

### Final Report of the College of Medicine Investigation Committee Concerning Allegations of Research Misconduct

### **February 9, 2021**

### **Executive Summary**

According to The Ohio State University Policy and Procedures Concerning Research Misconduct ("the Policy"¹) (<a href="http://orc.osu.edu/files/Misconduct Policy.pdf">http://orc.osu.edu/files/Misconduct Policy.pdf</a>), a College of Medicine Investigation Committee (the "COMIC") reviewed allegations of potential Research Misconduct against Samson Jacob, Ph.D., Professor Emeritus, Department of Cancer Biology and Genetics, College of Medicine, The Ohio State University (OSU) (the "Respondent"). A series of allegations against Dr. Jacob were received or identified between March 11, 2017 and October 22, 2019. In total, sixty-seven (67) allegations in twenty (20) publications were reviewed by the COMIC. All twenty (20) publications cite support from the Public Health Service (see <a href="https://orc.osu.edu/files/Misconduct ("the Policy">Appendix</a>). The Manuscript and Allegation numbers correspond to the numbers used in the Inquiry plus additional allegations added during the Investigation.

The COMIC determined, by a preponderance of the evidence and/or by clear and convincing evidence, that fourteen (14) allegations (Allegations 8-11, 17, 23, 25, 44-45, 47, 50-51, 71, 76) do constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b). The COMIC determined, by a preponderance of the evidence and/or by clear and convincing evidence, that fifty-three (53) allegations (Allegations 1-7, 12-16, 18-20, 24, 26-37, 39-40, 43, 48, 55-57, 60-61, 63, 66, 69-70, 72-75, 77-84) do not constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b) and should be dismissed. A review of each specific allegation is found in the "Investigation Committee Analysis" section of this report.

### Allegations Summary<sup>2</sup>

#### Dr. Samson Jacob reported falsified data in the following figures/manuscripts:

Manuscript #1<sup>3</sup>: Majumder S\*, Ghoshal K\*, Datta J\*, Bai S, Dong X, Quan N, Plass C, Jacob ST. "Role of de novo DNA methyltransferases and methyl CpG-binding proteins in gene silencing in a rat hepatoma." J Biol Chem. 2002 May 3; 277(18):16048-58. Epub 2002 Feb 13. [Supported by: NIH ES10874 and CA81024] **RETRACTED 07/19/18<sup>4</sup>** \* **co-first authors** 

- Allegation #1 Splicing between lanes 1 and 2 in Figure 3A<sup>5</sup> (slide 3<sup>6</sup>)
- Allegation #2 Splicing between samples 4 and 5 in Figure 5A (slide 4)
- Allegation #3 Splicing between samples 2 and 3 in Figure 5C (slide 5)
- Allegation #4 Reuse of same data in lane 1 and in lane 3 in Figure 6B (slide 6)

Manuscript #2<sup>7</sup>: Motiwala T, Kutay H, Ghoshal K, Bai S, Seimiya H, Tsuruo T, Suster S, Morrison C, Jacob ST. "Protein tyrosine phosphatase receptor-type O (PTPRO) exhibits characteristics of a candidate tumor suppressor

<sup>&</sup>lt;sup>1</sup> Ex. 1 - University Policy and Procedures Concerning Research Misconduct

<sup>&</sup>lt;sup>2</sup> Due to nature of when allegations arose and/or when Dr. Jacob was notified, the numbering of allegations is not consecutive.

<sup>&</sup>lt;sup>3</sup> Ex. 5 - Majumder et al., JBC 2002

<sup>&</sup>lt;sup>4</sup> Ex. 31 - 20180817-Retraction-J. Biol. Chem.-2018-Majumder-12948

<sup>&</sup>lt;sup>5</sup> Original allegation posted on PubPeer noted Figure 1A incorrectly

<sup>&</sup>lt;sup>6</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final

<sup>&</sup>lt;sup>7</sup> Ex. 6 - Motiwala et al., PNAS 2004

in human lung cancer." Proc Natl Acad Sci U S A. 2004 Sep 21; 101(38):13844-9. Epub 2004 Sep 8. [Supported by: NIH ES10874, CA81024, and CA86978]

- Allegation #5 Reuse of same data in lanes 1 and 2 and in lanes 7 and 8, and in lanes 3 and 4, (though as a horizontal mirror image) in the 18S rRNA blot in Figure 2 (slides 8-10)
- Allegation #6 RT-PCR data were falsified by falsely labeling normal and tumor matched pairs #3 and #4 when compared to the original research record<sup>8</sup> (slides 11-20)
- Allegation #43 Reuse of same data for serum starved images for both A549/vector and A549/PTPRO in Figure 5A (slides 21-24)

Manuscript #39: Ghoshal K\* \*\*, Datta J\*, Majumder S, Bai S, Kutay H, Motiwala T, Jacob ST\*\*. "5-Azadeoxycytidine induces selective degradation of DNA methyltransferase 1 by a proteasomal pathway that requires the KEN box, bromo-adjacent homology domain, and nuclear localization signal." Mol Cell Biol. 2005 Jun; 25(11):4727-41. [Supported by: NIH ES10874, CA81024, and CA86978] **CORRECTED 04/30/18** 10, 11 \* co-first authors \*\* co-corresponding authors

- Allegation #7 Reuse of same IHC images in both panels f and g in Figure 2A (slide 28)
- Allegation #8 Reuse of same data in lanes 1-5 and in lanes 6-10 (flipped 180 degrees) of the NS blot in Figure 3D (slide 29)
- Allegation #9 Reuse of same data in lanes 1-3 and in lanes 7-9 of the GFP blot in Figure 6C-1 (slide 30)
- Allegation #10 Reuse of same data in lane 2 and in lane 4 of the Dnmt1 blot in Figure 6C-2 (slide 31)
- Allegation #11 Reuse of the same data in lanes 1-2/lanes 8-9 of the GFP blot in Figure 6C-1 and in lanes 1-2/lanes 7-8 of the beta-tubulin blot in Figure 2, J Nutr. 136, 2006 (Manuscript #6) (slide 32-33)
- Allegation #44 Reuse of same data in lane 1 and in lane 7; reuse of same data in lane 5 and in lane 6 (horizontal flip of image) in Dnmt3a blot in Figure 1A (slide 34-36)
- Allegation #45 Reuse of same data in lanes 1,2 and in lanes 4,5 of the Ku70 blot in Figure 1B (slide 37)
- Allegation #76 Reuse of the lower bands in lanes 1-2 and 5-6 in the DNMT3B blot of Figure 1B (slide 38-39)

Manuscript #4<sup>12</sup>: Bai S, Ghoshal K, Datta J, Majumder S, Yoon SO, Jacob ST. "DNA methyltransferase 3b regulates nerve growth factor-induced differentiation of PC12 cells by recruiting histone deacetylase 2." Mol Cell Biol. 2005 Jan; 25(2):751-66. [Supported by: NIH ES10874, CA81024, and CA86978]

- Allegation #12 Reuse of same data in lane 2 and lane 3 of the Dnmt3a blot in Figure 2D (slide 44)
- Allegation #13 Reuse of same data in lane 1 and lane 3 of the Alu I blot in Figure 5 (slide 45)
- Allegation #14 Reuse of same data in lanes 3, 4 of the Ku-70 blot in Figure 1D and as lanes 1, 2 of the Ku-70 blot in Figure 8A (slide 46)
- Allegation #15 Splicing between lanes 4 and 5 of the Dnmt3b blot and lanes 1 and 2 of the Hdac2 blot in Figure 8B (slide 47)

<sup>&</sup>lt;sup>8</sup> Original allegation was splicing between lanes 2 and 3 and between 6 and 7 of the PTPRO-FL blot in Figure 2. Review of the original source data by the CII uncovered additional issues with data misrepresentation and mislabeling.

<sup>&</sup>lt;sup>9</sup> Ex. 7 - Ghoshal et al., Mol Cell Biol 2005

<sup>&</sup>lt;sup>10</sup> Correction was posted 04/30/18 regarding Figure 2A and Figure 4C only

<sup>&</sup>lt;sup>11</sup> Ex. 28 - 20180430 Correction-Mol.Cell.Biol-2018-Ghoshal

<sup>&</sup>lt;sup>12</sup> Ex. 8 - Bai et al., Mol Cell Biol 2005

- Allegation #16 Splicing between samples 1 and 2 in the Hdac2 blot in Figure 8C (slide 48)
- Reinstated and Expanded Allegation #17 Reuse of multiple bands and background images in Figure 8C. Specifically:
  - a. Reuse of the same data in sample 3 and sample 4 (with possible erasure of the band) in the Hdac2 blot (slide 49-50)
  - b. Reuse of the same blank background image in samples 15-16 and 17-18 of the Hdac2 blot (slide 49-50)
  - c. Reuse of the same data in samples 7-8 and 9-10 (with possible erasure of the bands) Dnmt3a blot (slide 51-52)
  - d. Reuse of the same blank background image in sample 16 and sample 18 (with possible erasure of background artifact) of the Dnmt3a blot (slide 51-52)
- Allegation #77 Reuse of the same cell images representing 'Vector' and 'Parental' for -NGF samples in Figure 2F (slide 53)

Manuscript #5<sup>13</sup>: Datta J, Majumder S, Bai S, Ghoshal K, Kutay H, Smith DS, Crabb JW, Jacob ST. "Physical and functional interaction of DNA methyltransferase 3A with Mbd3 and Brg1 in mouse lymphosarcoma cells." Cancer Res. 2005 Dec 1; 65(23):10891-900. [Supported by: NIH ES10874, CA81024, and CA86978]

Allegation #18 – Reuse of same data in lanes 2-4 (figure label is 3-5) and in lanes 7-9 (figure label is 8-10) of the Hdac1 blot in Figure 1C (slide 55-56)

Manuscript #6<sup>14</sup>: Ghoshal K, Li X, Datta J, Bai S, Pogribny I, Pogribny M, Huang Y, Young D, Jacob ST. "A folate- and methyl-deficient diet alters the expression of DNA methyltransferases and methyl CpG binding proteins involved in epigenetic gene silencing in livers of F344 rats." J Nutr. 2006 Jun; 136(6):1522-7. [Supported by: NIH CA 86978]

- Allegation #19 Reuse of same data in lanes 2-4, and 7 of the Dnmt1 blot, 18 weeks, and in lanes 4-6, and 7 of the Dnmt1 blot, 36 weeks in Figure 2 (slide 58)
- Allegation #20 Reuse of same data in lanes 1, 2 and in lanes 7, 8 of the beta-tubulin blot in Figure 2. [Note the same data is also reused in lanes 1, 2 and in lanes 8, 9 of the GFP blot in Figure 6C-1, Mol Cell Biol. 2005 (Manuscript #3)] (slide 59-60)

Manuscript #7<sup>15</sup>: Majumder S\*, Ghoshal K\*, Datta J, Smith DS, Bai S, and Jacob ST." Role of DNA methyltransferases in regulation of human ribosomal RNA gene transcription." J Biol Chem. 2006 Aug 4; 281(31):22062-72. Epub 2006 May 30. [Supported by: NIH ES10874 and CA86978] **RETRACTED 02/13/18** \* co-first authors

- Allegation #47 –Reuse of same data in lane 2 (flipped), and in lane 3, and in lane 6 in Figure 6C (slides 62-63)
- Allegation #78 Splicing present between lanes of the Nucleolin blot in Figure 2B (slide 64-65)
- Allegation #79 Possible erasure of band in the RNA Pol II blot (Nucleolus) in Figure 2B (slide 64-65)

Manuscript #8<sup>17</sup>: Bai S, Datta J, Jacob ST, Ghoshal K. "Treatment of PC12 cells with nerve growth factor induces

<sup>&</sup>lt;sup>13</sup> Ex. 9 - Datta et al., Cancer Res 2005

<sup>&</sup>lt;sup>14</sup> Ex. 10 - Ghoshal et al., J Nutr. 2006

<sup>&</sup>lt;sup>15</sup> Ex. 11 - Majumder et al., JBC. 2006

<sup>&</sup>lt;sup>16</sup> Ex. 25 - 20180213-Retraction-J. Biol. Chem.-2018-Majumder-3591

<sup>&</sup>lt;sup>17</sup> Ex. 12 - Bai et al., JBC. 2007

proteasomal degradation of T-cadherin that requires tyrosine phosphorylation of its cadherin domain." J Biol Chem. 2007 Sep 14; 282(37):27171-80. Epub 2007 Jul 13. [Supported by: NIH CA86978 and CA101956<sup>18</sup>] **RETRACTED 02/13/18**<sup>19</sup>

- Allegation #23 Reuse of same data in lanes 1-4 and in lanes 5-8 of the GAPDH blot in Figure 2C (slide 68)
- Allegation #24 Reuse of same data in lane 1 and in lane 4 of the NS blot in Figure 3C (slide 69)
- Allegation #25 Reuse of same data in lanes 1-3 and in lanes 6-8 of the NS blot in Figure 3E (slide 70)
- Allegation #26 Reuse of same data in lanes 5 and 6, and in lanes 8 and 9, and in lanes 10 and 11 in beta-tubulin blot, in Figure 5C. Reuse of same data in lane 4 and in lane 7 of the beta-tubulin blot in Figure 5C (slides 71-72)
- Allegation #27 Reuse of same data in lane 1 and in lane 4 of the NS blot in Figure 7A (slide 73)
- Allegation #48 Reuse of same data in multiple lanes within the blots in Figure 1B (Ku-70), Figure 5A (beta-tubulin) and Figure 5C (beta-tubulin) as follows (slide 74-81):
  - Reuse of same data in lane 3, Ku70 blot in Figure 1B and, and in lanes 6, 9 and 11 of the beta-tubulin blot in Figure 5C (slides 76-77)
  - Reuse of same data in lanes 1 and 2, and in lanes 4 and 5, Ku70 blot in Figure 1B; and in lanes 5 and 6, beta-tubulin blot in Figure 5A; and in lanes 4 and 5 and lanes 7 and 8, betatubulin blot in Figure 5C (slides 78-79)
  - Reuse of same data in lanes 2-4, beta-tubulin blot in Figure 5A and in lanes 1-3 beta-tubulin blot in Figure 5C (slides 80-81)
- Allegation #50 Reuse of same data in lane 4 and in lane 5, and in lane 6 (0, 2 and 4 hours) in the deltaCD2-5 sample +NGF (lower panel) in Figure 6B (slides 82-85)
- Allegation #51 Reuse of same data in lanes 1-3 in the top panel (-NGF) in Figure 6B and in lanes 1-3 of the Tcadflag blot in Figure 7D. Reuse of same data in lanes 1-3 in the bottom panel (+NGF) in Figure 6B, and in lanes 7-9, Tcadflag blot, in Figure 7D (slides 86-89)

Manuscript #9<sup>20</sup>: Datta J\*, Kutay H\*, Nasser MW, Nuovo GJ, Wang B, Majumder S, Liu CG, Volinia S, Croce CM, Schmittgen TD, Ghoshal K\*\*, Jacob ST\*\*. "Methylation mediated silencing of MicroRNA-1 gene and its role in hepatocellular carcinogenesis." Cancer Res. 2008 Jul 1; 68(13):5049-58 [Supported by: NIH CA86978, CA122695, and CA101956] \*co-first authors\*\*co-corresponding authors

- Allegation #28 Reuse of the FOXP1 blot and the GAPDH blot to represent data from two different cell lines (SK-Hep1 and SNU-449 cell lines) in Figure 5A (slide 92-98)
- Allegation #29 Reuse of the same data as sample 1 and as sample 8 (T\* and N lanes) of the FOXP1 blot in Figure 6A (slide 99-105)
- Allegation #80 Reuse of multiple DNA bands and background images in Supplemental Figure 1. (slides 106-111). Specifically:
  - a. DNA ladder band #3 in lane 1 was reused in lane 4 (Taq1/control) as bands #2 and #3 (slide 108)
  - b. DNA ladder band #4 in lane 1 was reused in lane 3 (Aci/control) as band #2 (slide 109)
  - c. Band #1 in lane 3 (Aci/control) was reused in lane 4 (Taq1/control) (slide 110)
  - d. Band #1 in lane 2 (uncut/control) was reused in lane 6 (uncut/5-Azac) and lane 9 (Tsp5091/5-Azac) (slide 110)
  - e. The same blank background image was reused in lanes 4, 5 and 9 (slide 111)

<sup>&</sup>lt;sup>18</sup> The publication itself references support by NIH CA10195

<sup>&</sup>lt;sup>19</sup> Ex. 23 - 20180309-Retraction-J. Biol. Chem-2018-Bai-3590

<sup>&</sup>lt;sup>20</sup> Ex. 13 - Datta et al., Cancer Res 2008

f. The same blank background image was reused in lanes 7 and 8 (slide 111)

Manuscript #10<sup>21</sup>: Datta J, Ghoshal K\*, Denny WA, Gamage SA, Brooke DG, Phiasivongsa P, Redkar S, Jacob ST\*. "A new class of quinoline-based DNA hypomethylating agents reactivates tumor suppressor genes by blocking DNA methyltransferase 1 activity and inducing its degradation." Cancer Res. 2009 May 15;69(10):4277-85. Epub 2009 May 5. [Supported by: NIH CA101956 and Supergen grant] \* co-corresponding authors

- Allegation #30 Reuse of same data in lane 1, lane 2, and lane 3 in the GAPDH blot in Figure 5B (slides 115-118)
- Allegation #81 Reuse of the same data in lane 5 (SGI-1027-12d) and lane 6 (SGI-1027-15d) in the P16-U-R1 151 bp sample in Figure 4A (slide 119-120)
- Allegation #82 Reuse of the same data in lane 2 (control), lane 3 (Decitabine-12d) and lane 4 (Decitabine-15d) in the P16-M-R2 234 bp sample in Figure 4A (slide 121)
- Allegation #83 Reuse of the same data in lane 4 (Decitabine-7d) and lane 5 (SGI-1027-5d) in the TIMP-3-M 116BP sample in Figure 4B (slide 122)

Manuscript #11<sup>22</sup>: Ramaswamy B\*, Majumder S\*, Roy S, Ghoshal K, Kutay H, Datta J, Younes M, Shapiro CL, Motiwala T\*\*, Jacob ST\*\*. "Estrogen-mediated suppression of the gene encoding protein tyrosine phosphatase PTPRO in human breast cancer: mechanism and role in tamoxifen sensitivity." Mol Endocrinol. 2009 Feb; 23(2):176-87. Epub 2008 Dec 18. [Supported by: NIH CA101956, CA122523, and CA086978] \*co-first authors \*co-corresponding authors\*

- Allegation #31 Reuse of same data in lane 4 and in lane 5 in the 18S rRNA gel image in Figure 2A (slide 125)
- Allegation #32 Reuse of same data in lane 1 and in lane 5 of the 18S rRNA gel image in Figure 2D (slide 126)
- Allegation #33 Reuse of same data in lane 1 and in lane 4 of the ERβ blot in Figure 4C (slide 127)

Manuscript #12<sup>23</sup>: Lu Y, Roy S, Nuovo G, Ramaswamy B, Miller T, Shapiro C, Jacob ST\*, Majumder S\*. "AntimicroRNA-222 (anti-miR-222) and -181B suppress growth of tamoxifen-resistant xenografts in mouse by targeting TIMP3 protein and modulating mitogenic signal." J Biol Chem. 2011 Dec 9; 286(49):42292-302. Epub 2011 Oct 18. [Supported by: NIH CA137567] <u>RETRACTED 02/13/18<sup>24</sup>\* co-corresponding authors</u>

- Allegation #34 Splicing between lanes 2 and 3 in the p-p42/44-MAPK blot and between lanes 3 and 4 of the total MAPK blot in Figure 5E (slide 130)
- Allegation #35 Reuse of same data in lanes 4-6 of the total MAPK blot in Figure 6C and in lanes 4-6 of the total MAPK blot in Figure 6D (slide 131). Figures 6C and 6D in JBC are also reported in grant application R21 CA137567-01A1, as Figures 6C and 6A, respectively.
- Allegation #55 Splicing between lane 1 and lane 2 of p-p42/44 MAPK blot in Figure 6B (slides 132-133)
- Allegation #56 Cut and paste of lane 4 of p-AKT blot in Figure 7A; and splicing between lane 3 and lane 4 in total AKT blot in Figure 7A (slides 134-135)
- Allegation #57 Cut and paste of lane 6 of total AKT blot in Figure 7C; and splicing between lane 3 and lane 4 in both p-AKT and total AKT blots in Figure 7C (slides 136-137)
- Allegation #60 Splicing around bands in lane 4 and between lane 5 and 6 in Figure S3 (slides 138-

<sup>&</sup>lt;sup>21</sup> Ex. 14 - Datta et al., Cancer Res. 2009

<sup>&</sup>lt;sup>22</sup> Ex. 15 - Ramaswamy et al., Mol Endo 2009

<sup>&</sup>lt;sup>23</sup> Ex. 16 - Lu et al., JBC 2011

<sup>&</sup>lt;sup>24</sup> Ex. 24 - 20180213-Retraction-J. Biol. Chem.-2018-Lu-3588

139)

Manuscript #13<sup>25</sup>: Datta J\*, Ghoshal K\* \*\*, Motiwala T, Jacob ST\*\*. "Novel Insights into the Molecular Mechanism of Action of DNA Hypomethylating Agents: Role of Protein Kinase C  $\delta$  in Decitabine-Induced Degradation of DNA Methyltransferase 1." Genes Cancer. 2012 Jan; 3(1):71-81. [Supported by: NIH CA101956 and CA86978] \* co-first authors \*\* co-corresponding authors

- Allegation #36 Reuse of same data in lanes 2-5 of the GAPDH blot in Figure 4B and in lanes 1-4 of the GAPDH blot in Figure 4D (slide 142)
- Allegation #37 Reuse of same data in lanes 4-9 of the GAPDH blot in Figure 5A and in lanes 1-6 of the GAPDH blot in Figure 5B (slide 143)
- Allegation #39 Reuse of the same data in lane 1, lane 3, and in lane 4 of the DNMT1 blot in Figure 6E (slide 144)
- Allegation #61 Reuse of same data in lane 11 and in lane 12 (Rottlerin treatment), DNMT1 blot, in Figure 5A (slide 145)

Manuscript #14<sup>26</sup>: Wang B, Hsu SH, Wang X, Kutay H, Bid HK, Yu J, Ganju RK, Jacob ST, Yuneva M, Ghoshal K. "Reciprocal regulation of microRNA-122 and c-Myc in hepatocellular cancer: role of E2F1 and transcription factor dimerization partner 2." Hepatology (2014) 59(2): 555–566. [Supported by: NIH DK088076 and CA086978]

 Allegation #40 – Reuse of same data in lanes 1-4 of the GAPDH blot in Figure 1B and in lanes 2-5 of the GAPDH blot in Figure 1E (slides 146-148)

Manuscript #15<sup>27</sup>: Motiwala T\*, Majumder S\*, Ghoshal K, Kutay H, Datta J, Roy S, Lucas DM, Jacob ST. "PTPROt inactivates the oncogenic fusion protein BCR/ABL and suppresses transformation of K562 cells." J Biol Chem. 2009 Jan 2; 284(1):455-64. [Supported by: NIH CA122695, CA101956, and CA086978] **RETRACTED 02/13/18<sup>28</sup>** \* **co-first authors** 

 Allegation #63 – Splicing between lane 2 and lane 3 in the PTPROt-flag blot in Figure 1A (slides 149-151)

Manuscript #16<sup>29</sup>: Bai S, Ghoshal K, Jacob ST. "Identification of T-cadherin as a novel target of DNA methyltransferase 3B and its role in the suppression of nerve growth factor-mediated neurite outgrowth in PC12 cells." J Biol Chem. 2006 May 12; 281(19):13604-11. [Supported by: NIH ES10874 and CA86978] **RETRACTED 02/13/18**<sup>30</sup>

 Allegation #66 – Reuse of same data in lane 1 and in lane 5, T-cad gel images in Figure 3B (slides 152-154)

Manuscript #17<sup>31</sup>: Nasser MW\*, Datta J\*, Nuovo G, Kutay H, Motiwala T, Majumder S, Wang B, Suster S, Jacob ST\*\*, Ghoshal K\*\*. "Down-regulation of Micro-RNA-1 (miR-1) in Lung Cancer." J Biol Chem. 2008 Nov

<sup>&</sup>lt;sup>25</sup> Ex. 17 - Datta et al., Genes Cancer 2012

<sup>&</sup>lt;sup>26</sup> Ex. 18 - Wang et al., Hepatology 2014

<sup>&</sup>lt;sup>27</sup> Ex. 19 - Motiwala et al., JBC 2009

<sup>&</sup>lt;sup>28</sup> Ex. 26 - 20180309- Retraction- J. Biol. Chem.-2018-Motiwala-3589

<sup>&</sup>lt;sup>29</sup> Ex. 20 - Bai et al., JBC 2006

<sup>&</sup>lt;sup>30</sup> Ex. 27 - 20180309-Retraction-J. Biol. Chem-2018-Bai-3592

<sup>&</sup>lt;sup>31</sup> Ex. 21 - Nasser et al., JBC. 2008

28;283(48):33394-405. [Supported by: NIH CA122695 and P01CA101956] RETRACTED 07/19/18<sup>32</sup> \* co-first authors \*\* co-corresponding authors

 Allegation #69 – Reuse of same data in lanes 12-19 (samples 17-20) 18S rRNA (upper blot) and in lanes 2-9 (samples 22-25) 18S rRNA (lower blot) in Figure 8A (slides 155-160)

Manuscript #18<sup>33</sup>: Dong, X., Ghoshal, K., Majumder, S., Yadav, S. P., & Jacob, S. T. (2002). Mitochondrial transcription factor A and its downstream targets are up-regulated in a rat hepatoma. *The Journal of biological chemistry*, *277*(45), 43309-18. [Supported by: NIH CA 81024 and ES 10874] **RETRACTED-07/19/18**<sup>34</sup>

- Allegation #70 Reuse of the same data in lanes 1-2 of the NS blot in Figure 1B and in lanes 1-2 of the NS blot in Figure 6B (slides 162-164)
- Allegation #71 Reuse of the same beta-actin blot for Figure 1D, Figure 2A, Figure 5 and Figure 6A (slides 165-167)
- Allegation #72 Cut and paste of lane 2 (Liver/V) of "UPPER STRAND" blot and cut and paste of lane 1 (Liver/N) of "LOWER STRAND" blot in Figure 4B (slides 168-169)
- Allegation #73 COX1 and ND1 seem to be stretched horizontally and vertically with respect to the rest of Figure 5 (slide 170)

Manuscript #19<sup>35</sup>: Majumder S\*, Varadharaj S\*, Ghoshal K, Monani U, Burghes AHM, Jacob ST. "Identification of a Novel Cyclic AMP-response Element (CRE-II) and the Role of CREB-1 in the cAMP-induced Expression of the Survival Motor Neuron (SMN) Gene." The Journal of Biological Chemistry. 2004; 279(15):14803-14811. doi:10.1074/jbc.M308225200. [Supported by: NIH NS 41649] **RETRACTED-07/19/18**<sup>36</sup> \* co-first authors

Manuscript #19 (Majumder JBC 2004) was included as an attachment to the progress report and referenced on page 2 of funded grant R01 NS041649-04. Arthur Burghes is PI, Samson Jacob is Co-PI, and Sarmila Majumder is Key Personnel.

- Allegation #74 Cut and paste of lane 2 and lane 3 in Figure 2A (slides 172-173)
- Allegation #75 Cut and paste of lane 3 (FI.SMN band) in Figure 7A (slides 174-176)

Manuscript #20<sup>37</sup>: Ghoshal K\*, Motiwala T, Claus R, Yan P, Kutay H, Datta J, Majumder S, Bai S, Majumder A, Huang T, Plass C, and Jacob S\*. (2010) "HOXB13, a Target of DNMT3B, Is Methylated at an Upstream CpG Island, and Functions as a Tumor Suppressor in Primary Colorectal Tumors." PLoS ONE 5(4): e10338. doi:10.1371/journal.pone.0010338. [Supported by: NIH CA086978 and CA101956] \*co-corresponding authors

- Allegation #84 Falsification of the DNMT3B Western blot in Figure 1, PLoS One 2010, for WT and DNMT1-/- in HCT cells, for RKO cells, and for the ladder (slides 180-186), specifically by:
  - using the bands from raw data file, "HCT-RKO-DNMT3B.tiff" labeled for WT and DNMT1-/-, but flipped horizontally in Figure 1 to give the desired result
  - using the ladder from raw data file "Marker.tiff," which is an unrelated experiment labeled with a
    date prior to the date on the raw data file "HCT-RKO-DNMT3B" used for Figure 1

<sup>&</sup>lt;sup>32</sup> Ex. 32 - 20180817-Retraction-J. Biol. Chem.-2018-Nasser-12945

<sup>&</sup>lt;sup>33</sup> Ex. 33 - Dong et al., JBC 2002

<sup>&</sup>lt;sup>34</sup> Ex. 30 - 20180817-Retraction-J.Biol Chem.-2018-Dong-12947

<sup>&</sup>lt;sup>35</sup> Ex. 34 - Majumder et al., JBC 2004

<sup>&</sup>lt;sup>36</sup> Ex. 29 - 20180817-Retraction-J.Biol Chem.-2018-Majumder-12946

<sup>&</sup>lt;sup>37</sup> Ex. 274 - Ghoshal et al., PLoS One 2010

 using an unidentified source for the RKO bands in Figure 1, when the raw data file "HCT-RKO-DNMT3B.Tiff" showed no RKO expression

#### **Subsequent Use Summary**

Seventeen (17) of the questioned publications (Manuscripts # 1-11, #15-20) were outside the six-year time limitation as defined in 42 C.F.R. §93.105(a) and the Policy, Section V.I. and therefore were reviewed under the subsequent use exception process.<sup>38</sup> The Office of Research Compliance (ORC) determined that the six-year time limitation did not apply as Dr. Jacob had continued to cite the questioned publications in grant applications, either funded or submitted within the past six years, where Dr. Jacob was listed as the PI (see Sub Use Grants - JacobV5)<sup>39</sup> and/or in additional publications as follows:

### Manuscript #1-JBC 2002:

1. Cited in Kutay H, Klepper C, Wang B, Hsu S, Datta J, Yu L, Zhang X, Majumder S, Motiwala T, Khan, N, Belury M, McClain C, Jacob S, Ghoshal K. Reduced Susceptibility of DNA Methyltransferase 1 Hypomorphic (Dnmt1N/+) Mice to Hepatic Steatosis upon Feeding Liquid Alcohol Diet. PLoS ONE. 2012. 7(8), e41949.

### Manuscript #2 - PNAS 2004:

1. Cited in Hsu S, Motiwala T, Roy S, Claus R, Mustafa M, Plass C, Freitas MA, Ghoshal K and Jacob ST. (2013) Methylation of the PTPRO gene in human hepatocellular carcinoma and identification of VCP as its substrate. J. Cell. Biochem. 114: 1810-1818.

### Manuscript #3: MCB 2005:

 Cited in Datta J\*, Ghoshal K\*, Motiwala T, and Jacob ST. "Novel Insights into the Molecular Mechanism of Action of DNA Hypomethylating Agents: Role of Protein Kinase C δ in Decitabine-Induced Degradation of DNA Methyltransferase 1." Genes Cancer. 2012 Jan; 3(1):71-81. \*Equal contribution.

#### Manuscript #4: MCB 2005:

1. Cited in Manuscript #13, Genes Cancer 2012.

### Manuscript #5: Cancer Res 2005:

1. Cited in Manuscript #13, Genes Cancer 2012.

### Manuscript #6: J Nutr 2006:

1. Cited in Wani NA, Zhang B, Teng K, Barajas JM, Motiwala T, Hu P, Yu L, Brüschweiler R, Ghoshal K, Jacob ST. "Reprograming of Glucose Metabolism by Zerumbone Suppresses Hepatocarcinogenesis." Mol Cancer Res. 2018 (16) (2) 256-268.

#### Manuscript #7: JBC 2006:

 Cited in Kutay H, Klepper C, Wang B, Hsu S, Datta J, Yu L, Zhang X, Majumder S, Motiwala T, Khan, N, Belury M, McClain C, Jacob S, Ghoshal K. Reduced Susceptibility of DNA Methyltransferase 1 Hypomorphic (Dnmt1N/+) Mice to Hepatic Steatosis upon Feeding Liquid Alcohol Diet. PLoS ONE. 2012. 7(8), e41949.

### Manuscript #9: Cancer Res 2008:

<sup>&</sup>lt;sup>38</sup> Ex. 2 - Subsequent Use Exception Process-V1

<sup>&</sup>lt;sup>39</sup> Ex. 556 - Sub Use Grants – JacobV5

- 1. Cited in Barajas JM., Reyes R, Guerrero MJ, Jacob ST, Motiwala T, Ghoshal K. "The role of miR-122 in the dysregulation of glucose-6-phosphate dehydrogenase (G6PD) expression in hepatocellular cancer." Scientific Reports 2018. Vol. 8, Article 9105.
- 2. Cited in Ghoshal K, Motiwala T, Claus R, Yan P, Kutay H, Datta, J., Majumder, S., Bai, S., Majumder, A., Huang, T., Plass, C. & Jacob, S.T. (2010) HOXB13, a Target of DNMT3B, Is Methylated at an Upstream CpG Island, and Functions as a Tumor Suppressor in Primary Colorectal Tumors. PLOS ONE 5(4): e10338. <a href="https://doi.org/10.1371/journal.pone.0010338">https://doi.org/10.1371/journal.pone.0010338</a> (subsequently added to the investigation as Manuscript #20)

#### Manuscript #10: Cancer Res 2009

- 1. Cited in Manuscript #13, Genes Cancer 2012.
- 2. Cited in Kutay H, Klepper C, Wang B, Hsu S, Datta J, Yu L, Zhang X, Majumder S, Motiwala T, Khan, N, Belury M, McClain C, Jacob S, Ghoshal K. Reduced Susceptibility of DNA Methyltransferase 1 Hypomorphic (Dnmt1N/+) Mice to Hepatic Steatosis upon Feeding Liquid Alcohol Diet. PLoS ONE. 2012. 7(8), e41949.

#### Manuscript #11: Mol Endo 2009

- 1. Cited in Motiwala T, Kutay H, Zanesi N, Frissora F W, Mo X, Muthusamy N, and Jacob, ST. "PTPROt-mediated regulation of p53/Foxm1 suppresses leukemic phenotype in a CLL mouse model." Leukemia. 2015; 29(6), 1350–1359.
- 2. Cited in Hsu, S.\*, Motiwala, T.\*, Roy, S., Claus, R., Mustafa, M., Plass, C., Freitas, M. A., Ghoshal, K.^ and Jacob, S. T.^ (2013), Methylation of the PTPRO gene in human hepatocellular carcinoma and identification of VCP as its substrate. J. Cell. Biochem., 114: 1810-1818.

### Manuscript #15: JBC 2009

1. Cited in Motiwala T, Kutay H, Zanesi N, Frissora F W, Mo X, Muthusamy N, and Jacob, ST. "PTPROt-mediated regulation of p53/Foxm1 suppresses leukemic phenotype in a CLL mouse model." Leukemia. 2015; 29(6), 1350–1359.

#### Manuscript #16: JBC 2006

1. Cited in Cited in Ghoshal K, Motiwala T, Claus R, Yan P, Kutay H, Datta, J., Majumder, S., Bai, S., Majumder, A., Huang, T., Plass, C. & Jacob, S.T. (2010) HOXB13, a Target of DNMT3B, Is Methylated at an Upstream CpG Island, and Functions as a Tumor Suppressor in Primary Colorectal Tumors. PLOS ONE 5(4): e10338. <a href="https://doi.org/10.1371/journal.pone.0010338">https://doi.org/10.1371/journal.pone.0010338</a> (subsequently added to the investigation as Manuscript #20)

### Manuscript #17: JBC 2008:

1. Cited in Barajas JM., Reyes R, Guerrero MJ, Jacob ST, Motiwala T, Ghoshal K. "The role of miR-122 in the dysregulation of glucose-6-phosphate dehydrogenase (G6PD) expression in hepatocellular cancer." Scientific Reports 2018. Vol. 8, Article 9105.

#### Manuscript #20: PLoS One 2010

1. Cited in Hsu, S.\*, Motiwala, T.\*, Roy, S., Claus, R., Mustafa, M., Plass, C., Freitas, M. A., Ghoshal, K.^ and Jacob, S. T.^ (2013), Methylation of the PTPRO gene in human hepatocellular carcinoma and identification of VCP as its substrate. J. Cell. Biochem., 114: 1810-1818.

### **Preliminary Assessment Summary**

On June 7, 2017, Robert A. Bornstein, Ph.D., former Vice Dean for Academic Affairs, Administrative Vice Dean, College of Medicine, met with David Wright, Ph.D., External, Independent Research Integrity Officer (RIO),

and Julia Behnfeldt, Ph.D., former OSU RIO, Associate Director, Office of Research Compliance, to review the allegations<sup>40</sup> and conduct a Preliminary Assessment (PA) under the Policy.

The PA determined that the allegations regarding manuscripts #1-#13 were credible and specific so that potential evidence of Research Misconduct may be identified. The allegation regarding the manuscript originally considered #14 was determined to not be specific and credible and was dismissed. On October 18, 2017, the Preliminary Assessment letter regarding the allegations of possible Research Misconduct was submitted to the Deciding Official in this matter, Karla Zadnik, O.D., Ph.D., Dean and Glenn A. Fry Professor in Optometry and Physiological Optics,<sup>41</sup> recommending that the allegations in Manuscripts #1-13 be moved forward to a Committee of Initial Inquiry (CII). On October 20, 2017, Dr. Zadnik concurred with the PA and indicated that a CII should be initiated.<sup>42</sup>

### Sequestration of Data and Respondent Notification Summary

Per the Policy (IV.B.2) and federal regulations (42 C.F.R. 93.305a), immediate action to protect data and other materials (including hard drives) relevant to the allegations is required at or before the notification of allegations to Respondents. On September 21, 2017, Dr. Julia Behnfeldt and Dr. Jennifer Yucel, former Associate Vice President for Research Compliance, sequestered Dr. Jacob's computers from his office.<sup>43</sup> The computers were forensically imaged by the Office of Research Information Services (ORIS) on October 9, 2017.<sup>44</sup>

As Dr. Jacob is retired and not present on campus regularly, he was notified of the allegations via email and by certified overnight letter to his current address in Florida on October 18, 2017. 45,46 On November 14, 2017, in a teleconference with Drs. Wright, Behnfeldt and Bornstein, Dr. Jacob discussed the notification memo, his questions about policy and procedures, and his general lab structure. During that teleconference, Dr. Jacob declined to have the conversation recorded. Dr. Jacob stated that his lab group would meet at least twice a month with lab meetings occurring once a week on Fridays. Dr. Jacob indicated that when a manuscript was ready to be prepared, the first or first and second authors would prepare a draft along with the figures and then provide those to him for his review. The paper would then get reviewed multiple times with a final review by all authors. Dr. Jacob could not state who would have made each figure within the questioned publications. Dr. Jacob indicated that Dr. Ghoshal was a part of his lab group for many years but stated that she was now an independent faculty member.

Specifically regarding the allegations on splicing, Dr. Jacobs stated that some lanes may not have been relevant or "appropriate" to the figure they were generating so they would have removed them from the final figure. Dr. Jacob explained that no one had ever questioned the validity of the data, 47, 48, 49 that the allegations are from old manuscripts, and the allegations mostly involve control lanes. Finally, Dr. Jacob stated that the allegations only involve a small percentage of his published papers.

<sup>&</sup>lt;sup>40</sup> Ex. 4 - 20170311 - Initial Allegation - Claire Francis

<sup>&</sup>lt;sup>41</sup> Ex. 35 - 20171018 Jacob Preliminary Assessment Report

<sup>&</sup>lt;sup>42</sup> Ex. 36 - 20171020- DO to RIO PA Decision

<sup>&</sup>lt;sup>43</sup> Ex. 39 - 20170921 Sequestration SJ

<sup>&</sup>lt;sup>44</sup> Ex. 40 - 20171009 Note to file chain of custody

<sup>&</sup>lt;sup>45</sup> Ex. 37 - 20171018- Jacob Notification of Allegations

<sup>&</sup>lt;sup>46</sup> Ex. 38 - Jacob Tracking UPS

<sup>&</sup>lt;sup>47</sup> This statement by Dr. Jacob is false as there is evidence that as early as March 23, 2017 and June 30, 2017, Dr. Jacob had received formal notifications from Proceedings of the National Academy of Sciences and the Journal of Biological Chemistry, respectively, that there were concerns with data in a number of publications.

<sup>&</sup>lt;sup>48</sup> Ex. 276 - 20180313 - Email PNAS to Jacob - PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>49</sup> Ex. 277 - 20170630- Email JBC to Jacob

### **Committee of Initial Inquiry Summary**

A Committee of Initial Inquiry (the "CII") was formed on October 19, 2017 to review allegations of possible Research Misconduct against Dr. Jacob. On March 9, 2018, 50 the ORC was made aware of five (5) retractions posted by the Journal of Biological Chemistry (JBC), all of which had Dr. Jacob as a common author. Three (3) of the five (5) retracted papers were already under review by the CII (i.e. Manuscripts #7, #8, and #12); however, the JBC retraction notices included figures in additional papers that were not part of the allegations under review (subsequently numbered Manuscript #15 and #16). During their review of the JBC retractions, ORC also noted additional allegations from new postings of figure manipulations on the PubPeer website for papers with Dr. Jacob as a common author. The majority of the PubPeer allegations involved new figures in manuscripts already under review by the CII (Manuscripts #2, #3, and #13); plus two (2) additional papers that were not under review (subsequently numbered Manuscript #14 and #17). With the JBC retractions and the new PubPeer posts, there were a total of thirty (30) new allegations. The CII reviewed the thirty (30) new allegations on April 11, 2018, and voted 3-0 to include them in their review. As required by the Policy, Dr. Jacob was notified of the new JBC and PubPeer based allegations on April 11, 2018.

On September 21, 2018, Dr. Jacob was provided the CII Preliminary Report<sup>53, 54, 55</sup> and all referenced documents and given two weeks (due October 5, 2018) in which to review and provide comments to the Preliminary Report in accordance with Policy Section IV.C.4. Dr. Jacob requested two extensions (on September 25, 2018<sup>56</sup> and October 18, 2018<sup>57</sup>) of the deadline for providing comments on the Preliminary Report, which were granted, and on October 22, 2018 the University received comments submitted by Dr. Jacob.<sup>58</sup> On November 5, 2018, the CII issued its final report, <sup>59,60,61</sup> upholding its initial determinations that for fifty-one (51) allegations (Allegations #1-16, 18-20, 23-37, 39-40, 43-45, 47-48, 50-51, 55-57, 60, 61, 63, 66, 69) there was sufficient evidence to warrant further Investigation of Dr. Jacob under the University's Policy and disciplinary process. The CII determined that for eighteen (18) allegations (Allegations #17, 21-22, 38, 41, 42, 46, 49, 52-54, 58-59, 62, 64-65, 67-68) there was not sufficient evidence to warrant further Investigation under the Policy and that these allegations should be dismissed. As allowed for by the policy, Dr. Jacob filed an appeal<sup>62,63,64</sup> to the Deciding Official, Dr. Karla Zadnik, on November 13, 2018.

On December 5, 2018, Dr. Zadnik concurred with the CII determinations and denied the appeal.<sup>65, 66</sup> Dr. Jacob was notified of the DO decision on December 10, 2018. On December 12, 2018,<sup>67</sup> the decision to initiate an Investigation was referred to the College of Medicine where the Investigation would be conducted pursuant

<sup>&</sup>lt;sup>50</sup> The 03/09/18 JBC withdrawal notices link to papers with withdrawal dates of 02/13/18 but ORC was not aware of those retractions until the posting of the 03/09/18 online notice

<sup>51</sup> http://www.jbc.org/site/misc/jacob.xhtml

<sup>&</sup>lt;sup>52</sup> Ex. 148 - 20180411 - Notification of New Allegations-S Jacob

<sup>&</sup>lt;sup>53</sup> Ex. 234 - 20180921 Jacob Preliminary CII Report

<sup>&</sup>lt;sup>54</sup> Ex. 235 - 20180921- Letter RIO to SJ-PR

<sup>&</sup>lt;sup>55</sup> Ex. 236 - 20180921- Email RIO to SJ

<sup>&</sup>lt;sup>56</sup> Ex. 173 - 20180925- Email Jacob to RIO - Request Extension

<sup>&</sup>lt;sup>57</sup> Ex. 197 - 20181018 - Email RIO to Jacob- Deadline extended

<sup>&</sup>lt;sup>58</sup> Ex. 209 - 20181022 - Jacob Response CII with Exhibits

<sup>&</sup>lt;sup>59</sup> Ex. 239 - 20181105 Jacob Final CII Report

<sup>&</sup>lt;sup>60</sup> Ex. 222 - 20181105 - Letter CII Chair to DO- Jacob Final Report

<sup>&</sup>lt;sup>61</sup> Ex. 240 - 20181105 Email RIO to Jacob- Final CII Report

<sup>62</sup> Ex. 249 - Jacob Appeal.Zadnik

<sup>&</sup>lt;sup>63</sup> Ex. 209 - Jacob Response to CII with Exhibits

<sup>&</sup>lt;sup>64</sup> Ex. 248 - 20181113 - Jacob to RIO - appeal to CII Report

<sup>&</sup>lt;sup>65</sup> Ex. 255 - 20181205- Email DO to RIO-Dismiss CII Appeals

<sup>&</sup>lt;sup>66</sup> Ex. 257 - 20181210- DO to Jacob- DO Decision

<sup>&</sup>lt;sup>67</sup> Ex. 269 - 20181212 - Letter Chair CII to Dean COM-Jacob

to Policy and under University Rule 3335-5-04(E).<sup>68</sup> On January 11, 2019, the Office of Research Integrity was notified of the CII Final Report and the determination that an Investigation was warranted.<sup>69, 70</sup>

Additional individuals were considered to be possible Respondents in this case as they were either the first author on a manuscript for which Dr. Jacob was the corresponding author, or they were a co-corresponding author. A separate report, specific to the allegations and findings for each of the additional Respondents, was generated and included with the CII Final Report.<sup>71</sup> The CII found that there <u>was</u> sufficient evidence to warrant further Investigation of Dr. Jacob under the University's Policy and disciplinary process as well as for four (4) additional Respondents besides Dr. Jacob being handled separately by the university.<sup>72, 73, 74, 75</sup>

### **College of Medicine Investigation Committee**

After screening each potential College of Medicine Investigation Committee (the "COMIC") member to ensure that each was free from any possible conflict of interest that could prevent a fair and impartial review of the allegations, the COMIC members were charged on January 31, 2019 and February 5, 2019 to: (1) examine all evidence and collect any additional evidence it deemed appropriate; (2) determine if each allegation constitutes Research Misconduct (i.e., meets all of the criteria required for a finding of Research Misconduct as outlined in the Policy Section III.A), and if so, whether Dr. Jacob is responsible for the Research Misconduct; and (3) recommend sanctions if the COMIC determines that Dr. Jacob committed Research Misconduct.

In order to ensure that the Investigation was conducted with the appropriate scientific domain experience and expertise, the COMIC served as the primary body to determine if Research Misconduct had occurred. A member of the College of Medicine's Human Resources (COM HR) staff, Ms. Colleen Rupp, was appointed to the COMIC to consider the interests of staff members. Ms. Rupp did not vote on allegations for Dr. Jacob. The composition of the COMIC was as follows:

**Paul M.L. Janssen, Ph.D., F.A.H.A. (Chair),** Fred A. Hitchcock Professor of Environmental Physiology; Professor of Internal Medicine, Cardiology; Department of Physiology and Cell Biology

Jonathan P. Godbout, Ph.D., Professor of Neuroscience, Department of Neuroscience

**Richard Gumina, M.D., Ph.D.,** Associate Professor, Department of Internal Medicine, Division of Cardiovascular Medicine

**E. Douglas Lewandowski, Ph.D.,** Jack M. George Chair in Medicine; Professor, Department of Internal Medicine, Divisions of Endocrinology and Cardiovascular Medicine

Dana McTigue, Ph.D., Professor & Vice Chair for Research, Department of Neuroscience

**Michael Oglesbee, DVM, PhD, DACVP (non-COM representative)**, Director, Infectious Diseases Institute and Professor, Department of Veterinary Biosciences

**Lakshmi (Prasad) Dasi, Ph.D. (non-COM representative)**,<sup>76</sup> Associate Professor, Biomedical Engineering; Associate Professor, Department of Surgery

<sup>&</sup>lt;sup>68</sup> Ex. 271 - 3335 5 04 - Complaints against Faculty

<sup>&</sup>lt;sup>69</sup> Ex. 272 - 20190111 ORI Notice CII Final Report Jacob

<sup>&</sup>lt;sup>70</sup> Ex. 273 - 20190111 - Email Notification to ORI and NIH of Investigation - DIO 6428 (Jacob)

<sup>&</sup>lt;sup>71</sup> Ex. 239 - 20181105 Jacob Final CII Report

<sup>&</sup>lt;sup>72</sup> Ex. 228 - 20181105 - Datta CII Final Report

<sup>&</sup>lt;sup>73</sup> Ex. 229 - 20181105 - Ghoshal CII Final Report

<sup>&</sup>lt;sup>74</sup> Ex. 231 - 20181105 - Majumder CII Final Report

<sup>&</sup>lt;sup>75</sup> Ex. 232 - 20181105 - Motiwala CII Final Report

<sup>&</sup>lt;sup>76</sup> As of January 1, 2020, Dr. Dasi accepted a faculty appointment (Full Professor) at Georgia Institute of Technology. As allowed for per the Policy and the College of Medicine Patterns of Administration, Dr. Dasi has formally been retained as a "consultant" to the university and will continue in his role as a non-College representative in this matter until the conclusion of the case.

**Colleen Rupp,** Senior Employee and Labor Relations Consultant, College of Medicine Human Resources

### **College of Medicine Investigation Committee Meetings**

The COMIC met on the following dates to review the allegations and case materials and/or to interview participants:

- 1/31/19: COMIC Charge meeting (Gumina, Lewandowski, Oglesbee, McTigue, Dasi, Godbout, Mankowski, Yucel, Schriver, Lester, Behnfeldt, Garfinkel). Provided formal charge letter/policy and encrypted flash drive containing CII reports and exhibits.
- 2/05/19: COMIC Charge meeting (Janssen, Rupp, Behnfeldt, Mankowski, Yucel, Schriver, Lester). Provided formal charge letter/policy and encrypted flash drive containing CII reports and exhibits.
- 2/27/19: COMIC working meeting. Dr. Janssen chosen as committee chair.
- 3/13/19: COMIC working meeting.
- 3/20/19: COMIC working meeting.
- 3/27/19: COMIC working meeting.
- 4/03/19: COMIC working meeting.
- 4/10/19: COMIC working meeting.
- 4/24/19: COMIC working meeting.
- 5/08/19: COMIC working meeting.
- 6/12/19: COMIC Interviews of Dr. Sarmila Majumder and Dr. Tasneem Motiwala.
- 6/26/19: COMIC Working Meeting.
- 6/28/19: COMIC Interviews of Dr. Jharna Datta and Dr. Kalpana Ghoshal.
- 7/17/19: COMIC Interview of Dr. Sam Jacob.
- 8/14/19: COMIC working meeting.
- 8/21/19: COMIC working meeting.
- 9/4/19: COMIC working meeting.
- 9/25/19: COMIC working meeting.
- 10/09/19: COMIC working meeting.
- 10/16/19: COMIC working meeting.
- 10/23/19: COMIC working meeting.
- 10/30/19: COMIC voting meeting.
- 11/06/19: COMIC voting meeting.
- 11/13/19: COMIC voting meeting.
- 11/20/19: COMIC voting meeting.
- 12/03/19: COMIC voting meeting.
- 12/04/19: COMIC voting meeting.
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- 12/20/19: COMIC voting meeting.
- 5/27/20: COMIC working meeting.
- 01/2721: COMIC working meeting

### **Notification of Additional Allegations**

Through its review the COMIC identified sixteen (16) new, expanded and/or reinstated allegations of potential Research Misconduct. These allegations represent questioned figures in five (5) previously identified manuscripts (Manuscripts #3, 4, 7, 9, and 10), two (2) newly identified manuscripts (Manuscripts #18 and 19) from retraction notices posted by the Journal of Biological Chemistry on August 18, 2018, as outlined in the Committee of Initial Inquiry's Final Report ("20181105 Jacob Final CII Report"), and one (1) newly identified manuscript identified by the COMIC (Manuscript #20). By a majority vote, the COMIC determined that the new and/or expanded allegations detailed below may indicate possible Research Misconduct as defined in Section III of the Policy. Therefore, these new and/or expanded allegations were added to the scope of the Investigation. Per 42 C.F.R. § 93.310(c), written notice of the new allegations was provided to Dr. Jacob on May 23, 2019<sup>77, 78</sup> and October 22, 2019.<sup>79, 80, 81, 82</sup>

#### Manuscript #3

• New Allegation #76 – Reuse of the lower bands in lanes 1-2 and 5-6 in the DNMT3B blot of Figure 1B

#### Manuscript #4

- Original Allegation #17 (originally dismissed by CII) Duplicating backgrounds in samples 3 and 4 in the Hdac2 blot; duplicating backgrounds in samples 15-16 and 17-18 in the Dnmt3b, Hdac2, and Dnmt3a blots; duplicating backgrounds in samples 6-8 and 9-11 in the Dnmt3a blot in Figure 8C
- Reinstated and Expanded Allegation #17 Reuse of multiple bands and background images in Figure 8C. Specifically:
  - Reuse of the same data in sample 3 and sample 4 (with possible erasure of the band) in the Hdac2 blot
  - o Reuse of the same blank background image in samples 15-16 and 17-18 of the Hdac2 blot
  - Reuse of the same data in samples 7-8 and 9-10 (with possible erasure of the bands) Dnmt3a blot
  - Reuse of the same blank background image in sample 16 and sample18 (with possible erasure of background artifact) of the Dnmt3a blot
- New Allegation #77 Reuse of the same cell images representing 'Vector' and 'Parental' for -NGF samples in Figure 2F

#### Manuscript #7

- New Allegation #78 Splicing present between lanes of the Nucleolin blot in Figure 2B
- New Allegation #79 Possible erasure of band in the RNA Pol II blot (Nucleolus) in Figure 2B

#### Manuscript #9

- New Allegation #80 Reuse of multiple DNA bands and background images in Supplemental Figure 1.
   Specifically:
  - a. DNA ladder band #3 in lane 1 was reused in lane 4 (Taq1/control) as bands #2 and #3

<sup>&</sup>lt;sup>77</sup> Ex. 282 - 20190523 - Notification of new allegations-Jacob

<sup>&</sup>lt;sup>78</sup> Ex. 283 - 20190523 - Email RIO to Jacob - Notification of new allegations

<sup>&</sup>lt;sup>79</sup> Ex. 284 - 20191022 - Revised Notification of new allegations-Jacob

<sup>80</sup> Ex. 285 - 20191022 - Revised Notice of Allegations Jacob Figure

<sup>81</sup> Ex. 286 - 20191022 - Email RIO to Jacob – Revised Notification of new allegations

<sup>&</sup>lt;sup>82</sup> The single allegation related to Manuscript #20 (Ghoshal et al., PLoS One 2010) was incorrectly referred to as Allegation #76. The correct allegation number for Manuscript #20 is Allegation #84.

- b. DNA ladder band #4 in lane 1 was reused in lane 3 (Aci/control)
- c. Band #1 in lane 3 (Aci/control) was reused in lane 4 (Taq1/control)
- d. Band #1 in lane 2 (uncut/control) was reused in lane 6 (uncut/5-Azac) and lane 9 (Tsp5091/5-Azac)
- e. The same blank background image was reused in lanes 4, 5 and 9
- f. The same blank background image was reused in lanes 7 and 8

### Manuscript #10

- Original Allegation #30 Reuse of same data in lane 1 and in lane 3 of the GAPDH blot in Figure 5B
- Expanded Allegation #30 Reuse of same data in lane 1, lane 2 and lane 3 of the GAPDH blot in Figure 5B
- New Allegation #81 Reuse of the same data in lane 5 (SGI-1027-12d) and lane 6 (SGI-1027-15d) in the P16-U-R1 151 bp sample in Figure 4A
- New Allegation #82 Reuse of the same data in lane 2 (control), lane 3 (Decitabine-12d) and lane 4 (Decitabine-15d) in the P16-M-R2 234 bp sample in Figure 4A
- New Allegation #83 Reuse of the same data in lane 4 (Decitabine-7d) and lane 5 (SGI-1027-5d) in the TIMP-3-M 116BP sample in Figure 4B

#### Manuscript #18

- New Allegation #70 Reuse of the same data in lanes 1-2 of the NS blot in Figure 1B and in lanes 1-2 of the NS blot in Figure 6B
- New Allegation #71 Reuse of the same beta-actin blot for Figure 1D, Figure 2A, Figure 5 and Figure
   6A
- New Allegation #72 Cut and paste of lane 2 (Liver/V) of "UPPER STRAND" blot and cut and paste of lane 1 (Liver/N) of "LOWER STRAND" blot in Figure 4B
- New Allegation #73 COX1 and ND1 seem to be stretched horizontally and vertically with respect to the rest of Figure 5

#### Manuscript #19

- New Allegation #74 Cut and paste of lane 2 and lane 3 in Figure 2A
- New Allegation #75 Cut and paste of lane 3 (FI.SMN band) in Figure 7A

#### Manuscript #20

- New Allegation #84 Falsification of the DNMT3B Western blot in Figure 1, PLoS One 2010, for WT and DNMT1-/- in HCT cells, for RKO cells, and for the ladder by:
  - using the bands from raw data file, "HCT-RKO-DNMT3B.tiff" labeled for WT and DNMT1-/-, but flipped horizontally in Figure 1 to give the desired result
  - using the ladder from raw data file "Marker.tiff," which is an unrelated experiment labeled with a date prior to the date on the raw data file "HCT-RKO-DNMT3B" used for Figure 1
  - using an unidentified source for the RKO bands in Figure 1, when the raw data file "HCT-RKO-DNMT3B.Tiff" showed no RKO expression

### Notification to Respondent - Information Release

In its review of the publications and case materials, the COMIC became concerned about the potential continued use and citation in the scientific community of the falsified figures in these manuscripts given the impact of the figure errors on the conclusions reported. While it was clear to the committee that these figures had been falsified, they recognized that it would be some time before they would be able to finish their investigation and make a determination of possible Research Misconduct attributed to a specific respondent. The COMIC believed that it would be in the best interest of the scientific community to contact the journals to see if they would be willing to publish expressions of concern on manuscripts #2-6, 9-11, and 13. In accordance with the Policy Section I.D., on May 21, 2019, Ms. Mankowski requested approval from Dr. Morley Stone, OSU Senior Vice President for Research, to contact the six involved journals to request expressions of concern.<sup>83</sup> On May 22, 2019, Dr. Stone approved the request to make the external contacts requesting expressions of concern.84 Per the Policy, on May 23, 2019, Dr. Jacob was notified of the intention to make the external contacts for the purpose of requesting expressions of concern. 85, 86 Multiple authors filed objections 87 urging the university to reconsider its plan to request these expressions of concern. At that time the plans for external contact were put on hold as the university believed the investigation would be completed in relatively short order; however, identification of additional evidence, new allegations, and subsequent restrictions imposed by the COVID-19 pandemic have protracted the investigation process.

### **Interview/s Summary**

Dr. Jacob was interviewed (by phone) by the COMIC on July 17, 2019.<sup>88</sup> During the presentation, Dr. Jacob was shown a PowerPoint presentation<sup>89</sup> summarizing the allegations under investigation.<sup>90</sup> Dr. Jacob's specific statements are included in the "Investigation Committee Analysis" section below. During the interview, Dr. Jacob was asked about his lab in general, how papers were prepared and figures generated. In summary, Dr. Jacob stated that he would not be able to comment on the specifics of the allegations with respect to which person generated the figures, performed the experiments, or when the experiments were done. Dr. Jacob stated he never personally made any figures.<sup>91</sup> Therefore, the COMIC, as with the CII before, did not question him on each specific allegation.

Drs. Datta, Ghoshal, Majumder, Motiwala were interviewed as witnesses on the above listed dates (see College of Medicine Investigation Committee Meetings), regarding the allegations for publications on which they were the first and/or last author, the Jacob lab in general, how papers were prepared and figures generated, etc. Their specific responses are found within the Investigation Committee Analysis section.

An additional witness, Dr. Shoumei Bai, former OSU Graduate Student from 2000 to 2005, and then a Postdoctoral Fellow from 2005 to 2006 in the laboratory of Dr. Jacob, was not interviewed but she did provide written responses to questions from the COMIC regarding her time in the laboratory and specific concerns raised in three publications (Manuscript #4, #8, #16). 92, 93, 94

<sup>83</sup> Ex. 280 - 20190521 - Email ORC to SVPR - External Contact Request

<sup>84</sup> Ex. 281 - 20190522 - Email SVPR to ORC - External Contact Request Approved

<sup>85</sup> Ex. 287 - 20190523 - External Contact Notification - Jacob

<sup>86</sup> Ex. 288 - 20190523 - Email RIO to Jacob - External Contact

<sup>87</sup> Ex. 289 - 2019.05.28 - Ltr to Dr. Yucel in Resp. to May 23 Correspondence

<sup>&</sup>lt;sup>88</sup> Ex. 290 - 20190717 - Jacob Interview Participants

<sup>&</sup>lt;sup>89</sup> Ex. 291 - Jacob Image Forensics COMIC Interview Updated

<sup>&</sup>lt;sup>90</sup> Ex. 292 - 20190523 - Exhibit 1- Summary of Jacob Allegations for Investigation

<sup>&</sup>lt;sup>91</sup> Ex. 293 - 20190717 - COMIC Interview + errata - Jacob

<sup>92</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>93</sup> Ex. 295 - 20190618 - Email to Bai from ORC - COMIC Questions

<sup>94</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

### Criteria Required for a Finding of RM

Per the Policy, Section III.A., Research Misconduct means Fabrication, Falsification, or Plagiarism in proposing, performing, or reviewing research, or in reporting research results. The allegations reviewed in this Investigation Report are the Falsification of data. Falsification is defined as:

Section III.F: Falsification. "Falsification" is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

In the "Investigation Committee Analysis" section below, the COMIC used forensic analysis to determine which of the questioned figures have been falsified, e.g. by splicing, by the reuse of the same blot to represent different experimental conditions and proteins, etc.. In many instances, the Respondent and witnesses do not dispute the duplication of data. Additionally, in some instances, the apparent Falsification was supported by comparison of questioned images to raw data, and the publication of a correction for one questioned figure stating that data were "inadvertently duplicated." <sup>95</sup>

Per the Policy, Section III.A.1, a finding of Research Misconduct requires:

- **A.** That there be a significant departure from the accepted practices of the relevant research community; and
- B. The misconduct be committed intentionally, knowingly, or recklessly; and
- **C.** The allegation be proved by a Preponderance of the Evidence.

Analysis of criteria A: "That there be a significant departure from the accepted practices of the relevant research community." The COMIC determined that the relevant research community for this Investigation would be experienced biomedical researchers using molecular biology, biochemical and molecular genetic techniques in an academic setting with experience in publishing and grant writing. The COMIC members, with the exception of the HR staff representative, all represent this community with their experience and status as either associate or full professors with experience in molecular biology research with numerous grants and publications. Specifically, the COMIC faculty members have each been in various positions required in the academic pathway to become a faculty member who oversees trainees, including being a graduate student followed by post-doctoral researcher training. At each stage of their careers, the COMIC members have participated in Responsible Conduct of Research (RCR) training and have a firsthand understanding of the expected knowledge, independence, and responsibilities of a trainee at each level. As a collective, the COMIC has trained 38 post-doctoral researchers and 76 graduate students and have been involved directly in mentoring via NIH training and career development awards, graduate program management, and the formal teaching of responsible conduct of research (RCR) including, but not limited to, topics on professional ethics, proper figure generation, data analysis and plagiarism. Further, all of the COMIC members train their own mentees and lab members on accepted practices and RCR. Therefore, their assessment of what is an accepted practice is based on their collective knowledge of and active participation in the relevant academic biomedical research community. In addition, most, or in some cases all, COMIC members have served on NIH, NSF, and/or foundation grant review panels, are active manuscript reviewers, and are journal editors or have positions on journal editorial boards.

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<sup>95</sup> Ex. 28 – 20180430 Correction-Mol.Cell.Biol-2018-Ghoshal.pdf

**Analysis of criteria B:** "The misconduct be committed intentionally, knowingly, or recklessly." The definitions of "intentionally, knowingly, or recklessly" are not listed in the Policy, nor in the federal regulations (42 C.F.R § 93) applicable in this Investigation. Based on federal, state, and university guidance, the COMIC used the following definitions for this investigation:

Intentionally: Respondent directly engages in Fabrication, Falsification, or Plagiarism with the intent, or purpose, of misleading the readers of the research record.

Knowingly: Respondent has actual knowledge of the Fabrication, Falsification, or Plagiarism or acts in deliberate ignorance or plain indifference of the Fabrication, Falsification, or Plagiarism.

Recklessly: Respondent is on notice of a significant, increased risk of falsified, fabricated, or plagiarized data and/or text being used or generated, or the risk is so obvious that a typical researcher in the relevant research community should have known, and through action or inaction, the respondent uses, or allows the use of, the falsified, fabricated, or plagiarized data and/or text.

**Analysis of criteria C:** "The allegation be proved by a Preponderance of the Evidence". The preponderance of the evidence standard comes from the federal regulations under CFR 93.104 (c) and the University Policy Section III.H., which states:

"Preponderance of the Evidence" means proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

The COMIC generally will interpret preponderance of the evidence to mean at a certainty of greater than 50%. In addition, as required by the Policy and University Rule 3335-5-04, to determine appropriate sanction recommendations for a faculty Respondent, the COMIC must also consider the allegations at the 'Clear and Convincing' standard as required under the University Rule.

Per the Policy Section III.A.2, Research Misconduct specifically does not include honest error or differences of opinion. As stated in 42 CFR 93.106(b)(2), the Respondent has the burden of proving, by a preponderance of the evidence, any affirmative defense or honest error. The COMIC must determine whether any claim of honest error or an affirmative defense is proven by the preponderance of the evidence.

### **Investigation Committee Analysis**

During the Investigation and deliberations of the allegations, the COMIC found that there were several themes that repeatedly surfaced, which need to be taken into account when viewing the entire Investigation as a whole. In the paragraphs below, these major themes and the COMIC's approach to the case are outlined.

The COMIC conducted the Investigation with the understanding that the standards in the field are that Dr. Jacob, as the laboratory PI and/or corresponding author, is expected to review all figures and all text in any manuscript (or grant application submitted). The experiments in all manuscripts under Investigation were conducted when Dr. Jacob was a PI with staff under his guidance. Therefore, as PI of the laboratory and the senior author listed on the manuscripts, Dr. Jacob was responsible for the validity of the published data. It was clearly and consistently maintained by all members of the laboratory during both the Inquiry and Investigation that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. As such, the COMIC does not believe Dr. Jacob created any of the final figures for publication or generated any of the alleged falsified figures. However, the allegations against Dr. Jacob involve the reporting of falsified data. The COMIC believes that it was arguably irresponsible, and at times reckless for Dr. Jacob to assume, and not take any action to verify, that figures placed in publications where he was listed as a last/senior

author were reliable and accurately represented the experimental results.

Although the voting on each allegation is reflected as either a "yes" or a "no", the COMIC would like to stress that many of the recorded 'no' votes were reluctantly made. In some cases the COMIC did find that it was overwhelmingly clear that Falsification of the data or image had occurred, even purposefully, but it could not be directly attributed to specific individuals and not specifically to Dr. Jacob. As such, the presence of 'no' votes on any specific allegation should not be taken to mean that no purposeful Falsification was present regarding that allegation. Largely, the COMIC concludes that Dr. Jacob did not fully discharge his senior/corresponding author responsibilities to review figures against the raw data, but with limited exceptions delineated below does not find by a preponderance of evidence that he intentionally or knowingly allowed data falsification or acted in contradiction to the accepted practices of figure generation or laboratory management at the time. When taking into account the testimony and written responses of the other witnesses, the sheer number of allegations, the consistent overlap in authorship of the manuscripts under Investigation, and the definition of Research Misconduct as "Fabrication, Falsification or Plagiarism in proposing, performing, or reviewing research, or in reporting research results" (emphasis added), the Committee concluded that all of the first authors share responsibility for reporting falsified data and/or were complicit in performing the acts of falsification themselves when there was clear evidence that they were involved. Indeed, this is consistent with the policy stated by Dr. Jacob during his interview with the COMIC that the first and second authors were responsible for the construction of figures. However, in the absence of direct evidence to the knowing, intentional, or reckless falsification of data or reporting of falsified data, the respondent's position as corresponding author alone is insufficient to prove that research misconduct was committed. Nevertheless, the COMIC believes that Dr. Jacob's actions were reckless in instances where he was previously aware that allegations were raised against certain figures in the questioned paper and he disregarded the risk that other figures may be falsified, or when the falsification was so obvious that a typical researcher would have identified the falsification had the original raw data been reviewed.

When reviewing allegations involving only splicing (i.e., limited to the splicing of lanes without a clear demarcation of the cut/paste), the Committee determined that these allegations did not represent Research Misconduct. This decision was based on the fact that several of the manuscripts were published at a time when the standard in the field was emerging to clearly denote when/where blots were spliced together, however it was not yet a mandatory practice. As such, the Committee did not consider such practice to be Research Misconduct, whereas if this practice of splicing blots together without demarcations would occur at present, we would have considered the community standards as persuasive evidence in determining an act of Research Misconduct. The Committee would like to note that for several allegations, the Respondent and witnesses have argued that the lack of an obvious splice line should be interpreted as proof that splicing did not take place. This argument was refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected in published images, despite clear evidence or testimony that splicing had taken place (e.g., see Allegation #5, Allegation #28, and Allegation #29 below) suggesting that one or more Jacob Laboratory members had sufficient skill when manipulating the images to mask splice lines. As such, the Committee did not view the lack of visible splicing lines as proof that no splicing had occurred, and did not find credible the argument of the Respondent or witnesses regarding the lack of splice lines as proof that no splicing had occurred.

Another common defense put forward by the Respondent and witnesses during the Investigation was that for those allegations where the original data were not available, it would not be possible for the Committee to determine whether Research Misconduct had taken place. The Committee does not agree with this defense and concluded that the original data is not always needed to determine if Research Misconduct had occurred. In cases where forensic analysis clearly demonstrates that blots were manipulated and/or duplicated in the published version of a manuscript or the same data were published in two different manuscripts, this would confirm falsification and along with other evidence can be used to attribute responsibility to a specific Respondent and support a Research Misconduct finding. Although lack of original data may often hinder the Investigation process and in some instances makes it difficult to know how the manipulations impact the reported results, the original data is not always needed to determine that Research Misconduct had taken place. During the

Investigation but after witness interviews, the COMIC identified additional evidence in the Respondent's and/or witnesses' original data files that influenced the final findings.

One of the arguments put forward by the Respondent and witnesses was that no one had ever challenged their data before the OSU notification of allegations in November 2017. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, such statements have been found to be false. A review of selected and pertinent email records revealed that as early as March 23, 2017 and June 30, 2017, Dr. Jacob had received formal notifications from Proceedings of the National Academy of Sciences and the Journal of Biological Chemistry, respectively, that there were concerns with data in a number of publications. Additionally, the respondent and others in the laboratory were in receipt of notifications from PubPeer regarding concerns with multiple manuscripts. It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 discussed later in this report) or whether they proceeded directly to PubPeer's website without opening the email. One of the editors of the Journal of Biological Chemistry with whom Dr. Jacob was in correspondence specifically mentioned PubPeer concerns to Dr. Jacob via email on September 19, 2017.96 The ongoing investigation by the Journal of Biological Chemistry as well as the concerns that were already published on the web (i.e. PubPeer) were known to the Respondent and witnesses at the time of initial notification of allegations by OSU, yet every single person involved in this investigation failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by the Respondent and witnesses.

Interestingly, the Committee notes that in the overwhelming majority of the instances wherein blots were allegedly manipulated, it was the control lanes that had been changed. Generally speaking, it is the Committee's collective experience that when reviewing a manuscript for publication, or when reading a manuscript to gain information, reviewers/researchers primarily focus on the experimental data lanes, and typically only take a quick glance at the control lanes to confirm equal loading was used in the blots or some other controlled variable is correct. Given this, it is not unlikely that manipulations of control lanes would be less readily recognized by a reviewer. Had the alleged falsifications all been attributable to inadvertent errors as the Respondent and witnesses contend, the Committee would expect the errors to be randomly divided between experimental and control data, with the majority expected to occur in the more numerous experimental data lanes. However, the alleged falsifications occurred predominantly in the control lanes of the figures, which casts significant and overwhelming doubt on the likelihood of such duplications/manipulations being inadvertent errors. In addition, since these manipulations and duplications occurred over a large number of manuscripts, and over an extended period of time, the Committee concluded that there was a permissive culture of data manipulation in the lab, with emphasis on the control lanes to minimize detection, and that this was not due to inadvertent error.

. The Committee believes that throughout the Inquiry and Investigation members of the Jacob laboratory were not truthful when accounting for their communication practices and were in frequent communication with one another, providing remarkably similar, if not identical response statements, and mounted a "circle the wagons" defense to any allegations. Given this unity of defense (to both the JBC and OSU Inquiry/Investigation committees), it was clear to the COMIC that the Respondent and witnesses were closely aligned and that the credibility of written or oral exculpatory statements should be questioned.

A summary of the overarching statements that bore upon the COMIC's decisions are described in the "General Respondent/Witness Statements" section below. The COMIC noted the many similarities in the

<sup>&</sup>lt;sup>96</sup> Ex. 297 - 20170919 - Email - JBC Editor to Jacob - Re Response JBC articles

witnesses' responses. The specific allegations against Dr. Jacob and the responses to those allegations are subsequently discussed by the COMIC, with the forensic analysis for the questioned images included accordingly. In some cases, the forensics were performed by ORC, and in others the forensics were performed by the Journal of Biological Chemistry (JBC) for their own investigation and e-mailed to the authors. ORC subsequently identified the JBC forensic analysis during review of email records. Due to additional allegations of possible Research Misconduct being added to manuscripts already under review by the CII and COMIC, the numbering of allegations within each specific manuscript are not in sequential, consecutive order. Allegations identified at the Preliminary Assessment stage for Dr. Jacob are numbered #1 - 39, while allegations added to the Inquiry and Investigation by a majority vote of the CII/COMIC members are numbered #40 - 84. A concluding summary of the COMIC's final findings of Research Misconduct is provided in the "Summary of Investigation Committee Conclusions" section following the manuscript and allegation analysis below.

### **General Respondent/Witness Statements**

#### Dr. Jacob

- 1. In his response to the CII's preliminary report, <sup>97</sup> his appeal of their determination, <sup>98</sup> and a letter sent to the COMIC at the beginning of its investigation, <sup>99, 100</sup> Dr. Jacob indicated that he carefully reviewed every paper and every figure prior to journal submission and throughout the editing process. He "did not spot any of the errors in any of the seventeen papers containing the figures now being questioned," <sup>101</sup> and he did not compare "every figure in every paper to the raw data on which each such figure was based prior to its publication." <sup>102</sup> Dr. Jacob has maintained that comparing a composed figure to the raw data was not an accepted practice in the research community at the time the majority of manuscripts under investigation were published, and as such his failure to do so could not be considered a significant departure from the standard practices of the relevant research community. Dr. Jacob cited the age of the publications and lack of available original data (retention thereof only required for 5 and 6 years, per the OSU and NIH policies, respectively) as hindrances to his defense against the allegations. <sup>103</sup> Furthermore, Dr. Jacob challenged the application of the subsequent use exception allowing for the investigation of any allegation stemming from a manuscript greater than 6-years old. <sup>104, 105, 106</sup>
- 2. In his response to the CII's preliminary report, <sup>107</sup> his appeal of their determination <sup>108</sup>, and a letter sent to the COMIC at the beginning of its investigation, <sup>109</sup> Dr. Jacob challenged the use of forensic tools and interpretations of forensic findings:

"We do not believe that mere similarity of bands within a panel, even where the allegedly duplicated bands are very similar or identical in appearance, is sufficient for a finding of duplication where the forensic analysis does not show any splicing. We expect the bands, especially in control blots, to appear very, very similar. If there were duplication of bands within

<sup>97</sup> Ex. 209 - 20181022 - Jacob Response to CII with Exhibits

<sup>98</sup> Ex. 249 - Jacob Appeal Zadnik

<sup>&</sup>lt;sup>99</sup> Ex. 279 - Ltr. To Coll Commit.2.19\_.

<sup>&</sup>lt;sup>100</sup> Dr. Jacob provided the document "Jacob Response to CII with Exhibits" on three occasions: in response to the CII's preliminary report, in conjunction with his appeal to the Deciding Official, and in solicited correspondence with the COMIC.

<sup>&</sup>lt;sup>101</sup> Ex. 209 - 20181022 - Jacob Response to CII with Exhibits, page 3

<sup>&</sup>lt;sup>102</sup> Ex. 209 - 20181022 – Jacob Response to CII with Exhibits, page 4

<sup>&</sup>lt;sup>103</sup> Ex. 209 - 20181022 – Jacob Response to CII with Exhibits, page 5

<sup>&</sup>lt;sup>104</sup> Ex. 209 - 20181022 – Jacob Response to CII with Exhibits, page 6-7

<sup>&</sup>lt;sup>105</sup> Ex. 249 - Jacob Appeal Zadnik, pages 1-2

<sup>&</sup>lt;sup>106</sup> Ex. 279 - Ltr. to Coll.Commit.2.19 ., page 2

<sup>&</sup>lt;sup>107</sup> Ex. 209 - 20181022 – Jacob Response to CII with Exhibits

<sup>&</sup>lt;sup>108</sup> Ex. 249 - Jacob Appeal Zadnik

<sup>&</sup>lt;sup>109</sup> Ex. 279 - Ltr. To Coll Commit.2.19\_.

a panel, we would also expect that there would be evidence of the splicing that would have to occur to create such a duplication, especially back at the time that these papers were prepared. Yet, there is no evidence of splicing. We feel the CII completely ignored this point. In the absence of evidence of splicing, I do not believe there is any substance to allegations of reuse of bands that appear within a larger panel." 110, 111

Additionally, Dr. Jacob made claims regarding duplication and interpretation of forensic analysis in written documentation provided to OSU via his legal counsel on July 15, 2019:<sup>112, 113</sup>

"Thus, significant overlay between two lanes in forensic analysis does not mean a duplication occurred, but rather may be explained by how meticulous the researchers were in equalizing the loading controls. Further, if there is duplication within a panel, we would expect to see some evidence of splicing, which is completely absent in many cases." 114

3. In written documentation provided to OSU via his legal counsel on July 15, 2019<sup>115</sup>, Dr. Jacob specifically argued again that splicing to remove lanes was an allowable practice, cited limited publications or policies to the contrary before 2017, and stated that:

"Unless the CII is prepared to recommend investigation of every spliced figure in every published paper by every scientist where the original data is no longer available, it is inappropriate and selectively punitive to recommend investigation of such figures in papers by Dr. Jacob."<sup>116</sup>

4. In written documentation provided to OSU via his legal counsel on July 15, 2019<sup>117</sup> and November 15, 2019, <sup>118</sup> Dr. Jacob highlighted his background and career accomplishments, reiterated his argument regarding the age of the publication and lack of available raw data hindering defense against the allegations, reiterated his challenge to OSU's application of the subsequent use exception allowing for the investigation of this allegation, reiterated his assertions about the limitations of forensic analysis, and defended his oversight as consistent with the standards of the time.

Furthermore, Dr. Jacob described that he:

"...carefully read every paper and carefully reviewed every figure in every paper before it was submitted to a journal for peer review consideration. Dr. Jacob had lived with the research and the research results over many months or even years at that point. He knew what the results were, and he reviewed the figures for consistency with the results he knew had been obtained, based on his supervision, review and discussion of the research that was conducted over time." 119

<sup>&</sup>lt;sup>110</sup> Ex. 209 - 20181022 - Jacob Response to CII with Exhibits, page 11

<sup>111</sup> These arguments were refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected, despite clear evidence or testimony that splicing had taken place (e.g., see <u>Allegation #5</u>, <u>Allegation #28</u>, and <u>Allegation #29</u> below) suggesting that the Jacob laboratory members had sufficient skill when manipulating the images to mask splice and/or cut/paste lines.

<sup>&</sup>lt;sup>112</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>113</sup> Ex. 299 - 20190715 - Email Counsel to LA - letter from Dr. Jacob

<sup>&</sup>lt;sup>114</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 12

<sup>&</sup>lt;sup>115</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>116</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 7-9

<sup>117</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>118</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>119</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 6

### Similarly,

"He would have reviewed all of the figures in this paper at the time they were originally submitted for publication, and would have noted that they were consistent with the results he observed in the laboratory." <sup>120</sup>

But that,

"It is true that Dr. Jacob did not, prior to publication of every paper, compare each and every figure in that paper to the raw data on which each such figure was based." 121

- 5. In written documentation provided to OSU via his legal counsel on July 15, 2019, 122 Dr. Jacob asserted that he did not prepare any manuscript figures and claims that his "level of reliance on his colleagues to properly prepare figures was not a substantial departure from accepted practice and did not disregard a substantial risk of which Dr. Jacob was consciously aware."
- 6. In his interview with the COMIC on July 17, 2019, Dr. Jacob did not specifically address individual allegations, but stated that he did not record who prepared each figure for each manuscript, <sup>123</sup> that no one remembers who made the figures for the JBC papers, <sup>124</sup> and that he generally reviewed figures but did not compare the figure's representation of the data to original source data at the time of manuscript submission. <sup>125</sup> Dr. Jacob further explained that he did not submit manuscripts electronically but rather delegated that duty to the first or second author and didn't know that submissions typically required testament to or acknowledgment of the responsibilities of authorship. <sup>126</sup> Consistent with previous testimony and written responses, Dr. Jacob maintained that he wasn't involved in the construction of figures. Dr. Jacob indicated that the first and second author ultimately should be responsible for the construction of figures <sup>127</sup> and that the most senior laboratory personnel included Drs. Ghoshal and Majumder. <sup>128</sup> If there were to be any manipulation of data within his laboratory, Dr. Jacob was not aware of this, never orchestrated it, and would consider himself a victim of such activity. <sup>129</sup>
- 7. After claiming in his July 17, 2019 interview with the COMIC that he should be considered a victim of data manipulation activity by others in the laboratory within his laboratory, in his letter dated November 15, 2019, Dr. Jacob back-tracked to his previous arguments and placed trust in and reliance on Dr. Ghoshal's responses. 130 In the letter, Dr. Jacob maintained that data falsification had not occurred or was immaterial to the conclusions presented in the figure at question or the manuscript at large. 131

<sup>&</sup>lt;sup>120</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 1

<sup>&</sup>lt;sup>121</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 6

<sup>122</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 2-3, page 11

<sup>&</sup>lt;sup>123</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 11, line 5-8

<sup>&</sup>lt;sup>124</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 14

<sup>&</sup>lt;sup>125</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 25, lines 16-21; page 28, line 23 to page 29, line 19

<sup>&</sup>lt;sup>126</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 26-27; page 28, line 15

<sup>&</sup>lt;sup>127</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 48

<sup>&</sup>lt;sup>128</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 45-46

<sup>&</sup>lt;sup>129</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 12-13; page 22, line 13-15; page 67, line 1-9; page 70, line 10-11

<sup>&</sup>lt;sup>130</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>131</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 1

#### Dr. Datta

- 1. In her response to the CII's preliminary report<sup>132</sup> and her appeal of their determination, <sup>133, 134</sup> Dr. Datta highlighted the age of many of the publications and the lack of available original data as hindrances to her defense against the allegations, and using nearly identical language to that of Dr. Jacob in challenging the application of the subsequent use exception allowing for the investigation of any allegation stemming from a manuscript greater than 6-years old.
- 2. In her response to the CII's preliminary report, Dr. Datta stood by the validity of each manuscript's conclusions and argued that no motive exists for the falsification of images:

"When a paper or a figure is just as strong with or without an allegedly manipulated image, or where a repeat or similar experiment shows the same results, I see no reason why anyone would intentionally manipulate the image." 135

3. In her interview with the COMIC on June 28, 2019, Dr. Datta indicated that day-to-day operations in the laboratory were overseen by Drs. Ghoshal and Majumder with data ultimately being presented to Dr. Jacob. Dr. Datta said that original data were usually kept in laboratory notebooks with publication-quality blots stored in a separate folder and given to Dr. Jacob and/or his secretary, 137 figures were constructed by many authors/members of the laboratory with the exception of Dr. Jacob, 138 and that responsibility for the integrity of the data in a published manuscript should generally be shared regardless of authorship position. 139 Specifically,

COMMITTEE MEMBER: Okay. So since every -- so who do you view responsible for the scientific integrity and content of the paper, is it the first author alone, the corresponding author alone, or everybody on the paper?

DR. DATTA: Everybody on the paper, right. In my opinion, I feel -- I felt. 140

4. Dr. Datta explained to the COMIC that she would always repeat experiments rather than "clean up" an image and had no knowledge of anyone in the laboratory performing such activities, which she deemed unacceptable. 141 Furthermore, Dr. Datta indicated that it would not be acceptable to re-use control blots from separate experiments to generate figures, and that without the original data to refer to that she cannot explain the apparent duplications, or acknowledge that a figure might be falsified. 142

 $<sup>^{132}\</sup> Ex.\ 211$  - 20181022 - Jharna Datta Response to CII

<sup>133</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>134</sup> Dr. Datta provided the document "Datta Response to CII with Exhibits" in conjunction with her appeal to the Deciding Official. It is identical to Ex. 211 - 20181022 - Jharna Datta Response to CII

<sup>&</sup>lt;sup>135</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 8

<sup>&</sup>lt;sup>136</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 7-9, 11

<sup>137</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 12-13

<sup>&</sup>lt;sup>138</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 14-16, page 94

<sup>&</sup>lt;sup>139</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 28, line 12-18; page 98, line 15-24

<sup>&</sup>lt;sup>140</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 28, line 12-18

<sup>&</sup>lt;sup>141</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 19-20; page 21 line 16-23

<sup>&</sup>lt;sup>142</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 53-54, page 79, page 90

#### Dr. Ghoshal

- 1. In her response to the CII's preliminary report<sup>143</sup> and her appeal of their determination, <sup>144,145</sup> Dr. Ghoshal highlighted the age of many of the publications and lack of available original data as hindrances to her defense against the allegations, using nearly identical language to that of Dr. Jacob in challenging the application of the subsequent use exception allowing for the investigation of any allegation stemming from a manuscript greater than 6-years old.
- 2. In Dr. Ghoshal's response to the CII's preliminary report<sup>146</sup> and her appeal of their determination, <sup>147</sup> Ghoshal argued that comparison of figures by the senior/corresponding author to the underlying original data was not an accepted practice of the research community and that she had no evidence and was therefore not aware of any substantial risk in relying on her graduate students, post-docs, or senior researchers to assemble figures. <sup>148</sup> Additionally, she disagreed with the characterization that she was an integral part of all projects in the Jacob laboratory, but rather considered herself having played a key role in liver cancer projects and only a smaller role in leukemia and breast cancer projects. <sup>149</sup>
- 3. With respect to alleged duplications in loading controls and/or duplications within a panel, Dr. Ghoshal stated in her response to the CII's preliminary report<sup>150</sup> and her appeal of their determination<sup>151</sup> that extreme attention to loading equal amounts of protein may have yielded the similarity in bands. Additionally, she maintained,

"I do have some skepticism of the allegations where the panel does not show, even in the forensic analysis, any splice lines. I believe the absence of splice lines is evidence of non-duplication, and no one has explained to me how we could have duplicated data within a panel without splicing it in, or how spliced data can be created without splice lines." 152,153

- 4. In her response to the CII's preliminary report, <sup>154</sup> Dr. Ghoshal stood by the reproducibility of each manuscript's conclusions and argued that no motive exists for the falsification of images.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal indicated that the Jacob laboratory generally kept track of and knew who made each figure in a manuscript, 155 that senior postdocs usually made their own figures, 156 and that prepared figures were usually accepted by postdocs or research scientists without comparing the figure's representation of the data to original source data. 157 Dr. Ghoshal generally indicated that whoever performed the experiment or made the figure

<sup>&</sup>lt;sup>143</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits

<sup>&</sup>lt;sup>144</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>145</sup> Dr. Ghoshal provided the document "Ghoshal Response to CII with Exhibits" in conjunction with her appeal to the Deciding Official.

<sup>&</sup>lt;sup>146</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits

<sup>&</sup>lt;sup>147</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>148</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 3

<sup>&</sup>lt;sup>149</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 3-4

<sup>150</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 9, point 1

<sup>&</sup>lt;sup>151</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>152</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 9, point 2

<sup>&</sup>lt;sup>153</sup> These arguments were refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected, despite clear evidence or testimony that splicing had taken place (e.g., see <u>Allegation #5</u>, <u>Allegation #28</u>, and <u>Allegation #29</u> below) suggesting that the Jacob laboratory members had sufficient skill when manipulating the images to mask splice and/or cut/paste lines.

<sup>&</sup>lt;sup>154</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 9, points 3 & 4

<sup>155</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 23-24

<sup>&</sup>lt;sup>156</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 27-28

<sup>157</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 28-30

should be responsible for the authenticity of the figure <sup>158</sup> and that the responsibility for the integrity of the data in a published manuscript should generally be shared regardless of authorship position, <sup>159</sup> but that without original data that she could not be sure who may be responsible for the specific allegations. <sup>160</sup>

### Dr. Majumder

- 1. In her response to the CII's preliminary report<sup>161</sup> and her appeal of their determination,<sup>162</sup> Dr. Majumder highlighted the age of many of the publications and lack of available original data as hindrances to her defense against the allegations, using nearly identical language to that of Dr. Jacob in challenging the application of the subsequent use exception allowing for the investigation of any allegation stemming from a manuscript greater than 6-years old.<sup>163, 164</sup>
- 2. With respect to splicing, Dr. Majumder indicated:

"It is important to understand that removal of lanes of a gel when preparing figures for publication is common, even today, and there is nothing wrong with it. Journals have limited space and do not want scientists to include unnecessary data in published papers. Our desire to remove unnecessary lanes stems from the journal's desire not to take up valuable space with irrelevant data and confuse the reviewers. There is no reason to conclude that the removal of lanes was for any improper purpose. Indeed, if the Committee is going to say that mere removal of lanes is "sufficient substance" to warrant a research misconduct investigation, then it will need to open a research misconduct investigation into every paper by every scientist in which irrelevant data have been removed for publication." 165

3. In her response to the CII's preliminary report, as well as a written response provided to the COMIC in advance of her interview, <sup>166</sup> Dr. Majumder stood by the validity of each manuscript's conclusions and argued that no motive exists for the falsification of images:

"Where the figure and the paper would be just as strong irrespective of those bands, it seems incomprehensible to me that someone would fabricate them... I would think that reproducibility of the science would be an important consideration when an allegation of fabrication or falsification has been made." 167

4. In her interview with the COMIC on June 12, 2019, Dr. Majumder indicated that she and Dr. Ghoshal were the senior staff in the Jacob lab, <sup>168</sup> that whoever ran the experiment would provide the figure for a manuscript or in cases where Dr. Majumder had a student run the experiment then she would check the original data, <sup>169</sup> that Dr. Jacob would ask for original data during the preparation of a manuscript but not necessarily review original data at the final stage, <sup>170</sup> and that integrity of the data

<sup>&</sup>lt;sup>158</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 7-9

<sup>159</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 10-11

<sup>&</sup>lt;sup>160</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 85

<sup>&</sup>lt;sup>161</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918

<sup>&</sup>lt;sup>162</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>163</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 1-2

<sup>&</sup>lt;sup>164</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>165</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 4

<sup>&</sup>lt;sup>166</sup> Ex. 350a - 2019-06-07 Pre-Interview Submission Majumder, pages 6-7, 9-10; see page 9

<sup>&</sup>lt;sup>167</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 11

<sup>&</sup>lt;sup>168</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 3, lines 14-20; page 5, lines 2-10; page 34, lines 13-17

<sup>&</sup>lt;sup>169</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 13 line 23 to page 14, line 14

<sup>&</sup>lt;sup>170</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 18, lines 5-11

in a published manuscript would be her responsibility if she were the first author.<sup>171</sup> However, she described a highly collaborative lab environment where all authors participated in manuscript development and review, response to reviewers, etc.<sup>172</sup>

### Dr. Motiwala

- 1. In her response to the CII's preliminary report<sup>173</sup> and her appeal of their determination,<sup>174</sup> Dr. Motiwala highlighted the age of many of the publications and lack of available original data as hindrances to her defense against the allegations, using nearly identical language to that of Dr. Jacob in challenging the application of the subsequent use exception to the six-year time limitation allowing for the investigation of any allegation stemming from a manuscript greater than 6-years old.<sup>175, 176</sup>
- 2. In Dr. Motiwala's response to the CII's preliminary report<sup>177</sup> and her appeal of their determination, <sup>178</sup> Dr. Motiwala argued the limitations of forensic analysis and also maintained that reuse of data would not be possible if splice lines were not detected. <sup>179, 180, 181</sup> Dr. Motiwala highlighted the relatively low frequency of figure errors as being likely attributable to inadvertent or honest errors and was adamant about the validity and reproducibility of each manuscript's conclusions. <sup>182</sup>
- 3. In her interview with the COMIC on June 12, 2019, <sup>183</sup> Dr. Motiwala identified Drs. Ghoshal and Majumder as senior members of the laboratory when she started in the laboratory, with herself and Dr. Datta serving in more junior positions. <sup>184</sup> Dr. Motiwala indicated that she reported to Dr. Jacob but worked more closely with Dr. Ghoshal, <sup>185</sup> and indicated that junior members of the lab shared computers, while the senior members had their own. <sup>186</sup> Dr. Motiwala maintained that generally whoever ran the experiment would prepare the figure, <sup>187</sup> that cutting and pasting would have occurred to remove extraneous samples for a figure, <sup>188</sup> and that Dr. Jacob never made figures <sup>189</sup> but trusted the lab members to perform and deliver. <sup>190</sup>
- 4. Dr. Motiwala generally indicated that responsibility for the integrity of the data in a published manuscript would rest with the corresponding author, 191 but also indicated that the first author has to take responsibility for every figure. 192

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<sup>171</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder_Redaction 1, page 23, lines 13-23; page 36, lines 6-10
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<sup>172</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 14-24

<sup>&</sup>lt;sup>173</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>&</sup>lt;sup>174</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>&</sup>lt;sup>175</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 1

<sup>&</sup>lt;sup>176</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318, page 1, 4

<sup>&</sup>lt;sup>177</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>&</sup>lt;sup>178</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>&</sup>lt;sup>179</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 2-3

<sup>&</sup>lt;sup>180</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318, page 1

<sup>&</sup>lt;sup>181</sup> These arguments were refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected, despite clear evidence or testimony that splicing had taken place (e.g., see <u>Allegation #5</u>, <u>Allegation #28</u>, and <u>Allegation #29</u> below) suggesting that the Jacob laboratory members had sufficient skill when manipulating the images to mask splice and/or cut/paste lines.

<sup>&</sup>lt;sup>182</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 7

<sup>183</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1

<sup>184</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 5, lines 6-7 and 18-20

<sup>185</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 6, line 22 to page 7, line 1

<sup>186</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 10, line 13 to page 11, line 2

<sup>187</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 12 line 23-25

<sup>188</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 13, line 8-20

<sup>&</sup>lt;sup>189</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 20, line 8-11

<sup>&</sup>lt;sup>190</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 72, line 4-6

<sup>&</sup>lt;sup>191</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 22, page 72-74

<sup>&</sup>lt;sup>192</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 85, line 25 to page 86, line 5

5. Furthermore, in her interview with the COMIC, Dr. Motiwala admitted that removing blemishes from a figure was acceptable, 193 although pasting in representative results was not a practice of which she was aware of in the laboratory or done with intent to distribute false research results:

"I wouldn't say that's a practice, but like if we are observing that, I mean, it's possible that that was happening but, I mean, obviously we were not aware." 194

And,

"I mean, there may have been errors or manipulations to make the figures pretty, like you said, but I don't think that was intentional to change anything or deceive the scientific community, if that makes sense." 195

6. The COMIC questioned Dr. Motiwala on what appears to be a pattern of controls being replicated:

COMMITTEE MEMBER: Can you comment in general, maybe this is redundant but, you know, there's often a pattern we're seeing of controls being replicated. Do you think there was, I mean, do you feel that within your environment there was a feeling that it's something you could do, you could replicate controls and it didn't matter, or it wasn't -- if didn't impact the conclusions of the paper, that it was acceptable? Do you have a -- do you want to comment on that?

DR. MOTIWALA: I don't think that was a general acceptance, I mean, or kind of like, say norm or something. But like, you know, this is being observed, like I mean, obviously, it is happening, you know, without our knowledge. 196

And

COMMITTEE MEMBER: And, again, you know, part of where our questions are coming from is there's this pattern emerging. Do you have any insight as to why this pattern may have occurred in terms of cutting and pasting in order to splice, in order to replicate bands? Do you have any sense of, I mean, do you believe it has occurred?

DR. MOTIWALA: I mean, considering like so many instances like definitely, I mean, it has occurred at some point, like if not for all. I'm not sure if they were, you know, they could have been errors sometimes, sometimes it may be like data belonging to so many different people and kind of putting it together, or sometimes Photoshop problems.<sup>197</sup>

### Manuscript #1 under Review - Majumder et al., JBC 2002 (4 Allegations)

Majumder S\*, Ghoshal K\*, Datta J\*, Bai S, Dong X, Quan N, Plass C, and Jacob ST. "Role of de novo DNA methyltransferases and methyl CpG-binding proteins in gene silencing in a rat hepatoma." J Biol Chem. 2002 May 3; 277(18):16048-58. Epub 2002 Feb 13. **RETRACTED 07/19/18** \* co-first authors

<sup>&</sup>lt;sup>193</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 20, line 12-25

<sup>&</sup>lt;sup>194</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 85, line 2-5

<sup>&</sup>lt;sup>195</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 87, line 19-23

<sup>&</sup>lt;sup>196</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 69, line 24 to page 70, line 13

<sup>&</sup>lt;sup>197</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 83, line 1-14

**Manuscript #1, Allegation #1 –** S.T. Jacob reported falsified data by splicing between lanes 1 and 2 in Figure 3A<sup>198</sup> in Majumder et al., JBC 2002.

### **Finding of Fact:**

- Figure 3A shows a Northern blot analysis of polyA<sup>+</sup> RNA isolated from liver and hepatoma in tumor bearing mice. The blot was probed for DNA methyltransferases (DNMTs), DNMT1, DNMT3a, and DNMT3b, and showed a higher expression level of the DNMTs in the hepatoma compared with the liver.
- 2. Adobe Photoshop gradient mapping demonstrated splice lines between lanes 1 (liver) and 2 (hepatoma) in the DNMT3a and DNMT3b panels (see slide 3<sup>199</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>200</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day<sup>201, 202</sup> and Dr. Majumder on July 2, 2017.<sup>203</sup> All authors, including Dr. Datta, were notified in follow-up directly by JBC on July 31, 2017.<sup>204</sup> As such, the co-first and co-corresponding authors knew of potential issues with the research for approximately three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.<sup>205, 206, 207, 208</sup>
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a line between lanes 1 and 2 in the DNMT3a and DNMT3b panels, which the Committee concludes represents a splice line and could be indicative of falsification.
- 6. Dr. Sarmila Majumder was the first author of JBC 2002 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Jharna Datta was a co-first author of JBC 2002 and Post-doctoral Researcher in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Kalpana Ghoshal was a co-first author of JBC 2002 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

#### Respondent's Response:

- 1. In his interview with the CII on March 5, 2018, Dr. Jacob generally stated that splicing from different gels/blots was common practice in that era and that there was no requirement during that time to demarcate spliced gels by a box or line.<sup>209</sup> He did not comment on this specific allegation of splicing.
- 2. In her interview with the CII on March 1, 2018, Dr. Majumder, the first author on the paper, commented that the bands on the bottom panel corresponded to the housekeeping COX-1 gene, and that since they were overexposed, the background makes it appear like a splice line.<sup>210</sup> Dr. Majumder did not believe there was splicing present in this figure<sup>211</sup> and maintained that she did not remember if she ran this

<sup>&</sup>lt;sup>198</sup> Original allegation posted on PubPeer noted Figure 1A incorrectly

<sup>&</sup>lt;sup>199</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 3

<sup>&</sup>lt;sup>200</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>201</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>202</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>203</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>204</sup> Ex. 484 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles

<sup>&</sup>lt;sup>205</sup> Ex. 309 - 20171019 - Email Jacob to JBC - JBC response Majumder 2002

<sup>&</sup>lt;sup>206</sup> Ex. 310 - JBC Majumder M1116622002-10172017

<sup>&</sup>lt;sup>207</sup> Ex. 311 - 20171019 - Email Jacob to JBC #2 - JBC response Majumder 2002

<sup>&</sup>lt;sup>208</sup> Ex. 312 - JBC Majumder M1116622002-v2

<sup>&</sup>lt;sup>209</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 30, lines 4-24; page 31 lines 1-14

<sup>&</sup>lt;sup>210</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 36 lines 11-24, page 27 lines 1-10

<sup>&</sup>lt;sup>211</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 36 lines 4-6

experiment, but indicated she could have.212

Dr. Majumder echoed the sentiments of Dr. Jacob and indicated during her interview with the CII that splicing was a common practice in the field and she would have spliced things out if a lane wasn't required or important for the figure.

DR. MAJUMDER: "Whether I brought lanes from 5 different -- different figures, I would not say. But, you know, it depends on the circumstance. But if I had some in between that I wanted to not present, yes, I would".<sup>213</sup>

- 3. Co-first authors Dr. Jharna Datta and Dr. Kalpana Ghoshal were not identified as co-first authors during the inquiry and therefore were not questioned about this allegation in their respective interviews.
- 4. See Dr. Jacob's General Respondent/Witness statements #1, #3-7 above regarding laboratory practices, oversight, construction of figures, splicing, application of the subsequent use exception, and responsibility of authors.
- 5. In her response to the CII's preliminary report<sup>214</sup> and her appeal of their determination,<sup>215</sup> Dr. Majumder reiterated that she does not know whether she ran the gel or prepared the figure and states that no evidence exists that she did. In her response to the CII's preliminary report, as well as a written response provided to the COMIC in advance of her interview,<sup>216</sup> Dr. Majumder argued that the CII misinterpreted her interview comments and explains, "because of the low level of expression of DNMT3a and 3b (low copy number), compared to Cox-1 (a house keeping gene), overexposure of the Dnmt3a and 3b bands (but not the Cox-1) was necessary to get a reasonable signal, and caused the appearance of the white line, which is being incorrectly interpreted as a splice."<sup>217</sup> She again explained that splicing unnecessary gel lanes from a final figure was a common and accepted practice, that the line between the samples is visible with the naked eye, and that the journal did not raise any concerns about the figure, in the past or more recently.<sup>218</sup>

See also Dr. Majumder's General Respondent/Witness statements #1-4 above regarding laboratory practices, oversight, reproducibility of the manuscripts under investigation, splicing, application of the subsequent use exception, and responsibility of authors.

6. In her interview with the COMIC on June 12, 2019,<sup>219</sup> Dr. Majumder confirmed that she does not remember doing the experiment or constructing the figure, does not believe a splice line is present and without the raw data cannot determine whether there was splicing or not.<sup>220</sup> The COMIC acknowledged that there may be instances where splicing is appropriate or common, but that in those cases the splice line should extend through the entire experiment/figure:

COMMITTEE MEMBER: But before going to the next I guess the question was, because I understand that we've previously established that splicing sometimes occurs in the lab, I guess in this situation the question is really if splicing was appropriate here, then why doesn't the splice line run all the way down through the complete set of blots? Why have we selectively spliced the first two panels?

<sup>&</sup>lt;sup>212</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 40 lines 19-22

<sup>&</sup>lt;sup>213</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 39 lines 4-8

<sup>&</sup>lt;sup>214</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918

<sup>&</sup>lt;sup>215</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>216</sup> Ex. 350a - 2019-06-07 Pre-Interview Submission Majumder, pages 6-7, 9-10; see page 6-7

<sup>&</sup>lt;sup>217</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 3

<sup>&</sup>lt;sup>218</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 3

<sup>&</sup>lt;sup>219</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1

<sup>&</sup>lt;sup>220</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 26, line 30 – page 27, line 11

DR. MAJUMDER: I mean, as I told the CII committee also, I didn't believe that there is splicing...<sup>221</sup>

And

COMMITTEE MEMBER: So a question on the -- so I understand you to indicate that you don't believe that there's a splice in the first two panels, correct?

DR. MAJUMDER: No, I don't believe it.

COMMITTEE MEMBER: Okay. If there were, if those were spliced, would the figure be valid?

DR. MAJUMDER: If the splice went all the way through, like all along through all the lane, yes, it would.

COMMITTEE MEMBER: Okay.

DR. YUCEL: But if it didn't go all the way through all four panels, then it would not be correct?

DR. MAJUMDER: Yes. 222

- 7. In her interview with the COMIC on June 28, 2019, co-first author Dr. Jharna Datta, indicated that she was involved in attempting to identify original data prior to the retraction of the manuscript in July 2018 and could not find the original data but rather only standardization or antibody testing data. See also Dr. Datta's General Respondent/Witness statements #1-4 above regarding laboratory practices, oversight, motive, application of the subsequent use exception, and responsibility of authors.
- 8. This allegation was not specifically discussed with co-first author Dr. Kalpana Ghoshal during her interview with the COMIC on June 28, 2019. See Dr. Ghoshal's General Respondent/Witness statements #1-2, 4-5 above regarding laboratory practices, oversight, construction of figures, reproducibility, application of the subsequent use exception, and responsibility of authors.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation. None of the co-first authors has taken responsibility for generation of Figure 3A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Majumder indicated that her main responsibility on the paper was writing.<sup>224</sup>
- 2. It is the Committee's understanding that the standards in the field at the time of this 2002 publication may not have been to require demarcation of non-contiguous bands and the alleged splice is visible to the naked eye. In permitted instances, however, the splice line would be expected to run all the way down through the complete set of blots (panels), which is not the case in Figure 3A.
- 3. Without original data, the COMIC is not able to determine the significance of the splicing and how it may have altered the interpretation and conclusions of the manuscript, i.e. it is unclear if the splicing was performed to remove extraneous noncontiguous data and not properly documented with a demarcation), to combine results from different experiments in order to illustrate an ideal result, or to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony,

<sup>&</sup>lt;sup>221</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 26, line 11-22

<sup>&</sup>lt;sup>222</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 28, line 10-24

<sup>&</sup>lt;sup>223</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 33-35

<sup>&</sup>lt;sup>224</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 33, line 16-17

that Dr. Jacob was not responsible for the falsification of Figure 3A and that the actions of others caused the splicing within Figure 3A in Allegation #1, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT3a and DNMT3b panels in Figure 3A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT3a and DNMT3b panels in Figure 3A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #1, Allegation #2 -** S.T. Jacob reported falsified data in Figure 5A by splicing between samples 4 and 5 in Majumder et al., JBC 2002.

### **Finding of Fact:**

- 1. Figure 5 shows the expression of methyl CpG-binding protein (MBDs) messenger RNA (mRNA) in liver tissue and hepatoma. Figure 5A is an RT-PCR experiment for MBD1 mRNA (lanes 1 and 2), cytochrome C oxidase mRNA (COX-1) (lanes 3 and 4), and mRNA without reverse transcriptase as a control (lanes 6 and 7). Figure 5 showed no difference in expression of MBD1, MBD2, and MBD4 between liver and hepatoma.
- 2. Adobe Photoshop gradient mapping clearly demonstrates a line between samples 4 and 5 (correlating to lanes 5 and 6) in the gel image (see slide 4<sup>225</sup>). Red arrows on slide 4 mark the top and bottom of the splice line, which is evident throughout the entirety of the gel image.
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day<sup>227, 228</sup> and Dr. Majumder on July 2, 2017. All authors, including Dr. Datta, were notified in follow-up directly by JBC on July 31, 2017. As such, the co-first and corresponding authors knew of potential issues with the research for approximately three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 4. Dr. Jacob sent a formal response to JBC on October 19, 2017. 230, 231, 232, 233
- 5. No original data for this figure were available.
- 6. The Committee finds the forensic evidence and visual inspection demonstrate a line between lanes 4

<sup>&</sup>lt;sup>225</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 4

<sup>&</sup>lt;sup>226</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>227</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

 $<sup>^{228}</sup>$  Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 -  $\overline{FW}$  JBC articles

<sup>&</sup>lt;sup>229</sup> Ex. 484 - 20170731 - Email - JBC Editor to Authors - FW\_JBC Articles

<sup>&</sup>lt;sup>230</sup> Ex. 309 - 20171019 - Email Jacob to JBC - JBC response Majumder 2002

<sup>&</sup>lt;sup>231</sup> Ex. 310 - JBC Majumder M1116622002-10172017

<sup>&</sup>lt;sup>232</sup> Ex. 311 - 20171019 - Email Jacob to JBC #2 - JBC response \_Majumder 2002

<sup>&</sup>lt;sup>233</sup> Ex. 312 - JBC Majumder M1116622002-v2

- and 5, which the Committee concludes represents a splice line and could be indicative of falsification.
- 7. Dr. Sarmila Majumder was the first author of JBC 2002 and a Research Scientist (2007) in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Jharna Datta was a co-first author of JBC 2002 and Post-doctoral Researcher in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Kalpana Ghoshal was a co-first author of JBC 2002 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

### Respondent's Response:

- 1. In her interview with the CII on March 1, 2018, Dr. Majumder said that the alleged splice line was occurring between samples in which the RT reaction was performed (samples 1-4) and controls in which RT was omitted (samples 5, 6 and 7) and that this was done with an over-abundance of caution. The purpose of lanes 5, 6, and 7 was to demonstrate that the any PCR product was not due to the presence of genomic DNA. Without splicing, the gel would have had the same impact.<sup>234</sup>
- 2. However, Dr. Majumder indicated that her understanding of this figure was that certain lanes were spliced out and then the figure pasted together.

DR. MAJUMDER: "My feeling – understanding is, like, there were other lanes in between that we had to cut because we did not want to show every lane that was there, and then we put together."<sup>235</sup>

- 3. During his interview with the CII on March 5, 2018, Dr. Jacob was shown the figure forensics for Allegation #2 but not asked specifically about it, nor did he provide any response.<sup>236</sup>
- 4. Co-first authors Dr. Jharna Datta and Dr. Kalpana Ghoshal were not identified as co-first authors during the Inquiry and therefore were not questioned about this allegation in their respective interviews.
- 5. In her response to the CII's preliminary report<sup>237</sup> and her appeal of their determination,<sup>238</sup> Dr. Majumder reiterated that she does not believe she prepared the figure. She argued that the CII misunderstood the role of the figure in the paper: "Lanes 5 (DNA Ladder), 6 & 7 that were spliced together with lanes (1-4), show that in the absence of reverse transcriptase, there was no PCR product for MBD2 (lanes 5 & 6) and therefore, the MBD2 PCR products shown in lanes 1 & 2 are not due to genomic DNA contamination."<sup>239</sup> She again explained that splicing unnecessary gel lanes from a final figure was a common and accepted practice, that the line between the samples is visible with the naked eye, and that the journal did not raise any concerns about the figure, in the past or more recently.<sup>240</sup>
- 6. As explained in M#1, A#1 (Respondent Responses 7 & 8) above, co-first authors Dr. Datta and Dr. Ghoshal had no specific comment on this allegation and did not take responsibility for generation of Figure 5A.
- 7. In her interview with the COMIC on June 12, 2019,<sup>241</sup> Dr. Majumder confirmed the presence of a splice line that runs the length of the figure, indicated she couldn't remember if she did this PCR work and that original data was not available to confirm who performed the experiment or made the figure but that the experiment was of such a nature that anyone in the lab could have been skilled enough to perform. She

<sup>&</sup>lt;sup>234</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 42 lines 17-24; page 43 line 1

<sup>&</sup>lt;sup>235</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 43 lines 3-7

<sup>&</sup>lt;sup>236</sup> Ex. 56 - 20180305-CII Interview + errata – Jacob, page 31, lines 15-18

<sup>&</sup>lt;sup>237</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918

<sup>&</sup>lt;sup>238</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>239</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 4

<sup>&</sup>lt;sup>240</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 4

<sup>&</sup>lt;sup>241</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 29-31

further indicated that her main responsibility on the paper was writing.<sup>242</sup> See also Dr. Majumder's General Respondent/Witness statements  $\frac{\#1-4}{4}$  above.

8. In his interview with the COMIC on July 17, 2019, Dr. Jacob did not specifically address this allegation. See also Dr. Jacob's General Respondent/Witness statements #1, #3-7 above.

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation. None of the co-first authors have taken responsibility for generation of Figure 5A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Majumder did not refute the allegation or that splicing occurred and indicated that her main responsibility on the paper was writing.<sup>243</sup>
- 2. It is the Committee's understanding that the standards in the field at the time of this 2002 publication may not have been to require demarcation of non-contiguous bands and the alleged splice is visible to the naked eye. To be scientifically correct, the splice line would be expected to run all the way down through the entire figure, which it does in Figure 5A.
- 3. Without original data, the COMIC is not able to determine the significance of the splicing and how it may have altered the interpretation and conclusions of the manuscript, i.e., if the splicing was performed to remove extraneous noncontiguous data (but not properly documented with a demarcation), to combine results from different experiments in order to illustrate an ideal result, or to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 5A and that actions of others caused the splicing within Figure 5A in Allegation #2, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that these actions represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #1, Allegation #3-** S.T. Jacob reported falsified data in Figure 5C by splicing between sample 2 and 3 in Majumder et al., JBC 2002.

#### **Finding of Fact:**

1. Figure 5 shows the expression of methyl CpG-binding proteins (MBDs) messenger RNA (mRNA) in liver

<sup>&</sup>lt;sup>242</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 33, line 16-17

<sup>&</sup>lt;sup>243</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 33, line 16-17

- tissue and hepatoma. Figure 5C is an RT-PCR experiment for COX-1 (lanes 1 and 2), MBD4 (lanes 3 and 4), and RNA without reverse transcriptase as a control (lanes 5 and 6). Figure 5 showed no difference in expression of MBD1, MBD2, and MBD4 between liver and hepatoma.
- 2. Adobe Photoshop gradient mapping clearly demonstrates a splice line between samples 2 and 3 (see slide 5<sup>244</sup>). Red arrows on slide 5 mark the top and bottom of the splice line, which is evident throughout the entirety of the gel image.
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>245</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day<sup>246, 247</sup> and Dr. Majumder on July 2, 2017.<sup>248</sup> All authors, including Dr. Datta, were notified in follow-up directly by JBC on July 31, 2017.<sup>249</sup> As such, the co-first and corresponding authors knew of potential issues with the research for approximately three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 4. Dr. Jacob sent a formal response to JBC on October 19, 2017. 250, 251, 252, 253
- 5. No original data for this figure were available.
- 6. The Committee finds the forensic evidence and visual inspection demonstrate a line between samples 2 and 3, which the Committee concludes represents a splice line and could be indicative of falsification.
- 7. Dr. Sarmila Majumder was the first author of JBC 2002 and a Research Scientist (2007) in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Jharna Datta was a co-first author of JBC 2002 and Post-doctoral Researcher in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Kalpana Ghoshal was a co-first author of JBC 2002 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

### Respondent's Response:

1. In her interview with the CII on March 1, 2018, Dr. Majumder offered the same explanation for Figure 5C as she did for Figure 5A, i.e., they spliced out certain lanes that weren't vital for the figure then pasted together other control lanes (see allegation #2).

DR. MAJUMDER: "And that we splice together in order to have a composite picture." 254

- 2. During his interview with the CII on March 5, 2018, Dr. Jacob was shown the figure forensics for Allegation #3 but not asked specifically about it nor did he provide any response.<sup>255</sup>
- 3. Co-first authors Dr. Jharna Datta and Dr. Kalpana Ghoshal were not identified as co-first authors during the Inquiry and therefore were not questioned about this allegation in their respective interviews.
- 4. In her response to the CII's preliminary report<sup>256</sup> and her appeal of their determination,<sup>257</sup> Dr. Majumder reiterated the same arguments as in M#1, A#2 above and that she does not believe she prepared the

<sup>&</sup>lt;sup>244</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 5

<sup>&</sup>lt;sup>245</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>246</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW\_ JBC articles

<sup>&</sup>lt;sup>247</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>248</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>249</sup> Ex. 484 - 20170731 - Email - JBC Editor to Authors - FW\_JBC Articles

<sup>&</sup>lt;sup>250</sup> Ex. 309 - 20171019 - Email Jacob to JBC - JBC response Majumder 2002

<sup>&</sup>lt;sup>251</sup> Ex. 310 - JBC Majumder M1116622002-10172017

<sup>&</sup>lt;sup>252</sup> Ex. 311 - 20171019 - Email Jacob to JBC #2 - JBC response Majumder 2002

<sup>&</sup>lt;sup>253</sup> Ex. 312 - JBC Majumder M1116622002-v2

<sup>&</sup>lt;sup>254</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 43 lines 21-22

<sup>&</sup>lt;sup>255</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 31 lines 19-20

<sup>&</sup>lt;sup>256</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918

<sup>&</sup>lt;sup>257</sup> Ex. 252 - Majumder Zadnik-letter-111218

figure. She again explained that splicing unnecessary gel lanes from a final figure was a common and accepted practice, that the line between the samples is visible with the naked eye, and that the journal did not raise any concerns about the figure.<sup>258</sup>

- 5. As explained in M#1, A#1 (Respondent Responses 7 & 8) above, co-first authors Dr. Datta and Dr. Ghoshal had no specific comment on this allegation and did not take responsibility for generation of Figure 5C.
- 6. In her interview with the COMIC on June 12, 2019, 259 Dr. Majumder did not refute the presence of a splice line and indicated she couldn't remember if she did this PCR work or made the figure. She further indicated that the experiment was of such a nature that anyone in the lab could have been skilled enough to perform it and that her main responsibility on the paper was writing. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 7. In his interview with the COMIC on July 17, 2019, Dr. Jacob did not specifically address this allegation. See also Dr. Jacob's General Respondent/Witness statements #1, #3-7 above.

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation. None of the co-first authors has taken responsibility for generation of Figure 5C, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Majumder did not refute the allegation or that splicing occurred and indicated that her main responsibility on the paper was writing.<sup>263</sup>
- It is the Committee's understanding that the standards in the field at the time of this 2002 publication may
  not have been to require demarcation of non-contiguous bands and the alleged splice is visible to the
  naked eye. In permitted instances, the splice line would be expected to run all the way down through the
  complete figure, which does occur in Figure 5C.
- 3. Without original data, the COMIC is not able to determine the significance of the splicing and how it may have altered the interpretation and conclusions of the manuscript, i.e. if the splicing was performed to remove extraneous noncontiguous data (but not properly documented with a demarcation), to combine results from different experiments in order to illustrate an ideal result, or to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 5C and that the actions of others caused the splicing within Figure 5C in Allegation #3, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 5C, and therefore

<sup>&</sup>lt;sup>258</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 4-5

<sup>&</sup>lt;sup>259</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 29-31

<sup>&</sup>lt;sup>260</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 31, line 8-12

<sup>&</sup>lt;sup>261</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 31, line 16-19

<sup>&</sup>lt;sup>262</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 33, line 16-17

<sup>&</sup>lt;sup>263</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 33, line 16-17

this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 5C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #1, Allegation #4 -** S.T. Jacob reported falsified data by reuse of the same data in lane 1 and in lane 3 in Figure 6B in Majumder et al., JBC 2002.

- 1. Figure 6B shows results of a ChIP assay using antibodies against MeCP2 to determine the MBD associated with the methylated MT-1 promoter. Figure 6B shows Western blot analysis of nuclear extracts used in the immunoprecipitation reactions. Nuclear extracts are from liver (lane 1, pre immune sera and lane 2, immune (MeCP-1) sera) and hepatoma (lane 1, pre immune sera and lane 2, immune (MeCP-1) sera).
- 2. Adobe Photoshop image overlay demonstrated significant overlap and similarity between lanes 1 and 3 in Figure 6B (see slide 6<sup>264</sup>). This would not be scientifically valid as the two lanes represent two different experimental controls.
- 3. Lanes 1 and 3 are purported to represent controls from different nuclear extracts (lane 1=liver preimmune sera vs. lane 3=hepatoma pre-immune sera) but they have the same unique artifacts present within the bands (small circle on the right side of the bottom-most band) and within the background (triplicate banding underneath the top-most band), which indicates the lanes have been duplicated.
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 6B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, <sup>265</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day <sup>266, 267</sup> and Dr. Majumder on July 2, 2017. <sup>268</sup> All authors, including Dr. Datta, were notified in follow-up directly by JBC on July 31, 2017. <sup>269</sup> As such, the co-first and corresponding authors knew of potential issues with the research for approximately three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 5. Dr. Jacob sent a formal response to JBC on October 19, 2017. 270, 271, 272, 273
- 6. No original data for this figure were available.
- 7. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 1 and 3, which the Committee concludes is indicative of falsification.
- 8. Dr. Sarmila Majumder was the first author of JBC 2002 and a Research Scientist (2007) in the laboratory of Dr. Samson Jacob at the time of the publication.
- 9. Dr. Jharna Datta was a co-first author of JBC 2002 and Post-Doctoral researcher in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Kalpana Ghoshal was a co-first author of JBC 2002 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.

<sup>&</sup>lt;sup>264</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 6

<sup>&</sup>lt;sup>265</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>266</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>267</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>268</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>269</sup> Ex. 484 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles

<sup>&</sup>lt;sup>270</sup> Ex. 309 - 20171019 - Email Jacob to JBC - JBC response Majumder 2002

<sup>&</sup>lt;sup>271</sup> Ex. 310 - JBC Majumder M1116622002-10172017

<sup>&</sup>lt;sup>272</sup> Ex. 311 - 20171019 - Email Jacob to JBC #2 - JBC response \_Majumder 2002

<sup>&</sup>lt;sup>273</sup> Ex. 312 - JBC Majumder M1116622002-v2

11. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

### Respondent's Response:

- 1. In her interview with the CII on March 1, 2018, Dr. Majumder stated that there appears to be "erroneous duplication of these lanes". She further stated that the bands "looks duplicated to me" and suggested the error may have been inadvertent since this was not the only evidence that drove the conclusions of the paper.
- 2. In his interview with the CII on March 5, 2018, Dr. Jacob made statements regarding the "key emphasis" of Figure 6B, which were not the lanes in question. Dr. Jacob did state that a "pre-immune sera (which lanes 1 and 3 are labeled as) could give you identical pattern." Also during his interview, Dr. Jacob asked if the CII had talked to the person who had performed the experiment because he "won't be able to throw any light on this" but indicated that he would never have allowed a lab member to make an intentional duplication. 278
- 3. As explained in M#1, A#1 (Respondent Responses 7 & 8) above, co-first authors Dr. Datta and Dr. Ghoshal had no specific comment on this allegation and did not take responsibility for generation of Figure 6B.
- 4. In her interview with the COMIC on June 12, 2019, Dr. Majumder re-established her previous position that the data look similar and the duplication was probably an inadvertent error.<sup>279</sup> Dr. Majumder stated that she did not make the figure and did not remember who made the figure<sup>280</sup> and that her main responsibility on the paper was writing.<sup>281</sup> The COMIC questioned why only a single lane (e.g., lane 1) would have been duplicated when it is part of a set from the LNE (liver) sample, theorizing that an erroneous cut/paste action would have duplicated lanes 1 and 2 as lanes 3 and 4, but not merely lane 1 as lane 3.<sup>282</sup> Dr. Majumder understood the question from a scientific point of view, but only commented that she could not explain how the figure was prepared. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 5. In his interview with the COMIC on July 17, 2019, Dr. Jacob did not specifically address this allegation. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified a response from the authors to the Journal of Biological Chemistry regarding its concerns with this manuscript. In this October 19, 2017 response, <sup>283, 284, 285, 286</sup> the authors indicate:

"We found the original film containing the immunoprecipitation data with MeCP2 antibody (see corrected figure). We tested pre-immune and immune sera in earlier experiments to confirm that MeCP2 is pulled down by the anti-MeCP2 antiserum. We did not perform IP with pre-immune serum in this particular experiment. We have provided the corrected figure created using this original data."

<sup>&</sup>lt;sup>274</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 45 lines 8-9

<sup>&</sup>lt;sup>275</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 48 line 5

<sup>&</sup>lt;sup>276</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 34 lines 15-24, page 35 lines 1-2

<sup>&</sup>lt;sup>277</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 32 lines 23-34 and page 33 line 1

<sup>&</sup>lt;sup>278</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 36 lines 19-24, page 37 lines 1-22

<sup>&</sup>lt;sup>279</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 35

<sup>&</sup>lt;sup>280</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 36, line 1-5 and lines 10-13

<sup>&</sup>lt;sup>281</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 33, line 16-17

<sup>&</sup>lt;sup>282</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 37-39

<sup>&</sup>lt;sup>283</sup> Ex. 309 - 20171019 - Email Jacob to JBC - JBC response Majumder 2002

<sup>&</sup>lt;sup>284</sup> Ex. 310 - JBC Majumder M1116622002-10172017, page 1, 3

<sup>&</sup>lt;sup>285</sup> Ex. 311 - 20171019 - Email Jacob to JBC #2 - JBC response \_Majumder 2002

<sup>&</sup>lt;sup>286</sup> Ex. 312 - JBC Majumder M1116622002-v2

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation. None of the co-first authors have taken responsibility for generation of Figure 6B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Majumder did not refute the allegation or that splicing occurred and indicated that her main responsibility on the paper was writing.<sup>287</sup>
- 2. Original data was not available for the COMIC to review, though it was quoted as being available and the basis for a corrected figure in the authors' October 2017 response to the journal's concerns with this figure. An entire blot, however, was not provided, and as such the COMIC cannot confirm its validity and/or rely on the corrected figure. Without original data, the COMIC is not able to determine the significance of the duplication and how it may have altered the interpretation and conclusions of the manuscript. Regardless, reuse of a single image to represent two different experimental conditions (i.e., extracts from different tissues) would not be scientifically valid and compromises the integrity of the figure and therefore the manuscript itself. The duplication of a single band of an ordered pair argues against an honest cut/paste error and suggests that the single lane was specifically reused to present the data in a manner so as to deceive the reader.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 6B and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 6B in Allegation #4, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 4. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 1 in favor (reckless) and 6 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Pre-Immune data in Figure 6B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Pre-Immune data in Figure 6B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #2 under Review- Motiwala et al., PNAS 2004 (3 Allegations)

Motiwala T, Kutay H, Ghoshal K, Bai S, Seimiya H, Tsuruo T, Suster S, Morrison C, Jacob ST. "Protein tyrosine phosphatase receptor-type O (PTPRO) exhibits characteristics of a candidate tumor suppressor in human lung cancer." Proc Natl Acad Sci U S A. 2004 Sep 21; 101 (38): 13844-9. Epub 2004 Sep 8.

**Manuscript #2, Allegation #5 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1 and 2 and in lanes 7 and 8, and in lanes 3 and 4, (though as a horizontal mirror image) in the 18S rRNA blot in Figure 2 in Motiwala et al., PNAS 2004.

<sup>&</sup>lt;sup>287</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 33, line 16-17

- 1. Figure 2 shows RT-PCR analysis for PTPRO-FL (top panel) and the 18S RNA control (bottom panel) for RNA isolated from 4 sets (#1, #3, #4, #5) of primary lung tumors (T) and their matching adjacent normal tissues (N).
- 2. Adobe Photoshop image overlay and gradient map analysis demonstrated significant overlap and similarity exists between the bands for lanes 1 and 2, when compared with lanes 7 and 8, and with lanes 3 and 4 (when flipped horizontally) in the 18S RNA panel (see slides 8-9<sup>288</sup>). Additionally Adobe Photoshop gradient map analysis reveals a splice line between lanes 6 and 7 in the 18S rRNA control panel.
- 3. The film<sup>289, 290</sup> that Dr. Motiwala identified from the sequestered data as corresponding to the original data for the figure was not labeled and therefore could not be used to verify the image in question.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lanes 1 and 2 as lanes 7 and 8 as well as reuse of lanes 1 and 2 horizontally flipped as lanes 3 and 4, which the Committee concludes is indicative of falsification. The Committee does not find that the suggested pixel differences shown by Dr. Motiwala in her response to the Committee<sup>291</sup> to be a convincing argument since the forensic overlay, based on size, shape, and spatial relationships of the questioned bands clearly indicate that these are duplications.
- 5. PNAS Executive Editor, Diane Sullenberger, contacted Dr. Jacob via email<sup>292</sup> on March 23, 2017 and again on March 13, 2018 requesting his response to points raised in a communication PNAS had received from pseudonymynous reporter "Clare Francis" and the website PubPeer on March 11, 2017 regarding Motiwala et al. PNAS 2004 (i.e. Manuscript #2). Ms. Sullenberger's email specifically requested a response to the comments "regarding bands that appear similar to other bands" and included a link to the image concerns raised on PubPeer (which as of March 23, 2017 specifically included the concern as it appears here as Allegation #5). Ms. Sullenberger's initial March 23, 2017 email was sent to Dr. Jacob nearly seven (7) months before OSU first notified Dr. Jacob of the Research Misconduct allegations requiring inquiry.
- 6. Dr. Jacob forwarded Ms. Sullenberger's email to Dr. Motiwala on March 13, 2018, with the comment that he had not seen the previous year's message until that day.<sup>293</sup> Later that day (March 13, 2018), Dr. Jacob sent a preliminary response<sup>294</sup> to Ms. Sullenberger acknowledging receipt of her email. Jacob submitted a more complete response<sup>295</sup> to Ms. Sullenberger on March 15, 2018 indicating that they no longer had the original data for Figure 2 and providing no specific explanation of the alleged duplication other than offering that normalizer genes often look similar, that it would not make sense for someone to duplicate two lanes of a normalizer gene, and that no one has raised questions about the reproducibility of the manuscript.
- 7. Deputy Executive Editor, Daniel Salsbury, responded<sup>296</sup> to Dr. Jacob on March 16, 2018 acknowledging receipt of his response, indicating that PNAS considered Figure 2 to be a composite image as opposed to a contiguous gel and that PNAS now instructed authors to specifically indicate in a figure legend any such splicing or rearrangement of lanes, but acknowledging that this was not a requirement of PNAS in 2004. Mr. Salsbury further commented that Lanes 7and 8 of the 18S rRNA gel in Figure 2 "do appear very similar to lanes 1 and 2." Mr. Salsbury additionally requested a response to the concerns raised on

<sup>&</sup>lt;sup>288</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slides 8-9

<sup>&</sup>lt;sup>289</sup> Ex. 106 - 20180126 18sRNA Blot, Motiwala PNAS 2004

<sup>&</sup>lt;sup>290</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 10

<sup>&</sup>lt;sup>291</sup> Ex. 116 - New Allegations-response-041918, page 1

<sup>&</sup>lt;sup>292</sup> Ex. 276 - 20180313 - Email PNAS to Jacob - PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>293</sup> Ex. 313 - 20180313 - Email Jacob to Motiwala - FW PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>294</sup> Ex. 314 - 20180313 - Email Jacob to PNAS - Re PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>295</sup> Ex. 315 - 20180315 - Email Jacob to PNAS - Re\_ PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>296</sup> Ex. 316 - 20180316 - Email PNAS to Jacob - RE\_ PNAS Motiwala et al. 2004

PubPeer regarding Figures 3B and 5A,<sup>297</sup> which were added to PubPeer subsequent to Dr. Jacob's initial notification of the concerns by PNAS in March 2017. Any response from Dr. Jacob addressing these PubPeer concerns as requested by PNAS was not able to be identified in a targeted review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations.

- 8. Dr. Tasneem Motiwala was first author of PNAS 2004 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Jacob was the laboratory PI and corresponding author of PNAS 2004.

## Respondent's Response:

- 1. In his interview with the CII on March 5, 2018, Dr. Jacob said that the data in question are 18S rRNA bands used as a control and it did not change the scope of the paper or results.<sup>298</sup>
- 2. In her interview with the CII on February 12, 2018, Dr. Motiwala admitted to running the experiment, generating the images for the publication, and writing the first draft of the manuscript.<sup>299</sup>
- 3. In her February 20, 2018 follow up <sup>300</sup> to questions that the CII emailed to Dr. Motiwala after her interview, Dr. Motiwala indicated that she believed there were limitations of forensic software. <sup>301</sup>
- 4. Dr. Motiwala stated in her written response to the CII on April 19, 2018, that the Figure 2 18s rRNA blot was "prepared from phosphorimage scans since this blot is overexposed."<sup>302</sup> The blot she is referring to was the blot that she had identified as source data from the sequestered data.<sup>303</sup>
- 5. In the written response submitted to the CII on April 19, 2018, Dr. Motiwala wrote that the expanded image of the 18S panel showed pixel differences between the lanes alleged to be the same.<sup>304</sup>
- 6. In her response to the CII's preliminary report<sup>305</sup> and her appeal of their determination,<sup>306</sup> Dr. Motiwala challenged the existence of splice lines and indicated that in the absence of splice lines she would not be convinced that duplication had taken place.
- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above.
- 8. In her interview with the COMIC on June 12, 2019, Dr. Motiwala indicated that as the lead author she would have done experiments, prepared figures for the experiments she performed, and she both did the experiment and made Figure 2. 307 She again pointed to the absence of splice lines and indicated that in the absence of splice lines she would not be convinced that duplication had taken place. Dr. Motiwala confirmed that the original experiment would have included samples 1, 2, 3, 4, and 5 on the same gel, and indicated that sample 2 would have been removed, i.e. spliced out, in the upper PTPRO-FL portion of the figure. When challenged that the 18S rRNA would also need to be spliced if it's a control for PTPRO-FL, Dr. Motiwala indicated she doesn't remember but that it was possible she ran another 18s rRNA gel without sample 2.308
- 9. See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.

<sup>&</sup>lt;sup>297</sup> The PubPeer concern raised regarding Figure 5A corresponds to the concerns as they appear in Allegation #43.

<sup>&</sup>lt;sup>298</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 38 lines 20-24; page 40 lines 20-24

<sup>&</sup>lt;sup>299</sup> Ex. 60 - 20180212-CII Interview + errata - Motiwala, pages 15, 18, 20

<sup>&</sup>lt;sup>300</sup> Ex. 110 - 20180220 Motiwala Follow Up Questions for CII

<sup>&</sup>lt;sup>301</sup> Ex. 114 - CII response

<sup>&</sup>lt;sup>302</sup> Ex. 116 - New Allegations-response-041918, page 1

<sup>303</sup> Ex. 106 - 20180126 18sRNA Blot, Motiwala PNAS 2004

<sup>&</sup>lt;sup>304</sup> Ex. 116 - New Allegations-response-041918, page 1

<sup>&</sup>lt;sup>305</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 4

<sup>&</sup>lt;sup>306</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318, page 7

<sup>&</sup>lt;sup>307</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 24 line 15-19 and page 27, line 4-11

<sup>&</sup>lt;sup>308</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 29-33

## Respondent's Responsibility and Intent:

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. Dr. Motiwala took responsibility for running the experiment and generating Figure 2 early in her career as a Senior Research Associate in Dr. Jacob' laboratory.
- 3. Reuse of a single image to represent three different experimental conditions would not be scientifically valid and compromises the integrity of the paper. Multiple duplications of Lanes 1 and 2 within Figure 2, including duplication via a horizontal flip of the data, argues against an honest cut/paste error and suggests that the lanes were specifically reused to present the data in a manner so as to deceive the reader. The COMIC disagrees with Dr. Jacob's statement that since the allegation only involves control bands it wouldn't impact the manuscript as controls are required to prove that changes in expression for the experimental data are due to the experimental treatment, and not from unequal loading of the samples. Dr. Motiwala's contention that splice lines must be evident for duplication to have occurred is not accepted by the Committee as a valid argument. Dr. Motiwala admitted that the experiment would have included a sample #2 that was removed for the figure, yet no corresponding splice lines can be detected around between samples #1 and #3, suggesting that the she had sufficient skill when manipulating the images to mask splice and/or cut/paste lines. Motiwala did not convincingly refute the allegation or provide a logical explanation for the apparent reuse of data.
- 4. In order to contend that gene expression is suppressed in a tumor but not non-tumor tissue, loading controls are essential. Without verifiable original data, the COMIC is not able to determine if the published results represent a true experimental outcome. The COMIC finds the manipulation of Figure 2 is significant even though data elsewhere in the manuscript (e.g. Figure 3) supports suppressed expression of PTPRO-FL in human lung cancer cells. Furthermore, the number of duplications within the 18S rRNA panel coupled with the issues in the PTPRO-FL panel discussed in Allegation #6 below casts overwhelming doubt on the veracity of the results presented in Figure 2.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2 and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 2 in Allegation #5, as described above. Furthermore, as it remains unknown if and to what extent Dr. Jacob viewed or opened the 2017 email from PNAS Executive Editor, Diane Sullenberger, the Committee cannot conclude that Dr. Jacob was aware of the concerns with the validity of the PNAS 2004 data prior to notification of allegations by OSU in November 2017. In summary, the Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly falsified the 18S rRNA data in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly falsified the 18S r RNA data in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #2, Allegation #6 -** S.T. Jacob reported falsified data Figure 2 by splicing between lanes 2 and 3 and between 6 and 7 of the PTPRO-FL blot in Motiwala et al., PNAS 2004.

- 1. Figure 2 shows RT-PCR analysis for PTPRO-FL (top panel) and the 18S rRNA control (bottom panel) for RNA isolated from 4 sets (#1, #3, #4, #5) of primary lung tumors (T) and their matching adjacent normal tissues (N).
- 2. Using Adobe Photoshop gradient map forensic analysis, splice lines in the PTPRO-FL panel were evident between lanes 2 and 3 (see slide 11<sup>309</sup>).
- 3. The forensic overlay analysis of the PTPRO-FL panel compared to original data provided by Dr. Motiwala as being the source data for the published figure, show that normal and tumor tissue were mislabeled in Figure 2.310 The identity of the samples included in Figure 2 was shown in Dr. Motiwala's lab notebook.311
  - a. Forensic analysis showed that some of the lung tumor and normal tissue samples matched with the x-ray film Dr. Motiwala identified as source data:
    - Lanes labeled #1 in Figure 2, compared to lanes circled 1 on the source film (T1999/N2000) in an overlay show accurate representation of a tumor/normal tissue set.<sup>312</sup>
    - ii. Lanes labeled #5 in Figure 2, appear to match lanes circled 4 on the source film (T23/N24), accurately representing a tumor/normal tissue set.<sup>313</sup>
  - b. However, other lanes in Figure 2 do not match to accurate tumor/normal tissue sets:
    - i. Lanes labeled #3 in Figure 2, do not match circled 2 on the source film (T9/N10), but do match T9/N8 lane, which are not an accurate tumor/normal set.<sup>314</sup>
    - ii. Lanes labeled #4 in Figure 2, do not match circled 3 on source film (T17/N18), but do match T11/N10 lanes, which are not an accurate tumor/normal set.<sup>315</sup>
- 4. In reconciling the numbers from the source film with the published Figure 2, it is clear that normal tissues have been mislabeled as tumor tissue (e.g., N10), and tumor tissue has been mislabeled as normal tissue.
- 5. The Committee finds the lab notebook, forensic evidence and visual inspection of the figure against the original source data demonstrates splicing and mislabeling of the tumor/normal sets, which the Committee concludes is indicative of falsification.
- 6. PNAS Executive Editor, Diane Sullenberger, contacted Dr. Jacob via email<sup>316</sup> on March 23, 2017 and again on March 13, 2018 requesting his response to points raised in a communication PNAS had received from pseudonymynous reporter "Clare Francis" and the website PubPeer on March 11, 2017 regarding Motiwala et al. PNAS 2004 (i.e. Manuscript #2). Ms. Sullenberger's email specifically requested a response to the comments "regarding bands that appear similar to other bands" and included a link to the image concerns raised on PubPeer (which as of March 23, 2017 specifically included the concern as it appears in Allegation #5 above). Ms. Sullenberger's initial March 23, 2017 email was sent to Dr. Jacob nearly seven (7) months before OSU first notified Dr. Jacob of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Jacob forwarded Ms. Sullenberger's email to Dr. Motiwala on March 13, 2018, with the comment that he had not seen the previous year's message until that day. 317 Later that day (March 13, 2018), Dr.

<sup>&</sup>lt;sup>309</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 11

<sup>&</sup>lt;sup>310</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 12-20

<sup>&</sup>lt;sup>311</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 15

<sup>&</sup>lt;sup>312</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 16-19

<sup>&</sup>lt;sup>313</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 16-18, 20

<sup>&</sup>lt;sup>314</sup> Ex. 305 - Jacob Image Forensics COMIC Final slides 16-19

<sup>&</sup>lt;sup>315</sup> Ex. 305 - Jacob Image Forensics COMIC Final slides 16-18, 20

<sup>&</sup>lt;sup>316</sup> Ex. 276 - 20180313 - Email PNAS to Jacob - PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>317</sup> Ex. 313 - 20180313 - Email Jacob to Motiwala - FW PNAS Motiwala et al. 2004

Jacob sent a preliminary response<sup>318</sup> to Ms. Sullenberger acknowledging receipt of her email. Dr. Jacob submitted a more complete response<sup>319</sup> to Ms. Sullenberger on March 15, 2018 indicating that they no longer had the original data for Figure 2 and providing no specific explanation of the alleged duplication other than offering that normalizer genes often look similar, that it would not make sense for someone to duplicate two lanes of a normalizer gene, and that no one has raised questions about the reproducibility of the manuscript.

- 8. Deputy Executive Editor, Daniel Salsbury, responded<sup>320</sup> to Dr. Jacob on March 16, 2018 acknowledging receipt of his response, indicating that PNAS considered Figure 2 to be a composite image as opposed to a contiguous gel and that PNAS now instructed authors to specifically indicate in a figure legend any such splicing or rearrangement of lanes, but acknowledging that this was not a requirement of PNAS in 2004. Mr. Salsbury further commented that Lanes 7and 8 of the 18S rRNA gel in Figure 2 "do appear very similar to lanes 1 and 2." Mr. Salsbury additionally requested a response to the concerns raised on PubPeer regarding Figures 3B and 5A,<sup>321</sup> which were added to PubPeer subsequent to Dr. Jacob's initial notification of the concerns by PNAS in March 2017. Any response from Dr. Jacob addressing these PubPeer concerns as requested by PNAS was not able to be identified in a targeted review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations.
- 9. Dr. Tasneem Motiwala was first author of PNAS 2004 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Jacob was the laboratory PI and corresponding author of PNAS 2004.

### Respondent's Response:

- 1. Dr. Jacob did not specifically respond to this allegation during the Inquiry phase of the case.
- 2. In her interview with the CII on February 12, 2018, Dr. Motiwala confirmed that she ran the experiment, generated the images for the publication, and wrote the first draft of the manuscript. Dr. Motiwala, however could not explain how the bands in the published image corresponded with the bands from the original film she had identified as source data for Figure 2. Dr. When questioned about the numbering on the original film, Dr. Motiwala could not provide an explanation for why the normal tissue was mislabeled as tumor in the publication.
- 3. In Dr. Motiwala's response to the CII's preliminary report<sup>325</sup> and her appeal of their determination,<sup>326</sup> Dr. Motiwala maintained that the phosphorimage scan prevents signal from an adjacent overexposed band to spread (like in the x-ray exposure) allowing for the band next to it to be visualized without being masked,<sup>327</sup> offered her own overlay analysis,<sup>328</sup> and highlighted the representative nature of the figure.<sup>329</sup> Dr. Motiwala went on to argue that any errors in figure generation would have been unintentional, that the findings of the experiment are still supported, there was no incorrect reporting of results, and that there would be no motive to falsify the figure.<sup>330</sup>
- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above.

<sup>&</sup>lt;sup>318</sup> Ex. 314 - 20180313 - Email Jacob to PNAS - Re\_ PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>319</sup> Ex. 315 - 20180315 - Email Jacob to PNAS - Re PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>320</sup> Ex. 316 - 20180316 - Email PNAS to Jacob - RE PNAS Motiwala et al. 2004

<sup>321</sup> The PubPeer concern raised regarding Figure 5A corresponds to the concerns as they appear in Allegation #43.

<sup>&</sup>lt;sup>322</sup> Ex. 60 - 20180212-CII Interview + errata - Motiwala, pages 15, 18, 20

<sup>&</sup>lt;sup>323</sup> Ex. 60 - 20180212-CII Interview + errata - Motiwala, pages 20 – 27

<sup>&</sup>lt;sup>324</sup> Ex. 60 - 20180212-CII Interview + errata - Motiwala, pages 20-27

<sup>&</sup>lt;sup>325</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>&</sup>lt;sup>326</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>&</sup>lt;sup>327</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 4

<sup>&</sup>lt;sup>328</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 4-5, 8-10

<sup>&</sup>lt;sup>329</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 5

<sup>&</sup>lt;sup>330</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 5

5. In her interview with the COMIC on June 12, 2019<sup>331</sup>, Dr. Motiwala reiterated her position that the figure was intended to be representative in nature, specifically indicating that the point of Figure 2 was to show that where there was methylation, downregulation was also apparent, and not to show methylation and suppressed expression in all tumors tested.<sup>332</sup> Dr. Motiwala maintained,

DR. MOTIWALA: ...if you look at those samples that are marked, like the tumors are low. So those were the samples to be represented. Like if some error happened in making the figure, but that's like the same representation of like what's marked is there, like the tumors are known and the normal. So --

COMMITTEE MEMBER: So this practice is fair, then, to take data like this and cut it, flip it, move it around, and make that figure?

DR. MOTIWALA: Right. So, like I said, like splicing was allowed, and then like since like the gel was originally loaded in like tumor-normal kind of order and the representation had to be like normal-tumor, so then like I had to flip like each pair.<sup>333</sup>

However, Dr. Motiwala did ultimately acknowledge that a mistake could have been made during figure generation:

COMMITTEE MEMBER: Okay. And your position is that -- is what, that this was not intentional, or this was a potential mislabeling in constructing the final figure? What is your explanation?

DR. MOTIWALA: Definitely not intentional. And what I'm saying is like the representation is not wrong, like where there is no expression in the tumor there is no expression. I mean, maybe --maybe there was a mistake in like picking the right pair, but the representation is the same as what's in the original data.

COMMITTEE MEMBER: So you may have captured a wrong pair of bands in the gel or the phosphoimage -- phosphoimager in constructing the figure, but what you're saying is the -- the actual data from those samples remains evidence of --

DR. MOTIWALA: Consistent in pattern.

COMMITTEE MEMBER: Right. (Interruption for clarification.)

COMMITTEE MEMBER: And that's okay because it's a representative gel?

DR. MOTIWALA: I'm not saying it's okay. I mean, it's an error, but it's not -- it's not making the -- it's not negating the results or it's not like falsely representing the result that was not observed.<sup>334</sup>

6. As in previous interviews and communications, Dr. Motiwala continued to posit that the lack of perfect overlay is a function of saturation and the phosphoimager data supports the figure rather than the film presented as the original data:<sup>335</sup>

<sup>&</sup>lt;sup>331</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1

<sup>332</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 38

<sup>&</sup>lt;sup>333</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 39, line 2-17

<sup>&</sup>lt;sup>334</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 47, line 13 to page 48, line 14

<sup>335</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 46, line 11-19 and page 49-50

"Yeah, the other thing we have to remember is like this figure may not have been made from this exact blot because, like I said, like we put it on the film and we put it on phosphoimager. So the intensity on the phosphoimager is very different than what's on the film. So when you try to overlay from the figure that could have been made from the phosphoimager to the film, that saturation level is very different." 336

7. See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. Dr. Motiwala took responsibility for running the experiment and generating Figure 2 early in her career as a Senior Research Associate in Dr. Jacob' laboratory.
- 3. The COMIC agrees with Dr. Motiwala and confirms that the splice lines between lanes 2/3 and 6/7 occurred due to the fact that the source film samples were run in the order of tumor and then normal sample, while the published figure samples were presented in the order of normal and then tumor sample. Thus the sample pairs from the source film were spliced and rotated in the published figure. Therefore, the splicing between lanes 2/3 and 6/7 did not impact the experimental outcome as the published data matched the source film. However, the COMIC notes that the splicing should have been designated with a line of demarcation.
- 4. The COMIC confirms that some of the lung tumor and normal tissue samples published matched with the x-ray film Dr. Motiwala identified as source data:
  - a. Lanes labeled #1 in Figure 2, match lanes circled 1 on the source film (T1999/N2000), thus accurately representing a tumor/normal tissue set. No falsification.
  - b. Lanes labeled #5 in Figure 2, match lanes circled 4 on the source film (T23/N24), thus accurately representing a tumor/normal tissue set. No falsification.
- 5. A review of the data in the laboratory notebook indicates some instances of downregulation, while in other instances upregulation, and some instances showing equal expression, yet the figure seems to show a very consistent downregulation. Dr. Motiwala indicated that the intent of the paper was to show that where there was methylation, there was downregulated expression of PTPRO-FLO, and that the figure was intended to select those tumors in which this relationship was observed and not to indicate that expression was downregulated in all tumors. However, neither Dr. Motiwala nor Dr. Jacob were able to refute the forensic evidence supporting misrepresentation of tumor and normal tissue (lanes labeled #4), provide a logical explanation for the mislabeling, or provide additional contemporaneous data to support the validity of tissue pairs represented in lanes labeled #3 and #4 in Figure 2 as published.
- 6. With respect to Dr. Motiwala's explanation that a phosphoimager could change the intensity of one band compared to another, the experience of the COMIC leads it to conclude that a phosphor image increases sensitivity to allow less exposure time compared with x-ray films, uniformly impacts intensity across entire blots, and that phosphor imaging was highly unlikely to have anything to do with band intensity. The use of a phosphoimager additionally would not affect or lead to similarities in size, shape, artifact, etc. between or amongst bands. The number of duplications within the PTPRO-FL panel coupled with the issues in the 18S rRNA panel discussed in Allegation #5 above casts overwhelming doubt on the veracity of the results presented in Figure 2.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2 and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 2 in Allegation #6, as described above. Furthermore, as it remains unknown if and to what extent Dr. Jacob viewed or opened the 2017 email

<sup>336</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 46, line 11-19

from PNAS Executive Editor, Diane Sullenberger, the Committee cannot conclude that Dr. Jacob was aware of the concerns with the validity of the PNAS 2004 data prior to notification of allegations by OSU. In summary, Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

8. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified PTPRO-FL data in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified PTPRO-FL data in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #2, Allegation #43 –** S.T. Jacob reported falsified data by the reuse of the same data for serum starved panels for both A549/vector and A549/PTPRO in Figure 5A in Motiwala et al., PNAS 2004.

### **Finding of Fact:**

- 1. Figure 5A is the immunohistochemical detection of incorporated BrdU to show the DNA replication in A549 cells transfected with PTPRO (right panels) or vector only (control, left panels) following serum starvation or thymidine block. The cells transfected with PTPRO showed less BrdU incorporation, suggesting less DNA replication than the vector only control.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap of a small portion of image A (upper left image, A549/Vector, serum starved) and with a small portion of image B (upper right image, A549/PTPRO, serum starved), suggesting that image A and image B do not represent different transfected cell samples, as purported in the figure legend (see slides 21-24<sup>337</sup>).
- 3. No original data for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrate image duplication, which the Committee concludes could be indicative of falsification.
- 5. Dr. Tasneem Motiwala was first author of PNAS 2004 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 6. Dr. Jacob was the laboratory PI and corresponding author of PNAS 2004.

## Respondent's Response:

- 1. Dr. Jacob did not specifically respond to this allegation during the Inquiry phase of the case.
- 2. In her written response provided to ORC on April 19, 2018, Dr. Motiwala stated that the original data are no longer available, but the results are valid since they have been validated by others.<sup>338</sup>
- 3. In her response to the CII's preliminary report<sup>339</sup> and her appeal of their determination,<sup>340</sup> Dr. Motiwala stated that this was a representative section of the image with quantification (Figure 5B) and other experiments confirming the results. She maintained that if any duplication occurred it was by inadvertent or honest error.

<sup>&</sup>lt;sup>337</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 21-24

<sup>&</sup>lt;sup>338</sup> Ex. 116 - New Allegations-response-041918, page 2

<sup>&</sup>lt;sup>339</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 5

<sup>&</sup>lt;sup>340</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318, page 2, page 8



- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 4-7 above.
- 5. In her interview with the COMIC on June 12, 2019,<sup>341</sup> Dr. Motiwala indicated that as the lead author she would have done experiments, prepared figures for the experiments she performed, but does not know who was responsible for Figure 5.
- 6. In her interview with the COMIC on June 12, 2019, Dr. Motiwala indicated that original data are not available, this is a representative figure for which the conclusions are actually based on the quantification of the fields and for which another set of panels shows the same phenomena, that an error may have occurred in the generation of the figure, and that the figure should be corrected. <sup>342</sup> Furthermore, Dr. Motiwala maintained,

"So, based on that, the conclusions are not wrong. This figure may be misrepresented, but the conclusions that we have drawn from them are not wrong." 343

7. See Dr. Motiwala's General Respondent/Witness statements #1-6 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation. Dr. Motiwala did not take responsibility for generation of Figure 5A, but has maintained that an error may have occurred during figure generation. She acknowledged the duplication and indicated the publication should be corrected. Generally, Dr. Motiwala has espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content, while the first author should take responsibility for every figure.
- 2. There appears to be duplication of at least parts of the images, which would not be possible if the published images represent different treatment groups (A549/vector versus A549/PTPRO). The figure as published supports PTPRO being a tumor suppressor since overexpression of PTPRO leads to decreased proliferation. However, since the authors have used the same image to show both the control and PTPRO overexpressing cells, there is no evidence that PTPRO leads to suppression of proliferation. Showing that overexpression of PTPRO leads to delayed reentry of cells into the cell cycle is a significant finding supporting candidacy as a tumor suppressor. The Committee does not believe that the reuse is mitigated by the quantification and presence of the thymidine block results depicting the same phenomena. Overall, evidence that PTPRO delays entrance into the cell cycle is called into question, and this is one of three characteristics used to define PTPRO as a tumor suppressor gene, the latter being a major thrust of the paper. Data showing that PTPRO enhances susceptibility to apoptosis and inhibits anchorage independent growth are provided and they do support a role for PTPRO as a tumor suppressor gene. As such, the falsification serves to strengthen the case of PTPRO as a tumor suppressor gene, but the classification is not entirely dependent upon data presented in Figure 5. The Committee does not find Dr. Motiwala's early statements that these results have been confirmed by other groups relevant in determining whether these images are duplicated and/or accurately represent the experimental data as reported. One member of the Committee believed that poor data management, storage and assembly issues could be a plausible explanation that may have led to the inadvertent reuse of the same image in Figure 5A.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 5A and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 5A in Allegation #43, as described

<sup>&</sup>lt;sup>341</sup> Ex. 304a - 20190612 - COMIC Interview + errata – Motiwala\_Redaction 1, page 24 line 15-19 and page 27, line 4-8

<sup>&</sup>lt;sup>342</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 52, page 57-59

<sup>&</sup>lt;sup>343</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 52, line 18-21

above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

4. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified serum starved images in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the serum starved images in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #3 under Review - Ghoshal et al., Mol Cell Bio 2005 (8 Allegations)

Ghoshal K\* \*\*, Datta J\*, Majumder S, Bai S, Kutay H, Motiwala T, Jacob ST\*\*. "5-Aza-deoxycytidine induces selective degradation of DNA methyltransferase 1 by a proteasomal pathway that requires the KEN box, bromo-adjacent homology domain, and nuclear localization signal." Mol Cell Biol. 2005 Jun; 25 (11): 4727-41. CORRECTED 04/30/18<sup>344, 345</sup> \* co-first authors \*\* co-corresponding authors

**Manuscript #3, Allegation #7-** S.T. Jacob reported falsified data by the reuse of the same IHC images in both panels f and g in Figure 2A in Ghoshal et al., Mol Cell Biol 2005.

- 1. Figure 2A shows an immunohistochemical (IHC) experiment for the incorporation of BrdU (to monitor cell replication) in HeLa cells treated with or without AzaC and aphidicolin, an inhibitor of DNA synthesis. Panel f (-AzaC/+aphidicolin control) and g (+AzaC/+aphidicolin) both show no BrdU incorporation.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap of the HeLa cell images in panels f and g, indicating that the same source image had been used to represent two different experimental conditions (f=Control vs g=AzaC treated) (see slide 28<sup>346</sup>).
- 3. The original data for this figure were not available during the Inquiry. A copy of the purported original data was provided as part of Dr. Ghoshal's response to the preliminary report of the CII<sup>347</sup> and additionally to the journal as part of the figure correction. The validity of this original source data cannot be confirmed.
- 4. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. At that time, PubPeer had published four (4) comments, corresponding to Allegations #7-11.
- 5. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017.<sup>349</sup> The initial letter requesting correction was signed by all authors, including Drs. Jacob and Datta. Over the ensuing four months, Dr. Ghoshal corresponded <sup>350, 351</sup> with MCB editors to request additional

<sup>344</sup> Ex. 28 - 20180430 Correction-Mol.Cell.Biol-2018-Ghoshal

<sup>&</sup>lt;sup>345</sup> Correction was posted 04/30/18 regarding Figure 2A and Figure 4C only

<sup>&</sup>lt;sup>346</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 28

<sup>&</sup>lt;sup>347</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 14

<sup>&</sup>lt;sup>348</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>349</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re\_MCB00539-17\_ Electronic Copyright Form Complete

<sup>&</sup>lt;sup>350</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio\_Jacob

<sup>&</sup>lt;sup>351</sup> These data are reviewed elsewhere under DIO 6819.

time to submit the corrected materials (requests on October 26, 2017; November 8, 2017; November 20, 2017; February 21, 2018), ultimately not submitting acceptable figures until March 14, 2018 and accepting correction proofs on March 23, 2018. As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, two additional comments had been posted to PubPeer<sup>352</sup> (ultimately corresponding to Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018).

- 6. A correction of the figure was published by the journal on April 30, 2018. At the time the CII interviewed Dr. Datta on March 1, 2018 and Dr. Jacob and Dr. Ghoshal on March 5, 2018, the correction of the figure had not been published by the journal, and none of the authors mentioned a forthcoming correction during their interviews.
- 7. The Committee finds the forensic evidence and visual inspection demonstrate image duplication, which the Committee concludes could be indicative of falsification.
- 8. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Datta was a co-first author of Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

### Respondent's Response:

- 1. Dr. Jacob did not specifically respond to this allegation during the Inquiry phase of the case.
- 2. In her interview with the CII on March 5, 2018, Dr. Ghoshal said she did not remember who did the experiment or made the figure, and moreover, that the reuse of the image would have been an inadvertent error, which did not compromise the integrity of the paper and was not caught by any journal during the submission/review process.<sup>353</sup> At the time of her interview, the correction of the figure had not been published by the journal.
- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned specifically about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>354</sup> and her appeal of their determination,<sup>355</sup> Dr. Ghoshal touted this paper as a highly-cited, paradigm-shifting publication; that this was a rare case in which the original data was available/retrievable after so many years; that the reviewers from two journals didn't catch the duplication; and that this figure was not critical to the reported results and strength of the manuscript, hence no motive existed for falsification of the figure.<sup>356</sup>
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC on June 28, 2019.<sup>357</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal agreed that the panels had been duplicated.<sup>358</sup> See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

<sup>&</sup>lt;sup>352</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>353</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 30-33

<sup>&</sup>lt;sup>354</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>355</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>356</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10, page 14

<sup>&</sup>lt;sup>357</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1

<sup>358</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.
- 2. Dr. Ghoshal did not take responsibility for generation of Figure 2A, but has maintained that an error may have occurred during figure generation and there was no motive for falsification given the results were supported by another experiment/figure. Dr. Ghoshal ultimately acknowledged the duplication, and based on original data she was able to locate, a correction of this figure was issued for the publication on April 30, 2018. Generally, Dr. Ghoshal has espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content, while the first author should take responsibility for every figure.
- 3. Dr. Datta did not specifically address this allegation and has not taken responsibility for the performance of the experiment or generation of the figure. Generally, Dr. Datta has espoused the view that the integrity of the data in a published manuscript should generally be shared regardless of authorship position. 359
- 4. Panel f was reported to represent a control, while panel g was purported to represent the AzaC treated sample. The erroneous figure panel was used in the publication to support the hypothesis that BrdUrd incorporation is abolished in cells treated with aphidicolin in AzaC treated cells. The erroneous figure panel possibly changed the reported results by making it unknown whether BrdUrd incorporation would be abolished in cells treated with aphidicolin and AzaC. The image forensics clearly demonstrate that the same image was used to represent both samples. The image was not an exact duplication, but was partially shifted, calling into question the likelihood that it was an inadvertent error of uploading the wrong file/image. However, Figure 2B illustrates results of a companion experiment that supports inhibition of DNA synthesis in cells treated with Aphidicolin and AzaC, where DNA synthesis is quantified using [a <sup>3</sup>H<sub>1</sub>]-thymidine incorporation assay.
- 5. The authors issued an erratum<sup>360</sup> that stated: "Panel f was an inadvertent duplication of panel g. The corrected image, obtained from original data, should appear as shown below. This change does not affect the interpretation of the data or the conclusions of the study."
- The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 7. The Committee has determined that Drs. Jacob and Ghoshal failed in their roles as corresponding authors to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2A, but that honest error cannot be ruled out since both images would lack BrdUrd incorporation and other experiments support the result represented. Thus, it is plausible that the duplication in Figure 2A in Allegation #7, as described above may have resulted from the honest error of others. The Committee does not find a preponderance evidence that Dr. Jacob intentionally, knowingly, or recklessly allowed data falsification or acted in contradiction to the accepted practices of figure generation or laboratory management at the time.
- 8. While this allegation may represent honest error and was corrected by the Respondent, the Committee recommends retraction of the manuscript to correct the scientific record based on the evidence presented for other concerns with this manuscript in Allegations #8-11, #44-45, and #76 below.

<sup>359</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 28, line 12-18; page 98, line 15-24

<sup>&</sup>lt;sup>360</sup> Ex. 28 - 20180430 Correction-Mol.Cell.Biol-2018-Ghoshal

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images f and g in Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images f and g in Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #8 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-5 and in lanes 6-10 (flipped 180 degrees) of the NS blot in Figure 3D in Ghoshal et al., Mol Cell Biol 2005.

- 1. Figure 3D shows a Western blot of immunoprecipitated <sup>35</sup>S-labeled Dnmt1 in Cos-7 cells treated with or without Aza-CdR for 0, 3, 6, 9 hrs, and/or with the proteasomal inhibitor, Z-LLL. The "NS" panel is a control that represents the level of non-specific polypeptide immunoprecipitated by the antibody.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lanes 1-5 with lanes 6-10 (flipped horizontally) in Figure 3D, indicating that the same data had been reused and relabeled to represent different experimental conditions (see slide 29<sup>361</sup>).
- 3. The original data for this figure were not available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lanes 1-5 flipped 180° to become lanes 6-10 of the NS blot in Figure 3D, which the Committee concludes is indicative of falsification.
- 5. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then, PubPeer had published four (4) comments, corresponding to Allegations #7-11. The Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript. The timing suggests that at least Drs. Ghoshal and Datta knew of potential issues with the research requiring correction and for a timeframe of at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 6. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017. The initial letter requesting correction was signed by all authors, including Dr. Jacob and co-first author Dr. Datta. Over the ensuing four months, Dr. Ghoshal corresponded the Corrected materials (requests on October 26, 2017; November 8, 2017; November 20, 2017; February 21, 2018), ultimately not submitting figures acceptable by the journal until March 14, 2018 and accepting correction proofs on March 23, 2018. As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, two additional comments had been posted to PubPeer<sup>367</sup> (ultimately corresponding to Allegations #44 and

<sup>&</sup>lt;sup>361</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 29

<sup>&</sup>lt;sup>362</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>363</sup> These data are reviewed elsewhere under DIO 6819 and 6822.

<sup>&</sup>lt;sup>364</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>365</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio Jacob

<sup>&</sup>lt;sup>366</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>367</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were



- 45, about which Dr. Jacob was notified on April 11, 2018).
- 7. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

### Respondent's Response:

- 1. Dr. Jacob did not specifically respond to this allegation during the Inquiry phase of the case.
- 2. During her interview with the CII on March 5, 2018, Dr. Ghoshal questioned if the forensics could be a false positive because this was a non-specific band. Dr. Ghoshal further indicated these data were not used for any purpose in the data analysis or in the results and conclusion, since the sole purpose of this image was to show that the protein existed. Dr. Ghoshal maintained that other authors would usually publish a certified quantification as a control, no non-specific control, and that there was no significance to the band in question other than to demonstrate that the protein was present. In the absence of the original data, Dr. Ghoshal found it difficult to provide an explanation or to refute the allegation. Dr. Ghoshal also indicated none of the reviewers caught the error during the submission/review process.
- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>370</sup> and her appeal of their determination,<sup>371</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication, but did not comment specifically on Figure 3D.<sup>372</sup>
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019.<sup>373</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal agreed that these data were flipped and duplicated and agreed this data was manipulated, but said that she could not recall who made the figure.

  374 See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.
- Neither Dr. Datta nor Dr. Ghoshal took responsibility for generation of Figure 3D, though Dr. Ghoshal has
  acknowledged the duplication. The fact that concerns already published on the web (i.e. PubPeer)
  regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of

initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>368</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 34-39

<sup>&</sup>lt;sup>369</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, lines 15-24

<sup>&</sup>lt;sup>370</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>371</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>372</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10

<sup>&</sup>lt;sup>373</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1

<sup>&</sup>lt;sup>374</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 31 line 20 to page 34 line 14

allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.

- 3. The forensics analysis clearly demonstrated significant overlay with five bands/lanes in sequence and mirror-imaging, which would not be scientifically valid as they represent different experimental conditions. The nature of the manipulation (i.e., re-use with mirror-imaging) strongly suggests that this was not an error but rather a deliberate manipulation of the image.
- 4. The falsified figure was used in the publication to support that equal loading of the samples was used, and is key to validation of conclusions. Because the level of the NS control has been falsified and is now unknown, there is no way to confirm the impact on the reported results and, thus, the conclusions must be considered invalid.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 3D in Allegation #8, as described above.
- 6. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 375 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry, 376 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other known potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 7. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified NS images in Figure 3D, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified NS images in Figure 3D, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #9 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-3 and in lanes 7-9 of the GFP blot in Figure 6C-1 in Ghoshal et al., Mol Cell Biol 2005.

- 1. Figure 6C-1 represents a Western blot of whole cell extracts from Cos-7 cells transfected with expression vectors for wild type and mutant Dnmt with GFP (control). GFP panel, lanes 1-3 represent the blot for the KEN/FL Dnmt1 wild type and lanes 7-9 represent the AAA/FL Dnmt1 mutant.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lanes

<sup>&</sup>lt;sup>375</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>376</sup> Ex. 037 - 20171018- Jacob Notification of Allegations



- 1-3 and lanes 7-9 (see slide 30<sup>377</sup>) indicating that the same data had been reused. This would not be scientifically valid as these lanes represent different experimental conditions.
- 3. Visual inspection of the bands reveals unique band shapes (e.g., upper left slant both on bands 1 and 7; middle notch in bands 2 and 8) that further supports the allegation that the same data has been reused.
- 4. The original data for this figure were not available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 1-3 and lanes 7-9 of the GFP blot in Figure 6C-1, which the Committee concludes is indicative of falsification.
- 6. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017.<sup>378</sup> As of then, PubPeer had published four (4) comments, corresponding to Allegations #7-11. The Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript.<sup>379</sup> The timing suggests that at least Drs. Ghoshal and Datta knew of potential issues with the research requiring correction and for a timeframe of at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017. 380 The initial letter requesting correction was signed by all authors, including Dr. Jacob and co-first author Dr. Datta. Over the ensuing four months, Dr. Ghoshal corresponded 381, 382 with Dr. Jacob and MCB editors delaying the correction and requesting additional time to submit the corrected materials (requests on October 26, 2017; November 8, 2017; November 20, 2017; February 21, 2018), ultimately not submitting figures acceptable by the journal until March 14, 2018 and accepting correction proofs on March 23, 2018. As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, two additional comments had been posted to PubPeer 383 (ultimately corresponding to Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018).
- 8. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

#### Respondent's Response:

- 1. Dr. Jacob did not specifically respond to this allegation during the Inquiry phase of the case.
- 2. During her interview with the CII on March 5, 2018, Dr. Ghoshal indicated that she may have run the gel, that since the data is 11-12 years old she does not recollect the experiment or have the original data, 384 and that in the absence of the original data she finds it difficult to provide an explanation or to refute the allegation. 385 Furthermore, Dr. Ghoshal indicated that the bands in question were not important to the

<sup>&</sup>lt;sup>377</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 30

<sup>&</sup>lt;sup>378</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>379</sup> These data are reviewed elsewhere under DIO 6819 and 6822.

<sup>&</sup>lt;sup>380</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>381</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio Jacob

<sup>&</sup>lt;sup>382</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>383</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>384</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 41

<sup>&</sup>lt;sup>385</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 43-44



- findings since they were presented in the manuscript simply to show that the protein was present.<sup>386</sup>
- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>387</sup> and her appeal of their determination,<sup>388</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication, but did not comment specifically on Figure 6C-1.<sup>389</sup>
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019.<sup>390</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal deferred to the forensics and agreed with the duplication, stating:

"If you know your forensics is correct, then I have no idea how it happened, but, it seems like, according to forensics, it is correct." <sup>391</sup>

8. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.
- 2. Dr. Ghoshal initially indicated she may have run the gel,<sup>392</sup> but later firmly stated that she did not make the figure or run the experiment and does not remember who did make Figure 6C-1.<sup>393</sup> Dr. Ghoshal has maintained that the results were not foundational to the manuscript, but ultimately acknowledged the duplication.
- 3. Dr. Datta did not specifically address this allegation and has not taken responsibility for the performance of the experiment or generation of the figure.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 5. Reuse of the same series of three bands would not be scientifically valid as they represent different experimental conditions (KEN/FL vs. AAA/FL) within Figure 6-C1. The expression levels for control proteins can be similar but not identical, indicating that that a span of three bands was reused. The

<sup>&</sup>lt;sup>386</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 51, lines 16-24

<sup>&</sup>lt;sup>387</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>388</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>389</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10

<sup>&</sup>lt;sup>390</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1

<sup>&</sup>lt;sup>391</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 35 line 14-16

<sup>&</sup>lt;sup>392</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 41

<sup>&</sup>lt;sup>393</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 35 line 19 to page 38 line 17

preponderance of the evidence points toward this duplication being an intentional act not the result of honest error. The unique notch in the middle of the lane 2 band would have been obvious to a scientist preparing the figure and difficult to ignore if unintentionally replicated six lanes away in the same figure, further indicating that the same data had been reused intentionally.

- 6. The falsified data potentially changed the reported results because the levels of Dnmt1-Flag cannot be related to a loading control, and cannot be interpreted unambiguously. The falsified GFP panel was used in the publication to support that the experimental lanes where equally loaded.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 6C-1 in Allegation #9, as described above.
- 8. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 394 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry, 395 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other known potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 9. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified GFP images (reuse of the same data in lanes 1-3 and in lanes 7-9) in Figure 6C-1, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified GFP images (reuse of the same data in lanes 1-3 and in lanes 7-9) in Figure 6C-1 and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #10 –** S.T. Jacob reported falsified data by the reuse of the same data in lane 2 and in lane 4 of the Dnmt1 blot in Figure 6C-2 in Ghoshal et al., Mol Cell Biol 2005.

- 1. Figure 6C-2 represents a Western blot of whole cell extracts from Cos-7 cells transfected with expression vectors for GFP (Control), Dnmt with wild type Zinc binding domain (KEN) but lacking the catalytic domain (ΔCAT), and Dnmt with a mutant Zinc binding domain (AAA) and lacking the catalytic domain. The Dnmt1 (endogenous) panel, lane 2 is the level of endogenous Dnmt in the KEN-ΔCAT transfected cells and lane 4 is the level of endogenous Dnmt in the AAA-ΔCAT transfected cells.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lane 2 and lane 4, indicating that the same data had been reused. This would not be scientifically valid as the lanes represent two different experimental conditions and time points (see slide 31<sup>396</sup>).
- 3. The original data for this figure were not available.

<sup>&</sup>lt;sup>394</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>395</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

<sup>&</sup>lt;sup>396</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 31

- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 2 and 4 of the Dnmt1 blot in Figure 6C-2, which the Committee concludes is indicative of falsification.
- 5. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017.<sup>397</sup> As of then, PubPeer had published four (4) comments, corresponding to Allegations #7-11. The Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript.<sup>398</sup> The timing suggests that at least Drs. Ghoshal and Datta knew of potential issues with the research requiring correction and for a timeframe of at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 6. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017.<sup>399</sup> The initial letter requesting correction was signed by all authors, including Dr. Jacob and co-first author Dr. Datta. Over the ensuing four months, Dr. Ghoshal corresponded<sup>400, 401</sup> with Dr. Jacob and MCB editors delaying the correction and requesting additional time to submit the corrected materials (requests on October 26, 2017; November 8, 2017; November 20, 2017; February 21, 2018), ultimately not submitting figures acceptable by the journal until March 14, 2018 and accepting correction proofs on March 23, 2018. As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, two additional comments had been posted to PubPeer<sup>402</sup> (ultimately corresponding to Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018).
- 7. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

## Respondent's Response:

- 1. Dr. Jacob did not address the allegation.
- 2. In her interview with the CII on March 5, 2018, Dr. Ghoshal stated she may have made this figure 403 and that the Dnmt1 blots may look similar given similar amounts of protein but that they weren't duplicated. 404
- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>405</sup> and her appeal of their determination,<sup>406</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication, but did not specifically comment on Figure 6C-2.<sup>407</sup>

<sup>&</sup>lt;sup>397</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>398</sup> These data are reviewed elsewhere under DIO 6819 and 6822.

<sup>&</sup>lt;sup>399</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>400</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio Jacob

<sup>&</sup>lt;sup>401</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>402</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>403</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 48, lines 13-18

<sup>&</sup>lt;sup>404</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 47, lines 1-7

<sup>&</sup>lt;sup>405</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>406</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>407</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10



- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019. See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal initially disputed the forensics, but ultimately agreed that there was a duplication.<sup>409</sup> See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

## Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.
- 2. Neither Dr. Datta nor Ghoshal have taken responsibility for generation of Figure 6C-2, but Dr. Ghoshal ultimately acknowledged the duplication. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 3. The falsified data potentially changed the reported results because the levels of transfected Dnmt1 mutants cannot be related to endogenous Dnmt-1 levels, and cannot be interpreted unambiguously.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 6C-2 in Allegation #10, as described above.
- 5. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 410 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry 411 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other known potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Dnmt1 images in Figure 6C-2, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>408</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1

<sup>409</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 38 line 18 to page 39 line 20

<sup>&</sup>lt;sup>410</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>411</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Dnmt1 images in Figure 6C-2, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #11 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-2/lanes 7-8 of the GFP blot in Figure 6C-1 and in lanes 1-2/lanes 7-8 of the beta-tubulin blot in Figure 2, J Nutr. 136, 2006 (Manuscript #6).

**Revised Allegation #11 -** This allegation was revised because during the Inquiry the CII found that the forensic analysis showed reuse of the full panel (not just two lanes) to represent GFP in Figure 6C-1 (lanes 1-8 of a 9 lane blot) of MCB 2005, and  $\beta$ -tubulin in Figure 2 (lanes 1-8) of J Nutr. 2006. (See also Allegation #20)

- 1. Figure 6C-1, MCB 2005 includes a GFP blot as a control for a Western blot of whole cell extracts from Cos-7 cells transfected with expression vectors for wild type (KEN/FL) and mutant (CS/FL) Dnmt with GFP. Figure 2, J Nutr 2006 includes a β-tubulin blot as a control for hepatic Dnmt1 Western blots of nuclear extracts from 4 control rats and 4 rats fed a diet deficient of methionine and devoid of folic acid and choline.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and internal duplication of lanes 1-3 as lanes 7-9 of Figure 6C-1 (Manuscript #3). See also <u>Allegation #9</u>. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lanes 1-8 of the GFP blot in Figure 6C-1 (Manuscript #3) with lanes 1-8 of the 36 wk β-tubulin blot in J Nutr. 2006 (Manuscript #6) (see slide 32-33<sup>412</sup>).
- 3. Visual inspection of the bands reveals unique band shaping (e.g., upper left slant both on bands 1 and 7 and middle notch in bands 2 and 8 of Figure 6C-1 that reappear in lanes 1-2 and 7-8 of Figure 2 J. Nutr. 2006 that further supports the allegation that the same data has been reused.
- 4. The original data for these figures were not available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a reuse of a span of eight lanes of the GFP blot in in Figure 6C-1 (Manuscript #3) as the entirety of the 36 wk β-tubulin blot in Figure 2 J Nutr. 2006 (Manuscript #6) (i.e., cross-publication duplication), which the Committee concludes is indicative of falsification.
- 6. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then, PubPeer had published four (4) comments, corresponding to Allegations #7-11. The Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript. The timing suggests that at least Drs. Ghoshal and Datta knew of potential issues with the research requiring correction and for a timeframe of at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017. The initial letter requesting correction was signed by all authors, including Dr. Jacob and co-first author Dr. Datta. Over the ensuing four months, Dr. Ghoshal corresponded with Dr. Jacob and MCB editors delaying the correction and requesting additional time to submit the corrected materials (requests on October 26, 2017; November 8, 2017; November 20, 2017; February 21, 2018), ultimately

<sup>&</sup>lt;sup>412</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 32-33

<sup>&</sup>lt;sup>413</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>414</sup> These data are reviewed elsewhere under DIO 6819 and 6822.

<sup>&</sup>lt;sup>415</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>416</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio\_Jacob

<sup>&</sup>lt;sup>417</sup> These data are reviewed elsewhere under DIO 6819.

not submitting figures acceptable by the journal until March 14, 2018 and accepting correction proofs on March 23, 2018. As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, two additional comments had been posted to PubPeer<sup>418</sup> (ultimately corresponding to Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018).

- 8. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

## Respondent's Response:

- 1. Dr. Jacob did not address the allegation during the Inquiry phase of the case.
- 2. In her interview with the CII on March 5, 2018, Dr. Ghoshal stated that in the absence of the original data, she found it difficult to provide an explanation or to refute the allegation, though she ultimately acknowledged the lanes look similar. Dr, Ghoshal also indicated that two manuscripts were being prepared for two different journals at the same time, and it was possible that the wrong image was pasted into the wrong manuscript.<sup>419</sup>
- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>420</sup> and her appeal of their determination,<sup>421</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication, but neither commented on this figure, nor on J Nutr. 2006.<sup>422</sup>
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019.<sup>423</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal accepted the forensic findings of similarity.<sup>424</sup> She posited that a shared scanner folder containing blots could have resulted in a mistaken reuse of the same image for both manuscripts as they were both in development at the same time.<sup>425</sup> Dr. Ghoshal did not recall who made the figure and indicated that the majority of the experiments for J Nutr 2006 were performed by the manuscript's second author, Xin Li.<sup>426</sup>
- 8. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

#### Respondent's Responsibility and Intent:

1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation

<sup>&</sup>lt;sup>418</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 previously mentioned) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>419</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 50-51

 $<sup>^{\</sup>rm 420}$  Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>421</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>422</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10

<sup>423</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1

<sup>&</sup>lt;sup>424</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 42 line 7 to page 43 line 1; page 52 line 19 to page 54 line 21

<sup>425</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 43 line 1-13; page 46 line 23 to page 47 line 1

<sup>&</sup>lt;sup>426</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 42 line 5-7; page 45 line 8 to page 47 line 8; page 50 line 18-25

that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.

- 2. Dr. Ghoshal did not take responsibility for generation of the questioned figures in either manuscript, but has maintained that an error may have occurred during figure generation.
- 3. Dr. Datta did not specifically address this allegation and has not taken responsibility for the performance of the experiment or generation of the figure in Mol. Cell Biol. 2005. Additionally, Dr. Datta is not a named Respondent on J Nutr. 2006 (Manuscript #6), and the Committee believes her level of involvement to be more minor.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 5. The published blot representing GFP protein (also containing the internal duplication, addressed as Allegation #9) in Figure 6C-1 of Mol. Cell Biol. 2005 was used in near totality (i.e., eight of the first nine lanes) in a later publication to represent β-tubulin protein in Figure 2 of J Nutr. 2006. Dr. Ghoshal's explanation that the wrong image could have been pasted into the wrong manuscript because the number of lanes was the same<sup>427</sup> is not valid nor plausible, as the number of lanes in Figure 6C-1 is nine while the number of lanes in Figure 2 of J Nutr. 2006 is eight. Because no original data exists for either publication, the Committee is unable to determine which publication may have been the source, and both images have internal duplications, and therefore, the COMIC concludes based on the preponderance of the evidence that neither image is a correct representation of the experimental result. Furthermore, without original data to verify the accuracy of these data, it cannot be determined to what extent the findings impact the conclusions of Mol Cell Bio 2005, as the figure was used in two different manuscripts.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 6C-1 in Allegation #11, as described above.
- 7. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 428 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry 429 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 8. The Committee recommends retraction of the manuscript to correct the scientific record.

<sup>&</sup>lt;sup>427</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 51, lines 7-12

<sup>&</sup>lt;sup>428</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>429</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified GFP images in Figure 6C-1, in Mol. Cell. Biol. 2005 by the reuse of lanes 1-8 (of a 9 lane blot) as  $\beta$ -tubulin lanes 1-8 in Figure 2 of J Nutr. 2006, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified GFP images in Figure 6C-1, in Mol. Cell. Biol. 2005 by the reuse of lanes 1-8 (of a 9 lane blot) as  $\beta$ -tubulin lanes 1-8 in Figure 2 of J Nutr. 2006, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #44 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 7; and the reuse of same data in lane 5 and in lane 6 (horizontal flip of image) in Dnmt3a blot in Figure 1A in Ghoshal et al., Mol Cell Biol 2005.

- Figure 1A shows a Western blot of Dnmt1, Dnmt3a and Dnmt3b from mouse lymphosarcoma cells (P1798) whole cell extracts treated with 5-aza-CdR for various times. Lane 1 of the Dnmt3a blot is time 0 treatment and lane 7 is 24 hr treatment.
- 2. Adobe Photoshop gradient mapping and overlay analysis showed significant similarity and overlap when comparing Dnmt3a lanes 1 and 7 indicating that the same data was used for lanes 1 and 7 though the right edge of lane 7 band was truncated (see slide 34-35<sup>430</sup>).
- 3. Similarly, Adobe Photoshop gradient mapping and overlay analysis showed significant similarity and exact overlap when comparing Dnmt3a lanes 5 and 6 indicating that the same data from lane 5 was flipped horizontally to be used as lane 6 (see slide 35<sup>431</sup>). Reuse of the data would not be scientifically valid as the lanes represent different experimental conditions.
- 4. Furthermore, visual inspection of the Dnmt3a lane as published demonstrates a consistent light background behind the bands themselves aligning with a speckled background toward the bottom of the image, indicating a possible cut/paste or superimposition of the series of bands on a separate background (see slide 34-35<sup>432</sup>).
- 5. No original data for this figure were available.
- 6. Allegation #44 represents one of three allegations against Figure 1 (See also Allegations #45 and #76).
- 7. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lane 1 as lane 7, a sharp line truncating lane 7, and reuse of lane 5 as lane 6 via horizontal flip, which the Committee concludes is indicative of falsification.
- 8. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017, 433 ultimately not submitting acceptable figures until March 14, 2018 and accepting correction proofs on March 23, 2018. 434 As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, multiple comments had been posted to PubPeer 435 (ultimately corresponding to Allegations #7-11, about

<sup>&</sup>lt;sup>430</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 34-35

<sup>&</sup>lt;sup>431</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 35

<sup>&</sup>lt;sup>432</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 34-35

<sup>&</sup>lt;sup>433</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re\_MCB00539-17\_ Electronic Copyright Form Complete

<sup>&</sup>lt;sup>434</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio\_Redacted Jacob

<sup>&</sup>lt;sup>435</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 previously mentioned) or whether they proceeded directly to PubPeer's website without opening the email.

which Dr. Jacob was notified on October 18, 2017 and Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018). It is known that as early as September 2017 Dr. Ghoshal was aware of figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 that had been published on the web (i.e., PubPeer). 436

- 9. An erratum was published by the journal on April 30, 3018.
- 10. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 11. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 12. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

## Respondent's Response:

- 1. Dr. Jacob did not address the allegation.
- 2. In her written response, provided to ORC on April 19, 2018, Dr. Ghoshal emphatically denied that there was any wrongdoing and attributed any similarity in the image to the shape of the wells in the stacking gel:

"I completely disagree with the allegation because of the following reasons. The western data in this panel show that Dnmt1 level is specifically reduced in P1798 cells upon Aza-CdR treatment. Since Dnmt3a and Dnmt3b levels are not altered some bands in certain lanes may look similar. Mirror image may arise because of the shape of the wells formed during formation of the stacking gel. The conclusion of this panel demonstrating downregulation of Dnmt1 with increase in time of exposure to Aza-CdR remains unchanged".<sup>437</sup>

- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>438</sup> and her appeal of their determination,<sup>439</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication,<sup>440</sup> again disagreed with the forensic analysis, and reiterated her supposition that the similarity of lanes 5 and 6 could be attributed to the shape of the wells in the stacking gel.<sup>441</sup> Dr. Ghoshal maintained that she saw no splicing lines, which must be necessary for duplication to be evident,<sup>442</sup> and that:

"It is hard to imagine that DNMT3a bands in two consecutive lanes were generated by copying one band followed by horizontal flipping and pasting just next to it. One has to be very creative to do so."443

5. In her response to the CII's preliminary report,  $^{444}$  and her appeal of their determination,  $^{445}$  Dr. Ghoshal further proposed that many of the bands in the Dnmt3a, Dnmt3b, and  $\beta$  -tubulin panels looked very similar but were not alleged duplicates and that such similarity demonstrates equal protein levels.

<sup>&</sup>lt;sup>436</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>437</sup> Ex. 130 - New Allegations Ghoshal, page 1

<sup>&</sup>lt;sup>438</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>439</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>440</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits page 10

<sup>&</sup>lt;sup>441</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10, page 11

<sup>&</sup>lt;sup>442</sup> This argument was refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected, despite clear evidence or testimony that splicing had taken place (e.g., see Allegation #5, Allegation #28, and Allegation #29) suggesting that the Respondents had sufficient skill when manipulating the images to mask splice lines.

<sup>&</sup>lt;sup>443</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 11

<sup>&</sup>lt;sup>444</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 11

<sup>&</sup>lt;sup>445</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

- 6. Consequently, the Committee looked at the other panels in the figure and subjected the Dnmt3b, and the □-tubulin panels to the same forensic analysis and <u>does</u> find evidence of additional duplications (see slide 36<sup>446</sup>):
  - a. Dnmt3b lanes 1-2 are horizontally flipped to be reused as lanes 4-5.
  - β-tubulin lane 3 is reused as lane 4.

Thus, the Committee found additional duplications and rejects Dr. Ghoshal's response. However, given the large number of allegations and evidence of potential Research Misconduct (both overall and within this manuscript), as well as a sufficient number of other issues to recommended retraction of this manuscript, the COMIC did not believe the scientific community or university would benefit by adding additional allegations for this figure at this late stage of investigation.

- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 8. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019. See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 9. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.
- 2. Dr. Ghoshal did not agree with the duplications nor take responsibility for the generation of Figure 1A, but put forth various alternative explanations of the duplications. The Committee does not agree with nor find scientifically valid the statement from Dr. Ghoshal that the lanes are similar or that "mirror images may arise" because of the shape of the wells during the formatting of the stacking gel.
- 3. Dr. Datta did not specifically address this allegation and has not taken responsibility for the performance of the experiment or generation of the figure.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 5. The falsified data potentially changed the reported results because the levels of Dnmt3a in P1798 cells treated with Aza-CdR cannot be interpreted unambiguously. The falsified figure was foundational and used in the publication to support that Aza-CdR treatment effects are specific for Dnmt1 and not Dnmt3a or Dnmt3b; hence, the falsification of any Dnmt3a or Dnmt3b data weakens the argument for the specificity of Aza-CdR for Dnmt1. As published, the results support the notion that Aza-CdR treatment did not significantly affect Dnmt3 protein levels, which was further confirmed by unaltered levels of the ectopically expressed HA-Dnmt3a/3b as shown in Figure 6E.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 1A in Allegation #44, as described above.

<sup>&</sup>lt;sup>446</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 36

<sup>&</sup>lt;sup>447</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1

- 7. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 448 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry 449 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other known potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 8. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Dnmt3a images in Figure 1A, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Dnmt3a images in Figure 1A, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #3, Allegation #45 -** S.T. Jacob reported falsified data by the reuse of same data in lanes 1, 2 and in lanes 4, 5 in Ku70 blot in Figure 1B in Ghoshal et al., Mol Cell Biol 2005.

- Figure 1B shows a Western blot of Dnmt1, Dnmt3a, and Dnmt3b from HeLa whole cell extracts treated with different concentrations of 5-Aza-CdR. The Ku-70 protein was used as a loading control. The figure depicts the impact of treatment on all three DNMT levels, showing that DNMT1 declined whereas DNMT3A and DNMT3B were not affected.
- 2. Adobe Photoshop gradient mapping showed a splice line after lane 1 and significant similarity of the overall shape and internal coloring in lanes 1 and 2 with lanes 4 and 5 in the Ku-70 panel, highly suggestive that the bands in question were duplicates (see slide 37<sup>450</sup>). This would not be scientifically valid as they represent different experimental conditions.
- 3. No original data for this figure were available.
- 4. Allegation #45 represents one of three allegations against Figure 1 (See also Allegations #44 and #76).
- 5. The Committee finds the forensic evidence and visual inspection of the allegedly reused lanes indicative of falsification.
- 6. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017, 451 ultimately not submitting acceptable figures until March 14, 2018 and accepting correction proofs on March 23, 2018. 452, 453 As of the time Dr. Ghoshal submitted revised figures and accepted MCB's

<sup>&</sup>lt;sup>448</sup> These data are reviewed elsewhere in DIO 6819.

<sup>&</sup>lt;sup>449</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

<sup>&</sup>lt;sup>450</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 37

<sup>&</sup>lt;sup>451</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>452</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio\_Jacob

<sup>&</sup>lt;sup>453</sup> These data are also reviewed elsewhere under DIO 6819.

proofs, multiple comments had been posted to PubPeer<sup>454</sup> (ultimately corresponding to Allegations #7-11, about which Dr. Jacob was notified on October 18, 2017 and Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018). It is known that as early as September 2017 Dr. Ghoshal was aware of figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 that had been published on the web (i.e., PubPeer). An erratum was published by the journal on April 30, 3018.

- 7. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

## Respondent's Response:

- 1. Dr. Jacob did not address the allegation in the Inquiry phase of the case.
- 2. In her written response to the allegation provided to ORC on April 19, 2018, Dr. Ghoshal expressed her disagreement with the allegation, indicating:

"Ku-70 was used as a loading control (normalizer) as its level was not significantly altered after Aza-CdR treatment. For that reason, its level may look very similar if not identical in certain lanes. In addition to Ku-70, Dnmt3a and Dnmt3b levels were not significantly changed and could be considered as normalizer. Therefore, considering all controls, specific and profound dose – dependent decrease in the Dnmt1 level in HeLa cells upon treatment with this DNA methyltransferase inhibitor remains unchanged."

- 3. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 4. In her response to the CII's preliminary report<sup>457</sup> and her appeal of their determination,<sup>458</sup> Dr. Ghoshal touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication and again disagreed with the forensic analysis, even suggesting that lanes 1 & 4 and 2 & 5 look similar but not identical.<sup>459</sup>
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019. See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

#### Respondent's Responsibility and Intent:

1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible

<sup>&</sup>lt;sup>454</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>455</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>456</sup> Ex. 130 - New Allegations Ghoshal, page 1

<sup>&</sup>lt;sup>457</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>458</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>459</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 11-12

<sup>&</sup>lt;sup>460</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1

for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.

- 2. Dr. Ghoshal did not agree with the alleged duplications nor take responsibility for the generation of Figure 1B.
- 3. Dr. Datta did not specifically address this allegation and has not taken responsibility for the performance of the experiment or generation of the figure.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 5. The data in Figure 1B are foundational and used to justify the remainder of the research focusing on Dnmt1 as the primary target of Aza-CdR. The falsified data potentially changed the reported results because the levels of Dnmt1/3A/3B cannot be related to the Ku-70 loading control, and cannot be interpreted unambiguously. The falsified figure was used in the publication to support that lanes were equally loaded, but as it is likely that the true relative values of Dnmt1 are different from what is presented, the falsification may lead the scientific community to a faulty conclusion that Dmnt1, but not Dmnt3a or Dmnt3b, are degraded.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 1B in Allegation #45, as described above.
- 7. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 461 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry 462 the Committee believes that the entire manuscript should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other known potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.
- 8. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Ku-70 images in Figure 1B, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified Ku-70 images in Figure 1B, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>461</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>462</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

**Manuscript #3, Allegation #76 –** S.T. Jacob reported falsified data by the reuse of the lower bands in lanes 1-2 and 5-6 in the DNMT3B blot of Figure 1B in Ghoshal et al., Mol Cell Biol 2005.

### **Finding of Fact:**

- 1. Figure 1B shows a Western blot of Dnmt1, Dnmt3a, and Dnmt3b from HeLa whole cell extracts treated with different concentrations of 5-Aza-CdR. In the Dnmt3B panel, lanes 1-2 represent control and 0.1 µM 5-Aza-CdR treatment and lanes 5-6 represent 5.0 µM 5-Aza-CdR treatment, with lane 6 samples being treated with DNase I to enhance DNMT extraction.
- 2. Adobe Photoshop overlay analysis and gradient mapping showed significant overlap and similarity of the overall shape and internal coloring in lanes 1 and 2 with lanes 5 and 6 in the bottom row of the DNMT3B panel, highly suggestive that the bands in question were duplicates (see slide 38-39<sup>463</sup>). This would not be scientifically valid as the lanes represent different experimental conditions.
- 3. Visual inspection of the bands demonstrates a unique notch in the bottom band of lane 1 that reappears in the bottom band of lane 5 and also a unique dot at the top right of the bottom band in lane 2 that reappears in the bottom band of lane 6.
- 4. Allegation #76 represents one of three allegations against Figure 1 (see also Allegations #44-45).
- 5. The Committee finds the forensic evidence and visual inspection demonstrates duplication of the bottom row of bands in lanes 1 and 2 as the bottom row of bands in lanes 5 and 6 in the DNMT3B panel of Figure 1B, which the Committee concludes is indicative of falsification.
- 6. Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 Figures 2A and 4C on or about October 10, 2017, 464 ultimately not submitting acceptable figures until March 14, 2018 and accepting correction proofs on March 23, 2018. 465, 466 As of the time Dr. Ghoshal submitted revised figures and accepted MCB's proofs, multiple comments had been posted to PubPeer (ultimately corresponding to Allegations #7-11, about which Dr. Jacob was notified on October 18, 2017 and Allegations #44 and 45, about which Dr. Jacob was notified on April 11, 2018). It is known that as early as September 2017 Dr. Ghoshal was aware of figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 that had been published on the web (i.e., PubPeer). 468 An erratum was published by the journal on April 30, 3018.
- 7. Dr. Ghoshal was a co-first and co-corresponding author of Mol Cell Biol 2005 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Datta was a co-first author on Mol Cell Biol 2005 and a Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Drs. Jacob, Ghoshal, and Datta were not questioned about this allegation during the Inquiry phase of the case.
- 2. In her response to the CII's preliminary report<sup>469</sup> and her appeal of their determination,<sup>470</sup> Dr. Ghoshal

<sup>&</sup>lt;sup>463</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 38-39

<sup>&</sup>lt;sup>464</sup> Ex. 317 - 20171017 - Email Ghoshal to MCB - Re MCB00539-17 Electronic Copyright Form Complete

<sup>&</sup>lt;sup>465</sup> Ex. 318a - Ghoshal-MCB Correspondence Portfolio\_Jacob

<sup>&</sup>lt;sup>466</sup> These data are also reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>467</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 described later in this report) or whether they proceeded directly to PubPeer's website without opening the email.

<sup>&</sup>lt;sup>468</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>469</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>470</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal



- touted Ghoshal et al., Mol Cell Biol 2005 as a highly-cited, paradigm shifting publication. 471
- 3. In written documentation provided to OSU via his legal counsel on July 15, 2019<sup>472</sup>, Dr. Jacob disagreed that a duplication is present, indicated that there would be no reason to reuse the bands, and highlighted the number of figures and panels in "this seminal paper in epigenetics field. The key findings have been reproduced in multiple laboratories."<sup>473</sup>
- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 5. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC June 28, 2019.<sup>474</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 6. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Jacob did not respond to this allegation, but the Committee identified email showing that Dr. Ghoshal initiated a correction of Mol Cell Biol 2005 (Figures 2A and 4C) in October 2017 and email and notification records that Dr. Jacob was aware of additional figure concerns over the months it took to finalize and publish the correction.
- 2. Neither Dr. Datta nor Dr. Ghoshal has specifically addressed this allegation and neither has taken responsibility for the performance of the experiment or generation of the figure. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see ensuing discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 3. The reuse of a portion of a blot (i.e., just the bottom row of bands as opposed to complete top/bottom sets) as well as the duplication of adjacent lanes argues against honest error in figure construction. The falsified data potentially changed the reported results because the levels of Dnmt3B cannot be determined, and thus cannot be interpreted. The data in Figure 1B are foundational and used to justify the remainder of the research focusing on Dnmt1 as the primary target of Aza-CdR. As it is likely that the true relative values of DNMT3B are different from what is presented, the falsification may lead the scientific community to a faulty conclusion that DNMT1, but not DNMT3a or DNMT3b, are degraded.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author (along with Dr. Ghoshal) to ensure the validity of data submitted for publication and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 1B in Allegation #76, as described above.
- 5. An erratum was initiated by the authors in October 2017 and finally issued for this manuscript in April 2018 to correct the use of a duplicated image (see Allegation #7). Given this, and the fact that other inconsistencies regarding this manuscript had already been published on the web (e.g., PubPeer) and were known to the Respondent and witnesses, 475 and/or had been brought to their formal attention via the initiation of the Research Misconduct inquiry 476 the Committee believes that the entire manuscript

<sup>&</sup>lt;sup>471</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 10, page 14

<sup>&</sup>lt;sup>472</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>473</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, "Exhibit 3" page 23

<sup>&</sup>lt;sup>474</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1

<sup>&</sup>lt;sup>475</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>476</sup> Ex. 037 - 20171018- Jacob Notification of Allegations

should have been meticulously reviewed for additional errors by the authors before submitting revised figures and finalizing the erratum with the journal. The Committee concluded that since the Dr. Jacob was aware of other potential errors in this manuscript, but only issued an erratum limited to Figure 2A and Figure 4C without addressing or investigating these other potential errors that he acted recklessly, allowing falsified data to remain uncorrected in the scientific literature and adds to the significance of the falsification.

6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified DNMT3B images in Figure 1B, and that this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified DNMT3B images in Figure 1B, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #4 under Review - Bai et al., Mol Cell Bio 2005 (7 Allegations)

Bai S, Ghoshal K, Datta J, Majumder S, Yoon SO, Jacob ST. "DNA methyltransferase 3b regulates nerve growth factor-induced differentiation of PC12 cells by recruiting histone deacetylase 2." Mol Cell Biol. 2005 Jan; 25 (2): 751-66.

**Manuscript #4, Allegation #12 –** S.T. Jacob reported falsified data by the reuse of the same data in lane 2 and lane 3 of the Dnmt3a blot in Figure 2D in Bai et al., Mol Cell Biol 2005.

#### **Finding of Fact:**

- 1. Figure 2D shows Western blot analyses for Dnmt1, Dnmt3a, Dnmt3b and Ku-70 control from extracts of untransfected cells (P), vector transfected cells (V), or 2 cell lines transfected with antisense Dnmt3b (#21 and #28). The Dnmt3a panel, lanes 2 and 3 represent expression of Dnmt3a in the vector control (lane 2) and the Dnmt3b antisense cell line #21 (lane 3).
- 2. Adobe Photoshop overlay analysis demonstrated a strong overlay between lanes 2 and 3, which indicates that the same data had been reused to represent the Dnmt3a protein expression for two different experimental conditions (see slide 44<sup>477</sup>).
- 3. Additional evidence of the reuse of the same data for both lanes 2 and 3 is the presence of the small dot in the background above both bands in lane 2 and lane 3.
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 2 and 3, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

#### Respondent's Response:

1. In written documentation provided to OSU via his legal counsel on July 15, 2019, <sup>478</sup> Dr. Jacob maintained that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, Dr. Jacob argued:

"The similarity of Dnmt3a bands in lanes 2 and 3 is most probably due to similar amounts in the

<sup>&</sup>lt;sup>477</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 44

<sup>&</sup>lt;sup>478</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

vector and clone 21. Since I do not see any splicing between the two lanes, it is unlikely to be copy pasted. Further, the focus in this figure is on Dnmt3b. We could have unequivocally proven this if we had raw data for a paper published almost 14 years ago."<sup>479</sup>

- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, 4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 3. First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>480</sup> Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions relating to the research,<sup>481</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible.

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- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 2D,
- 3. Reuse of a single image to represent two different experimental conditions would not be scientifically valid and compromises the integrity of the paper. The persistence of similar duplications, in this paper and others reviewed in the Investigation, is difficult to reconcile with accidental duplication. The figure as published demonstrates that targeted down-regulation of Dnmt3b inhibits PC12 cell differentiation, and specifically demonstrate the specificity for 3bsi by showing that Dnmt3a and Dnmt1 expression is not impacted in #21 and #28. The reuse of the same immunoblots for the control and clone #21 showing the expression of Dnmt3a means that the data cannot rule out an impact on Dnmt3a in clone #21. The Committee does not find Dr. Jacob's early statements regarding similar amounts of loaded protein, his inability to detect splicing (for this specific allegation and in general), and the focus of the figure being on Dnmt3b as relevant in determining whether these bands are duplicated and/or accurately represent the experimental data as reported. However, the overall significance of the manipulation is relatively low because it does not change the results of Dnmt3b.
- 4. The Committee has determined that the evidence supports the falsification of Figure 2D, but based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2D. The Committee

<sup>&</sup>lt;sup>479</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>480</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>481</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>&</sup>lt;sup>482</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

has determined that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 2D in Allegation #12, as described above. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 3 in favor (reckless) and 4 against, that the Respondent recklessly reported falsified DNMT3a images in Figure 2D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the DNMT3a images in Figure 2D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #4, Allegation #13 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 3 of the Alu I blot in Figure 5 in Bai et al., Mol Cell Biol 2005.

### **Finding of Fact:**

- 1. Figure 5 examines the DNA methylation profile in NGF-induced PC12 cell differentiation. Figure 5 represents a Southern blot of genomic DNA from vector transfected cells (Vector), 2 cell lines transfected with antisense Dnmt3b (#21 and #28), an untreated parental cell line (Parental) and 3bsi transfected cells (3bsi), digested with either Hpall (H), a methylation sensitive enzyme, or Mspl (M), a methylation insensitive enzyme. Southern blots were examined with IAP, Alu I and Satellite 1 probes, for the major repetitive elements in the genome to assess the DNA methylation profile in Dnmt3b-depleted cells. The data show that the methylation pattern of genomic DNAs for the repetitive elements did not change with depletion of Dnmt3b.
- 2. Adobe Photoshop overlay analysis demonstrated a strong overlay between lanes 1 and 3, which indicates that the same data had been reused to represent Alu I methylation pattern for two different experimental conditions, vector transfected cells or cell line #21 both digested with Hpall (see slide 45<sup>484</sup>).
- 3. There is a unique line artifact that runs to the right within both bands in lane 1 and 3.
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 1 and 3, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005

# Respondent's Response:

1. In written documentation provided to OSU via his legal counsel on July 15, 2019, <sup>485</sup> Dr. Jacob maintained that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, Dr. Jacob argued:

"While Lanes 1 and 3 of vector and clone #21 in the Alu I Southern blot appear similar, I do not see any splicing for them that rules out the possibility of duplication. Further, we arrived at the

<sup>&</sup>lt;sup>484</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 45

<sup>&</sup>lt;sup>485</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

conclusion that the depletion of Dnmt3b by antisense expression (clone #21, 28) or siRNA-mediated depletion did not change DNA methylation profile by Southern blot analysis of 3 repeat elements (IAP, Alu I and Satellite 1)—two critical experiments."<sup>486</sup>

- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, 4-7 above.
- First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>487</sup>
   Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions relating to the research,<sup>488</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible.

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 5,
- 3. Reuse of a single image to represent two different experimental conditions would not be scientifically valid and compromises the integrity of the paper. Persistence of similar duplications is difficult to reconcile with accidental duplication. As these are indicated to be major mobile repetitive elements in the genome, such duplication can influence the interpretation by enhancing the appearance of consistency of the repetition. The duplication is not benign, because it augments the appearance of the claim that there is no significant alteration of the methylation pattern. The Committee does not find Dr. Jacob's statements regarding his inability to detect splicing relevant in determining whether these images are duplicated and/or accurately represent the experimental data as reported. However, the Committee does agree with Dr. Jacob's point that conclusions were reached via two experiments and finds that this mitigates the impact of the apparent falsification of Figure 5 on the reported results.
- 4. The Committee has determined that the evidence supports the falsification of Figure 5, but based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 5. The Committee has determined that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 5 in Allegation #13, as described above. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a

<sup>&</sup>lt;sup>486</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>487</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>488</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>&</sup>lt;sup>489</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

5. The Committee recommends retraction of the manuscript to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 3 in favor (reckless) and 4 against, that the Respondent recklessly reported falsified Alu I data in Figure 5, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the Alu I data in Figure 5, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #4, Allegation #14 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 3, 4 of the Ku-70 blot in Figure 1D and in lanes 1, 2 of the Ku-70 blot in Figure 8A in Bai et al., Mol Cell Biol 2005.

# **Finding of Fact:**

- 1. Figure 1D shows a Western blot for Dnmt1, Dnmt3a, Dnmt3b and Ku-70 control in NGF-induced PC12 cells over 0, 1, 2, 4, and 6 days. Figure 8A shows a Western blot for Hdac 2, Hdac3, Hdac1 and Ku-70 control in untreated and 6 day NGF treatment. Figure 1D, lanes 3, 4 represent Ku-70 expression at 2 day and 4 day NGF treatment, while Figure 8A lanes 1, 2 represent Ku-70 expression in untreated and 6 day NGF treatment.
- 2. Using Adobe Photoshop, an image overlay demonstrated a high degree of similarity between Ku-70 lanes in Figure 1D lanes 1-2 (NGF treatment at 2 and 4 days, respectively) and Figure 8A lanes 3-4 (NGF no treatment and NGF treatment, respectively) (see slide 46<sup>491</sup>)
- 3. The blots are distinct in shape and edge contrast, arguing against coincidence as the explanation for the similarity of the two figures.
- 4. The spacing between the lanes for each differs between the two figures, suggesting possible manipulation (e.g., stretching or magnification) during preparation of the figures.
- 5. The Ku-70 blots in Figure 2D (Allegation #12) differ in appearance from the blots in Figs. 1D and 8A, as is expected, and argues against coincidence as an explanation for the similarity seen in the bands present in Figs. 1D and 8A.
- 6. No original data for this figure were available.
- 7. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 3 and 4 of the Ku-70 blot in Figure 1D and in lanes 1 and 2 of the Ku-70 blot in Figure 8A, which the Committee concludes is indicative of falsification.
- 8. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

# Respondent's Response:

1. In written documentation provided to OSU via his legal counsel on July 15, 2019, <sup>492</sup> Dr. Jacob maintained that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, Dr. Jacob argued:

"Very similar Ku-70 bands in these two lanes of these two figure panels could be coincidental due to identical amounts of protein loading in all samples. Further, no splicing lines are visible on

<sup>&</sup>lt;sup>491</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 46

<sup>&</sup>lt;sup>492</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

either side of these bands. Interestingly, Hdac1 is almost identical in these two samples, which can also be considered as a normalizer."<sup>493</sup>

- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>494</sup>
   Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions related to the research,<sup>495</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible.

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figures 1D or 8A,
- 3. The Ku-70 antigen was used as a loading control, and the same loading control data was used for different experiments. Reused images are reported as day 2 and day 4 of NGF treatment in Fig 1D but also as 6 days for treated and untreated cells in Figure 8A. The use of the same images representing two different experimental conditions is irreconcilable since the loading controls provide an analytical basis for relative changes in experimental measurements. Thus, the data and integrity of the paper are compromised. Furthermore, duplicating an internal pair of bands from Figure 1D then apparently stretching or magnifying them for reuse in a separate figure (8A) argues against an honest cut/paste error and suggests that the lanes were specifically reused to present the data in a manner so as to deceive the reader. The Committee does not find Dr. Jacob's comments regarding the lack of splice lines (for this specific allegation and in general) to excuse the duplication
- 4. The Committee has determined that the evidence supports the falsification of Figure 1D and 8A, but based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 1D and 8A. The Committee has determined that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 8A in Allegation #14, as described above. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on

<sup>&</sup>lt;sup>493</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

<sup>&</sup>lt;sup>494</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>495</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>496</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 3 in favor (reckless) and 4 against, that the Respondent recklessly reported falsified Ku-70 data in Figures 1D and 8A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Ku-70 data in Figures 1D and 8A, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #4, Allegation #15 – S.T. Jacob reported falsified data by splicing between lanes 4 and 5 of the Dnmt3b blot and lanes 1 and 2 of the Hdac2 blot in Figure 8B in Bai et al., Mol Cell Biol 2005.

### Finding of Fact:

- Figure 8B represents a coimmunoprecipitation of Dnmt3b and Hdac2 from PC12 cells treated for 6 days with NGF.
- 2. Adobe Photoshop gradient mapping shows a distinct, abrupt change in background brightness suggesting splicing between lanes 4 and 5 for Dnmt3b and lanes 1 and 2 for Hdac2 in Figure 8B (see slide 47<sup>498</sup>).
- 3. No original data for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates a line between lanes 4 and 5 in the Dnmt3b blot and lanes 1 and 2 of the Hdac2 blot, which the Committee concludes represents a splice line and could be indicative of falsification.
- 5. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

#### Respondent's Response:

- In his interview with the CII on March 5, 2018, Dr. Jacob generally stated that splicing from different gels/blots was common practice in that era and that there was no requirement during that time to demarcate spliced gels by a box or line.<sup>499</sup> Dr. Jacob did not comment on this specific allegation of splicing.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, 500 Dr. Jacob maintained that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, he argued that he is not convinced splicing has occurred between these specific lanes. 501
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, #3-7 above.
- 4. First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>502</sup> Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions<sup>503</sup> relating to the research,

<sup>&</sup>lt;sup>498</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 47

<sup>499</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 30, lines 4-24; page 31 lines 1-14

<sup>&</sup>lt;sup>500</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>501</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

<sup>&</sup>lt;sup>502</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>503</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair, page 1-2

With regard to splicing, Dr. Bai indicated:

"I do believe that, back at that time, it was commonly accepted by journals to remove extraneous lanes of a blot, in order to present in a paper only the lanes that were relevant. I do not know of any journal that, at that time, instructed authors to put a line in the figure to indicate the removal of lanes. I believe everyone did the same as we did. Under today's standards, I would either put a line in the figure or I would re-run the experiment without the unnecessary lanes. However, I do not believe that was common practice at OSU or at other research institutions during the time I was in Dr. Jacob's lab, and I do not believe the journals were requiring it then." 504

# Respondent's Responsibility and Intent:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 8B,
- 3. It is the Committee's understanding that the standards in the field at the time of this 2005 publication may not have been to require demarcation of non-contiguous bands and the alleged splice is visible to the naked eye. In permitted instances, the splice line would be expected to run all the way down through the complete set of blots, which is not the case in Figure 8B. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 8B and that the actions of others caused the splicing of Figure 8B in Allegation #15, as described above. The Committee did not identify the requisite intent necessary to make a finding of Research Misconduct. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record based on the evidence presented for Allegations #12-14, and #17.

# **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Dnmt3b and Hdac2 images in Figure 8B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Dnmt3b and Hdac2 images in Figure 8B, and therefore this act **does not** constitute Research Misconduct as described as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>504</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair, page 1-2

Manuscript #4, Allegation #16 – S.T. Jacob reported falsified data by splicing between samples 1 and 2 in the Hdac2 blot in Figure 8C in Bai et al., Mol Cell Biol 2005.

### Finding of Fact:

- Figure 8C represents the cosedimentation of Dnmt3a, Hdac2, Hdac3a, and Hdac1 fractionated by glycerol density gradient and visualized by Western blots. The potential splicing is between Hdac2 fractions 1 and 2.
- 2. Adobe Photoshop gradient mapping shows a distinct, abrupt change in background brightness consistent with splicing between samples 1 and 2 (lanes 2 and 3) of the Hdac2 blot in Figure 8C (see slide 48<sup>506</sup>).
- 3. No original data for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates a line between lanes 1 and 2 in the Hdac2 blot, which the Committee concludes represents a splice line and could be indicative of falsification.
- 5. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

### Respondent's Response:

- 1. In his interview with the CII on March 5, 2018, Dr. Jacob generally stated that splicing from different gels/blots was common practice in that era and that there was no requirement during that time to demarcate spliced gels by a box or line. 507 Dr. Jacob did not comment on this specific allegation of splicing.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, <sup>508</sup> Dr. Jacob maintained that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, Dr. Jacob argued:

"It is not obvious to me that there is splicing between fraction #1 and fraction #2. Further, the key lanes in this figure are 9-11 in Dnmt3b and Hdac2 panels that clearly support the conclusion that Dnmt3b co-sedimented with Hdac2 during glycerol density gradient centrifugation. It does not make any sense about this kind of allegation." <sup>509</sup>

- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, #3-7 above.
- 4. First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>510</sup> Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions relating to the research,<sup>511</sup>

With regard to splicing, Dr. Bai indicated:

"I do believe that, back at that time, it was commonly accepted by journals to remove extraneous lanes of a blot, in order to present in a paper only the lanes that were relevant. I do not know of any journal that, at that time, instructed authors to put a line in the figure to indicate the removal of lanes. I believe everyone did the same as we did. Under today's standards, I would either put

<sup>&</sup>lt;sup>506</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 48

<sup>&</sup>lt;sup>507</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 30, lines 4-24; page 31 lines 1-14

<sup>&</sup>lt;sup>508</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>509</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

<sup>&</sup>lt;sup>510</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>511</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

a line in the figure or I would re-run the experiment without the unnecessary lanes. However, I do not believe that was common practice at OSU or at other research institutions during the time I was in Dr. Jacob's lab, and I do not believe the journals were requiring it then."<sup>512</sup>

### Respondent's Responsibility:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 8C
- 3. It is the Committee's understanding that the standards in the field at the time of this 2005 publication may not have been to require demarcation of non-contiguous bands and the alleged splice is visible to the naked eye. In permitted instances, the splice line would be expected to run all the way down through the complete set of blots, which is not the case in Figure 8C. Without original data, the COMIC is not able to confirm that the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) and not to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome. However, when considered with the evidence presented in Allegation #17 below, the sheer number of manipulations to this figure lead the Committee to believe that the manipulations were made intentionally with falsification as the goal.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 8C and that the actions of others caused the splicing of Figure 8C in Allegation #16, as described above. The Committee did not identify the requisite intent necessary to make a finding of Research Misconduct. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record based on the evidence presented for Allegations #12-14 and #17.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Hdac2 data in Figure 8C via splicing, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Hdac2 data in Figure 8C via splicing, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #4, Allegation #17 –** S.T. Jacob reported falsified data by the reuse of multiple bands and background images in Figure 8C in Bai et al., Mol Cell Biol 2005. Specifically:

a. Reuse of the same data in sample 3 and sample 4 (with possible erasure of the band) of the Hdac2 blot

<sup>&</sup>lt;sup>512</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair, page 1-2

- b. Reuse of the same blank background image in samples 15-16 and 17-18 of the Hdac2 blot
- c. Reuse of the same data in samples 7-8 and 9-10 (with possible erasure of the bands) of the Dnmt3a blot
- d. Reuse of the same blank background image in sample 16 and sample18 (with possible erasure of background artifact) of the Dnmt3a blot

# **Finding of Fact:**

- 1. Figure 8C represents the cosedimentation Dnmt3a, Hdac2, Hdac3a, or Hdac1 fractionated by glycerol density gradient and visualized by Western blots to demonstrate that Dnmt3b preferentially interacts in PC12 cells with Hdac2, which is up-regulated upon NGF treatment.
- 2. Adobe Photoshop gradient mapping and embossing filter show: 514
  - a. Allegation 17a: a splice line between lanes 3 and 4, a distinct white dot at the top of lane 3, which is replicated in lane 4; similar background artifacts (i.e. a pair of distinct white dots at the bottom of lane 3, which are replicated in lane 4); and a quarter circle marking at the top right corner of lane 3, which is replicated in lane 4 (see embossing filter) of the Hdac2 blot in Figure 8C. While the presence and relative location of these white dots is consistent between the two lanes, the only difference is the absence of the protein band in lane 4 and instead an area of probable erasure (see slide 49-50). In addition, a background inconsistency in lane 5 is also consistent with erasure of bands.
  - b. Allegation 17b: a splice line between lanes 16 and 17, unique background features across the top of the lanes 15-16, which are duplicated in lanes 17-18, and a series of vertical red dots at the edge of lane 16 that reappear at the edge of lane 18. Breaks in the top line are also noted at the top left corner of the Hdac2 blot in Figure 8C, which are indicative of imprecise cutting/pasting of the duplicated lanes (see slide 49-50).
  - c. Allegation 17c: a splice line between lanes 10 and 11, a series of five distinct white dots and a comma-shaped marking at the top of lanes 7-8, which are replicated in lanes 9-10, and a series of 3 distinct white dots and a comma-shaped marking at the top of lane 7, which is replicated in lane 9 of the Dnmt3a blot in Figure 8C (see slide 51-5253).
  - d. Allegation 17d: a series of rectangular-shaped, darkened areas at the top of lane 16, which are repeated in lane 18 of the Dnmt3a blot in Figure 8C. Breaks in the bottom line are also noted at the bottom left corner of the Dnmt3a blot in Figure 8C, which are indicative of imprecise cutting/pasting of the duplicated lanes (see slide 51-52).
- 3. No original data for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of multiple sections of the same data in the Hdac2 blot as well as the Dnmt3a blot of Figure 8C, which the Committee concludes is indicative of falsification.
- 5. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

### Respondent's Response:

1. In written documentation provided to OSU via his legal counsel on July 15, 2019,<sup>515</sup> Dr. Jacob maintains that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated, the conclusions remain intact, and that no one has questioned any figures in the past or more recently. Furthermore, Dr. Jacob argues:

"When a protein sediments in a specific region in a gradient, western blot of that protein in those fractions will, of course, show much more intense blot. It is not evident that there is any manipulation of background in samples listed here." <sup>516</sup>

<sup>&</sup>lt;sup>514</sup> Ex. 305 - Jacob Image Forensics COMIC Final, see slide 49-52

<sup>&</sup>lt;sup>515</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>516</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-7 above.
- First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>517</sup>
  Dr. Bai generally maintained that she has no access to any original data and does not have a memory
  from which she can answer specific questions relating to the research,<sup>518</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible.

*"519* 

### Respondent's Responsibility:

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 8C,
- 3. Reuse of multiple, separate bands to represent different experimental conditions would not be scientifically valid and compromises the integrity of the paper. Without original data, the Committee cannot determine to what extent the falsified data potentially changed the reported results and conclusions of the paper. For example, if there were bands in lanes 7-10 of the Hdac1 blot that have been obscured then there would not be preferential association of only Hdac2 as reported. Furthermore, the re-use of so many sections within the span of the Hdac2 blot as well as the Dnmt3a blot argues against an honest cut/paste error and suggests that the lanes were specifically reused to present the data in a manner so as to deceive the reader. Additionally, when considered with the evidence presented in Allegation #16 above, the sheer number of manipulations in this figure lead the Committee to conclude that the manipulations were made intentionally with falsification as the goal. The totality of manipulations within this figure and the manuscript as a whole compounds the significance of the falsification.
- 4. The Committee has determined that the evidence supports the falsification of Figure 8C, and that, based on witness testimony, Dr. Jacob was not responsible for the creation of Figure 8C itself. The Committee has determined that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 8C in Allegation #17, as described above. The Committee, however, finds Dr. Jacob was reckless in executing his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, given the complexity of the figure and its significance to the results reported in the manuscript (i.e., Dnmt3b preferentially interacts in PC12 cells with Hdac2, which is up-regulated upon NGF treatment), and that

<sup>&</sup>lt;sup>517</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>518</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>&</sup>lt;sup>519</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

these reckless actions caused the inclusion and reporting of falsified data within Figure 8C as described above.

5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 4 in favor and 3 against, that the Respondent recklessly reported falsified DNMT3a and Hdac2 panels in Figure 8C, and therefore this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT3a and Hdac2 panels in Figure 8C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #4, Allegation #77 – S.T. Jacob reported falsified data by the reuse of the same cell images representing 'Vector' and 'Parental' for -NGF samples in Figure 2F in Bai et al., Mol Cell Biol 2005

### Finding of Fact:

- Figure 2F shows a representative microscopy image for Parental, Vector only, and Dnmt3b antisense transfected PC12 cells (#21 and #28), with or without NGF treatment. The Parental and Vector images in question are controls for –NGF treatment.
- Adobe Photoshop overlay analysis demonstrated significant similarity and overlap of the left three-fourths
  of the Parental image with the right two-thirds of the Vector image, suggesting that the images do not
  represent samples from two different stable cell lines as purported in the figure legend (see slides 53<sup>521</sup>).
- 3. No original data for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in "Vector" and "Parental" –NGF cell samples, which the Committee concludes is indicative of falsification.
- 5. Dr. Jacob was the laboratory PI and corresponding author of Mol Cell Biol 2005.

# Respondent's Response:

- In written documentation provided to OSU via his legal counsel on July 15, 2019,<sup>522</sup> Dr. Jacob maintained
  that the novel and seminal observations presented via 8 figures with 32 subpanels should be appreciated,
  the conclusions remain intact, and that no one has questioned any figures in the past or more recently.
  No response specific to this allegation was issued.
- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>523</sup>
  Dr. Bai generally maintained that she has no access to any original data and does not have a memory
  from which she can answer specific questions relating to the research,<sup>524</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm

<sup>&</sup>lt;sup>521</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 53

<sup>&</sup>lt;sup>522</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 23

<sup>&</sup>lt;sup>523</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>524</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair



that the images have been duplicated	that	the	images	have	been	du	plicated
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### Respondent's Responsibility and Intent:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 2F
- 3. The image forensics clearly demonstrate that the same microscopy image was used to represent both samples. The image is not an exact duplication, but a partially shifted field, introducing the possibility that it was an inadvertent error of uploading the wrong file/image. The Committee does believe that poor data management/storage and assembly issues could be a plausible explanation and could have led to the inadvertent reuse of the same image in Figure 2F. The authors purport that Dnmt3b plays a role in differentiation of PC12 cells following treatment with NGF, and Figure 2F clearly shows the impact of down-regulating Dnmt3b on the differentiation of cells. Since both control images are called into question by the duplication, the data for the clones cannot be interpreted.
- 4. The Committee has determined that the evidence supports the duplication of Figure 2F, and based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2F. The Committee has determined that the actions of others caused the duplication within Figure 2F in Allegation #77, as described above. The Committee did not identify the requisite intent necessary to make a finding of Research Misconduct. The Committee finds Dr. Jacob failed in his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record based on the evidence presented for Allegations #12-14 and #17.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Vector and Parental –NGF images in Figure 2F, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Vector and Parental –NGF images in Figure 2F, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #5 under Review-Datta et al., Cancer Res 2005 (1 Allegation)

Datta J, Majumder S, Bai S, Ghoshal K, Kutay H, Smith DS, Crabb JW, Jacob ST. "Physical and functional interaction of DNA methyltransferase 3A with Mbd3 and Brg1 in mouse lymphosarcoma cells." Cancer Res. 2005 Dec 1; 65(23):10891-900.

<sup>&</sup>lt;sup>525</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

**Manuscript #5, Allegation #18 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 2-4 (figure label is 3-5) and in lanes 7-9 (figure label is lanes 8-10) of the Hdac1 blot in Figure 1C in Datta et al., Cancer Res 2005.

### **Finding of Facts:**

- 1. Figure 1 illustrates Western blot analysis of glycerol density gradient fractions to show polypeptides that co-purify with Dnmt3a (DNA methlytransferase 3A). The association between Dnmt3a with Brg1 and Mdb3 was the overarching focus of the paper. The allegation relates to a purported finding (Figure 1C) in which Dnmt3a is shown to co-purify with Hdac1 (histone deacetlyase).
- 2. Adobe Photoshop overlay analysis demonstrated a high degree of similarity between lanes 2-4 (figure label indicates lanes 3-5) and lanes 7-9 (figure label indicates lanes 8-10) of the Hdac1 blots in Figure 1C (see slide 55-56<sup>527</sup>).
- 3. The questioned lanes occur as a triplet sequence rather than as a single lane, making the strong similarity in the overlay very unlikely to have occurred by chance. There is a unique background artifact (i.e., a small dot) that appears below the bands in both lane 3 and lane 8 that is observable by visual inspection. Reuse and relabeling of the questioned lanes would misrepresent the data as different glycerol density gradient fractions. Different fractions cannot be represented by the same bands.
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a reuse of the same data in lanes 2-4 as lanes 7-9, which the Committee concludes is indicative of falsification.
- 6. Figure inconsistencies in Datta et al. 2005 were published on the web (i.e. PubPeer) and known at least to Dr. Datta and other authors on the publication as early as September 2017.<sup>528</sup> As of then, PubPeer had published three (3) comments, corresponding to Allegation #18. The timing suggests at least Dr Datta knew of potential issues with the research for at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Jharna Datta was the first author of Cancer Res 2005 and Senior Research Associate in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of Cancer Res 2005.

#### Respondent's Response:

- 1. Dr. Jacob did not address this specific allegation via written statements or interview during the Inquiry.
- 2. In her interview with the CII on March 1, 2018, Dr. Datta indicated that the original data was not available due to a computer crash,<sup>529</sup> but to her knowledge the bands were not copied and pasted.<sup>530</sup> Dr. Datta questioned the accuracy of the forensics software and whether or not the overlay might be a false positive.<sup>531</sup> Dr. Datta also presented her analysis of a pdf version of the figure (that she had previously emailed to the CII on 11/30/17)<sup>532</sup> that showed more dissimilarity than found in the OSU forensic analysis.<sup>533,534</sup> Additionally, Dr. Datta stated that there would be no scientific point to such duplication and that the scientific content of the paper had been replicated by another lab in Cleveland.<sup>535</sup>
- 3. Two months later, in a written response provided to ORC on May 18, 2018, Dr. Datta indicated that she remembered doing the experiment and preparing the figure, and while she believed that the lanes in question are very similar, she did not believe they are identical. Dr. Datta commented again that the

<sup>&</sup>lt;sup>527</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 55-56

<sup>&</sup>lt;sup>528</sup> These data are reviewed elsewhere under DIO 6822.

<sup>&</sup>lt;sup>529</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 17 lines 4-8

<sup>&</sup>lt;sup>530</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 35 lines 10-11; page 45 lines 6-10; page 27 lines 5-8

<sup>&</sup>lt;sup>531</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 33 lines 19-21

<sup>&</sup>lt;sup>532</sup> Ex. 75 - 20171130- Email Datta to RIO Cancer Res 2005

<sup>&</sup>lt;sup>533</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 33 lines 21-24

<sup>&</sup>lt;sup>534</sup> Ex. 82 - Can Res 2005-Explanation-JD-113017

<sup>&</sup>lt;sup>535</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 35 lines 11-19; page 37 lines 2-3



original data were not available, but that the major conclusions of the paper are supplemented by other analyses and that the conclusions of the paper remain valid. 536, 537

4. In her response to the CII report<sup>538</sup> and her appeal of their determination,<sup>539</sup>, Dr. Datta maintained:

"...that splicing would have been required in order to accomplish the alleged duplication, and that, if splicing had occurred, it would be visible from the image analysis. However, the image analysis I provided and the analysis performed by OSU do not show any splice lines on either side of the alleged duplicated bands. I believe this is evidence of non-duplication that was not considered by the Committee." 540

and

"There would have been nothing for us to gain by duplicating the bands in the Hdac1 panel of Figure 1C. If Hdac1 had peaked only at fraction 4, we would still have sent fraction 9 for LC-MS/MS analysis, and it would still have shown the association with Hdac1 that is evidenced in Fig. 1B. Further, if Hdac1 had not been associated with Dnmt3a at all, our paper would have been no less strong. The focus of this paper is on the components of Brg1 complex (Brg1, Baf155 and Baf57), not Hdac1. We do not understand what possible motive we would have for duplicating bands..."541

- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 6. In her interview with the COMIC on June 28, 2019, <sup>542</sup> Dr. Datta continued to disagree with the allegation of duplication, to appeal to her previous analysis of a pdf version of the figure she scanned and enlarged via Photoshop and which she posited demonstrated pixel differences, and to take responsibility for generating the figure. Dr. Datta could not find the original data. Dr. Datta generally described the laboratory process for generating and submitting manuscripts and the collective responsibility all manuscript authors have for the review and validity of the data. <sup>543</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. Dr. Datta was listed as first author on Cancer Res 2005. In her written response, provided to ORC on May 18, 2018, Dr. Datta indicated that the first six authors were involved in performing the experiments and preparing figures, but she did remember performing the experiment and preparing the figure. Dr. Datta admitted she was the person who generated Figure 1C and the Committee finds that as a first author, she had the responsibility to ensure that all figures included in the publication were correct.
- 3. The Committee did not find compelling Dr. Datta's analysis of a pdf version of the figure she claimed shows more dissimilarity than found in the OSU forensic analysis, but believes that the lower resolution of the pdf version provided by Dr. Datta was not as accurate as the higher resolution forensic analysis performed by ORC. The Committee disagrees with Dr. Datta's conclusion that the bands were dissimilar.

<sup>&</sup>lt;sup>536</sup> Ex. 78 - OSU Response 1-JD, page 1

<sup>&</sup>lt;sup>537</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 1

<sup>&</sup>lt;sup>538</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII

<sup>&</sup>lt;sup>539</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>540</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 3

<sup>&</sup>lt;sup>541</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 3

<sup>&</sup>lt;sup>542</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 38 line 21 – page 39 line 22; page 40 lines 17-18

<sup>&</sup>lt;sup>543</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, pages 23-28; page 98 line 15-24

- 4. The Committee agrees with Dr. Datta<sup>544</sup> that this Western blot analysis of the glycerol density gradient fractions is not the only experiment that showed the association/co-fractionation of Hdac1 protein with Dnmt3a. The presence of all the proteins shown in the Western blot analysis of Figure 1C, including Hdac1, was determined by mass spectrometry (LC-MS/MS) and bioinformatics analysis (performed at Cole Eye Institute and Lerner research Institute, Cleveland clinic Foundation, Cleveland, Ohio under the supervision of Dr. John W. Crabb), as shown in Figure 1B. The Committee agrees with Dr. Datta that the key conclusions of the paper remains valid.
- 5. Dr. Datta maintained that there was nothing to be gained by manipulating the Hdac1 Western blot by the duplication of a series of bands. The Committee disagrees with Dr. Datta's assessment. The presence of bands in lanes 6-10 in the Hdac1 panel confirms the hypothesis of co-purification of Dnmt3a and Hdac1. If lanes 6-10 in the Hdac1 panel were manipulated, the experimental results would be in question. Without original data, it cannot be determined to what extent the falsifications impact on the reported conclusions of the paper.
- 6. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Datta at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Datta.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 1C and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 1C in Allegation #18, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the Committee failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the increased risk of falsified information) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 8. Because this specific falsification is the only allegation in this manuscript, the Committee would normally recommend that the authors work with the journal to correct this figure. However, on account of original data not being available and the Jacob laboratory no longer being actively assembled, the Committee believes that correction is not possible, and, therefore, recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Hdac1 data in Figure 1C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the Hdac1 data in Figure 1C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #6 under Review - Ghoshal et al., J. Nutr. 2006 (2 Allegations)

Ghoshal K, Li X, Datta J, Bai S, Pogribny I, Pogribny M, Huang Y, Young D, Jacob ST. "A folate- and methyl-deficient diet alters the expression of DNA methyltransferases and methyl CpG binding proteins involved in epigenetic gene silencing in livers of F344 rats." J. Nutr. 2006 Jun; 136 (6): 1522-7.

<sup>&</sup>lt;sup>544</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, pg 3

**Manuscript #6, Allegation #19 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 2-4, and 7 of the Dnmt1 blot (18 weeks) and in lanes 4-6, and 7 of the Dnmt1 blot (36 weeks) in Figure 2 in Ghoshal et al., J Nutr 2006.

### **Finding of Fact:**

- 1. Figure 2 shows hepatic Dnmt1 and β-tubulin control Western blots of nuclear extracts from 4 control rats and 4 rats fed a diet deficient in methionine and devoid of folic acid and choline (FMD). Dnmt1 middle blot, lanes 2-7, [lanes 2-4 are 18 wk Control and lane 7 is 18 wk FMD] and Dnmt1 bottom blot, lanes 4-7 [lane 4 is 18 week Control and lanes 5-7 are 36 wk FMD].
- 2. Adobe Photoshop overlay analysis demonstrated a very high degree of similarity and overlap when comparing lanes 2, 3, 4, and 7 of the 18 wk Dnmt1 blot with lanes 4, 5, 6, and 7 of the 36 wk Dnmt1 blot in Figure 2 (see slide 58<sup>545</sup>). This would not be scientifically valid as the lanes all represent different experimental conditions.
- 3. These blots have very distinct features in both the curvature and height of the bands. The high degree of similarity in overlay between them strongly suggests duplication rather than supporting an argument of similarity occurring by simple coincidence.
- 4. The similarity of bands occurring as a triplet lane sequence rather than as a single lane argues against coincidence or honest error.
- 5. There is a unique background artifact (i.e., a small dot) that appears above the band in lane 7, of 18 wk Dnmt1 blot, that is also present in lane 7 of the wk 36 Dnmt1 blot, strongly suggesting that the data have been duplicated and reused.
- 6. No original data for this figure were available.
- 7. The Committee finds the forensic evidence and visual inspection demonstrates duplication of lanes 2, 4, 7 in the wk 18 Dnmt1 blot as lanes 4-6, 7 in the wk 36 Dnmt1 blot, which the Committee concludes is indicative of falsification.
- 8. Dr. Ghoshal was first author of J. Nutr. 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of J. Nutr. 2006.

### Respondent's Response:

- 1. During her interview with the CII on March 5, 2018, Dr. Ghoshal disputed the exactness of the forensics overlay, feeling that the bands were similar but not identical.<sup>546</sup> Dr. Ghoshal offered a theory that high molecular weight samples run on the same gel would have a similar appearance.<sup>547</sup> The Committee pointed out that the bands appeared more than similar and that their similar appearance in sequence argued against false positive coincidence.<sup>548</sup> Dr. Ghoshal was unwilling to confirm or deny the possibility of copying and pasting without access to original data.<sup>549</sup> Generally, Dr. Ghoshal denied ever intentionally copying and pasting lanes from one experiment or figure into another.<sup>550</sup> Dr. Ghoshal stated that alterations to a figure were limited to brightness or contrast.<sup>551</sup> Dr. Ghoshal claimed that any such duplication would have been inadvertent<sup>552</sup> and that she did not recall making this specific figure.<sup>553</sup>
- 2. In his interview with the CII on March 5, 2018, senior corresponding author/laboratory PI, Dr. Jacob,

<sup>&</sup>lt;sup>545</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 58

<sup>&</sup>lt;sup>546</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 59 lines 4-6

<sup>&</sup>lt;sup>547</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 60 lines 9-12

<sup>&</sup>lt;sup>548</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 61 lines 1-6

<sup>&</sup>lt;sup>549</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 60 lines 16-20

<sup>&</sup>lt;sup>550</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 26 lines 5-9

<sup>&</sup>lt;sup>551</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 24 lines 23-24

<sup>&</sup>lt;sup>552</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 31 lines 15-16

<sup>&</sup>lt;sup>553</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 62 line 19



stated that he was not prepared to comment on the figure. 554

- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal agreed that the forensics demonstrated duplication, but could offer no explanation for the duplication as she did not have the original data available, and argued that no splice line was evident, which she believed should be present if copying/pasting had taken place.<sup>555</sup> Dr. Ghoshal indicated she had no recollection of who made the figure, but knew that she did not.<sup>556</sup> See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

# Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.
- 2. First author, Dr. Ghoshal, did not offer an explanation for the alleged duplications nor take responsibility for the generation of Figure 2. Generally, Dr. Ghoshal has espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content while the first author should take responsibility for every figure.
- 3. The duplications and shifting of lanes (control lanes 3 and 4 at 18 weeks repeated as experimental FM deficient diet lanes 5 and 6 at 36 weeks) would not be scientifically valid as the same bands represent not only different weeks but also different experimental conditions. Without original data, the Committee cannot determine to what extent the falsified data potentially changed the reported results and conclusions of the paper. However, these data are meant to support a major conclusion of the paper that folate and methyl deficiency alters hepatic DNA methylation machinery. As these are the only raw data shown in this manuscript (the rest are in tables), the data manipulation present calls into question the entire study.
- 4. The similarity of bands occurring as a triplet lane sequence rather than as a single lane argues against coincidence or honest error. This triplicate duplication, the additional duplication of a single lane, and finally the fact that the results were to have depicted control vs. treatment across different rats signifies to the Committee that the intention was to deceive the reader.
- 5. The Committee has determined that Dr. Jacob failed in his roles as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2 and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 2 in Allegation #19, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent recklessly reported falsified Dnmt1 images in Figure 2, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>554</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 42 lines 20-22

<sup>&</sup>lt;sup>555</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 56-58

<sup>&</sup>lt;sup>556</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 58, line 16-22

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent recklessly reported falsified Dnmt1 images in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #6, Allegation #20 - S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-2 and in lanes 7-8 of the 36 wk β-tubulin blot in Figure 2 in Ghoshal et al., J. Nutr. 2006.

This allegation was revised because the CII found that the forensic analysis showed reuse of the same blot to represent GFP in Figure 6C-1 (lanes 1-8 of a 9 lane blot) of Mol. Cell. Biol 2005, and  $\beta$  -tubulin in Figure 2 (lanes 1-8) of J. Nutr. 2006. (See also Allegation #11)

# **Finding of Fact:**

- 1. Figure 2 shows hepatic Dnmt1 and β-tubulin control Western blots of nuclear extracts from 4 control rats and 4 rats fed a diet deficient of methionine and devoid of folic acid and choline (FMD). β-tubulin, 36 wk lanes 1-2 represent control rats and lanes 7-8 represent FMD rats. Figure 6C-1, Mol. Cell. Biol, 2005 includes a GFP blot as a control for a Western blot of whole cell extracts from Cos-7 cells transfected with expression vectors for mutant Dnmt with GFP.
- 2. Adobe Photoshop overlay analysis showed significant similarity and overlap when comparing lanes 1-2 and lanes 7-8 of the 36 wk  $\beta$ -tubulin blots in Figure 2 (see slide  $59^{557}$ ). This would not be scientifically valid as the lanes represent different experimental conditions.
- 3. Adobe Photoshop overlay analysis also demonstrated significant similarity and overlap when comparing lanes 1-8 of the 36 wk  $\beta$ -tubulin blot in J. Nutr. 2006 (Manuscript #6) with lanes 1-8 of the GFP blot in Figure 6C-1 (Manuscript #3) (see slide  $60^{558}$ ).
- 4. Visual inspection of the bands reveals unique band shaping (e.g., upper left slant both on bands 1 and 7; middle notch in bands 2 and 8) that further supports the allegation that the same data has been reused.
- 5. The original data for these figures were not available.
- 6. The Committee finds the forensic evidence and visual inspection demonstrates internal duplication of lanes 1-2 as lanes 7-8 within the 36 wk β-tubulin blot in Figure 2 and also reuse of a span of eight lanes of the 36 wk β-tubulin blot in Figure 2 J. Nutr. 2006 (Manuscript #6) as the entirety of the GFP blot in Figure 6C-1 (Manuscript #3), which the Committee concludes is indicative of falsification.
- 7. Figure inconsistencies in Ghoshal et al., Mol Cell Biol. 2005 (Manuscript #3) were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then, PubPeer had published comments, corresponding to Allegation #11 discussed above and consequently allegation #20. This indicates Dr. Ghoshal knew of potential issues with the research for at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. As of late September 2017PubPeer had also published three (3) comments regarding J Nutr. 2006, corresponding to Allegations #19-20.
- 8. Dr. Ghoshal was first author of J. Nutr. 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of J. Nutr. 2006.

### Respondent's Response:

 During the interview with the CII on March 5, 2018, Dr. Ghoshal stated that it was possible that similar samples on the same gel would end up with a similar appearance.<sup>560</sup> Dr. Ghoshal also questioned whether the similarity might be a false positive, that is an artifact.<sup>561</sup> Dr. Ghoshal stated that her

<sup>&</sup>lt;sup>557</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 59

<sup>&</sup>lt;sup>558</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 60

<sup>&</sup>lt;sup>559</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>560</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 64 line 22

<sup>&</sup>lt;sup>561</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 65 lines 1-4

recollection of the specifics of a figure would be better if she had access to the original data.<sup>562</sup> In considering the allegation against Mol. Cell. Biol. 2005, Dr. Ghoshal ultimately acknowledged the lanes look similar, that the two manuscripts were being prepared for two different journals at the same time, and that it was possible that the wrong image got pasted into the wrong manuscript.<sup>563</sup>

- 2. In his interview with the CII, Dr. Jacob, was shown the forensic analysis but did not comment.
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal was questioned about this allegation in conjunction with discussion of Mol. Cell. Biol. 2005 and accepted the forensic findings of similarity. Dr. Ghoshal posited that a shared scanner folder containing blots could have resulted in a mistaken reuse of the same image for both manuscripts as they were both in development at the same time. Dr. Ghoshal did not recall who made the figure and indicated that the majority of the experiments for J. Nutr. 2006 were performed by the manuscript's second author, Xin Li. Sec.
- 5. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. First author, Dr. Ghoshal, did not take responsibility for generation of the questioned figures in either manuscript, but has maintained that an error may have occurred during figure generation.
- 2. β-tubulin serves as a normalization control for the experiment; however, the data is misrepresented because duplication of blots with control lanes 1 and 2 repeated as experimental lanes 7 and 8 would have the same bands representing different experimental conditions (i.e., control for lanes 1-4, FM deficient diet in lanes 5-8). The additional presence of the entire blot in an earlier publication (and representing a different protein) calls into question the validity of both publications. Because no original data exists for either publication, the Committee is unable to determine which publication may have been the source and therefore must conclude based on the preponderance of the evidence that they have both been falsified. Furthermore, without original data, it cannot be determined to what extent the findings impact on the conclusions of the paper. However, these data are meant to support a major conclusion of the paper that folate and methyl deficiency alters hepatic DNA methylation machinery. As these are the only raw data shown in this manuscript (the rest are in tables), the data manipulation present calls into question the entire study.
- 3. An internal duplication of lanes 1-2 as lanes 7-8 occurs in the β-tubulin blot in Figure 2. The β-tubulin blot in Figure 2 of J. Nutr. 2006 appears as eight lanes of a nine-lane blot representing GFP protein in Figure 6C-1 of Mol. Cell. Biol. 2005. Dr. Ghoshal's explanation that the wrong image was pasted into the wrong manuscript because the number of lanes was the same <sup>567</sup> is not valid nor plausible, as the number of lanes in Figure 6C-1 is nine while the number of lanes in Figure 2 of J. Nutr. 2006 is eight. Furthermore, her explanation does not account for the internal duplication.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose

<sup>&</sup>lt;sup>562</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 69 lines 13-14

<sup>&</sup>lt;sup>563</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 50-51

<sup>&</sup>lt;sup>564</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 42 line 7 to page 43 line 1; page 52 line 19 to page 54 line 21

<sup>&</sup>lt;sup>565</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 43 line 1-13; page 46 line 23 to page 47 line 1

<sup>&</sup>lt;sup>566</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 42 line 5-7; page 45 line 8 to page 47 line 8; page 50 line 18-25

<sup>&</sup>lt;sup>567</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 51, lines 7-12



this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness.

- 5. The Committee has determined that Dr. Jacob failed in his roles as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2 and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 2 in Allegation #20, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent recklessly reported falsified  $\beta$ -tubulin images in Figure 2, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent recklessly reported falsified  $\beta$ -tubulin images in Figure 2, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #7 under Review - Majumder et al., JBC 2006 (3 Allegations)

Majumder S\*, Ghoshal K\*, Datta J, Smith DS, Bai S, Jacob ST." Role of DNA methyltransferases in regulation of human ribosomal RNA gene transcription." J Biol Chem. 2006 Aug 4; 281 (31): 22062-72. Epub 2006 May 30. **RETRACTED - 02/13/18** \* **co-first authors** 

**Manuscript #7, Allegation #47 -** S.T. Jacob reported falsified data by reuse of same data in lane 2, lane 3, and lane 6 in Figure 6C in Majumder et al., J Biol Chem 2006.

#### Finding of Fact:

- Figure 6C is a Western blot analysis of HeLa cells transfected with wild-type and deletion mutants to monitor the expression of Dnmt3b and determine the domains on Dnmt3b involved in the transcriptional repression of the ribosomal RNA gene promoter (rDNA). Figure 6C, lane 2 is wild-type and lanes 3 and 6 are different mutants, ΔCAT and ΔN-term.
- 2. Adobe Photoshop gradient mapping, performed by JBC, showed significant similarity between the bands, strongly suggesting that duplication had occurred (see slide 62<sup>568</sup>). Adobe Photoshop overlay analysis, performed by OSU, demonstrates significant similarity and overlap of lane 2 reused in lane 3 (when flipped vertically) and again as lane 6 (when flipped vertically) in Figure 6C. This is further apparent in the near perfect overlay of lane 6 on lane 3 (see yellow boxes, slide 63<sup>569</sup>). Furthermore, Adobe Photoshop overlay analysis, performed by OSU, demonstrates significant similarity and overlap of the lower band in lane 2 reused as the lower band in lane 3 (when rotated 180°) in Figure 6C.
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 6C) within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>570</sup> Dr. Jacob subsequently notified Dr.

<sup>&</sup>lt;sup>568</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 62

<sup>&</sup>lt;sup>569</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 63

<sup>&</sup>lt;sup>570</sup> Ex. 277 - 20170630- Email JBC to Jacob

Ghoshal the same day<sup>571, 572</sup> and Dr. Majumder on July 2, 2017.<sup>573</sup> All authors, including Dr. Majumder, were notified in follow-up directly by JBC on July 31, 2017.<sup>574</sup> As such, the co-first and corresponding authors knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.

- 4. Dr. Jacob sent a formal response to JBC on October 26, 2017. 575, 576
- 5. No original data were available for this figure.
- 6. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lane 2 as both lanes 3 and 6 (via 180° rotation and vertical flip, respectively) in Figure 6C, which the Committee concludes is indicative of falsification.
- 7. Dr. Sarmila Majumder was co-first and co-corresponding author of JBC 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Kalpana Ghoshal was co-first author of JBC 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2006.

# Respondent's Response:

- This allegation was added to the Inquiry after the initial interviews of Dr. Jacob and Dr. Majumder upon retraction of the manuscript by JBC. Co-first author Dr. Kalpana Ghoshal was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 2. Dr. Jacob later acknowledged the apparent duplications. In a written response provided to ORC on April 19, 2018, Dr. Jacob, writes:

"In Fig. 6C, we have shown expression of different truncation mutants of Flag-tagged DNMT3B. In absence of the original figure, we are not certain why gel splices were used to create the figure. However, Bai et.al (who generated the mutants) from our lab have published western blot analysis of different DNMT3B mutants including ones following ectopic expression in the year 2005 [Mol Cell Biol. 2005 Jan; 25(2): 751–766.Fig. 6A] and 2006 [J Biol Chem. 2006 May 12; 281(19): 13604-11 (Fig. 4E, lower panel and Fig. 4F, lower panel)]. In absence of the original gel picture used in Fig. 6C, we would like to remove the figure from the paper and refer to the paper by Bai.et.al in the "Result" section." 577

- 3. Dr. Jacob's response provided to ORC on April 19, 2018 was the same as that provided to JBC on October 26, 2017.<sup>578, 579, 580</sup>
  - a. The response to both JBC and ORC cited Bai et al., Mol Cell Biol. 2005 (Manuscript #4) as containing confirmatory results for the figure in question here in Manuscript #7. As such, Dr. Jacob knew of potential issues with Bai et al., Mol Cell Biol. 2005 (Manuscript #4) (upon being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry) when he then used the publication to defend Majumder et al. JBC 2006. Six months later (on April 19, 2018), Dr. Jacob again uses Bai et al., Mol Cell Biol 2005 (Manuscript #4) to defend Majumder et

<sup>&</sup>lt;sup>571</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>572</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW\_ JBC articles

<sup>&</sup>lt;sup>573</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>574</sup> Ex. 487 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles Majumder 2006

<sup>&</sup>lt;sup>575</sup> Ex. 324 - 20171026 - Email Jacob to JBC - JBC response Majumder 2006

<sup>&</sup>lt;sup>576</sup> Ex. 154 - Response-Majumder 2006-JBC601155-220-M-102517

<sup>&</sup>lt;sup>577</sup> Ex. 154 - Response-Majumder 2006-JBC601155-22-M-102517

<sup>&</sup>lt;sup>578</sup> Ex. 324 - 20171026 - Email Jacob to JBC - JBC response Majumder 2006

<sup>&</sup>lt;sup>579</sup> Ex. 154 - Response-Majumder 2006-JBC601155-220-M-102517

<sup>&</sup>lt;sup>580</sup> Ex. 149 - Cover letter .4.19.18 pdf

- al., JBC 2006 (Manuscript #7) to OSU when Manuscript 7 was added to the scope of the research misconduct inquiry. Though the particular figure of reference in Bai et al., Mol Cell Biol. 2005 (Manuscript #4) (Figure 6A) was not the subject of research misconduct allegations, five (5) of 29 figure panels within Manuscript #4 were already the subject of concern on October 26, 2017 when Dr. Jacob reported them to JBC, as well as later on April 19, 2018 when Dr. Jacob proposed that manuscript's data to OSU as an adequate replacement for Figure 6C in Majumder et al., JBC 2006 (Manuscript #7).<sup>581</sup>
- b. The October 2017 response to JBC's concerns further cited Bai et al., JBC 2006 (Manuscript #16) as containing confirmatory results for the figure in question in Manuscript #7. Dr. Jacob was aware that Bai et al. JBC 2006 was already the subject of concern by the journal itself, having received formal notice of concerns with figures 2B, 3B, and 5A from JBC on June 30, 2017. Dr. Jacob knew of potential issues with Bai et al., JBC 2006 (Manuscript #16) when he then used the publication to defend Majumder et al. JBC 2006. Six months later (on April 19, 2018), with both manuscripts retracted, Dr. Jacob again used Bai et al., JBC 2006 (Manuscript #16) to defend Majumder et al., JBC 2006 (Manuscript #7) to OSU when each manuscript (#7 and #16) was added to the scope of the research misconduct inquiry. Though the particular figures of reference in Bai et al., JBC 2006 (Manuscript #16) (Figures 4E and 4F) were not the subject of research misconduct allegations at the time, three (3) of 23 figure panels within Manuscript #16 were already the subject of concern on October 26, 2017 when Dr. Jacob reported them to JBC, and the manuscript had already been retracted by April 19, 2018 when Dr. Jacob proposed that manuscript's data as an adequate replacement for Figure 6C in Majumder et al., JBC 2006 (Manuscript #7).
- 4. In her written response provided to ORC on July 26, 2018, Dr. Majumder stated that Dr. Jacob already provided a response and she had nothing further to add regarding this allegation. Dr. Majumder indicated that she did not remember doing this experiment or preparing the figure, but that they are "honest and correctable errors [that] did not change the interpretation or conclusions of the paper." 583
- 5. In her response to the CII's preliminary report<sup>584</sup> and her appeal of their determination,<sup>585</sup> Dr. Majumder disagreed with the allegation, reiterated her belief in the limitations of forensic analysis, and defended Figure 6C with the argument that duplication could not have taken place without splice lines being evident.<sup>586</sup> Dr. Majumder again denied memory of personally performing the experiment or preparing the figure.
- 6. In her interview with the COMIC on June 12, 2019, Dr. Majumder did not recall who generated Figure 6C, but clearly remembered which figures she generated, none of which happen to have any allegations of falsification against them.<sup>587</sup>
- 7. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 8. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 9. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.

<sup>&</sup>lt;sup>581</sup> A sixth panel was later added to the research misconduct allegations as Allegation #77 on May 23, 2019.

<sup>&</sup>lt;sup>582</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>583</sup> Ex. 100 - Response-OSU-07262018

<sup>&</sup>lt;sup>584</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 5-6

<sup>&</sup>lt;sup>585</sup> Ex. 252 - Majumder Zadnik-letter-111218

These arguments were refuted by evidence found by the Committee where, in multiple instances, splice lines were not visibly detected, despite clear evidence or testimony that splicing had taken place (e.g., see <u>Allegation #5</u>, <u>Allegation #28</u>, and <u>Allegation #29</u> below) suggesting that the Respondents had sufficient skill when manipulating the images to mask splice and/or cut/paste lines.

<sup>&</sup>lt;sup>587</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 42-46

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors have taken responsibility for generation of Figure 6C, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. Without original data, the COMIC is not able to determine the significance of the duplication and how it may have altered the interpretation and conclusions of the manuscript. Regardless, reuse of a single image to represent three different experimental conditions would not be scientifically valid and argues against the duplication occurring as a result of an honest error. Furthermore, the rotation and flipping of that band also argues against an honest cut/paste error and suggests that the single lane was specifically reused to present the data in a manner so as to deceive the reader.
- 3. Dr. Jacob seemingly acknowledged that the data was spliced together when he proposed to JBC that, "...we are not certain why gel splices were used to create the figure...In absence of the original gel picture used in Fig. 6C, we would like to remove the figure from the paper and refer to the paper by Bai.et.al in the "Result" section." The Committee believes that Dr. Jacob's admission to and careful selection of the words "gel splices" does not reflect a straight splicing as may have been allowable at the time of publication in 2006, but rather obfuscates the actual falsification by the flipping, rotating, and reuse of multiple bands within the figure. The Journal of Biological Chemistry similarly rejected Dr. Jacob's argument and required the retraction of the manuscript.
- 4. It should be noted that one paper to which he referred for confirmatory results is also included in this Investigation as Manuscript 4 (Bai et al., Mol. Cell. Biol. 2005), a fact that would have been known to Dr. Jacob at the time of his correspondence with JBC. Furthermore, a second paper to which he referred for confirmatory results (Bai et al., JCB 2006; Manuscript #16) was also the subject of concurrent concern by JBC. The Committee has serious reservations about Dr. Jacob's judgement to refer journal editors with concerns in one of his published manuscripts (i.e., Manuscript #7, Majumder et al., JBC 2006) to the results of other publications he knows to be of concern in a Research Misconduct proceeding (i.e., Manuscript #4, Bai et al., Mol Cell Biol 2005) or of concern to the journal itself (i.e. Manuscript #16, Bai et al., JBC 2006, which then became the subject of this research misconduct inquiry/investigation upon its retraction). The Committee believes that the preservation of publications appears to be compelling Dr. Jacob more than critically reviewing the people working on his behalf and potentially fraudulent results emanating from his laboratory.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication, but that, based on consistent witness testimony, Dr. Jacob was not responsible for the falsification of Figure 6C itself. However, the Committee has determined that Dr. Jacob admitted to figure manipulation and was on notice of the significantly increased risk of falsified information being generated/used in his laboratory (based on the fact that he had been contacted by the Journal of Biological Chemistry to address concerns with multiple manuscripts (including Manuscript #16) in June 2017 and had already been informed of research misconduct proceedings against Manuscript #4 on October 18, 2017) and acted recklessly in disregarding that risk and reporting research results in defense of Majumder et al, JBC 2006 to the Journal of Biological Chemistry on October 26, 2017. The Committee believes that the entirety of the manuscripts and responses to JBC should have been meticulously reviewed for additional errors by the authors before submitting responses and revised figures to the Journal of Biological Chemistry, and in not doing so, Dr. Jacob deviated from the accepted practices of typical researchers in the biomedical field.
- 6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

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<sup>&</sup>lt;sup>588</sup> Ex. 154 - Response-Majumder 2006-JBC601155-220-M-102517

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified data in and for Figure 6C, and therefore this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 5 in favor and 2 against, that the Respondent recklessly reported falsified data in and for Figure 6C, and therefore this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #7, Allegation #78 –** S.T. Jacob reported falsified data by the presence of splice lines between lanes 1 and 2 of the Nucleolin blot in Figure 2B in Majumder et al., J Biol Chem 2006.

### **Finding of Fact:**

- 1. Figure 2B is a Western blot of nucleolin, Dnmt1, Dnmt3a, Dnmt3b, and RNA Pol II in both nucleolar and nuclear extracts of HeLa cells.
- 2. Adobe Photoshop gradient map analysis demonstrates a splice line between lanes 1 and 2 of the Nucleolin blot in Figure 2B (see slide 64-65<sup>589</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day and Dr. Majumder on July 2, 2017. All authors, including Dr. Majumder, were notified in follow-up directly by JBC on July 31, 2017. As such, the co-first and corresponding authors knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 26, 2017. Sep. 596
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a line between lanes 1 and 2 in the Nucleolin blot in Figure 2B, which the Committee concludes represents a splice line and could be indicative of falsification.
- 6. Dr. Sarmila Majumder was co-first and co-corresponding author of JBC 2006 and a Research Scientist (2007) in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Kalpana Ghoshal was co-first author of JBC 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2006.

### Respondent's Response:

- 1. As this allegation was added during the course of the Investigation, no responses from Drs. Jacob, Ghoshal, or Majumder exist from the Inquiry stage of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, Dr. Jacob argued:
  - "1. If there is splicing, one should expect splice line through the lane. If there is an apparent line at the upper and lower edge of these two lanes, it is how this gel ran and does not involve any manipulation. We could have easily authenticated it if we had the raw data.
  - 2. It should also be noted that JBC software did not pick up this problem." 597

<sup>&</sup>lt;sup>589</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 64-65

<sup>&</sup>lt;sup>590</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>591</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>592</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW\_ JBC articles

<sup>&</sup>lt;sup>593</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>594</sup> Ex. 487 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles Majumder 2006

<sup>&</sup>lt;sup>595</sup> Ex. 324 - 20171026 - Email Jacob to JBC - JBC response Majumder 2006

<sup>&</sup>lt;sup>596</sup> Ex. 154 - Response-Majumder 2006-JBC601155-220-M-102517

<sup>&</sup>lt;sup>597</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

- 3. Dr. Jacob did not address this allegation during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1, #3-7 above.
- 4. In written documentation provided to OSU via her legal counsel on June 7, 2019, <sup>598</sup> Dr. Majumder argued that the concern with Figure 2B was not brought forward by JBC, "suggesting there should be no concern about the figure." Dr. Majumder maintained that she was unable to find the raw data and has no memory of conducting the experiment or preparing the figure, but based on her current knowledge would opine that a clear line between lanes 1 and 2 of the Nucleolin blot in Figure 2B appears because "that is how the gel ran and that there is no falsification of data."
- 5. In her interview with the COMIC on June 12, 2019, Dr. Majumder did not recall who generated Figure 2, but clearly remembered which figures she generated, none of which happen to have any allegations of falsification against them. <sup>599</sup> Dr. Majumder further indicated that this allegation of splicing was not brought up by JBC and that,

"And I don't really -- I see a sharp, I would say even a sharp -- there are like, even in the black and white picture, there are some sharp white places, but even if there's splicing, there is no space between the two lanes. So I would have a hard time to believe there was splicing." 600

Furthermore, when questioned by the COMIC if splicing in this figure would concern her, Dr. Majumder indicated that she could not make an assertion without the raw data. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

6. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors have taken responsibility for generation of Figure 2B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. It is the Committee's understanding that the standards in the field at the time of this 2006 publication may not have been to require demarcation of non-contiguous bands, and the alleged splice is visible to the naked eye. In permitted instances, the splice line would be expected to run all the way down through the complete set of blots, which is not the case in Figure 2B.
- 3. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2B and that the actions of others caused the splicing within Figure 2B in Allegation #78, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

<sup>&</sup>lt;sup>598</sup> Ex. 350a - 2019-06-07 Pre-Interview Submision Majumder, pages 6-7, 9-10; see page 10

<sup>&</sup>lt;sup>599</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 44-46

<sup>600</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 47 line 8-13

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 2B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figure 2B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #7, Allegation #79 –** S.T. Jacob reported falsified data by the presence of a possible erasure in the first RNA Pol II blot (Nucleolus) in Figure 2B in Majumder et al., J Biol Chem 2006.

# **Finding of Fact:**

- 1. Figure 2B is a Western blot of nucleolin, Dnmt1, Dnmt3a, Dnmt3b, and RNA Pol II in both nucleolar and nuclear extracts of HeLa cells.
- 2. Adobe Photoshop gradient map analysis demonstrates irregularity in the background as well as sharp horizontal lines at the top and bottom of the space where you would expect the band to be, which suggest potential pasting of a blank background in the Nucleolus sample of the RNA Pol II blot or some other erasure in Figure 2B (see slide 64-65<sup>601</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day and Dr. Majumder on July 2, 2017. All authors, including Dr. Majumder, were notified in follow-up directly by JBC on July 31, 2017. As such, the co-first and corresponding authors knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 26, 2017. Dr. 608
- 4. No original data for this figure were available
- 5. The Committee finds the forensic evidence and visual inspection of the allegedly blank lane indicative of falsification.
- 6. Dr. Sarmila Majumder was co-first and co-corresponding author of JBC 2006 and a Research Scientist (2007) in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Kalpana Ghoshal was co-first author of JBC 2006 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2006.

# Respondent's Response:

1. As this allegation was added during the course of the Investigation, no responses from Drs. Jacob, Ghoshal, or Majumder exist from the Inquiry stage of the case.

 $<sup>^{601}</sup>$  Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 64-65

<sup>&</sup>lt;sup>602</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>603</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>604</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>605</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>606</sup> Ex. 487 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles Majumder 2006

<sup>&</sup>lt;sup>607</sup> Ex. 324 - 20171026 - Email Jacob to JBC - JBC response \_Majumder 2006

<sup>&</sup>lt;sup>608</sup> Ex. 154 - Response-Majumder 2006-JBC601155-220-M-102517

- 2. In written documentation provided to OSU via her legal counsel on June 7, 2019,<sup>609</sup> Dr. Majumder argued that the concern with Figure 2B was not brought forward by JBC, "suggesting there should be no concern about the figure." Dr. Majumder maintained that she was unable to find the raw data and has no memory of conducting the experiment or preparing the figure, but based on her current knowledge would firmly opine "that there is no erasure as it is not apparent in the figure."
- 3. In written documentation provided to OSU via his legal counsel on July 15, 2019, Dr. Jacob indicated that he did not believe any erasure was evident in this figure. Dr. Jacob did not address this allegation during his interview with the COMIC on July 17, 2019. See also Dr. Jacob's General Respondent/Witness statements #1, #4-7 above.
- 4. In her interview with the COMIC on June 12, 2019, Dr. Majumder did not recall who generated Figure 2B, but clearly remembered which figures she generated, none of which happen to have any allegations of falsification against them. Dr. Majumder further indicated that this issue was not brought up by JBC and that she was not convinced an erasure had taken place. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

### Respondent's Responsibility:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors have taken responsibility for generation of Figure 2B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Majumder was also co-corresponding author on this publication.
- 2. Erasure of a band from a figure and/or pasting a blank background into a figure would be an intentional action, whether it was done in an effort to beautify the image or significantly alter the presented results so as to deceive the reader. Erasure would be an intentional act, and was not a permitted practice in 2006, nor is it now.
- 3. Without original data, the COMIC is not able to determine if the erasure was performed to remove extraneous data or non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 2B and that the actions of others caused the falsification within Figure 2B in Allegation #79, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified RNA Pol II data in Figure 2B,

<sup>&</sup>lt;sup>609</sup> Ex. 350a - 2019-06-07 Pre-Interview Submission Majumder, pages 6-7, 9-10; see page 10

<sup>&</sup>lt;sup>610</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 24

<sup>611</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 44-46

<sup>&</sup>lt;sup>612</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 47 line 2-15

and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified RNA Pol II data in Figure 2B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

# Manuscript #8 under Review - Bai et al., JBC 2007 (8 Allegations)

Bai S, Datta J, Jacob ST, Ghoshal K. "Treatment of PC12 cells with nerve growth factor induces proteasomal degradation of T-cadherin that requires tyrosine phosphorylation of its cadherin domain. J Biol Chem. 2007 Sep 14; 282 (37): 27171-80. Epub 2007 Jul 13. **RETRACTED-02/13/18** 

**Manuscript #8, Allegation #23 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-4 and in lanes 5-8 of the GAPDH blot in Figure 2C in Bai et al., J Biol Chem 2007.

### **Finding of Fact:**

- 1. Figure 2C is a Western blot for T-Cad in PC-12 cells, untreated or treated with NGF and cyclohexamide for 1, 2 or 4 hr to monitor the half-life of endogenous T-Cad. GAPDH is used as a loading control.
- 2. Adobe Photoshop overlay analysis shows significant similarity and overlap when comparing lanes 1-4 and lanes 5-8 of the GAPDH blot in Figure 2C (see slide 68<sup>613</sup>). This would not be scientifically valid as these lanes represent different experimental conditions.
- 3. The band shapes are very distinctive and the repetition occurring in a sequence of four lanes rather than in isolation strongly suggests that the similarity is not due to coincidence. The blot has very distinctive background artifacts (e.g., vertical marks and dots) that appear above the bands in lanes 1-2 and are also present in lanes 5-6.
- 4. No original data for the figure were available
- 5. The Committee finds the forensic evidence and visual inspection demonstrate reuse of the same data in lanes 1-4 and in lanes 5-8 of the GAPDH blot in Figure 2C, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob received formal notice of concerns with figures (including Figure 2C) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day. Figure inconsistencies in Bai et al., JBC 2007 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then,, PubPeer had published four (4) comments, corresponding to Allegations #23-27. As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Jacob sent a formal response to JBC on October 19, 2017.618, 619
- 8. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

# Respondent's Response:

<sup>613</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 68

<sup>&</sup>lt;sup>614</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>615</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>616</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>617</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>618</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response \_Bai 2007

<sup>619</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

- 1. During her interview with the CII on March 5, 2018, the final author, Dr. Ghoshal, stated that she did not recall who made the figure, 620 and that if there was duplication of bands that it would be due to human error. 621 Dr. Ghoshal was hesitant to offer any further perspectives without access to the original data, 622 but admitted that the presence of a line might indicate splicing that may also have included inadvertent duplication of the four lanes. 623
- 2. In a written response provided to ORC on April 19, 2018, 625 Dr. Jacob indicated that in general the lab tried to retrieve as much data as possible and tried to keep all original data for 5-6 years as was consistent with university, federal, and journal guidelines. However, Dr. Jacob stated that a computer with a large volume of their original data had crashed. Dr. Jacob indicated that he did not have access to the original figures and was not involved in their preparation. Dr. Jacob further maintained that no figures or images were intentionally manipulated; that splicing of a figure to remove duplicate samples was allowed by many journals in the past without requiring that vertical lines be provided to indicate splicing; that any minor errors are few in comparison to the high number of figures/lanes included in a publication, errors are inadvertent, are correctable, and do not impact the overall conclusions of the paper; that there has been no plagiarism in any paper published from their laboratory; and that the reproducibility of their work has never been an issue. 626, 627 Specifically, Dr. Jacob stated,

"This is about GAPDH normalizer in first 4 lanes duplicated in the last 4. Since we were unable to find this blot, we could not submit a corrected figure. However, the results of this experiment complements the results in Fig. 2A, B (pulse-chase studies) that demonstrated reduced half-life of T-cad after NGF treatment." 628

- Dr. Jacob's response provided to ORC on April 19, 2018 was the same as that provided to JBC on October 19, 2017. 629, 630
- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 6. First author, Dr. Shoumei Bai, provided witness statements via written communication with the COMIC.<sup>631</sup> Dr. Bai generally maintained that she has no access to any original data and does not have a memory from which she can answer specific questions relating to research,<sup>632</sup>

Regarding duplication, Dr. Bai indicated:

<sup>620</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 70 line 24

<sup>621</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 69 lines 18-19

<sup>622</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 70 lines 14-15, 20

<sup>623</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 72 lines 4-7

<sup>625</sup> Ex. 149 - Cover letter .4.19.18 pdf

<sup>626</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>627</sup> Ex. 149 - Cover letter .4.19.18 pdf

<sup>628</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 1

<sup>629</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>630</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>631</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>632</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible. It is possible that in some instances the same control was appropriately used in more than one figure in a publication, such as where the same samples/gels were used for data presented in separate figures. It is possible that like any human we could have made inadvertent errors while preparing figures for manuscripts but I do not believe anyone I worked with made up any research results." 633

7. Dr. Jacob's January 20, 2021 response to the preliminary report claimed that he could not have been responsible for identifying duplications of loading controls when forensic analysis was not available to him and that at least one committee member had conceded this point.<sup>634</sup> However, it must be noted that the portion of the interview to which Dr. Jacob refers does not make reference to a necessity for forensic analysis, but rather includes statements by a committee member that controls were often overlooked or not scrutinized during the peer review process and that considering them more carefully (including a comparison of the figures to the raw data) would have shed light on the figure manipulations.<sup>635</sup>

- 1. The alleged duplication is visible to the naked eye and would have been obvious had Drs. Jacob and/or Ghoshal reviewed the figure prior to publication.
- 2. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 3. Dr. Ghoshal has not taken responsibility for the generation of Figure 2C, but has generally espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content while the first author should take responsibility for every figure. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 2C.
- 5. Figure 2C was used in the publication to support the hypothesis that NGF significantly reduces the half-life of T-Cad. This is the main point of the paper, and as such, the data falsification impacts the scientific validity of the entire paper. The falsified data may have drastically changed the reported results because it is impossible to know if NGF truly reduced levels of T-Cadflag without original data. Because the blot is unreliable, the quantification data in Figure 2D are also not scientifically valid. The argument that these data match prior data in the paper is not sufficient to prove the veracity of the figure in question. Given the number of allegations within and across figures in this manuscript, the Committee believes that it is more likely than not that this duplication is not the result of honest error.
- 6. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.

<sup>633</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

<sup>634</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), page 21-22

<sup>635</sup> Ex. 293 - 20190717 - COMIC Interview + errata - Jacob, page 15-16

- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication and that the actions of others caused the falsification within Figure 2C in Allegation #23, as described above. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2C itself. However, the distinctive band shapes and background artifacts and the repetition occurring in a sequence of four lanes (lanes 1-4) reappearing immediately adjacent (lanes 5-8) is so obvious that the majority of voters determined that Dr. Jacob did act recklessly, at the preponderance of the evidence standard, in his oversight of this project. They believe that so blatantly failing to review the figure and identify such a visible data duplication represents a significant departure from community standards.
- 8. The Committee agreed that the duplications were obvious, however, the lack of consensus centered on the attribution/state of mind required for a finding. The dissenting voters found Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, but did not believe that this rose to the level of recklessness as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 9. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 4 in favor and 3 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified GAPDH data in Figure 2C, and this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified GAPDH data in Figure 2C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #8, Allegation #24 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 4 of the NS blot in Figure 3C in Bai et al., J Biol Chem 2007.

#### **Finding of Fact:**

- 1. Figure 3C is a Western blot for T-Cadflag in PC-12 cells untreated or treated with NGF and chloroquine, a lysosomal protease inhibitor. NS, nonspecific band, serves as a loading control.
- 2. Adobe Photoshop overlay analysis demonstrates significant similarity and overlap when comparing lane 1 and lane 4 in the NS (non-specific) blot in Figure 3C (see slide 69<sup>636</sup>). This would not be scientifically valid as the same data is reused to represent two different experimental conditions.
- 3. The original data for this figure were not available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lane 1 as lane 4, which the Committee concludes is indicative of falsification.
- 5. Dr. Jacob received formal notice of concerns with figures (including Figure 3C) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day. Figure inconsistencies in Bai et al., JBC 2007 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then,, PubPeer had published four (4) comments, corresponding to Allegations #23-27. As such, Drs. Jacob and Ghoshal

<sup>636</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 69

<sup>637</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>638</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>639</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW\_ JBC articles

<sup>&</sup>lt;sup>640</sup> These data are reviewed elsewhere under DIO 6819.

knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.

- Dr. Jacob sent a formal response to JBC on October 19, 2017.641, 642
- 7. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

### Respondent's Response:

1. During the interview with the CII on March 5, 2018, Dr. Ghoshal stated that she did not make the figure and that she could not recall who did.<sup>643</sup> Dr. Ghoshal stated that the bands looked similar but she did not have the data in order to able to comment further on whether there was or was not duplication of the blot.<sup>644</sup>

However, when asked specifically if Dr. Bai, the first author, made the figure, Dr. Ghoshal responded, "No, I don't remember how it happened, whether—whether indeed there was duplication." 646

- Dr. Jacob's general statements regarding Manuscript #8 can be found above in the analysis for Allegation #23. Specifically for Figure 3C, Dr. Jacob only indicated "we could not find the original data." This response was the same as that provided to JBC on October 19, 2017. 648, 649
- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 5. In written communication with the COMIC,<sup>650</sup> the first author, Dr. Shoumei Bai indicated that she has no access to any original data and that experiments were repeated multiple times for accuracy, with results tested via multiple methods such that lab members were confident the results were reproducible though inadvertent human errors were possible. Furthermore she could not affirm duplication of any image, believed bands of normalizers could look very similar, and deemed duplication impossible in the absence of visible splicing.<sup>651</sup>

- 1. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- Dr. Ghoshal has not taken responsibility for the generation of Figure 3C, but has generally espoused the
  view that the corresponding author on a publication is responsible for its scientific integrity and content
  while the first author should take responsibility for every figure. The COMIC believes, as seemingly do

<sup>641</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>642</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>643</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 73 line 1; page 74 line 9

<sup>644</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 74 line 5, lines 9-11

<sup>&</sup>lt;sup>646</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 74, lines 7-11

<sup>647</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 1

<sup>648</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>649</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>650</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>651</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2



the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.

- 3. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 3C.
- 4. Figure 3C was used in the publication to support the hypothesis that T-Cadflag is not degraded by a lysosomal protease. Without a proper control, this conclusion cannot be drawn. The Falsified data may have a significant impact on the reported results by making it impossible to know if T-Cadflag is or is not degraded by a lysosomal protease. Reuse of a single image to represent two different experimental conditions would not be scientifically valid and compromises the integrity of the paper. Without original data, the COMIC is not able to determine if the duplication was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome. Given the number of allegations within and across figures in this manuscript, the Committee believes it is more likely than not that this duplication is not the result of honest error.
- 5. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee has determined, based on witness testimony, that Dr. Jacob was not responsible for the falsification of Figure 3C and that the actions of others caused the falsification within Figure 3C in Allegation #24, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 7. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 3C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 3C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #8, Allegation #25 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-3 and in lanes 6-8 of the NS blot in Figure 3E in Bai et al., J Biol Chem 2007.

#### Finding of Fact:

- Figure 3E is a Western blot for T-Cadflag in PC-12 cells untreated or treated with NGF for 12, 24, 36, or 48 hr and the proteasomal inhibitor, ZLLL, for 12 or 24 hr. NS, nonspecific band, serves as a loading control.
- 2. Adobe Photoshop overlay analysis showed significant similarity and overlap when comparing lanes 1-3

and lanes 6-8 of the NS blot in Figure 3E (see slide 70<sup>652</sup>). This would not be scientifically valid as the same data has been reused in the NS blot to demonstrate different experimental conditions. The repetition of the overall pattern seen within the group of three lanes rather than as single lanes in isolation, argues very strongly for intentional duplication.

- 3. The original data for this figure were not available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of lanes 1-3 as lanes 6-8 of the NS blot in Figure 3E, which the Committee concludes is indicative of falsification.
- 5. Dr. Jacob received formal notice of concerns with figures (including Figure 3E) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day. Figure inconsistencies in Bai et al., JBC 2007 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then,, PubPeer had published four (4) comments, corresponding to Allegations #23-27. As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 6. Dr. Jacob sent a formal response to JBC on October 19, 2017. 657, 658
- 7. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

# Respondent's Response:

- During her interview with the CII on March 5, 2018, Dr. Ghoshal stated that she did not make the figure and had no further comments to offer without seeing the raw, original data.<sup>659</sup> However, Dr. Ghoshal admitted the bands looked very similar to each other.<sup>660</sup>
- Dr. Jacob's general statements regarding Manuscript #8 can be found above in the CII analysis for <u>Allegation #23</u>. Specifically for Figure 3E (and Figure 3A), Dr. Jacob indicated the issue is about common, nonspecific bands, however they could not find the original data. 662, 663 This response is the same as that provided to JBC on October 19, 2017. 664, 665
- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 5. In written communication with the COMIC, 666 first author, Dr. Shoumei Bai indicated that she has no

<sup>652</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 70

<sup>653</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>654</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>655</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>656</sup> These data are reviewed elsewhere under DIO 6819.

<sup>657</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>658</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>659</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 75 lines 6-7, page 74 lines 22-24

<sup>660</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, pages 74-75 lines 24-1

<sup>662</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>663</sup> Ex. 149 - Cover letter .4.19.18 pdf

<sup>664</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>665</sup> Ex. 151 - JBC M700691200\_Bai 2007-10172017

<sup>666</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

### access to any original data

6. Dr. Jacob's January 20, 2021 response to the preliminary report claimed that he could not have been responsible for identifying duplications of loading controls when forensic analysis was not available to him and that at least one committee member had conceded this point.<sup>668</sup> However, it must be noted that the portion of the interview to which Dr. Jacob refers does not make reference to a necessity for forensic analysis, but rather includes statements by a committee member that controls were often overlooked or not scrutinized during the peer review process and that considering them more carefully (including a comparison of the figures to the raw data) would have shed light on the figure manipulations.<sup>669</sup>

- 1. The alleged duplication is visible to the naked eye and would have been obvious had Drs. Jacob and/or Ghoshal reviewed the figure prior to publication.
- 2. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 3. Dr. Ghoshal has not taken responsibility for the generation of Figure 3E, but has generally espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content while the first author should take responsibility for every figure. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 3E.
- 5. Figure 3E was used in the publication to support the hypothesis that T-Cadflag is degraded by a proteosomal process. The falsified data significantly impacts the reported results by making it impossible to determine if the proteosomal inhibitor ZLLL truly prevents T-Cadflag breakdown. The NS blot serves as controls for different experimental conditions. The manipulations have the same blots representing different time points and experimental conditions of exposure to ZLLL (absent in lane 2, but present in lane 7; present in lane 3, but absent in lane 8). Because the control bands are manipulated and unreliable, the quantification data presented in Figure 3F are also unreliable.
- 6. The similarity of bands occurring as a triplet lane sequence rather than as single lane argues against coincidence or honest error. This triplicate duplication and the fact that the results were to have depicted different treatments and different time points signifies to the Committee that the intention was to deceive the reader. Given the number of allegations within and across figures in this manuscript, the Committee believes it is more likely than not that this duplication is not the result of honest error.
- 7. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose

<sup>668</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), page 21-22

<sup>669</sup> Ex. 293 - 20190717 - COMIC Interview + errata - Jacob, page 15-16

<sup>&</sup>lt;sup>670</sup> Ex. 12 - Bai et al., JBC 2007, page 5 (i.e. journal page 27175)

this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.

- 8. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication and that the actions of others caused the falsification within Figure 3E in Allegation #25, as described above. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 3E itself. However, the repetition occurring in a sequence of three lanes (lanes 1-3) and reappearing so closely adjacent (lanes 6-8) is so obvious that the majority of voters determined that Dr. Jacob did act recklessly, at the preponderance of the evidence standard, in his oversight of this project. They believe that so blatantly failing to review the figure and identify such a visible data duplication represents a significant departure from community standards.
- 9. The Committee agreed that the duplications were obvious, however, the lack of consensus centered on the attribution/state of mind required for a finding. The dissenting voters found Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, but did not believe that this rose to the level of recklessness as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 10. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 4 in favor and 3 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 3E, and that this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 3E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #8, Allegation #26 - S.T. Jacob reported falsified data by the reuse of the same data in lanes 5-6, and lanes 8-9, and in lanes 10-11 in the  $\beta$ -tubulin blot in Figure 5C; and also the reuse of same data in lane 4 and in lane 7 of the  $\beta$ -tubulin blot in Figure 5C in Bai et al., J Biol Chem 2007.

### **Finding of Fact:**

- 1. Figure 5C is a Western blot for T-Cadflag in PC-12 cells co-transfected with T-Cadflag, vector control, Cdh1, Cdh20, or Cullin 1, the polypeptides involved in the substrate recognition of E3 ligase that is needed for proteasomal degradation. β-tubulin serves as a loading control.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lanes 4 and 7, and when comparing lanes 5-6 with lanes 8-9 and 10-11 for  $\beta$  -tubulin in Figure 5C (see slides 71-72<sup>671</sup>). Thus, there is reuse of the same data in lanes 4-6 and in lanes 7-9; and reuse of the same data in lanes 5-6, in lanes 8-9, and in lanes 10-11. This would not be scientifically valid as the same data are being reused to represent  $\beta$  -tubulin protein expression for different experimental conditions.
- 3. Although the blots are not very distinctive in shape, the similarities occur in sequences of two or three lanes, which argues strongly for the duplication not being a result of honest error.
- 4. No original data for this figure were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates duplication and reuse of the same data lanes 4-6 and lanes 7-9, and also the same data used in lanes 5-6, lanes 8-9, and lanes

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<sup>&</sup>lt;sup>671</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 71-72



- 10-11 of the β-tubulin blot in Figure 5C, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob received formal notice of concerns with figures (including Figure 5C) within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>672</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day.<sup>673, 674</sup> Figure inconsistencies in Bai et al., JBC 2007 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017.<sup>675</sup> As of then,, PubPeer had published four (4) comments, corresponding to Allegations #23-27. As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 7. Dr. Jacob sent a formal response to JBC on October 19, 2017. 676, 677
- 8. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

#### Respondent's Response:

- During her interview with the CII on March 5, 2018, Dr. Ghoshal stated that she did not make the figure and that she could not recall who did.<sup>678</sup> Dr. Ghoshal stated that she did not have the data in order to able to comment further.<sup>679</sup>
- 2. Dr. Jacob's general statements regarding Manuscript #8 can be found above in the CII analysis for Allegation #23. Specifically for Figure 5C (and Figures 1B, 5A), Dr. Jacob stated "The question raised is about use of the normalizers (Ku-70 and b-tubulin) for different experiments. We used nonspecific polypeptides detected by the antibodies or appropriate proteins as normalizers wherever possible. We have presented those in each figure, if available." This response is the same as that provided to JBC on October 19, 2017. 682, 683
- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 5. In written communication with the COMIC,<sup>684</sup> first author, Dr. Shoumei Bai indicated that she has no access to any original data and

<sup>672</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>673</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>674</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>675</sup> These data are reviewed elsewhere under DIO 6819.

<sup>676</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>677</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>&</sup>lt;sup>678</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 77 lines 17 and 24

<sup>679</sup> Ex. 58 - 20180305-CII Interview + errata -Ghoshal, page 77 line 19-21

<sup>&</sup>lt;sup>681</sup> Ex. 151 - JBC\_M700691200\_Bai 2007-10172017, page 1

<sup>682</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>683</sup> Ex. 151 - JBC M700691200\_Bai 2007-10172017

<sup>&</sup>lt;sup>684</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

#### Respondent's Responsibility and Intent:

- 1. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 2. Dr. Ghoshal has not taken responsibility for the generation of Figure 5C, but has generally espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content while the first author should take responsibility for every figure. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 5C.
- 4. Figure 5C was used in the publication to support the hypothesis that degradation of T-Cadflag is proportional to the amount of Cdh1 expressed. β-tubulin serves as a normalization control; however, the data is misrepresented with the same β-tubulin blots used to represent different experimental conditions (Cdh1 in lanes 4-6, Cdc20 in lanes 7-9, and Cullin1 in lanes 10-12). The falsified data significantly impact the reported results by making it impossible to know if T-Cadflag levels were truly different in the different conditions.
- 5. The similarity of bands occurring in multiple lane sequences rather than as single lane argues against coincidence or honest error. The duplication of a series of three bands (in lanes 4-6 and 7-9) as well as a series of two bands used three separate times (in lanes 5-6, 8-9, and 10-11), and the fact that the results were to have depicted treatment with various polypeptides signifies to the Committee that these results as presented are inaccurate, may impact the overall conclusions to be drawn from the figure, and thus mislead the reader. Given the sheer number of duplications in this single panel along with the number of allegations within and across other figures in this manuscript, the Committee believes it is more likely than not that these duplications are not the result of honest error.
- 6. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 5C and that the actions of others caused the falsification within Figure 5C in Allegation #26, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 8. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified β-tubulin data in Figure 5C, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified  $\beta$  -tubulin data in Figure 5C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #8, Allegation #27 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 4 of the NS blot in Figure 7A in Bai et al., J Biol Chem 2007.

#### **Finding of Fact:**

- 1. Figure 7A is a Western blot of PC12 cells transfected with T-Cadflag, untreated or treated with the tyrosine kinase inhibitor genistein and +/- NGF treatment. However, the figure legend does not match the figure: there does not seem to be an upper and lower panel in the figures as described in the legend, and the results do not appear to represent each of three different antibodies listed in the legend as being used.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing lanes 1 and 4 (see slide 73<sup>686</sup>). This would not be scientifically valid as the same data have been used to represent two different experimental conditions.
- 3. No original data records for this figure were available.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates duplication of lane 1 as lane 4 of the NS blot in Figure 7A, which the Committee concludes is indicative of falsification.
- 5. Dr. Jacob received formal notice of concerns with figures (including Figure 7A) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Ghoshal the same day. Figure inconsistencies in Bai et al., JBC 2007 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then, PubPeer had published four (4) comments, corresponding to Allegations #23-27. As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 6. Dr. Jacob sent a formal response to JBC on October 19, 2017. 691, 692
- 7. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

#### Respondent's Response:

- 1. In her interview with the CII on March 5, 2018, Dr. Ghoshal noted that she did not make this figure Dr. Ghoshal did not refute or confirm the specifics of the allegation.
- 2. Dr. Jacob's general statements regarding Manuscript #8 can be found above in the CII analysis for <u>Allegation #23</u>. Dr. Jacob did not provide a specific response for Figure 7A.
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

<sup>&</sup>lt;sup>686</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 73

<sup>&</sup>lt;sup>687</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>688</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>689</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>690</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>691</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>692</sup> Ex. 151 - JBC M700691200\_Bai 2007-10172017

- 4. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- In written communication with the COMIC,<sup>694</sup> first author, Dr. Shoumei Bai indicated that she has no access to any original data

#### Respondent's Responsibility and Intent:

- 1. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 2. Dr. Ghoshal has not taken responsibility for the generation of Figure 7A, but has generally espoused the view that the corresponding author on a publication is responsible for its scientific integrity and content while the first author should take responsibility for every figure. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 7A.
- 4. Figure 7A was used to support the manuscript's conclusion that protein tyrosine phosphorylation is needed for NGF-induced T-Cad degradation. The falsified data significantly impacted the reported results by making it impossible to if know NGF-induced degradation depends on protein tyrosine phosphorylation.
- Reuse of a single band to represent two different experimental conditions would not be scientifically valid
  and compromises the integrity of the paper. Given the number of allegations within and across figures
  in this manuscript, the Committee believes it is more likely than not that this duplication is not the result
  of honest error.
- 6. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 7A and that the actions of others caused the falsification within Figure 7A in Allegation #27, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 8. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

<sup>&</sup>lt;sup>694</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS data in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #8, Allegation #48 - S.T. Jacob reported falsified data by the reuse of the same data in multiple lanes within the blots in Figure 1B (Ku-70), Figure 5A (β-tubulin) and Figure 5C (β-tubulin) in Bai et al., JBC 2007 as follows:

- Reuse of same data in lane 3 of the Ku70 blot in Figure 1B, and again in lanes 6, 9 and 11 of the β-tubulin blot in Figure 5C;
- Reuse of same data in lane 1 and in lane 2 of the Ku70 blot in Figure 1B, and in lane 4 and in lane 5 of the Ku70 blot in Figure 1B; and in lane 5 and in lane 6 of the β-tubulin blot in Figure 5A; and in lanes 4 and 5 and in lanes 7 and 8 of the β-tubulin blot in Figure 5C;
- Reuse of same data in lanes 2-4 of the  $\beta$ -tubulin blot in Figure 5A and in lanes 1-3 of the  $\beta$ -tubulin blot in Figure 5C.

#### **Finding of Fact:**

- 1. Figure 1B, 5A and 5C all represent Western blots of PC12 cells for different experiments. Figure 1B shows T-Cad degradation upon NGF treatment. Figure 5A and 5C show PC12 cells co-transfected with T-Cad and the Cbl family of proteins.
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC, demonstrated significant similarity when comparing between the bands in the Ku70 and  $\beta$ -tubulin blots in Figures 1B, 5A and 5C as detailed above (see slide 74<sup>696</sup>). Additional Adobe Photoshop overlay analysis performed by ORC strongly suggests:
  - a. Duplication and reuse of the same data in lane 3 of the Ku-70 blot in Figure 1B, and again in lanes
     6, 9,11 of the β-tubulin blot in Figure 5C (see slide 76-77<sup>697</sup>);
  - b. Duplication and reuse of the same data in lanes 1, 2 and lanes 4, 5 of the Ku-70 blot and in lanes 5, 6 of the  $\beta$ -tubulin blot in Figure 5A, and in lanes 4, 5 and lanes 7, 8 of the  $\beta$ -tubulin blot in Figure 5C (see slide 78-79<sup>698</sup>); and
  - c. Duplication and reuse of the same data in lanes 2-4 of the  $\beta$ -tubulin blot in Figure 5A and in lanes 1-3 of the  $\beta$ -tubulin blot in Figure 5C (see slide 80-81<sup>699</sup>).
- 3. Forensic analyses clearly show that the same data has been duplicated and reused to represent Ku-70 and β-tubulin protein expression levels. Reuse of the data would not be scientifically valid as the same data is being used to represent the expression level of two different proteins and many different experimental conditions.
- 4. No original data for these figures were available.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of multiple bands within and across the Ku70 and  $\beta$ -tubulin blots of Figures 1B, 5A and 5C, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob received formal notice of concerns with figures (including Figures 1B, 5A, and 5C) within this

<sup>&</sup>lt;sup>696</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 74

<sup>&</sup>lt;sup>697</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 76-77

<sup>&</sup>lt;sup>698</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 78-79

<sup>&</sup>lt;sup>699</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 80-81

manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>700</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day.<sup>701, 702</sup> As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.<sup>703, 704</sup>

- 7. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

#### Respondent's Response:

- 1. During her interview with the CII on March 5, 2018, Dr. Ghoshal noted
- 2. In her written response to the allegation provided to ORC on April 19, 2018, Dr. Ghoshal referred the CII to the response provided by Dr. Jacob to JBC. 706, 707
- 3. Dr. Jacob's general statements regarding Manuscript #8 can be found above in the CII analysis for <u>Allegation #23</u>. Specifically regarding Figures 1B, 5A, and 5C, Dr. Jacob states "The question raised is about use of the normalizers (Ku-70 and b-tubulin) for different experiments. We used nonspecific polypeptides detected by the antibodies or appropriate proteins as normalizers wherever possible. We have presented those in each figure, if available." This response is the same as that provided to JBC on October 19, 2017. 709, 710
- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- In written communication with the COMIC,<sup>711</sup> first author, Dr. Shoumei Bai indicated that she has no access to any original data

#### Respondent's Responsibility and Intent:

Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which
the research originated. It is unlikely he generated this figure, as it has been clearly and consistently
maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally

<sup>700</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>701</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>702</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW\_ JBC articles

<sup>703</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>704</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>&</sup>lt;sup>706</sup> Ex. 130 - New Allegations Ghoshal, page 2

<sup>&</sup>lt;sup>707</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>708</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 1

<sup>&</sup>lt;sup>709</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>710</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>&</sup>lt;sup>711</sup> Ex. 296 - 20190630 - Email response Bai to COMIC



- create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 2. Dr. Ghoshal has not taken responsibility for the generation of Figure 1B, 5A, or 5C, but was considered a faculty member at the time of publication of this manuscript. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 2B, 5A, or 5C.
- 4. Figure 1B is used to justify the entire thesis of this study that T-cad protein is decreased in the presence of NGF. Duplication of the Ku-70 bands invalidates this control making all conclusions from this figure (and Fig 1C upon which it is based) untrustworthy. Figure 5 is also highly problematic since lanes from Figure 1B are used multiple times in Figures 5A and 5C, and multiple lanes from Fig 5A are used in 5C. Since Fig 5A and 5C are used for quantification shown in Figure 5B and 5D, those data are also compromised and untrustworthy. Collectively Figure 5 was put forth to prove that the E3 ligase APC/C<sup>CDH1</sup> is required for proteasomal degradation of T-Cad. These collective manipulations invalidate one of the major conclusions of the manuscript. Given the number and complexity of duplications within this and across other figures in this manuscript, the preponderance of the evidence points toward these duplications being an intentional act and not the result of honest error.
- 5. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 1B, 5A, or 5C and that the actions of others caused the falsification within Figures 1B, 5A and 5C in Allegation #48, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 7. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figures 1B, 5A and 5C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figures 1B, 5A and 5C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #8, Allegation #50 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 4, lane 5, and in lane 6 (0, 2 and 4 hours) in the  $\Delta$ CD2-5 sample +NGF (lower panel) in Figure 6B in Bai et al., J Biol Chem 2007.

#### **Finding of Fact:**

- 1. Figure 6B is a Western blot for T-Cad wild type and mutant-transfected PC12 cells treated 0, 2, 4 hr with cyclohexamide (CHX).
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC, clearly demonstrated significant similarity when comparing the +NGF panel lanes 4, 5 and 6 in Figure 6B (see slide 83<sup>713</sup>). The JBC gradient map clearly shows repetition of shape amongst the three bands, the presence of a small notch at the lower left edge of each band, and the similarity of the background artifacts below each band. This would not be scientifically valid as it indicates that the same data had been reused to represent different experimental conditions.
- 3. From the JBC analysis of Figure 6B, the contrast of the entire +NGF panel has been changed in the grayscale so that the entire panel appears darker and a box around lanes 4, 5 and 6 becomes visually observable (indicated by the red arrows on slide 83 & 85), which suggests that the lanes had been pasted into the figure.
- 4. Additional Adobe Photoshop overlay analysis performed by ORC strongly suggests significant similarity and near perfect overlap when comparing lane 4 to 5 and lane 4 to 6 (see slide 84<sup>714</sup>).
- 5. The original data for these figures were not available. The authors, however, proposed a corrected figure to JBC, which was purportedly assembled from the original data (see slide 85<sup>715</sup>).
- 6. The Committee finds the forensic evidence and visual inspection clearly demonstrates the duplication and reuse of the same data in lanes 4, 5 and 6 and the "superimposing" of those lanes into ΔCD2-5 sample +NGF (lower panel) to compose the final figure as Figure 6B, which the Committee concludes is indicative of falsification.
- 7. Dr. Jacob received formal notice of concerns with figures (including Figure 6B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>716</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day.<sup>717, 718</sup> As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.<sup>719, 720</sup>
- 8. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

#### Respondent's Response:

- 1. During her interview with the CII on March 5, 2018, Dr. Ghoshal noted
- 2. In her written response to the allegation provided to ORC on April 19, 2018, Dr. Ghoshal referred the CII to the response provided by Dr. Jacob to JBC.<sup>722,723</sup>

<sup>&</sup>lt;sup>713</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 83

<sup>714</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 84

<sup>&</sup>lt;sup>715</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 85

<sup>&</sup>lt;sup>716</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>717</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>718</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>719</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>720</sup> Ex. 151 - JBC M700691200\_Bai 2007-10172017

<sup>&</sup>lt;sup>722</sup> Ex. 130 - New Allegations Ghoshal, page 2

<sup>723</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017



3. Dr. Jacob's general statements regarding Manuscript #8 can be found above in the analysis for <u>Allegation</u> #23. Specifically regarding Figure 6B (and Figure 7D discussed below), Dr. Jacob provided a response<sup>724</sup> to the CII that he'd previously submitted to JBC and a new Figure 6B, which he stated corrected the errors.<sup>725, 726</sup> Dr. Jacob indicated:

"The published figure was a composite created from original data. Since there was a problem in detecting the bands corresponding to  $\Delta$ CD2-5 in lanes 4, 5 (see upper panel in the corrected figure for original data), the WT and  $\Delta$ CD2-5 samples were repeated separately (see bottom panel in corrected figure). The panel of three lanes from the repeat experiment (for  $\Delta$ CD2-5) was superimposed over the rest of the data to create the figure for the paper. We have now provided the original data for all Tcadflag deletion and point mutant along with the wild type with and without NGF treatment in two different panels (i and ii). T27

- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 6. In written communication with the COMIC,<sup>728</sup> first author, Dr. Shoumei Bai indicated that she has no access to any original data
- 7. In his January 20, 2021 response to the preliminary investigation report, Dr. Jacob argued that the Committee had not provided him with an opportunity to discuss the publication and associated allegations and has arrived at its conclusions erroneously. However, Dr. Jacob made it known to former Research Integrity Officer, Dr. Jen Yucel, in a phone call on Friday, July 12, 2019 that he wanted the Committee to understand that he would not be able to participate in the upcoming interview for very long based on his health, that he didn't want to discuss the original allegations as they had already been addressed, that he would leave it up to his laboratory members to discuss technical details, that he would like to focus the interview on the new allegations, and that he would be submitting a response 131 via his attorney for committee consideration.

#### Respondent's Responsibility and Intent:

- 1. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure, as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 2. Dr. Ghoshal has not taken responsibility for the generation of Figure 6B, but was considered a faculty

<sup>&</sup>lt;sup>724</sup> Ex. 149 - Cover letter .4.19.18 pdf

<sup>&</sup>lt;sup>725</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>726</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 2 and 7

<sup>&</sup>lt;sup>727</sup> Ex. 151 - JBC\_M700691200\_Bai 2007-10172017, page 2

<sup>&</sup>lt;sup>728</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>&</sup>lt;sup>730</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), pages 18-20

<sup>731</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

member at the time of publication of this manuscript. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.

- 3. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 6B.
- 4. In response to concerns raised by the journal (JBC), Dr. Jacob acknowledged the "panel of three lanes from the repeat experiment (for ΔCD2-5) was superimposed over the rest of the data to create the figure for the paper."<sup>732</sup> The Committee reviewed the response and the new Figure 6B provided by Dr. Jacob<sup>733</sup> and noted that there are discrepancies between the new data and the published Figure 6B (see slide 85<sup>734</sup>).
  - a. The expression pattern for the ΔCD2-5 original data (see red box in lower panel +NGF, lanes 4-6) does not match the steady expression pattern reported in the published Figure 6B, suggesting a possible motive to superimpose the three new bands into the final figure.
  - b. The decreasing expression pattern for ΔCD3-5 reported in the published Figure 6B (see green box in lower panel +NGF, lanes 10-12) does not match the steady expression pattern shown in the proposed correction. The text in the paper states that the degradation of T-Cad with the ΔCD3-5 deletion shows more pronounced degradation after NGF treatment, supporting the main conclusion that the CD2 domain is essential for NGF-mediated degradation. The proposed correction does not support this conclusion. The Committee believes that the additional falsification of the published Figure 6B in this case is significant.
- 5. The Committee believes that the brazen use and later acknowledgment of creating a composite figure from multiple sources of data because there had been a problem detecting bands during experimentation falls well outside the established practices and standards of the field. Further, providing original data that allows the Committee to identify an additional falsification reinforces the conclusion that Dr. Jacob shows a disregard for the accepted practices and rigors of scientific inquiry and an intention to manipulate and deceive the reader. The key knowledge that Dr. Jacob provided in defense of this allegation was above and beyond that previously provided for any other allegations, which indicated to the Committee that he was involved in the falsification and/or knew who perpetrated the falsification.
- 6. In deferring to Dr. Jacob's response, Dr. Ghoshal appears to stand by and accept his explanation of events as her own. 735, 736
- 7. Further, the ongoing investigation by the journal (i.e. JBC), as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript, were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 8. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 6B, but that, based on his own admission, Dr. Samson Jacob intentionally or knowingly reported falsified data in Figure 6B in Allegation #50, as described above.
- As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### Committee Conclusion:

<sup>732</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 2

<sup>&</sup>lt;sup>733</sup> Ex. 151 - JBC\_M700691200\_Bai 2007-10172017, page 2 and 7

<sup>&</sup>lt;sup>734</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 85

<sup>735</sup> Ex. 130 - New Allegations Ghoshal, page 2

<sup>&</sup>lt;sup>736</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

By a preponderance of the evidence, the Committee finds by a vote of 6 in favor and 1 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in the  $\Delta$ CD2-5 sample +NGF (lower panel) and the  $\Delta$ CD3-5 sample +NGF (lower panel) in Figure 6B, and this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 6 in favor and 1 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in  $\Delta$ CD2-5 sample +NGF (lower panel) and the  $\Delta$ CD3-5 sample +NGF (lower panel) in Figure 6B, and this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #8, Allegation #51 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-3 in the top panel (-NGF) in Figure 6B and in lanes 1-3 of the Tcadflag blot in Figure 7D; and also by the reuse of same data in lanes 1-3 in the bottom panel (+NGF) in Figure 6B, and in lanes 7-9, Tcadflag blot in Figure 7D in Bai et al., J Biol Chem 2007.

#### **Finding of Fact:**

- 1. Figures 6B and 7D are both Western blots for T-Cadflag wild type and mutant-transfected PC12 cells treated 0, 2, 4 hr with cyclohexamide (CHX).
  - a. Figure 6B, lanes 1-3 (top panel) represent WT, -NGF, +0, 2, 4 hr CHX and Figure 7D also represents WT, -NGF, and +0, 2, 4 hr CHX.
  - b. Figure 6B, lanes 1-3 (bottom panel) represent WT, +NGF, +0, 2, 4 hr CHX and Figure 7D, lanes 7-9 represent *Nsp-ΔCD1 mutant*, +NGF, +0, 2, 4 hr CHX.
  - c. Note also that the quantification graph of 7D indicates  $Nsp-\Delta CA1$  as opposed to  $Nsp-\Delta CD1$ .
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC demonstrated:
  - a. Significant similarity when comparing lanes 1-3 (top panel, -NGF, flag blot) in Figure 6B, and lanes 1-3 of the Tcadflag blot in Figure 7D (red boxes, slide 86), indicating that the same data have been duplicated and reused. This may be scientifically valid as the lanes appear to represent the same experimental conditions as reported.
  - a. Significant similarity when comparing lanes 1-3 (bottom panel, +NGF, flag blot) in Figure 6B, and lanes 7-9, of the Tcadflag blot in Figure 7D (blue boxes, slide 86<sup>737</sup>), indicating that the same data have been duplicated and reused. This would not be scientifically valid as, according to the labels on the figure, the lanes represent different experimental conditions.
- 3. Additional Adobe Photoshop overlay analysis performed by ORC shows significant similarity and near perfect overlay of lanes 1-3 (top panel, -NGF, Flag blot) in Figure 6B, and lanes 1-3, of the Tcadflag blot in Figure 7D. Adobe Photoshop overlay analysis performed by ORC strongly suggests significant similarity and near perfect overlap when comparing lanes 1-3 (bottom panel, +NGF, Flag blot) in Figure 6B, and lanes 7-9 (labeled Nsp-ΔCD-1), of the Tcadflag blot in Figure 7D. See slide 87. 738
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 6B and 7D) within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>739</sup> Dr. Jacob subsequently notified Dr. Ghoshal the same day.<sup>740, 741</sup> As such, Drs. Jacob and Ghoshal knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.<sup>742, 743</sup>

<sup>&</sup>lt;sup>737</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 86

<sup>&</sup>lt;sup>738</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 87

<sup>&</sup>lt;sup>739</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>740</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>741</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>742</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response \_Bai 2007

<sup>&</sup>lt;sup>743</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017



- No original data for the figures were provided. The authors, however, proposed to JBC a corrected figure of Figure 6B incorporating results from Figure 7D, which was purportedly assembled from the original data (see slide 88-89<sup>744</sup>).
- 6. The Committee finds the forensic evidence and visual inspection demonstrates reuse of multiple lanes of data across figures 6B and 7D, which the Committee concludes is indicative of falsification.
- 7. Dr. Kalpana Ghoshal was the final author of JBC 2007 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2007.

#### Respondent's Response:

- 1. During her interview with the CII on March 5, 2018, Dr. Ghoshal noted
- In her written response to the allegation provided to ORC on April 19, 2018, Dr. Ghoshal referred the CII to the response provided by Dr. Jacob to JBC. 746, 747
- 3. Dr. Jacob's general statements regarding Manuscript #8 can be found above in the analysis for <u>Allegation</u> #23. Specifically regarding Figure 7D (and Figure 6B discussed above), Dr. Jacob provided a response<sup>748</sup> to the CII that he'd previously submitted to JBC and a new Figure 6B, which he stated corrected the errors. <sup>749, 750</sup> Dr. Jacob stated:

"In the manuscript, we first described the results on deletion mutants in Fig. 6B and then phosphorylation site mutant (Y327F) in Fig. 7D. We realized that there was an inadvertent error in labeling of Fig. 7D. Lanes 7-9 are actually WT and not Nsp- ΔCD1. Since they represent the same samples that were shown in lanes 1-3 of Fig. 6B, we had intentionally duplicated them in Fig. 7D. In the corrected figure, all samples including the Y327F are presented all together in Fig. 6B. As a result Fig. 7D should be deleted."

- 4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 6. In written communication with the COMIC<sup>752</sup>, first author, Dr. Shoumei Bai indicated that she has no access to any original data
- 7. In his January 20, 2021 response to the preliminary investigation report, Dr. Jacob argued that the Committee had not provided him with an opportunity to discuss the publication and associated allegations

<sup>744</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 888-89

Ex. 130 - New Allegations Ghoshal, page 2

<sup>747</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017

<sup>&</sup>lt;sup>748</sup> Ex. 149 - Cover letter .4.19.18 pdf

<sup>&</sup>lt;sup>749</sup> Ex. 325 - 20171019 - Email Jacob to JBC - JBC response Bai 2007

<sup>&</sup>lt;sup>750</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 2 and 7

<sup>&</sup>lt;sup>751</sup> Ex. 151 - JBC M700691200 Bai 2007-10172017, page 2

<sup>&</sup>lt;sup>752</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

and has arrived at its conclusions erroneously. The However, Dr. Jacob made it known to former Research Integrity Officer, Dr. Jen Yucel, in a phone call on Friday, July 12, 2019 that he wanted the Committee to understand that he would not be able to participate in the upcoming interview for very long based on his health, that he didn't want to discuss the original allegations as they had already been addressed, that he would leave it up to his laboratory members to discuss technical details, that he would like to focus the interview on the new allegations, and that he would be submitting a response to his attorney for committee consideration.

#### Respondent's Responsibility and Intent:

- 1. Dr. Jacob is the corresponding author on this paper and the Principal Investigator of the lab in which the research originated. It is unlikely he generated this figure, as it has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication. However, as laboratory PI, he is responsible for reviewing the figure for accuracy and fidelity with the original data before publication.
- 2. Dr. Ghoshal has not taken responsibility for the generation of Figure 6B or 7D. The COMIC believes, as seemingly do the members of the Jacob laboratory itself, that being named the final author of a biomedical manuscript denotes a level of seniority and bears as much responsibility for its content and overall accuracy as does the named corresponding author.
- 3. The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 6B or 7D.
- 4. Dr. Jacob did not dispute the allegation but rather indicated that the lanes in 7D had been intentionally duplicated because they represent the same samples in Figure 6B. In deferring to Dr. Jacob's response, Dr. Ghoshal appears to stand by and accept the same explanation as her own.
- 5. The Committee reviewed Figures 6B, 7D and the corresponding text in JBC 2007, and the Committee believes that both figures as initially published likely present the same experimental design. The Committee notes that Figure 7D focused on the degradation of T-Cad and examined the effect of a mutation in the tyrosine 327 site (the Y327F mutant). The text describes the differences in protein degradation of wt and the Y327F mutant. Dr. Jacob contends that whoever created Figure 7D made labeling errors: as published, what should be the "+NGT WT" blot in Figure 7D is erroneously labeled "Nsp-ΔCD1," while in the accompanying graph it is also erroneously labeled "Nsp-ΔCA1." The Committee is skeptical about the honest error explanation and at best finds that the generation of the figures and the review of the figures were a significant departure from acceptable standards: the incorrect Nsp-ΔCD1 and Nsp-ΔCA1 labels in Figure 7D are so obvious that even if Dr. Jacob performed a cursory review of the figure, he should have noted the errors. The labeling of the graph in Figure 7D with Nsp-ΔCA1 is completely irrelevant to the figure or text.
- 6. The Committee notes that, according to Dr. Jacob, Figure 7D was created by cropping parts of the original data for the experiment in Figure 6B, since Dr. Jacob stated in the correction he provided, "In the corrected figure, all samples including the Y327F are presented all together in Fig. 6B. As a result Fig. 7D should be deleted." Dr. Jacob provided a new Figure 6B, which he stated corrected the errors in the published Figure 6B and 7D. The Committee reviewed the proposed correction for Figure 6B as compared to the published Figure 7D, and found the following inconsistencies (see slide 88-89757):
  - a. The proposed correction of +NGF Y327F, CHX 4 hour (lane 15) in Figure 6B (a downward curving band) does not match +NGF Y327F, CHX 4 hour (lane 12) in the original Figure 7D (an upwardly

<sup>&</sup>lt;sup>754</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), pages 18-20

<sup>755</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>756</sup> Ex. 151 - JBC\_M700691200\_Bai 2007-10172017, page 2 and 7

<sup>757</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 88-89

- curving band) (see blue boxes, slide 88758).
- b. None of the NS bands in published Figure 7D match the NS bands in the proposed correction.<sup>759</sup> The expression pattern of the –NGF Y327F NS control (lanes 4-6) shows equal expression in the original Figure 7D, but not in the proposed, corrected Figure 6B (lanes 13-15, upper panel), which shows no expression at CHX 0 hr (see pink boxes, slide 89<sup>760</sup>).
- c. The expression pattern of the +NGF Nsp-ΔCD1 NS control (lanes 7-9, which according to the authors should have been labeled "WT") shows expression (roughly equal) in the original Figure 7D, but not in the proposed, corrected Figure 6B (lanes 1-3, lower panel), which shows no expression at all (see yellow boxes, slide 89<sup>761</sup>).
- d. The expression pattern of the +NGF Y327F NS control (lanes 10-12) shows expression (roughly equal) in the original Figure 7D, but not in the proposed, corrected Figure 6B (lanes 13-15, lower panel), which shows decreasing expression (see blue boxes, slide 89<sup>762</sup>).
- 7. The ongoing investigation by the journal (i.e. JBC) as well as the concerns that were already published on the web (i.e. PubPeer) regarding this manuscript were known to Dr. Jacob and Dr. Ghoshal at the time of their initial notification of allegations by OSU, yet both Dr. Jacob and Dr. Ghoshal failed to disclose this. The Committee concludes that such failure to disclose represents dishonesty and damages the credibility of arguments made by Drs. Jacob and Ghoshal.
- 8. The Committee believes that, similar to Allegation #50 involving Figure 6B, the key knowledge that Dr. Jacob provided in defense of this allegation was above and beyond that provided for any of the other allegations, which indicated to the Committee that he was involved in the falsification and/or knew who perpetrated the falsification. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 6B or 7D, but that Dr. Jacob intentionally or knowingly reported falsified data in Figures 6B and 7D in Allegation #51, as described above. While the significance of the original duplication in isolation may be low, taken in the context of all the allegations (in particular Allegation #50), the additional findings in the proposed corrected version of Figure 6B, the level and experience of Dr. Jacob (which he has repeatedly touted throughout the investigation), and the fact that Dr. Jacob knew about the concerns with Figure 7D when this investigation began and said nothing, the Committee believes Dr. Jacob showed a disregard for the accepted practices and rigors of scientific inquiry and an intention to manipulate the trust of the scientific community.
- 9. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 6 in favor and 1 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figures 6B and 7D, and this act **does** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 6 in favor and 1 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified data in Figures 6B and 7D, and this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

#### Manuscript #9 under Review- Datta et al., Cancer Res 2008 (3 Allegations)

Datta J\*, Kutay H\*, Nasser MW, Nuovo GJ, Wang B, Majumder S, Liu CG, Volinia S, Croce CM, Schmittgen TD,

<sup>&</sup>lt;sup>758</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 88

<sup>&</sup>lt;sup>759</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 89

<sup>&</sup>lt;sup>760</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 89

<sup>&</sup>lt;sup>761</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 89

<sup>&</sup>lt;sup>762</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 89

Ghoshal K\*\*, Jacob ST\*\*. "Methylation mediated silencing of MicroRNA-1 gene and its role in hepatocellular carcinogenesis." Cancer Res. 2008 Jul 1; 68(13):5049-58 \*\* co-first authors \*\* co-corresponding authors

**Manuscript #9, Allegation #28 -** S.T. Jacob reported falsified data by the reuse of the FOXP1 blot and GAPDH blot to represent data from two different cell lines (SK-Hep1 and SNU-449 cell lines) in Figure 5A in Datta et al., Cancer Res 2008.

#### **Finding of Fact:**

- Figure 5A shows a Western blot for expression of miR1 targets (FoxP1, MET, HDAC4), and GAPDH as a loading control, in six different hepatocellular carcinoma (HCC) cell lines treated with 5-AzaC, a DNA demethylating agent.
- 2. Adobe Photoshop overlay analysis demonstrated that when the FOXP1 blots for the SK-Hep1 and SNU-449 images were overlaid, there was significant overlap of the bands as evidenced by the red colocalization with very little surrounding (white) border (see slide 92<sup>763</sup>).
- 3. Adobe Photoshop overlay analysis demonstrated that when the GAPDH blots for the SK-Hep1 and SNU-449 images were overlaid, there was significant overlap of the bands as evidenced by the red colocalization with very little surrounding (white) border (see slide 92<sup>764</sup>).
- 4. Adobe Photoshop analysis demonstrated significant overlap when the published FOXP1, SK-Hep1 and SNU-449 blots were overlaid on each other as well as when the published blots were overlaid on original/contemporaneous data provided by Dr. Datta as "Exhibit 2"<sup>765</sup> (see slides 93, 95-97<sup>766</sup>).
- 5. Exhibit  $3,^{767}$  as provided by Dr. Datta, is labeled as " $\alpha$ -Met" on the film and not GAPDH as stated by Dr. Datta, suggesting that the blot is not stained for GAPDH but instead stained for  $\alpha$ -Met and therefore would not be a "*relevant experiment*." Furthermore, certain bands (outlined in yellow on Exhibit 3) appear to have been used in the final Figure 5A for the  $\alpha$ -MET blot, further suggesting it is not the "*relevant experiment*" for GAPDH staining. <sup>768</sup> See slides 94, 98. <sup>769</sup>
- The Committee finds the forensic evidence, visual inspection, and comparison to the raw data demonstrates reuse of the same FOXP1 data to represent two different cell lines as well as reuse of the same GAPDH data to represent two different cell lines, which the Committee concludes is indicative of falsification.
- 7. Dr. Datta was co-first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Ghoshal was a co-corresponding author and contributed equal work as first author of Cancer Res 2008 and was a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2008.

#### Respondent's Response:

1. In her interview with the CII on March 1, 2018, Dr. Datta indicated that she could not remember who made this figure, but did not dispute the fact that these bands looked similar. Dr. Datta did state that she did the experiment, however, this would be confirmatory as was routine. <sup>770</sup> Dr. Datta noted that she could not retrieve the original hard disk for this figure, <sup>771</sup> but went on to note that these figures (i.e., the

<sup>&</sup>lt;sup>763</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 92

<sup>&</sup>lt;sup>764</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 92

<sup>&</sup>lt;sup>765</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 2

<sup>&</sup>lt;sup>766</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 93, 95-97

<sup>&</sup>lt;sup>767</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 3

<sup>&</sup>lt;sup>768</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 98

<sup>&</sup>lt;sup>769</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 94, 98.

<sup>&</sup>lt;sup>770</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 50, line 15

<sup>&</sup>lt;sup>771</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 47 lines 18-20



- representative blots for FOXP1 and GAPDH from SK-Hep1 and SNU-449) do look "very similar, if not identical." <sup>772</sup>
- 2. In her written response provided to ORC on May 18, 2018, Dr. Datta reiterated that she was unable to produce the original data and could not remember who prepared the final figures. Specifically, Dr. Datta expressed disagreement with the allegation, indicated that the lanes are very similar but not identical, and provided data from a related experiment showing that the bands can look very similar. Additionally, Dr. Datta offered the following caveat,

"In case the GAPDH lanes had been duplicated (as figures made by multiple authors, there is probability of this kind of unintentional errors), it is an inadvertent error. However, raw data from a relevant experiment (Please see attached PPT file: **Exhibit 3**) demonstrate that intensities of GAPDH bands are more or less identical and hence the conclusion of the data in the figure does not change."<sup>773, 774</sup>

3. In her response to the CII report<sup>775</sup> and her appeal of their determination, <sup>776</sup> Dr. Datta challenged the forensic evidence and stated that though she can acknowledge similarity, in the absence of original data she "cannot affirmatively agree that a duplication occurred." Dr. Datta recanted her knowledge of who performed the experiment that was ultimately used for the generation of the figure, argued that the data presented in the figure are consistent with those that could be drawn from the times she performed the experiment, and concluded that any errors in figure generation would have been inadvertent. Furthermore, she maintained that inclusion of the data for SNU449 and SK HEP-1 cell lines was redundant, having already been shown in four other cell lines, and argued that the conclusions of the paper remain unchanged. Finally, regarding the GAPDH data she presented in her Exhibit 3 which the CII found to be labeled as "α-Met", Dr. Datta indicated:

"My understanding is that the blot was cut into two pieces, while the upper part was probed with anti-Met antibody and the lower part was probed with anti-GAPDH antibody. Next, the blots were washed with stripping solution to remove MET signal and the upper part was probed with anti-FOXP1 antibody. I continue to believe that Exhibit 3 shows GAPDH bands (bottom darker bands while the top lighter bands represent MET). While I continue to believe the blot in my Exhibit 3 was not the blot from which Figure 5A was made, I do believe the blot shows even loading, reflected in consistent GAPDH bands."777

- 4. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 5. As this allegation was added during the course of the investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

<sup>&</sup>lt;sup>772</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 47, lines 22-24

<sup>&</sup>lt;sup>773</sup> Ex. 78 - OSU Response 1-JD, page 1

<sup>&</sup>lt;sup>774</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 3

<sup>&</sup>lt;sup>775</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 3-4

<sup>&</sup>lt;sup>776</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>777</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 4

8. In her interview with the COMIC on June 28, 2019,<sup>778</sup> Dr. Datta referred to the data she previously provided, reiterated her belief that the data look similar but not identical, and indicated that she could not recall who performed the experiment or made the figure or whether she made any figures for this paper. She argued that if a duplication exists, it would have been an inadvertent error.<sup>779</sup> Dr. Datta again argued that without the original data, she could not explain how the data look identical and maintained that the findings were replicated in other cell lines so there would be no motive to falsify the data. <sup>780</sup> See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors has taken responsibility for generation of Figure 5A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. The expression levels for proteins obtained from different cell sources can be similar but not identical, making it very likely that a single blot was reused to represent FOXP1 expression levels for two different experimental conditions, and a single blot was reused to represent GAPDH expression levels for two different experimental conditions. Though in this rare instance, original data for this 2008 publication was provided by the first author, the data does not mirror the published image.
- 3. An intermediary lane present on the FOXP1 SNU-449 raw data does not appear in the published figure (see slide 98<sup>781</sup>) and by Dr. Jacob's argument a splice line should be visible in the published figure, which is not the case. This suggests that laboratory members had sufficient skill when manipulating the images to mask splice and/or cut/paste lines.
- 4. Given the number of allegations within and across figures in this manuscript, the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error. The COMIC has found sufficient evidence to prove that other laboratory members had sufficient skill in manipulating images to mask splice and/or cut/paste lines (see <u>Allegation #29</u> below), and insufficient evidence to prove that Dr. Jacob was responsible for this duplication.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 5A and that the actions of others caused the falsification within Figure 5A in Allegation #28, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified FOXP1 and GAPDH images in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified FOXP1 and GAPDH images in

<sup>&</sup>lt;sup>778</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 38 line 21 – page 39 line 22; page 40 lines 17-18

<sup>&</sup>lt;sup>779</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 49-56

<sup>780</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 54, lines 15-18; page 55 line 21 to page 56 line 15

<sup>&</sup>lt;sup>781</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 98

Figure 5A, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #9, Allegation #29 -** S.T. Jacob reported falsified data by the reuse of the same data as sample 1 and as sample 8 (T\* and N lanes) in the FOXP1 blot in Figure 6A in Datta et al., Cancer Res 2008.

#### **Finding of Fact:**

- 1. Figure 6A shows Western blots for FOXP1, MET, HDAC and Ku-70 as a control, in human primary HCCs (T) and matching liver tissue (N).
- 2. Adobe Photoshop overlay analysis demonstrated that samples 1 and 8, for the T (tumor) and N (normal) lanes in the FOXP1 blot, showed nearly perfect overlay (see slide 99<sup>782</sup>).
- 3. Adobe Photoshop overlay analysis performed on "Datta Exhibit 1a"<sup>763</sup> demonstrates that this is the original source data of Figure 6A (see slide 104-105<sup>784</sup>). The image forensics further confirm that samples 2-11 in Figure 6A correspond to the 10 matched pair samples in Datta Exhibit 1a.<sup>785</sup>
- 4. "Exhibit 4"<sup>786</sup> provided by Dr. Datta corresponds to the data sequestered and reviewed on 11/30/17 labeled as "Datta Exhibit 1a."<sup>787</sup>
- 5. Despite Dr. Datta's disagreement that Exhibit 4/Datta Exhibit 1a are the original source data for Figure 6A, the COMIC, like the CII before it, determined that it is in fact the source data used in the final published figure.
- 6. Files dating back to 2007 show evidence of manipulation of the data published in Figure 6A as compared to the original data for the FOXP1, MET, and Ku-70 lanes of Figure 6A.<sup>788</sup> These data were not associated with Dr. Jacob and serve as additional evidence that Dr. Jacob was likely not responsible for the data manipulation in composing this figure or in masking splice lines.
- 7. The Committee finds the forensic evidence and visual inspection of the raw data demonstrate reuse of sample set 8 as sample set 1 in Figure 6A, which the Committee concludes is indicative of falsification.
- 8. Dr. Datta was co-first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 9. Dr. Ghoshal was a co-corresponding author and contributed equal work as first author of Cancer Res 2008 and was a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.
- 10. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2008.

#### Respondent's Response:

- 1. In her interview with the CII on March 1, 2018, Dr. Datta did not recall if she had made this figure, and she did not have the original data.<sup>789</sup> Dr. Datta introduced "Exhibit 4," which she claimed was a "*similar autorad*" to what is published in Figure 6A of Cancer Res 2008.<sup>790</sup> Dr. Datta did not believe that this was the original source data that was used to make the final Figure 6A.<sup>791</sup>
- 2. In her written response provided to ORC on May 18, 2018, Dr. Datta argued that the samples have not been duplicated and offered supplemental evidence that "10 out of 11 pairs FOXP1 has been upregulated in tumors. Therefore, even if we remove one of the two pairs (1 and 8) under

<sup>&</sup>lt;sup>782</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 99

<sup>&</sup>lt;sup>783</sup> Ex. 68 - Datta\_Exhibit\_1a. A blot that was pulled from the sequestered data by Dr. Datta in the 11/30/17 data review.

<sup>&</sup>lt;sup>784</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 104-105

<sup>&</sup>lt;sup>785</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 103

<sup>&</sup>lt;sup>786</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 4

<sup>&</sup>lt;sup>787</sup> Ex. 68 - Datta\_Exhibit\_1a

<sup>&</sup>lt;sup>788</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>789</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 56 lines 3-12

<sup>&</sup>lt;sup>790</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 56 lines 15-16

<sup>&</sup>lt;sup>791</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 59 lines 14-15

question, the conclusion of the data remains unaltered" (emphasis added by author). 792

3. In her response to the CII report<sup>793</sup> and her appeal of their determination,<sup>794</sup> Dr. Datta reiterated her belief that she did not prepare the figure and/or that the figure was not prepared from the data she located within material sequestered by ORC, specifically stating,

"Either the figure was made from a different experiment, or it was made by someone else, who read the data differently than I did. With the passage of more than 10 years, and without all of the original data for this paper, I am not able to reconstruct how the figure was prepared or by whom." 795

Additionally, Dr. Datta argued against the possibility of reuse given no visible splice lines and asserted that there would be no motive for duplication given their conclusion that FoxP1 is upregulated in a majority of samples tested would be true regardless of the specific number of pairs shown and that the conclusion was also validated in Figure S4. Dr. Datta conceded that if in fact there was duplication, it would have been the result of some error.

- 4. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 5. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 8. In her interview with the COMIC on June 28, 2019, <sup>796</sup> Dr. Datta confirmed that she ran the experiment <sup>797</sup> and maintained that she did not know who made the figure, but that an error had been made. <sup>798</sup> Even though she was the first author, Dr. Datta said that she could not remember her or anyone else's role in generating figures for this manuscript, but indicated that experimental results may have been given to other members of the laboratory to scan or to make the figure. Dr. Datta said that she did not identify the discrepancy between her original data and the final figure, and that the duplication had to be an error because she didn't see any reason to purposely manipulate the data. <sup>799</sup> When pressed further to explain how Lane 1 as depicted in the published manuscript was not present in the raw data, Dr. Datta seemed incredulous and visibly upset:

DR. YUCEL: ... so the most logical or the easiest way to explain how you could get that would be that the sample, Sample Set 1, in Photoshop was copied and pasted for lane 8, or vice versa, it could have been lane 8 original data was copied and pasted on top of the image for Sample Set 1. Do you agree that that is probably the simplest explanation for how you could get a figure that doesn't match your data in that specific way?

DR. DATTA: If the data is there, why someone will do that?

<sup>&</sup>lt;sup>792</sup> Ex. 78 - Datta OSU Response 1-JD, page 2

<sup>&</sup>lt;sup>793</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 5

<sup>&</sup>lt;sup>794</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>795</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 5

<sup>&</sup>lt;sup>796</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1

<sup>&</sup>lt;sup>797</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 60 line 21

<sup>&</sup>lt;sup>798</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 57 line 3-12

<sup>&</sup>lt;sup>799</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 56-62, page 66-68

DR. YUCEL: I'm not asking why. We're not asking why they might do it, but can you tell -- can you say, in your mind does that make sense to you, that that is the simplest, most straightforward way to explain why the figure doesn't match your data, specifically how it doesn't match?

DR. DATTA: I don't know.800

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts.
- 2. Dr. Datta ran the experiment and provided original data for Figure 6A. Neither Dr. Datta nor Dr. Ghoshal have taken responsibility for generation of Figure 6A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 3. In this rare instance, original data for this 2008 publication was identified by the first author ("Exhibit 4/Datta Exhibit 1a"), and the data does appear to be the source data for the published figure. The forensics performed on the source data by ORC, however, verify that the image labeled as sample set 1 has been falsified by the reuse and relabeling of sample set 8.
- 4. Figure 6A reinforces the overall conclusions of the paper because it shows that FOXP1 (a target of miR-1) is upregulated in liver tumor tissue as compared to normal liver tissue. It is possible that the duplication was entered to increase the statistical significance shown in 6B, but without the raw data from the image quantification it is not possible to say conclusively.
- 5. The original data and other files reviewed by the COMIC provide evidence Dr. Jacob was not responsible for the data manipulation for Figure 6A in composing this figure or in masking the splice lines.
- 6. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 6A and that the actions of others caused the falsification within Figure 6A in Allegation #29, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 7. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified FOXP1 images in Figure 6A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified FOXP1 images in Figure 6A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #9**, **Allegation #80** – S.T. Jacob reported falsified data by the reuse of multiple DNA bands and background images in Supplemental Figure 1 (slides 106-111) in Datta et al., Cancer Res 2008. Specifically:

a. DNA ladder band #3 in lane 1 was reused in lane 4 (Taq1/control) as bands #2 and #3 (slide 106-111)

<sup>800</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 70 line 12 to page 71 line 4

- b. DNA ladder band #4 in lane 1 was reused in lane 3 (Aci/control) as band #2 (slide 106-107, 109)
- c. Band #1 in lane 3 (Aci/control) was reused in lane 4 (Taq1/control) (slide 110)
- d. Band #1 in lane 2 (uncut/control) was reused in lane 6 (uncut/5-Azac) and lane 9 (Tsp5091/5-Aza) (slide 110)
- e. The same blank background image was reused in lanes 4, 5 and 9 (slide 111)
- f. The same blank background image was reused in lanes 7 and 8 (slide 111)

#### **Finding of Fact:**

- Figure S1A shows a COBRA assay of CGI in Huh-7 cells. COBRA is a quantitative technique that allows DNA methylation levels to be determined at specific gene loci, using restriction enzyme digestion of PCR products to reveal differences in methylation.
- 2. Both Adobe Photoshop gradient mapping and overlay analysis demonstrate significant similarity and near perfect overlap of the DNA ladder band #3 in lane 1 with lane 4 (Taq1/control) bands #2 and #3 (see slides 106-108<sup>801</sup>). Use of the same band to represent three experimental conditions is not scientifically valid. Further the band used comes from the commercially obtained DNA ladder and is not an experimental sample.
- 3. Both Adobe Photoshop gradient mapping and overlay analysis demonstrate significant similarity and near perfect overlap of the DNA ladder band #4 with lane 3 (Aci/control) band #2 (see slides 106-107, 109<sup>802</sup>). Use of the same band to represent two different experimental conditions is not scientifically valid.
- 4. Both Adobe Photoshop gradient mapping and overlay analysis demonstrate significant similarity and near perfect overlap of band #1 in lane 3 (aci/control) with band #1 in lane 4 (Taq1/control) (see slide 106-107, 110<sup>803</sup>). Use of the same band to represent two different experimental conditions is not scientifically valid. Further the band used comes from the commercially obtained DNA ladder and is not an experimental sample.
- 5. Both Adobe Photoshop gradient mapping and overlay analysis demonstrate significant similarity and near perfect overlap of band #1 in lane 2 (uncut/control) with band #1 in lane 6 (uncut/5-Azac) and lane 9 (Tsp5091/5-Azac) (see slides 106-107, 110<sup>804</sup>). Use of the same band to represent three experimental conditions is not scientifically valid.
- 6. Adobe Photoshop gradient mapping demonstrates significant similarity of the background features below the top bands of lanes 4, 5, and 9 (see slides 106-107, 111<sup>805</sup>).
- 7. Adobe Photoshop gradient mapping demonstrates significant similarity of the background features of below the top bands of lanes 7 and 8 (see slides 106-107, 111806).
- 8. Adobe Photoshop gradient mapping shows multiple splice lines, abrupt changes in background intensity, and boxes around bands indicative of splicing or cutting and pasting bands into the figure (see slides 106-107<sup>807</sup>).
- 9. No original data were available for this figure.
- 10. The Committee finds the forensic evidence and visual inspection demonstrates reuse of numerous bands and background lanes, which the Committee concludes is indicative of falsification.
- 11. Dr. Datta was co-first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 12. Dr. Ghoshal was a co-corresponding author and contributed equal work as first author of Cancer Res 2008 and was a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of publication.

<sup>801</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 106-108

<sup>802</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 106-107, 109

<sup>803</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 106-107, 110

<sup>804</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 106-107, 110

<sup>805</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 106-107, 111

<sup>806</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 106-107, 111

<sup>807</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 106-107

13. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2008.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Drs. Jacob, Ghoshal, and Datta were not guestioned about this allegation during the Inquiry phase of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, Dr. Jacob indicated that the bands look similar although he didn't believe the backgrounds had been duplicated, that DNA bands when separated on polyacrylamide gels and stained with ethidium bromide might look similar or not run evenly, and that there would be no reason to duplicate undigested DNA bands.<sup>808</sup>
- 3. In his interview with the COMIC on July 17, 2019, Dr. Jacob indicated that he would not be making any statement about the allegation without the raw data and that he didn't see any problem.<sup>809</sup> He added:

"... this paper was published 11 years ago, and we looked at this paper with all the technology I had at that time, there was nothing wrong with this figure. And this was peer reviewed by --extensively. And, in fact, if I recall correctly, reviewers didn't even ask for this figure. You know, we had all the supplemental figures.

So it's very difficult for me to say who made this figure after 11 years. You know, I don't make a note of who prepared each figure for each paper because this is not something -- I don't know if anybody in my capacity will be able to do that."<sup>810</sup>

- 4. See also Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal first indicated that she did not know if she made this figure, 811 then later indicated she could not recall who made the figure but knew she did not make this or any figures in the manuscript, having mostly written the paper and coordinated the project. 812 Dr. Ghoshal was surprised and appalled 813 about the level of manipulation evident in the forensic review of the figure, but maintained that she would not have been able to find the manipulations in a review of the gel itself. 814 See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 6. In her interview with the COMIC on June 28, 2019, Dr. Datta recalled performing the experiment and explained how it would have been run, but indicated that she did not make the figure. B15 Dr. Datta acknowledged the similarity between many of the bands, but believed that was the way the experiment must have run and didn't believe any duplication occurred. Dr. Datta denied knowing anyone on the author list specifically who would not have been able to run the experiment and/or make the figure, indicating that everyone had the required expertise.

#### Respondent's Responsibility:

1. None of the co-first authors have taken responsibility for generation of Supplemental Figure 1, but

<sup>808</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 25

<sup>&</sup>lt;sup>809</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 9 lines 13-18 and 20-24

<sup>&</sup>lt;sup>810</sup> Ex. 293 - 20190717 - COMIC Interview + errata – Jacob, page 9 line 21 to page 11 line 8

<sup>811</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 65 lines 8-9

<sup>812</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 66 lines 3-12

<sup>813</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal\_Redaction 1, page 65 lines 21-22

<sup>814</sup> Ex. 302a - 20190628 - COMIC Interview + errata - Ghoshal Redaction 1, page 67 line 1-8

<sup>815</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 41-42, page 45 line 8-9

<sup>816</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta\_Redaction 1, page 44 line 6-11 and 23-24

<sup>817</sup> Ex. 301a - 20190628 - COMIC Interview + errata - Datta Redaction 1, page 44 line 11 to page 48 line 13



espouse the view that all authors on a publication are responsible for its scientific integrity and content.

- 2. Duplicate and triplicate repetition of unique bands across multiple experimental conditions is nearly impossible to have occurred by chance. Similarly, duplicate and triplicate repetition of unique background features across a gel is quite unlikely to have occurred by chance. Given the sheer number of duplications within this figure and the number of allegations across multiple figures in this manuscript, the preponderance of the evidence points toward these duplications being intentional acts and not the result of honest error.
- 3. The authors purport that the mechanism of miR-1 silencing is methylation of the CpG island. Figure 2B is key in demonstrating this in liver cancer cell lines. However, Figure S1 takes it one step further and shows that when treated with aza, demethylation occurs, thereby strengthening the results of Figure 2.
- 4. The COMIC has found clear evidence of the manipulation of multiple sections of other figures within the manuscript (see <u>Allegation #29</u> above), which is sufficient to suggest that Dr. Jacob was not responsible for these duplications and prove that others had sufficient skill in manipulating images to mask splice and/or cut/paste lines.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Supplemental Figure 1 and that the actions of others caused the falsification within Supplemental Figure 1 in Allegation #80, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Supplemental Figure 1, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Supplemental Figure 1, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

#### Manuscript #10 under Review - Datta et al., Cancer Res 2009 (4 Allegations)

Datta J, Ghoshal K\*, Denny WA, Gamage SA, Brooke DG, Phiasivongsa P, Redkar S, Jacob ST\*. "A new class of quinoline-based DNA hypomethylating agents reactivates tumor suppressor genes by blocking DNA methyltransferase 1 activity and inducing its degradation." Cancer Res. 2009 May 15; 69 (10): 4277-85. Epub 2009 May 5. \*\*co-corresponding authors\*

**Manuscript #10, Allegation #30 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1, lane 2, and in lane 3 in the GAPDH blot in Figure 5B in Datta et al., Cancer Res 2009.

#### **Finding of Fact:**

1. Figure 5B is a Western blot for DNMT1 and GAPDH from HCT116 cells (human colon cancer cells) treated for various times with SGI-1027, a quinolone-based inhibitor of DNMTs. The figure shows the depletion of DNMT1 as early as 6hrs.

- 2. Both Adobe Photoshop overlay analysis and gradient mapping demonstrate significant similarity of the bands in lanes 1, 2, and 3 of the GAPDH blot (see slides 114-115818).
- 3. A small band artifact (notch) on the right upper end of the band appears in lanes 1, 2, and 3, providing further evidence that the same data has been used for all three lanes even though they purport to represent different experimental conditions.
- 4. No original data were available for this figure. The files identified as relevant data by Dr. Datta on February 26, 2018, do not correspond to the data published in Figure 5B (see slides 116-117<sup>819</sup>).
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in each of the first three GAPDH lanes in Figure 5B, which the Committee concludes is indicative of falsification.
- 6. On September 28, 2017, Dr. Ghoshal received a "New Comment" email notification from PubPeer<sup>820</sup> indicating there was a new comment on Datta et al. 2009. The next day, September 29, 2017, Dr. Ghoshal forwarded the PubPeer email notice to Dr. Datta,<sup>821</sup> thus indicating that at least Drs. Ghoshal and Datta knew of potential issues with the research for at least three (3) weeks prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. As of the September 28, 2017, PubPeer had published one (1) comment, corresponding to Allegation #30.
- 7. Dr. Datta was first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Kalpana Ghoshal was a co-corresponding author of Cancer Res 2009 and a Research Assistant Professor in the laboratory of Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2009.

#### Respondent's Response:

- 1. Dr. Datta said in her interview with the CII on March 1, 2018 that she did the experiment for this figure, but could not recall who made the figure and was not able to find the original data for this figure. But a did agree that the data seemed similar, but countered, "if you run the same amount of proteins, especially like --- like the normalizer, they might look the same". But a said that this was a second run of the experiment whereby the conditions were being optimized. But a said that this was a second run of the experiment whereby the conditions were being optimized. But a said that this was a second run of the experiment whereby the conditions were being optimized. But a said that this was a second run of the experiment whereby the conditions were being optimized.
- 2. In her written response provided to ORC on May 18, 2018, Dr. Datta reiterated that she was unable to produce the original data, expressed disagreement with the allegation, indicating that the lanes are very similar but not identical, and provided data from a related experiment showing that the bands can look very similar. Dr. Datta further argues and has provided a new figure in support that "even if we remove either one of the GAPDH and corresponding DNMT1 data (lanes 1 and 3) under question, the major conclusion (SGI-1027 treatment results in DNMT1 degradation and it is an early event) of the data in the figure remains valid" (emphasis added by author). 825
- 3. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 4. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

<sup>818</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 114-115

<sup>819</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 116-117

<sup>820</sup> Ex. 347 - 20170928 - Email PubPeer to Ghoshal - New comment (Datta et al. Cancer Res 2009)

<sup>821</sup> Ex. 348 - 20170929 - Email Ghoshal to Datta - New comment (Datta et al. Cancer Res 2009)

<sup>822</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 71, lines 20-21

<sup>823</sup> Ex. 57 - 20180301-CII Interview + errata - Datta, page 72, lines 1-3

<sup>824</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 72 line 19

<sup>825</sup> Ex. 78 - OSU Response 1-JD, pages 2-3



- 6. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 7. This allegation was not specifically discussed with Dr. Datta during her interview with the COMIC on June 28, 2019. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the first nor the corresponding author have taken responsibility for generation of Figure 5B, but both espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. The expression levels for control proteins can be similar but not identical, making it very likely that a single blot was reused to represent three different experimental conditions (i.e. three of the figure's five timepoints). The preponderance of the evidence points toward this duplication being an intentional act and not the result of honest error. The lack of a verified loading controls invalidate the stated impact of the expression levels of the proteins, as this is dependent on a valid loading control, which is now not available. Since DNMT1 expression is relative to the GAPDH controls, the conclusion that DNMT1 expression decreases after treatment with SGI-1027 cannot be supported.
- 3. The COMIC has found clear evidence of the manipulation of other figures within other manuscripts (see <u>Allegation #29</u> above), which is sufficient to prove that others had sufficient skill in manipulating images to mask splice and/or cut/paste lines and strongly suggest that Dr. Jacob was not the primary person involved in the falsification of data within the Jacob laboratory.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Drs. Ghoshal and Datta at the time of their initial notification of allegations by OSU, yet both failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by both Dr. Ghoshal and Dr. Datta.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 5B and that the actions of others caused the falsification within Figure 5B in Allegation #30, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figure 5B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figure 5B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #10, Allegation #81 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 5 (SGI-1027-12d) and lane 6 (SGI-1027-15d) in the P16-U-R1 151 bp sample in Figure 4A in Datta et al., Cancer Res 2009.

#### **Finding of Fact:**

- Figure 4 shows the results of methylation-specific PCR and COBRA analysis of the P16 and TIMP genes in colon cancer cells (RKO). Figure 4A shows the PCR results for bisulfite-converted genomic DNA using P16 PCR primers for unmethylated (P16-U-R1 and P16-U-R2) and methylated (P16-M-R1 and P16-M-R2) CpG islands of P16 exon 1. Cells were treated with decitabine or SGI-1027. Allegation #81 is the re-use of a band in the P16-U-R1 panel for both the SGI-1027 -12d and -15d treated samples.
- 2. Both Adobe Photoshop overlay analysis and gradient mapping demonstrate significant similarity of the bands in lanes 5 and 6 of the P16-U-R1 151 bp sample in Figure 4A (see slide 119826).
- 3. No original data were available for this figure.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 5 and 6 of the P16-U-R1 151 bp sample in Figure 4A, which the Committee concludes is indicative of falsification.
- 5. Dr. Datta was first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 6. Dr. Kalpana Ghoshal was a co-corresponding author of Cancer Res 2009 and a Research Assistant Professor in the laboratory of Samson Jacob at the time of publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2009.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Drs. Jacob, Ghoshal, and Datta were not questioned about this allegation during the Inquiry phase of the case.
- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 3. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the first nor the corresponding authors have taken responsibility for generation of Figure 4A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. The expression levels for amplicons can be similar but not identical, making it very likely that a single band was reused to represent expression levels for two different experimental conditions. The authors contend that SGI-1027 causes demethylation of P16 CpG islands, similar to that of Decitabine. Duplicating bands (151 bp amplicon for unmethylated targets) for Decitabine treatment at 12 and 15d raises questions as to whether treatment had any effect in these cells. Given the number of allegations within Figure 4 in this manuscript, the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr.

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<sup>826</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 119

Jacob was not responsible for the creation of Figure 4A and that the actions of others caused the falsification within Figure 4A in Allegation #81, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

4. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the P16-U-R1 151 bp images in Figure 4A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the P16-U-R1 151 bp images in Figure 4A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #10, Allegation #82 –** S.T. Jacob reported falsified data by the reuse of the same data in lane 2 (control), lane 3 (Decitabine-12d) and lane 4 (Decitabine-15d) in the P16-M-R2 234 bp sample in Figure 4A, in Datta et al., Cancer Res 2009.

#### **Finding of Fact:**

- Figure 4 shows the results of methylation-specific PCR and COBRA analysis of the P16 and TIMP genes in colon cancer cells (RKO). Figure 4A shows the PCR results for bisulfite-converted genomic DNA using P16 PCR primers for unmethylated (P16-U-R1 and P16-U-R2) and methylated (P16-M-R1 and P16-M-R2) CpG islands of P16 exon 1. Cells were treated with decitabine or SGI-1027. Allegation #82 for Figure 4A is reuse of bands in the P16-M-R2 panel for lanes 2 (control), 3 (decitabine treated 12d), and 4 (decitabine treated 15d).
- 2. Both Adobe Photoshop overlay analysis and gradient mapping demonstrate significant similarity of the bands in lanes 2, 3, and 4, in the P16-U-R2 234 bp sample in Figure 4A (see slide 120<sup>827</sup>). Splice lines are evident at the edges of each lane, as well as especially sharp rectangular lines around the lane 3 (Decitabine-12d) blot. A unique, darkened spot appears in the lower third of each lane's background, further indicating that the same data have been reused.
- 3. No original data were available for this figure.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 2, 3, and 4 of the P16-U-R2 234 bp sample in Figure 4A, which the Committee concludes is indicative of falsification.
- 5. Dr. Datta was first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 6. Dr. Kalpana Ghoshal was a co-corresponding author of Cancer Res 2009 and a Research Assistant Professor in the laboratory of Samson Jacob at the time of publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2009.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Drs. Jacob, Ghoshal, and Datta were not questioned about this allegation during the Inquiry phase of the case.
- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July

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<sup>827</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 120



- 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 3. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the first nor the corresponding authors have taken responsibility for generation of Figure 4A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. The expression levels for amplicons can be similar but not identical, making it very likely that a single band was reused to represent three different experimental conditions, in this case as a control and two different treatment conditions. Given the number of allegations within Figure 4 in this manuscript, the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error. Figure 4A shows the methylated and unmethylated PCR products of P16 when treated with decitabine and other novel compounds. Key to interpretation of the figure as a whole is the ability to show consistent methylation of P16 CpG islands in RKO cells. Duplication raises concerns that methylation may not be consistently observed in these control cells, raising concern that unmethylated targets (in Decitabine or SGI-1027 treated cells) may not in fact represent a treatment effect. Since the control lane cannot be trusted, the conclusion that "only methylated amplicons were obtained in the untreated RKO cells" cannot be made. The authors do, however, show this same trend with another primer pair, which may decrease the significance of the duplication on the outcome.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 4A and that the actions of others caused the falsification within Figure 4A in Allegation #82, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 4. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the P16-M-R2 234 bp images in Figure 4A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the P16-M-R2 234 bp images in Figure 4A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #10, Allegation #83 –** S.T. Jacob reported falsified data by the reuse of the same data in lane 4 (Decitabine-7d) and lane 5 (SGI-1027-5d) in the TIMP-3-M 116BP sample in Figure 4B in Datta et al., Cancer Res 2009.

#### **Finding of Fact:**

- Figure 4 shows the results of methylation specific PCR and COBRA analysis of the P16 and TIMP genes in colon cancer cells (RKO). Figure 4B shows the PCR results for bisulfite-converted genomic DNA using TIMP3 PCR primers for unmethylated (TIMP-3-U) and methylated (TIMP-3-M) CpG islands of TIMP3. Allegation #83 is the reuse of a band in lanes treated with decitabine (lane 4) and SGI-1027 (lane 5).
- 2. Both Adobe Photoshop overlay analysis and gradient mapping demonstrate significant similarity of the bands in lanes 4 and 5 in the TIMP-3-M 116BP sample in Figure 4B (see slide 121828). Gradient map features are strikingly similar for both the bands and lower half of the backgrounds of these two lanes, which is not likely to have occurred by chance.
- 3. No original data were available for this figure.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the bands and background of lane 4 as lane 5 indicative of falsification.
- 5. Dr. Datta was first author of Cancer Res 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 6. Dr. Kalpana Ghoshal was a co-corresponding author of Cancer Res 2009 and a Research Assistant Professor in the laboratory of Samson Jacob at the time of publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Cancer Res. 2009.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Drs. Jacob, Ghoshal, and Datta were not questioned about this allegation during the Inquiry phase of the case.
- 2. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 3. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 4. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the first nor the corresponding authors have taken responsibility for generation of Figure 4B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. The expression levels for amplicons can be similar but not identical, making it very likely that a single band was reused to represent two different experimental conditions. The duplication is meant to show residual methylated CpG islands following Decitabine and SGI-1027 treated cells. Given the number of allegations within Figure 4 in this manuscript, the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error. The impact of the manipulation in TIMP-3 in Figure 4B is more significant because only one primer pair is used, although the significance of this duplication to the overall conclusions of the paper is likely minimal.
- 3. Files found on Dr. Ghoshal's hard drive provide clear evidence of her figure manipulation skills dating back to 2007 (see <u>Allegation #29</u> above) and strongly suggest Dr. Ghoshal as the primary person involved

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<sup>828</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 121

in the falsification of data within the Jacob laboratory. However, as Dr. Datta has not provided satisfactory explanations or an affirmative defense, the Committee must conclude that she shares responsibility as first author and/or was complicit in the act of falsification.

- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 4B and that the actions of others caused the falsification within Figure 4B in Allegation #83, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the TIMP-3-M 116BP images in Figure 4B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the TIMP-3-M 116BP images in Figure 4B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

#### Manuscript #11 under Review - Ramaswamy et al., Mol Endo 2009 (3 Allegations)

Ramaswamy B\*, Majumder S\*, Roy S, Ghoshal K, Kutay H, Datta J, Younes M, Shapiro CL, Motiwala T\*\*, Jacob ST\*\*. "Estrogen-mediated suppression of the gene encoding protein tyrosine phosphatase PTPRO in human breast cancer: mechanism and role in tamoxifen sensitivity." Mol Endocrinol. 2009 Feb; 23 (2): 176-87. Epub 2008 Dec 18 \* co-first authors \*\* co-corresponding authors

**Manuscript #11, Allegation #31 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 4 and in lane 5 in the 18S rRNA gel image in Figure 2A in Ramaswamy et al., Mol Endocrinol 2009.

#### **Finding of Fact:**

- 1. Figure 2A shows RT-PCR for PTPRO, ERα, ERβ and 18S rRNA control from normal human epithelial cells (HMEC-184, HMEC-48R) and breast cancer cell lines (MCF-7, MB-231, Hs578t).
- 2. Adobe Photoshop overlay analysis demonstrated that significant overlap and similarity exists between lanes 4 and 5 of the 18S rRNA gel image (see slide 124829).
- 3. No original data could be located for this manuscript.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 4 and 5 of the 18S rRNA image in Figure 2A, which the Committee concludes is indicative of falsification.
- 5. Figure inconsistencies in Ramaswamy et al. Mol Endo 2009 were published on the web (i.e. PubPeer) and known at least to Dr. Majumder and other members of the laboratory as early as March 2018. 830 At that time, PubPeer had published three (3) comments, corresponding to Allegations #31-33. Given the consistent level of communication amongst members of the Jacob laboratory and the evidence that Dr. Jacob was corresponding with other laboratory members about concerns and PubPeer comments

<sup>829</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 124

<sup>830</sup> These data are reviewed elsewhere under DIO 6820.

for an additional manuscript on which Dr. Jacob is a primary author (see previous discussions of Manuscript #2), the Committee believes that it is reasonable to conclude that Dr. Jacob would have also been aware of the PubPeer concerns for this manuscript.

- 6. Dr. Sarmila Majumder was a co-first author of Mol Endocrinol 2009 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Tasneem Motiwala was a co-corresponding author of Mol Endocrinol 2009 and a Research Scientist from 2006-2014 in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Mol Endocrinol 2009.

#### Respondent's Response:

- 1. During her interview with the CII on March 7, 2018,<sup>831</sup> co-first author, Dr. Ramaswamy, generally described that she was not involved in the generation of figures for manuscripts during her time in the lab and specifically that she left the lab in 2005, well before the manuscript's publication in 2009.<sup>832</sup> Dr. Ramaswamy stated that her role as first author was primarily due to the fact that the provided the clinical subjects and associated samples.<sup>833</sup> Dr. Ramaswamy noted that she did not make the figure in question.<sup>834</sup>
- 2. Co-first author, Dr. Majumder, described in her written response provided to ORC on April 18, 2018<sup>835</sup> that the original data had been lost, discarded, or unavailable. Dr. Majumder did not remember who made the figures in this publication. Specifically, Dr. Majumder stated:

"In this figure expression of PTPRO, ERα and ERβ in different breast cancer cell lines were presented. 18S RNA was used as loading control in the western blot. In my analysis of the zoomed-in figure, three of the five 18S appears very similar, which is expected as this is a house-keeping gene. It is important to note that the only conclusion drawn from Fig.2A is whether PTPRO was expressed but not the level of its expression in these cell lines that would depend on level of 18S in each cell line. Therefore, if an error was made, it was plainly inadvertent; it does not change the conclusion. There was no possible motive to fabricate this data."836

- 3. Co-corresponding author, Dr. Motiwala, stated in her written response provided to ORC on June 22, 2018, that the figure "did not show any signs of splicing of the gel that would result from the use of the same data in two lanes." B37 Dr. Motiwala also stated in her written response that she did not recall who conducted each experiment or who prepared the figures for publication. Dr. Motiwala wrote that she was listed as co-corresponding author "primarily due to my contribution in conception and design of the study."
- 4. Dr. Jacob did not provide a specific response to this allegation during the Inquiry phase of the case.
- 5. In her response to the CII's preliminary report<sup>839</sup> and her appeal of their determination, <sup>840</sup> Dr. Majumder reiterated her assertion that data represents a quantitative analysis, that the bands look similar because they are housekeeping bands, and "that all five lanes look very similar and they are supposed to be

<sup>831</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy

<sup>832</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, pages 14-15

<sup>833</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 20

<sup>834</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 25, lines 15-16

<sup>835</sup> Ex. 99 - OSU Response 041818.SM

<sup>836</sup> Ex. 99 - OSU Response 041818.SM, page 1

<sup>837</sup> Ex. 119 - CII response-Mol Endo-062218, page 1

<sup>838</sup> Ex. 119 - CII response-Mol Endo-062218, page 1

<sup>839</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918

<sup>840</sup> Ex. 252 - Majumder Zadnik-letter-111218

- similar, as rRNAs constitute the bulk of the total RNA in any organism/cells."841 Dr. Majumder maintained that any overlap is coincidental and argued that duplication could not have occurred without a visible splice line.
- 6. In her response to the CII's preliminary report<sup>842</sup> and her appeal of their determination, <sup>843</sup> Dr. Motiwala continued to stand behind her assertion that "the forensic analysis is still not showing splice lines, just the similarity between the bands. I would request the committee to demonstrate splice lines or explain how it would be possible to duplicate lanes without splicing." <sup>844</sup>

Furthermore, Dr. Motiwala stood behind the scientific findings represented by the figure and argued the CII's description of 18S rRNA as a loading control:

"This figure demonstrates the presence or absence of PTPRO, ERα and ERβ in different breast cancer cell lines. Our studies have shown that PTPRO is completely silenced in the MCF-7 and MB231 cells... Thus, no matter how much cDNA we would use, we would not see expression of these genes since they are silenced in the respective cell lines. Thus, this is an all or none expression experiment v/s differential expression based on intensity of the band. In this context the 18S rRNA panel is not a true loading control to show "experimental outcomes are due to the experimental treatments only". 845

Finally, Dr. Motiwala referred also to the response provided by Dr. Majumder for this manuscript.

- 8. In her interview with the COMIC on June 12, 2019, 846 Dr. Majumder reconfirmed that the project had initially been that of Dr. Ramaswamy who worked initially with Dr. Motiwala then later with Dr. Majumder, that should could not recall the contributions of all authors, and that she would have performed some experiments that might have been "left over" once Dr. Ramaswamy left the laboratory<sup>847</sup> and may have constructed the figure. 848 Dr. Majumder indicated that her answers would be the same as those previously provided to the CII and via her appeal, that in the absence of raw data she disagreed that there was a duplication in the figure, and that there would be no motive for duplication as the conclusion wouldn't change. 849 See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 9. In her interview with the COMIC on June 12, 2019,<sup>850</sup> Dr. Motiwala again challenged the forensic findings and questioned the possibility of duplication in the absence of a visible splice line. See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.
- 10. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

#### Respondent's Responsibility and Intent:

1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the

<sup>841</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 8-9

<sup>&</sup>lt;sup>842</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>843</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>844</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 3

<sup>&</sup>lt;sup>845</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 6

<sup>846</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1

<sup>847</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 74 line 20 to page 75 line 15

<sup>848</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 77 line 3-6

<sup>849</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 75 line 24 to page 76 line 12

<sup>850</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 67 line 10 to page 68 line 8

co-corresponding author have taken responsibility for generation of Figure 2A, though Dr. Majumder has indicated she could have prepared the figure and any error would have been an inadvertent one. They both espouse the view that all authors on a publication are responsible for its scientific integrity and content (or at least the first author's responsibility, in the opinion of Dr. Majumder<sup>851</sup>). However, as Dr. Majumder (who was considered a faculty member at the time of publication of this manuscript) has not provided satisfactory explanation for or an affirmative defense of the duplication, the Committee must conclude that she bore responsibility as first author for creating or verifying the validity of the figure and/or was complicit in the act of falsification.

- 2. The expression levels for proteins can be similar but not identical, making it very likely that a single band was reused to represent two different experimental conditions. The authors' description of the data as qualitative is correct; however, the Committee disagrees that variability in a control lane would not change the figure's conclusions. The lack of a verified loading controls invalidate the stated impact of the expression levels of the proteins, as this is dependent on a valid loading control, which is now not available.
- 3. The Committee found unacceptable Dr. Majumder's argument that if a "mix up" in data presentation did occur the conclusions drawn are not changed. Such rationale fails to meet the standards of data presentation and accurate disclosure of laboratory results in published research findings, and the Committee finds this to be unacceptable practice and unacceptable rationale in addressing the allegation.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2A and that the actions of others caused the falsification within Figure 2A in Allegation #31, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The dissenting voter believed that Dr. Jacob did act recklessly at the preponderance of the evidence standard in his oversight of this project, contending that the community standard would involve higher levels of oversight when a clinical trainee was involved in laboratory research and that as PI, Dr. Jacob was on notice that he should have reviewed the data and figures with additional scrutiny when it was deemed time to publish the research two years later.
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 1 in favor (reckless) and 6 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the 18S rRNA images in Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the 18S r RNA images in Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #11, Allegation #32 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 5 of the 18S rRNA gel image in Figure 2D in Ramaswamy et al., Mol Endocrinol 2009.

#### **Finding of Fact:**

1. Figure 2D shows an RT-PCR for PTPRO and 18S rRNA control in breast cancer cell lines (MCF7 and

<sup>851</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 23, lines 13-23; page 36, lines 6-10



MB231) untreated or treated with AzaC and for untreated Brain RNA.

- 2. Adobe Photoshop overlay analysis demonstrated that significant overlap and similarity exists between lanes 1 and 5 of the 18S rRNA blot (see slide 125<sup>852</sup>).
- 3. No original data could be located for this manuscript.
- 4. The Committee finds the forensic evidence and visual inspection demonstrates lanes 1 and 5 of the 18S rRNA gel in Figure 2D are duplicated, which the Committee concludes is indicative of falsification.
- 5. Figure inconsistencies in Ramaswamy et al. Mol Endo 2009 were published on the web (i.e. PubPeer) and known at least to Dr. Majumder and other members of the laboratory as early as March 2018. 853 At that time, PubPeer had published three (3) comments, corresponding to Allegations #31-33. Given the consistent level of communication amongst members of the Jacob laboratory and the evidence that Dr. Jacob was corresponding with other laboratory members about concerns and PubPeer comments for an additional manuscript on which Dr. Jacob is a primary author (see previous discussions of Manuscript #2), the Committee believes that it is reasonable to conclude that Dr. Jacob would have also been aware of the PubPeer concerns for this manuscript.
- 6. Dr. Sarmila Majumder was a co-first author of Mol Endocrinol 2009 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Tasneem Motiwala was a co-corresponding author of Mol Endocrinol 2009 and a Research Scientist from 2006-2014 in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Mol Endocrinol 2009.

#### Respondent's Response:

- 1. During her interview with the CII on March 7, 2018,<sup>854</sup> co-first author, Dr. Ramaswamy, generally described during her interview that she was not involved in the generation of figures for manuscripts during her time in the lab and specifically that she left the lab in 2005, well before the manuscript's publication in 2009.<sup>855</sup> Dr. Ramaswamy said her role as first author was primarily due to the fact that the provided the clinical subjects and associated samples.<sup>856</sup> Dr. Ramaswamy noted that she did not make any of figures noted here.<sup>857</sup>
- 2. Co-first author, Dr. Majumder, described in her written response provided to ORC on April 18, 2018, 858 that the original data had been lost, discarded, or unavailable. Dr. Majumder did not remember who made the figures in this publication. Dr. Majumder asserted,

"18S in lane 1 and 5 looks similar but not identical, which again is expected as this is a house-keeping gene. The conclusion drawn from this experiment was that if PTPRO was re-expressed upon AZAC treatment but **not** to what extent where 18S level would have been important. Therefore, if an error was made, it was plainly inadvertent; it does not change the conclusion. There was no possible motive to fabricate this data".<sup>859</sup>

3. Dr. Motiwala stated in her written response provided to ORC on June 22, 2018 that the figure showed qualitative data and as 18s rRNA was a loading control so any variability in its expression would not impact the results. 860 Dr. Motiwala further stated that she did not recall who conducted each experiment or who prepared the figures for publication.

<sup>852</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 125

<sup>853</sup> These data are reviewed elsewhere under DIO 6820.

<sup>854</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy

<sup>855</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, pages 14-15

<sup>856</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 20

<sup>857</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 25, lines 15-16

<sup>858</sup> Ex. 99 - OSU Response 041818.SM

<sup>859</sup> Ex. 99 - OSU Response 041818.SM, page 1

<sup>860</sup> Ex. 119 - CII response-Mol Endo-062218, page 1

- 4. Dr. Jacob did not provide a specific response to this allegation during the Inquiry phase of the case.
- 5. In her response to the CII's preliminary report<sup>861</sup> and her appeal of their determination,<sup>862</sup> Dr. Majumder contested the forensic findings, argued that as a housekeeping gene 18S rRNA would be expected to be similar across lanes, and maintained that the findings were still valid and replicated across different experiments within the publication leaving no motive for fabricating results.
- 6. In her response to the CII's preliminary report<sup>863</sup> and her appeal of their determination,<sup>864</sup> Dr. Motiwala again maintained that "this is a qualitative comparison where loading control is not necessarily used to show that 'experimental outcomes are due to the experimental treatments only'." Finally, Dr. Motiwala referred also to the response provided by Dr. Majumder.
- 7. In her interview with the COMIC on June 12, 2019, 866 Dr. Majumder indicated she had the same set of answers as previously and that while the blots look similar, if there was a duplication, it does not impact the findings of the figure or manuscript. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 9. In her interview with the COMIC on June 12, 2019, <sup>867</sup> Dr. Motiwala indicated that she had the same set of answers as previously and that if there was a duplication, it would not impact the qualitative findings of the figure or manuscript. Dr. Motiwala stated that she did not think she generated this figure and wouldn't know who might have based on his/her expertise. See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.
- 10. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the co-corresponding author have taken responsibility for generation of Figure 2D, though Dr. Majumder has indicated she could have prepared the figure and any error would have been an inadvertent one. They both espouse the view that all authors on a publication are responsible for its scientific integrity and content (or at least the first author's responsibility, in the opinion of Dr. Majumder<sup>868</sup>). However, as Dr. Majumder (who was considered a faculty member at the time of publication of this manuscript) has not provided satisfactory explanation for or an affirmative defense of the duplication, the Committee must conclude that she bore responsibility as co-first author for creating or verifying the validity of the figure and/or was complicit in the act of falsification.
- 2. The expression levels for proteins can be similar but not identical, making it very likely that a single band was reused to represent two different experimental conditions. The authors' description of the data as qualitative is correct; however, the Committee disagrees that variability in a control lane would not change the figure conclusions because equal loading of samples is required to show that the experimental outcomes are due to the experimental treatments only and not unequal loading or failure of experimental conditions. The lack of a verified loading controls invalidate the stated impact of the expression levels of the proteins, as this is dependent on a valid loading control, which is now not available.

<sup>&</sup>lt;sup>861</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 9-10

<sup>862</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>863</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>&</sup>lt;sup>864</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>865</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 6

<sup>866</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 77

<sup>867</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 68-69

<sup>868</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 23, lines 13-23; page 36, lines 6-10

- 3. The Committee found the argument that, if duplication did occur, it does not impact the findings of the paper, inconsistent with standard scientific practice and unacceptable for standards of data presentation and accurate disclosure of laboratory results. Thus, the Committee does not agree with the arguments provided by Dr. Motiwala and Dr. Majumder that if duplication of data exists in the figure that it does not matter, and the Committee does not accept this line of argument as valid.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2D and that the actions of others caused the falsification within Figure 2D in Allegation #32, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The dissenting voter believed that Dr. Jacob did act recklessly at the preponderance of the evidence level in his oversight of this project, contending that the community standard would involve higher levels of oversight when a clinical trainee was involved in laboratory research and that as PI, Dr. Jacob was on notice that he should have reviewed the data and figures with additional scrutiny when it was deemed time to publish the research two years later.
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 1 in favor (reckless) and 6 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the 18S rRNA images in Figure 2D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the 18S rRNA images in Figure 2D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #11, Allegation #33 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 4 of the ER $\beta$  blot in Figure 4C in Ramaswamy et al., Mol Endocrinol 2009.

#### **Finding of Fact:**

- 1. Figure 4C shows RT-PCR for PTPRO, ERα, ERβ and β-actin as a control, from the Hs578t breast cancer cell line transfected with either ERα or ERβ, and untreated or treated with 17β-estradiol.
- 2. Adobe Photoshop overlay analysis and gradient mapping demonstrated significant overlap and similarity between lanes 1 and 4 of the ERβ blot (see slide 126<sup>869</sup>). Furthermore, application of Adobe Photoshop gradient maps and embossing features demonstrated sharp lines and boxes around bands in lane 2, and abrupt changes in background intensity and splice lines at both edges of lane 4, indicative of image splicing or cutting and pasting bands into the figure.
- 3. No original data could be located for this manuscript.
- 4. The Committee finds the forensic evidence and visual inspection demonstrate near perfect overlay of lanes 1 and 4 of the ERβ blot of Figure 4C as well as a box around the band in lane 2 of the ERβ blot of Figure 4C, which the Committee concludes is indicative of falsification.
- 5. Figure inconsistencies in Ramaswamy et al. Mol Endo 2009 were published on the web (i.e. PubPeer) and known at least to Dr. Majumder and other members of the laboratory as early as March 2018.870

<sup>869</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 126

<sup>&</sup>lt;sup>870</sup> These data are reviewed elsewhere under DIO 6820.

At that time, PubPeer had published three (3) comments, corresponding to Allegations #31-33. Given the consistent level of communication amongst members of the Jacob laboratory and the evidence that Dr. Jacob was corresponding with other laboratory members about concerns and PubPeer comments for an additional manuscript on which Dr. Jacob is a primary author (see previous discussions of Manuscript #2), the Committee believes that it is reasonable to conclude that Dr. Jacob would have also been aware of the PubPeer concerns for this manuscript.

- 6. Dr. Sarmila Majumder was a co-first author of Mol Endocrinol 2009 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Tasneem Motiwala was a co-corresponding author of Mol Endocrinol 2009 and a Research Scientist from 2006-2014 in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Mol Endocrinol 2009.

### Respondent's Response:

- 1. During her interview with the CII on March 7, 2018,<sup>871</sup> co-first author, Dr. Ramaswamy, generally described during her interview that she was not involved in the generation of figures for manuscripts during her time in the lab and specifically that she left the lab in 2005, well before the manuscript's publication in 2009.<sup>872</sup> Dr. Ramaswamy's role as first author was primarily due to the fact that the provided the clinical subjects and associated samples.<sup>873</sup> Dr. Ramaswamy noted that she did not make the figure noted here.<sup>874</sup>
- 2. Co-first author, Dr. Majumder, described in her written response provided to ORC on April 18, 2018, 875 that the original data had been lost, discarded, or unavailable. Dr. Majumder maintains that no conclusions were drawn from these lanes, there would be no motive to falsify the data, and that if a mistake were made it would be completely inadvertent. 876
- 3. In a written response provided to ORC on April 18, 2018, Dr. Motiwala stated: "Since the data in lanes 1 and 4 of the ERβ blot were not significant to the conclusion drawn from this figure, I do not see any motive for falsification of data in those lanes."

  877 Dr. Motiwala also stated in her written response that she did not recall who conducted each experiment or who prepared the figures for publication.
- 4. In her response to the CII's preliminary report<sup>878</sup> and her appeal of their determination,<sup>879</sup> Dr. Majumder described the science underlying the figure and that the bands in question were not used in any conclusions drawn by the paper and that there would have been no motive for duplication. Dr. Majumder further argued that duplication should be coincident with visible splice lines, contested the forensic findings, argued that as a housekeeping gene 18S rRNA would be expected to be similar across lanes, and maintained that the findings were still valid and replicated across different experiments within the publication leaving no motive for fabricating results.
- 5. In her response to the CII's preliminary report<sup>880</sup> and her appeal of their determination,<sup>881</sup> Dr. Motiwala challenged the forensic analysis and referred to the response provided by Dr. Majumder.<sup>882</sup>
- 6. In her interview with the COMIC on June 12, 2019, 883 Dr. Majumder could not remember who performed the experiment or constructed the figure, was not convinced that a duplication had occurred, and could

<sup>871</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy

<sup>872</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, pages 14-15

<sup>873</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 20

<sup>874</sup> Ex. 61 - 20180307-CII Interview + errata -Ramaswamy, page 25, lines 15-16

<sup>875</sup> Ex. 99 - OSU Response 041818.SM

<sup>876</sup> Ex. 99 - OSU Response 041818.SM, page 1

<sup>877</sup> Ex. 119 - CII response-Mol Endo-062218, page 1

<sup>878</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 9-10

<sup>879</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>880</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218

<sup>881</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>882</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 2 and 6

<sup>883</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1



- not rely on the software showing such.<sup>884</sup> See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 7. In her interview with the COMIC on June 12, 2019, <sup>885</sup> Dr. Motiwala indicated that she wouldn't know who constructed the figure and that anyone could have performed the experiment. Dr. Motiwala was reluctant to accept the forensics showing a duplication in the absence of visible splicing. <sup>886</sup> Dr. Motiwala described the role of corresponding author as someone with responsibility to see that the data are accurately represented, that the interpretations are correct: someone who above all others stands for the credibility and accuracy of the data presented. <sup>887</sup> See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.
- 8. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the co-corresponding author have taken responsibility for generation of Figure 4B, nor acknowledged the alleged duplication. They both espouse the view that all authors on a publication are responsible for its scientific integrity and content (or at least the first author's responsibility, in the opinion of Dr. Majumder<sup>888</sup>). However, as Dr. Majumder (who was considered a faculty member at the time of publication of this manuscript) has not provided satisfactory explanation for or an affirmative defense of the duplication, the Committee must conclude that she bore responsibility as first author for creating or verifying the validity of the figure and/or was complicit in the act of falsification.
- 2. Evidence points to lanes 1 and 4 being duplicates of the same data though reported to represent entirely different experimental conditions, which would not be scientifically valid or acceptable. The expression levels for proteins can be similar but not identical, making it very likely that a single band was reused to represent two different experimental conditions. Additional splice lines and a box around the band in lane 2 suggest that data were also pasted into the figure, raising further doubts as to these being unintentional or honest errors. The duplication and insertion of additional data directly points to an intent to mislead the reader as to the experimental findings. Figure 4 demonstrates that estrogen receptor beta (not alpha) is involved in the estrogen mediated suppression of PTPRO. Increased expression of estrogen receptor beta ablates PTPRO expression when treated with estradiol. This is significant to the overall conclusions of the paper. The lanes that were duplicated are in estrogen receptor beta expression and not PTPRO, so the overall significance of the duplication is relatively minor.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 4C and that the actions of others caused the falsification within Figure 4C in Allegation #33, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>884</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 78 line 8 to page 79 line 1; page 81 line 3-12

<sup>885</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 70-71; page 75 line 17

<sup>886</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 75 line 5-13

<sup>887</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala\_Redaction 1, page 73 line 3-11

<sup>888</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 23, lines 13-23; page 36, lines 6-10

- 4. The dissenting voter believed that Dr. Jacob did act recklessly in his oversight of this project, contending that the community standard would involve higher levels of oversight when a clinical trainee was involved in laboratory research and that as PI, Dr. Jacob was on notice that he should have reviewed the data and figures with additional scrutiny when it was deemed time to publish the research two years later.
- 5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 1 in favor (reckless) and 6 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified ERβ images in Figure 4C, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified ER $\beta$  images in Figure 4C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

## Manuscript #12 under Review - Lu et al., JBC 2011 (6 Allegations)

Lu Y, Roy S, Nuovo G, Ramaswamy B, Miller T, Shapiro C, Jacob ST\*, Majumder S\*. "Anti-microRNA-222 (anti-miR-222) and -181B suppress growth of tamoxifen-resistant xenografts in mouse by targeting TIMP3 protein and modulating mitogenic signal. J Biol Chem. 2011 Dec 9; 286 (49): 42292-302. Epub 2011 Oct 18. **RETRACTED** 02/13/18<sup>889</sup> \* co-corresponding authors

**Manuscript #12, Allegation #34 -** S.T. Jacob reported falsified data by splicing between lanes 2 and 3 in the p-p42/44-MAPK blot and between lanes 3 and 4 of the total MAPK blot in Figure 5E in Lu et al., J Biol Chem 2011.

#### **Finding of Fact:**

- 1. Figure 5E shows Western blots for MAPK phosphorylation (p-p42/44-MAPK) and total MAPK in MCF-7 cells transfected with vector or miR-221/222, and treated with 0, 0.1, and 1.0 ng/ml EGF.
- 2. Adobe Photoshop gradient mapping showed that splicing was likely used between lanes 2 and 3 of the p-p42/44-MAPK blot as well as between lanes 3 and 4 of the total MAPK blot (see slide 129<sup>890</sup>). Gradient mapping shows less definitively that splicing may have also occurred between lanes 3 and 4 and between lanes 4 and 5 of the p-p42/44-MAPK blot.
- 3. The proposed corrected Figure 5E, submitted by Dr. Jacob, does not address the first subpart of this allegation regarding the splicing between lanes 2 and 3 in the p-p42/44-MAPK blot.
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 5E) within this manuscript from the Journal of Biological Chemistry on June 30, 2017,<sup>891</sup> Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017.<sup>892</sup> As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on November 2, 2017.<sup>893, 894</sup>
- 5. No original data could be located.
- 6. The Committee finds the forensic evidence, visual inspection, the CII interview of Dr. Majumder, and the statement provided by Dr. Jacob to JBC confirms a line between lanes 2 and 3 of the p-p42/44-MAPK

<sup>889</sup> Ex. 24 - 20180213-Retraction-J. Biol. Chem.-2018-Lu-3588

<sup>890</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 129

<sup>891</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>892</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>893</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>894</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

blot as well as between lanes 3 and 4 of the total MAPK blot in Figure 5E, which the Committee concludes represents splicing and could be indicative of falsification.

- 7. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

#### Respondent's Response:

1. In her interview with the CII on March 1, 2018, the final author Dr. Majumder agreed that there is splicing between lanes 3 and 4; however, she disagreed that there is splicing between lanes 2 and 3. Dr. Majumder described the reason for the splicing between lanes 3 and 4 in this figure was due to the conditions of the experiment. Dr. Majumder said that four concentrations of EGF were run; however, one of the conditions (10 ng/ml EGF) caused complete signal blow-out, which was removed from the figure. 

By Dr. Majumder confirmed that she would have been the one to remove a lane:

DR MAJUMDER: "And I -- I'm agreeing with that, yes, I removed it. Like, for every experiment we did, we had four different concentrations. I removed the 10 nanogram concentration and I spliced it together. And I reviewed that." 896

2. In the written response provided to ORC on April 19, 2018, Dr. Jacob provided a proposed corrected Figure 5E, that has a black line between lanes 3 and 4897 and indicated,

"This data showed difference in phospho-MAPK activation in response to EGF in parental MCF7 cells and TIMP3 depleted (shTIMP3) MCF7 cells. In all these experiments we routinely included extracts from cells treated with EGF at three different concentrations (0, 0.1, 1.0 and 10.0 μg/ml) in order to capture the best condition showing the difference between the two cell lines Splicing of the gel was done to remove the oversaturated phospho-MAPK band due to high EGF concentration (10.0 μg/ml), which should have been separated by a line. We have now provided the corrected figure including the line to indicate splicing of a lane in between." 898

- 3. Dr. Jacob's response provided to ORC on April 19, 2018 was the same as that provided to JBC on November 2, 2017. 899, 900
- 4. In his written response provided to ORC on June 11, 2018, the first author, Dr. Lu, indicated that he only made Figure 8 of JBC 2011, and therefore did not respond to this allegation. Dr. Lu stated: "Dr. Majumder, a corresponding author for this paper have answered all questions regarding the figure preparation and presenting in the paper."901
- 5. In her response to the CII's preliminary report<sup>902</sup> and her appeal of their determination,<sup>903</sup> Dr. Majumder again explained why there is "likely" a splice line between lanes 3 and 4 in both pMAPK and total MAPK in this figure. She continued to disagree with the presence of a splice line appearing between lanes 2 and 3, and further indicated that JBC had not asserted the presence of a splice in that location. Dr. Majumder explained that, "if a splice is present there (of which, again, I am doubtful), it would have resulted from an inadvertent removal of the irrelevant lane when the 10ng/ml EGF data was being

<sup>895</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, pages 60-62

<sup>896</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, pages 60-62, page 62 lines 2-6

<sup>&</sup>lt;sup>897</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926, page 4

<sup>&</sup>lt;sup>898</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>899</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>&</sup>lt;sup>900</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>&</sup>lt;sup>901</sup> Ex. 89 - 20180611 - Responses to the questions from OSU

<sup>&</sup>lt;sup>902</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 6-8

<sup>903</sup> Ex. 252 - Majumder Zadnik-letter-111218

removed."904

- 6. In her interview with the COMIC on June 12, 2019, 905 Dr. Majumder was not convinced that a splice line had occurred between lanes 2 and 3, but explained a 10 ng/ml sample would have been removed accounting for the splicing between lanes 3 and 4 (which she believes is present in both the top and bottom blots). 906 See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 8. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

I apologize sincerely for my mistakes."907

#### Respondent's Responsibility and Intent:

- It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.
- 2. Dr. Majumder admits to manipulating the figure via splicing between lanes 3 and 4 of the total MAPK blot, but not between lanes 2 and 3 in the p-p42/44-MAPK blot in Figure 5E.
- 3. It is the Committee's understanding that the standards in the field at the time of this 2011 publication may not have been to require demarcation of non-contiguous bands and the alleged splicing is visible to the naked eye. Additional instances of splicing in the figure, however, appear visible via Adobe Photoshop gradient mapping. In permitted instances of splicing, the splice line would be expected to run through the complete set of blots, which is not the case in the entirety of Figure 3E.
- 4. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.

<sup>&</sup>lt;sup>904</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 7

<sup>905</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1

<sup>906</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 59 line 14 to page 60 line 3; page 61 line 10-19

<sup>&</sup>lt;sup>907</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE\_ PUB. COMMIT:

- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 5E and that the actions of others caused the splicing within Figure 5E in Allegation #34, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 5E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 5E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #12, Allegation #35 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 4-6 of the total MAPK blot in Figure 6C and in lanes 4-6 of the total MAPK blot in Figure 6D in Lu et al., J Biol Chem 2011. *Figures 6C and 6D in JBC are also reported in grant application R21 CA137567-01A1, as Figures 6C and 6A, respectively.* 

#### **Finding of Fact:**

- 1. Figure 6C and 6D in JBC show Western blots for MAPK phosphorylation (p-p42/44-MAPK) and total MAPK in OHT<sup>R</sup>-Vec or OHT<sup>R</sup>-TIMP3 transfected cells treated for 0, 5, and 10 min with 50 pM 17β-estradiol (Figure 6C) or 50 nM 4-OH-Tamoxifen (Figure 6D). Allegation #35 is the reuse of the same bands in the total MAPK panels in OHT<sup>R</sup>-TIMP3 cells for the different experimental conditions of either estrogen or tamoxifen treatment.
- 2. Adobe Photoshop overlay analysis demonstrated significantly overlapping bands when comparing lanes 4-6 of the total MAPK blot in Figure 6C with lanes 4-6 of the total MAPK blot in Figure 6D (see slide 130<sup>908</sup>), which would not be scientifically valid with same image being used to represent two different experimental conditions (Figure 6C = treatment with estradiol for 0,5,10 minutes versus Figure 6D = treatment with tamoxifen for 0,3,5 minutes).
- 3. Of note, the unique dot/notch on the middle upper portion of band 4 in Figure 6C is also present in the middle upper portion of band 4 in Figure 6D, further indicating that the same data had been reused.
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 6C and 6D) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on

<sup>908</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 130

<sup>&</sup>lt;sup>909</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>910</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

November 2, 2017.911, 912

- 5. No original data were available for this figure.
- 6. The Committee finds the forensic evidence and visual inspection demonstrates reuse of Total MAPK lanes 4-6 data in Figure 6C and 6D, which the Committee concludes is indicative of falsification.
- 7. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

### Respondent's Response:

- 1. In her interview with the CII on March 1, 2018, Dr. Majumder indicated she could not specify if she or a post-doc had done this experiment, <sup>913</sup> Dr. Majumder described how the figure could have been constructed with erroneous cutting and pasting, <sup>914</sup> and said that any errors were unintentional labeling errors <sup>915</sup> that would not change the result of the experiment. <sup>916</sup>
- 2. Dr. Majumder also stated in her interview with the CII that she had to cut and paste the figure to prepare the figure since when the gels were run they weren't always set in up the order that the authors wanted to present in the final figure and then one area may have been "erroneously" copied:

DR. MAJUMDER: ""-- in my mind, yes, I think -- you know, there could be a duplication of this three lane to this three lane. And that is -- the reason is, like, I had to cut and paste this figure."917

- 3. The first author, Dr. Lu deferred to Dr. Majumder regarding this figure (see statement in Allegation #34).
- 4. Dr. Jacob did not provide a specific response to this allegation during the Inquiry phase of the case.
- 5. Dr. Jacob did not address Figure 6 in his November 2, 2017 response to JBC.
- 6. In her response to the CII's preliminary report<sup>918</sup> and her appeal of their determination, <sup>919</sup> as well as a written response provided to the COMIC in advance of her interview, <sup>920</sup> Dr. Majumder disagreed that she had admitted to the CII that she'd cut/pasted this figure, explained the purpose of the experiment, and maintained:

"We did not manipulate the figure, we constructed a figure from existing data to logically lay out our findings in the paper. Reuse of the total MAPK, if that occurred, was not intentional but erroneous."921

7. However, in her interview with the COMIC on June 12, 2019<sup>922</sup>, Dr. Majumder returned to the narrative that she did make the figure and that the duplication was an error that was not made purposely:

"And I explained in the past like how I made this figure out of a contiguous eight lanes, had to take apart like -- let me see. So estradiol and tamoxifen treatments were done side by side and we took -- I took out the tamoxifen in a different figure. And in my mind, of course if I had known then I would have not done this mistake while I was putting -- cutting and pasting the TIMP3. I

<sup>911</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

 $<sup>^{912}</sup>$  Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>913</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, pages 63-64

<sup>914</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, pages 65-66

<sup>915</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 67

<sup>916</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 69, line 23 to page 70, line 1

<sup>917</sup> Ex. 59 - 20180301-CII Interview + errata - Majumder, page 64, lines 10-12

<sup>918</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 7

<sup>919</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>920</sup> Ex. 350a - 2019-06-07 Pre-Interview Submision Majumder, pages 6-7, 9-10; see page 7

<sup>&</sup>lt;sup>921</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 7

<sup>922</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 62-63

must have erroneously put that same MAPK over there. That I admit like this is an error and I probably have erroneous figures in that."923

See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

- 8. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 9. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

I apologize sincerely for my mistakes."924

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.
- 2. Despite a reversal of accounts, Dr. Majumder ultimately admits to constructing the figure, but explains the duplication as an error.
- 3. This duplication of a series of three bands and the fact that the results were to have depicted treatment with estrogen versus tamoxifen signifies to the Committee that the intention was to deceive the reader. The unique dot/notch on the middle upper portion of band 4 in Figure 6C would have been difficult to ignore if unintentionally replicated in Figure 6D, further indicating that the same data had been reused intentionally.
- 4. Figure 6D shows phosphorylation of MAPK in response to estrogen and tamoxifen when treated for 0, 3, 5 or 10 minutes with total MAPK used as a control to determine the extent of phosphorylation. Though the figures under question represent total MAPK from the same cell line (OHTR-TIMP3) and the authors expected that these cells would have similar amounts of total MAPK, if similar amounts of total MAPK were not seen during actual experimentation, replication of data across the panels could be used to mislead the reader as to the actual effect of estrogen versus tamoxifen.

<sup>923</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 62 line 19 to page 63 line 4

<sup>&</sup>lt;sup>924</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE\_ PUB. COMMIT:

- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 6C and 6D and that the actions of others caused the falsification within Figure 6C and 6D in Allegation #35, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified total MAPK images in Figures 6C and 6D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified total MAPK images in Figures 6C and 6D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #12, Allegation #55 -** S.T. Jacob reported falsified data by splicing between lane 1 and lane 2 of p-p42/44 MAPK blot in Figure 6B in Lu et al., J Biol Chem 2011.

#### **Finding of Fact:**

- 1. Figure 6B shows Western blots for MAPK phosphorylation (p-p42/44-MAPK) and total MAPK in MCF-7/Vec or MCF-7/221/222 transfected cells treated for 0, 3, and 5 min with 50 nM 4-OH-Tamoxifen.
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC and ORC, showed that there was an abrupt change in background darkness between lanes 1 and 2 that indicated splicing had occurred (see slide 131-132<sup>925</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 6B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, 926 Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on November 2, 2017. 928, 929
- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a line between lane 1 and 2, which the Committee concludes represents splicing and could be indicative of falsification.
- 6. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

#### Respondent's Response:

<sup>925</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 131-132

<sup>&</sup>lt;sup>926</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>927</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>928</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>&</sup>lt;sup>929</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

- 1. In her written response provided to ORC on April 18, 2018, Dr. Majumder described how the original data were lost, discarded, or unavailable. Dr. Majumder disagreed that the lanes looked spliced together. 930
- 2. The first author, Dr. Lu, deferred to Dr. Majumder regarding this figure (see statement in Allegation #34).
- 3. Dr. Jacob did not provide a specific response to this allegation during the Inquiry phase of the case.
- 4. Dr. Jacob did not address Figure 6 in his November 2, 2017 response to JBC.
- 5. In her response to the CII's preliminary report<sup>931</sup> and her appeal of their determination,<sup>932</sup> Dr. Majumder disputed the presence of a splice line and indicated she could not recall if she prepared the figure.
- 6. However, in her interview with the COMIC on June 12, 2019,<sup>933</sup> Dr. Majumder disagreed with the allegation and indicated she had not done this experiment, but did make the figure.<sup>934</sup> See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 8. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

I apologize sincerely for my mistakes."935

#### Respondent's Responsibility:

- 1. Despite a reversal of accounts, Dr. Majumder ultimately admits to constructing the figure, but does not acknowledge the alleged splicing.
- 2. It is the Committee's understanding that the standards in the field at the time of this 2011 publication may not have been to require demarcation of non-contiguous bands and the alleged splicing is visible to the naked eye. In permitted instances of splicing, the splice line would be expected to run all the way down through the complete set of blots, which is not the case in the entirety of Figure 6B.
- 3. The figure shows that the cells at the 0 minute time point (lane1) were serum starved for 48 hours to

<sup>930</sup> Ex. 99 - OSU Response 041818.SM, page 3

<sup>931</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 7-8

<sup>932</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>933</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 62-63

<sup>934</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 63 line 13 to page 64 line 5

<sup>935</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE\_PUB. COMMIT:

reduce the basal level of phosphoMAPK to a minimum, which has been demonstrated elsewhere in the manuscript (e.g. Figure 5Di, lane 1 and Figure 6A, lane 1). Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.

- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 6B and that the actions of others caused the splicing within Figure 6B in Allegation #55, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 6B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 6B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #12, Allegation #56 -** S.T. Jacob reported falsified data by the cut and paste of lane 4 of p-AKT blot in Figure 7A and splicing between lane 3 and lane 4 in total AKT blot in Figure 7A in Lu et al., J Biol Chem 2011.

#### **Finding of Fact:**

- 1. Figure 7A shows Western blots for AKT phosphorylation (p-AKT) and total AKT in MCF-7 or OHT<sup>R</sup> cells treated with 0, 0.1 and 1.0 ng/ml EGF.
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC, showed that the p-AKT band in lane 4 appears to be rectangular in shape with very sharp borders, suggesting a crop followed by a cut and paste (see slide 133-134<sup>936</sup>).
- 3. The change in background between total AKT in lanes 3 and 4 appears to be too abrupt between lanes to be explained by anything other than splicing.
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 7A) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, 937 Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. 938 As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on November 2, 2017. 939, 940
- 5. No original data were available for this figure

<sup>936</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 133-134

<sup>&</sup>lt;sup>937</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>938</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>939</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>&</sup>lt;sup>940</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

- 6. The Committee finds the forensic evidence and visual inspection demonstrates a line between lane 3 and 4 of the total AKT blot, which the Committee concludes represents splicing and insertion of data into lane 4 of the p-AKT blot, which the Committee concludes could be indicative of falsification.
- 7. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

#### Respondent's Response:

- 1. Dr. Jacob indicated in his written response provided to ORC on April 19, 2018, that original data were not able to be retrieved, but that splicing was performed to remove oversaturated bands and should have been separated by a line (and refers to the same reasoning Dr. Jacob provided for Figure 5E in Allegation #34). 941 No response was provided for alleged copying and pasting of lane 4 of the p-Akt blot. Dr. Jacob's response provided to ORC on April 19, 2018 was the same as that provided to JBC on November 2, 2017. 942, 943
- 2. In her written response provided to ORC on April 18, 2018, Dr. Majumder described how the original data were lost, discarded, or unavailable. Dr. Majumder stated that any error in producing the figure would have been inadvertent and not intended to deceive. No response was provided for alleged copying and pasting of lane 4 of the p-Akt blot. Dr. Majumder admitted that splicing likely took place between lanes 3 and 4 to remove an oversaturated Total AKT band and that a line of demarcation would have been appropriate:

DR. MAJUMDER: "I agree there is likely a splice between lanes 3 and 4 in total Akt (and also pAkt lane), which would have occurred in order to remove the oversaturated pAkt band due to high EGF concentration". 944

- 3. The first author, Dr. Lu, deferred to Dr. Majumder regarding this figure (see statement in Allegation #34).
- 4. In her response to the CII's preliminary report<sup>945</sup> and her appeal of their determination,<sup>946</sup> Dr. Majumder indicated she did not perform this experiment and did not believe she had prepared the figure, but maintained that if an error had been made it had been made inadvertently.
- 5. In her interview with the COMIC on June 12, 2019<sup>947</sup>, Dr. Majumder indicated that either of the first two authors would have performed the experiment and that,

"And, again, the splicing in the bottom line is for the same reason. We had another -- I cannot explain the top one. Even if I have -- I cannot deny that I made this figure, I cannot recall absolutely I made this figure, but I don't have explanation like how that has happened without the raw data." 948

See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

<sup>941</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926, page 2

<sup>942</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>943</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>944</sup> Ex. 99 - OSU Response 041818.SM page 3

<sup>945</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 8

<sup>946</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>947</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 64-65

<sup>948</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 65 line 3-9

7. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

I apologize sincerely for my mistakes."949

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts.
- 2. Dr. Majumder admits she may have constructed the figure and acknowledges the splicing between lanes 3 and 4. She could not explain the apparent cut/paste of data into lane 4 of p-AKT blot.
- 3. It is the Committee's understanding that the standards in the field at the time of this 2011 publication may not have been to require demarcation of non-contiguous bands and the alleged splicing is visible to the naked eye. In permitted instances of splicing, the splice line would be expected to run all the way through the complete set of blots, which is not the case in the entirety of Figure 7A. The Committee believes the allegation of simple splicing does not fully reflect what they believe to be an intentional cut/paste falsification. The apparent insertion of a highly rectangular blot into lane 4 of the p-AKT blot strongly suggests intent to deceive rather than honest error. Without original data, the COMIC is not able to determine if the splicing and the apparent cut and paste of lane 4 were performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if they were performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 4. The authors maintain that conclusions drawn in this figure were substantiated elsewhere in the manuscript (e.g., Figures 5 and 6), however those figures have also been called into question, casting doubt as to the true experimental outcomes. Inserting or modifying a single band signals an intentional action, not merely the inadvertent duplication via cut/paste actions.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 7A and that the actions of others caused the manipulations within Figure 7A in Allegation #56, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness

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<sup>&</sup>lt;sup>949</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE PUB. COMMIT:

(i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #12, Allegation #57 -** S.T. Jacob reported falsified data by the cut and paste of lane 6 of total AKT blot in Figure 7C; and splicing between lane 3 and lane 4 in both p-AKT and total AKT blots in Figure 7C in Lu et al., J Biol Chem 2011.

### **Finding of Fact:**

- 1. Figure 7C shows Western blots for AKT phosphorylation (p-AKT) and total AKT in OHT<sup>R</sup>-Vec or OHT<sup>R</sup>-TIMP3 transfected cells treated 0, 0.1 or 1.0 ng/ml EGF.
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC and ORC, demonstrates the presence of a dark line in the top row between lanes 3 and 4 and a bright line in the bottom row between lanes 3 and 4 suggestive of splicing, as well as a dark rectangular "halo" around the band in lane 6 for total AKT blot, displaying as a distinct, sharp rectangular border that makes an abrupt change in brightness between it and the rest of the background (see slide 135-136<sup>950</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 7C) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, 951 Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. 952 As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on November 2, 2017. 953, 954
- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates a line between lane 3 and 4 of the both AKT blots, which the Committee concludes represents splicing; and an insertion of data into lane 6 of the Total AKT blot, which the Committee concludes could be indicative of falsification.
- 6. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

#### Respondent's Response:

1. Dr. Jacob indicated in his written response provided to ORC on April 19, 2018 that original data were not able to be retrieved and that splicing was performed to remove oversaturated bands and should have

<sup>950</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 135-136

<sup>&</sup>lt;sup>951</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>952</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>953</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>&</sup>lt;sup>954</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

been separated by a line (and refers to the same reasoning Dr. Jacob provided for Figure 5E in <u>Allegation</u> #34). 955 Dr. Jacob's response provided to ORC on April 19, 2018 was the same as that provided to JBC on November 2, 2017. 956, 957

- 2. In her written response provided to ORC on April 18, 2018, Dr. Majumder described how the original data were lost, discarded, or unavailable. Dr. Majumder admitted that splicing likely took place between lanes 3 and 4 to remove an oversaturated AKT band and that a line of demarcation would have been appropriate. 958 With respect to the allegation of pasting data into lane 6, Dr. Majumder maintained that comparable levels of AKT would be expected in all these cells and that any error in producing the figure would have been inadvertent and not intended to deceive. 959
- 3. The first author, Dr. Lu, deferred to Dr. Majumder regarding this figure (see statement in Allegation #34).
- 4. In her response to the CII's preliminary report<sup>960</sup> and her appeal of their determination,<sup>961</sup> Dr. Majumder indicated she did not perform this experiment and did not believe she had prepared the figure, but maintained that if an error had been made it had been made inadvertently.
- 5. In her interview with the COMIC on June 12, 2019, 962 Dr. Majumder admitted that the splicing was done purposefully, but that she couldn't explain the alleged cut/paste of data into lane 6 without the raw data. 963 Dr. Majumder ultimately agreed that she should have denoted the splicing and that lane 6 did not look correct, appearing to have had data pasted into it. 964 See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

<sup>955</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926, page 2

<sup>956</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response \_Lu 2011

<sup>&</sup>lt;sup>957</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>958</sup> Ex. 99 - OSU Response 041818.SM page 3

<sup>959</sup> Ex. 99 - OSU Response 041818.SM page 4

<sup>&</sup>lt;sup>960</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 8

<sup>&</sup>lt;sup>961</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>&</sup>lt;sup>962</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1

<sup>&</sup>lt;sup>963</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 66 line 7-10

<sup>964</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 70 line 16 to page 71 line 10

I apologize sincerely for my mistakes."965

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts.
- 2. Dr. Majumder admits she may have constructed the figure, acknowledges the splicing between lanes 3 and 4, and acknowledges that lane 6 is incorrect.
- 3. It is the Committee's understanding that the standards in the field at the time of this 2011 publication may not have been to require demarcation of non-contiguous bands and the alleged splicing is visible to the naked eye. In permitted instances of splicing, the splice line would be expected to run all the way through the complete set of blots, which is the case in Figure 7C, indicating that the author's explanation that the splicing was done to remove the oversaturated sample is plausible. In contrast, the apparent insertion of a band into lane 6 of the Total AKT panel strongly suggests intent to deceive the reader rather than honest error.
- 4. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome. In regards to the cut/paste of a band in lane 6, this action strongly suggests that the true experimental outcome for that lane was not ideal and was replaced by the pasted in band to support the author's conclusions.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 7C and that the actions of others caused the splicing and cut/paste of data within Figure 7C in Allegation #57, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7C, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #12, Allegation #60 -** S.T. Jacob reported falsified data by splicing around lane 4 and between lane 5 and 6 in Figure S3 in Lu et al., J Biol Chem 2011.

<sup>&</sup>lt;sup>965</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE PUB. COMMIT:

### **Finding of Fact:**

- 1. Figure S3 shows MMP9 and MMP2 matrix metalloprotease activity by zymography, an electrophoretic method for measuring proteolytic activity. Samples are loaded onto a gel embedded with a protease substrate and after separation, the gel is submerged in a solution with the necessary cofactors for enzyme activity. Coomassie blue staining distinguishes clear regions of the gel with proteolytic activity against a dark background. Proteases are identified based on their migration through the gel.
- 2. Adobe Photoshop gradient mapping, performed and provided by JBC and ORC, shows abrupt sharp-bordered changes in background brightness between lanes, consistent with splicing (see slide 137-138<sup>966</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure S3) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, 967 Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on November 2, 2017. 969, 970
- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates lines around lane 4 and between lanes 5 and 6, which the Committee concludes represents splicing and could be indicative of falsification.
- 6. Dr. Sarmila Majumder was final and co-corresponding author of JBC 2011 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2011.

### Respondent's Response:

- 1. In her written response provided to ORC on April 18, 2018, Dr. Majumder described how the original data were lost, discarded, or unavailable. Dr. Majumder stated that splicing was possible and might have been done in order to remove a duplicate sample.<sup>971</sup>
- 2. In his written response provided to ORC on April 19, 2018, Dr. Jacob reiterated Dr. Majumder's explanation for the irregularity in the figure. 972
- 3. Dr. Jacob did not address Figure S3 in his November 2, 2017 response to JBC.
- 4. The first author, Dr. Lu deferred to Dr. Majumder regarding this figure (see statement in Allegation #34).
- 5. In her response to the CII's preliminary report<sup>973</sup> and her appeal of their determination,<sup>974</sup> Dr. Majumder indicated she did not perform this experiment and did not believe she had prepared the figure. Dr. Majumder explained that splicing may have been performed to remove duplicate lanes, but disagreed with the forensic analysis demonstrating vertical lines in lane 4.<sup>975</sup>
- 6. In her interview with the COMIC on June 12, 2019, 976 Dr. Majumder stated that the experiment was performed by the first author (Lu), that she did not know if Dr. Lu had made the figure or if she had herself, and that she did not know if any data had been removed for the figure without consulting the raw data. 977 See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

<sup>966</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 137-138

<sup>&</sup>lt;sup>967</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>968</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>969</sup> Ex. 330 - 20171102 - Email Jacob to JBC - JBC response Lu 2011

<sup>&</sup>lt;sup>970</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>&</sup>lt;sup>971</sup> Ex. 99 - OSU Response 041818.SM, page 5

<sup>&</sup>lt;sup>972</sup> Ex. 153 - Response Lu Y et al., 2011-JBC-270926

<sup>&</sup>lt;sup>973</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 8

<sup>974</sup> Ex. 252 - Majumder Zadnik-letter-111218

<sup>975</sup> Ex. 215 - 20181022 - Majumder Response-CII -101918, page 8

<sup>&</sup>lt;sup>976</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1

<sup>977</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder Redaction 1, page 73 line 18 to page 74 line 3



- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1, 3-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 8. Via a limited review of respondent email records that are routinely put on hold upon the university's receipt of initial allegations, the Committee identified correspondence between Drs. Majumder and Jacob regarding the Journal of Biological Chemistry concerns with this manuscript. In this September 19, 2017 exchange, Dr. Jacob indicates,

"I am very disappointed that you cannot retrieve some of the original data. It appears the problem with Yuanzi's ms is in regard to the western blots you did. His animal work appears intact and well done. If you cannot produce at least some of the original data, your papers will have a real problem—sadly."

To which Dr. Majumder responds,

"I take full responsibility of the experiments I did and I have not blamed first, last or any coauthors. If I fail retrieve all my original data I will retract the HHg paper. I have worked hard and with multiple people and on multiple projects, but have not kept good back up records as evident now. There could be several reasons and I am not going to find excuse for what I did then. Like everyone I would like to end this and move on with life, even if that means I end up my scientific career here.

I apologize sincerely for my mistakes."978

### Respondent's Responsibility and Intent:

- It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Dr. Majumder does not recall if she constructed the figure and neither confirms nor denies the apparent splicing.
- 2. It is the Committee's understanding that the standards in the field at the time of this 2011 publication may not have been to require demarcation of non-contiguous bands, though through their use of a white line of separation between lanes 2 and 3, the authors did denote that two gels were being presented. The alleged splicing is visible to the naked eye. In permitted instances of splicing, the splice line would be expected to run all the way down which is the case between lane 5 and 6, but not lane 4 in Figure S3. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome.
- 3. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure S3 and that the actions of others caused the splicing within Figure S3 in Allegation #60, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 4. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

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<sup>&</sup>lt;sup>978</sup> Ex. 331 - 20170917 - Email Majumder to Jacob - RE\_ PUB. COMMIT:

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure S3, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure S3, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

#### Manuscript #13 under Review- Datta et al., Genes and Cancer 2012 (4 Allegations)

Datta J\*, Ghoshal K\* \*\*, Motiwala T, Jacob ST\*\*. "Novel Insights into the Molecular Mechanism of Action of DNA Hypomethylating Agents: Role of Protein Kinase C  $\delta$  in Decitabine-Induced Degradation of DNA Methyltransferase 1." Genes Cancer. 2012 Jan; 3 (1): 71-81. \*\*co-first authors\*\* \*\*co-corresponding authors\*\*

**Manuscript #13, Allegation #36 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 2-5 of the GAPDH blot in Figure 4B and in lanes 1-4 of the GAPDH blot in Figure 4D in Datta et al., Genes Cancer 2012.

### **Finding of Fact:**

- Figure 4B shows Western blot analysis for DNMT1 from HCT116 cells pretreated with the PKC inhibitor Ro318220, and then exposed to decitabine. Figure 4D shows Western blot analysis for DNMT1 from Hep3B cancer cells pretreated with the PKC inhibitor Ro318220, and then exposed to 5-Aza or decitabine. GAPDH is used as a loading control.
- 2. Adobe Photoshop overlay analysis demonstrated significantly overlapping bands when comparing lanes 2-5 of the GAPDH blot in Figure 4B with lanes 1-4 of the GAPDH blot in Figure 4D (see slide 141<sup>979</sup>). This would not be scientifically valid as these figures represent different experimental conditions.
- 3. No original data were available for this figure.
- 4. Figure inconsistencies in Datta et al., Genes & Cancer 2012 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. As of then, PubPeer had published 4 comments on Manuscript #13, corresponding to Allegations #36-37 & #39.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of GAPDH lanes 2-5 in Figure 4B as GAPDH lanes 1-4 in Figure 4D, which the Committee concludes is indicative of falsification.
- 6. Dr. Datta was the first author of Genes Cancer 2012 and a Research Scientist (2006-2012) in the laboratory of Dr. Samson Jacob prior to the publication.
- 7. Dr. Kalpana Ghoshal was a co-first and co-corresponding author of Genes Cancer 2012 and an Associate Professor collaborating with Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Genes Cancer 2012.

### Respondent's Response:

1. Dr. Datta did confirm in her interview with the CII on March 2, 2018, that she, and potentially others, had made this figure.<sup>981</sup> Dr. Datta stated that she could not produce the original data, partly because she had moved labs and also because the data could have been produced long before the 2012 publication date.

<sup>&</sup>lt;sup>979</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 141

<sup>&</sup>lt;sup>980</sup> These data are reviewed elsewhere under DIO 6819.

<sup>981</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 80, lines 6-10

2. In her written response provided to ORC on May 18, 2018, Dr. Datta reiterated that she was unable to produce the original data and expressed disagreement with the allegation, indicating that the lanes are very similar but not identical. Dr. Datta offered the following caveat,

"In absence of the original scans it is not possible to determine whether it is duplication, but if there is duplication, it is an inadvertent mistake. However, we repeated the experiments so many times and in my recollection GAPDH lanes used to be very similar." <sup>982</sup>

- 3. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 4. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- 5. In her response to the CII report<sup>983</sup> and her appeal of their determination, <sup>984</sup> Dr. Datta clarified that while she believed she performed one iteration of this experiment, she did not know whether the figure was made from her experimental results or who prepared the figure. Dr. Datta indicated that the bands looked similar but not identical to her and further posited that "the care we took to ensure equal proteins may have resulted in very similar bands." <sup>985</sup>
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 8. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the co-corresponding authors have taken responsibility for generation of Figure 4B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Based on her own testimony and written responses, Dr. Datta indicated she may have made the figure and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts.
- 2. Lanes 2-5 of the GAPDH blot in Figure 4B represent treatment of HCT116 cells with Ro-318220, 5-AzadC, 5-AzadC plus Ro-318220, and 5-AzaC, respectively whereas lanes 1-4 of the GAPDH blot in Figure 4D represent control and treatment of Hep3B cells with Ro-318220, 5-Azad plus Ro-318220, and 5-AzaC, respectively. Reuse of the same series of four bands would not be scientifically valid as they represent different cell types used across the two figures. In addition, the labeled lanes in Figure 4B do not correspond to the labeled lanes in Figure 4D, showing that the reuse of the four bands represent different experimental conditions. The expression levels for control proteins can be similar but not identical, making it very likely that a span of four blots representing four experimental conditions was reused to represent a control and three different experimental conditions. The preponderance of the evidence strongly suggests that this duplication was not the result of honest error. In this manuscript, the authors conclude that PKCδ is involved in decitabine-induced degradation of DNMT1, that Rottlerin was as effective as MG-132, staurosporine, and Ro-318220 in blocking decitabine-induced degradation of DNMT1 in HCT116 cells, and that their observations suggest the probable involvement of PKCδ in

<sup>&</sup>lt;sup>982</sup> Ex. 78 - OSU Response 1-JD, pages 3-4

<sup>983</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7

<sup>&</sup>lt;sup>984</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>985</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7

drug-induced depletion of DNMT1 in human cancer cell lines. The manipulation of controls associated with the abovementioned inhibitors is highly significant to the hypotheses and conclusions of the manuscript, and taken together, the falsification of Figures 4, 5, and 6 (Allegations #36-37, 39, 61) negates the conclusion that PKCdelta is involved in decitabine induced DNMT1 degradation. Furthermore, when considered in the context of all the allegations within this and across all manuscripts, the Committee believes the falsification shows a lack of regard for the importance of control data and makes the falsification more significant.

- 3. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see previous discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 4B and 4D and that the actions of others caused the falsification within Figures 4B and 4D in Allegation #36, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figures 4B and 4D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figures 4B and 4D, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #13, Allegation #37 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 4-9 of the GAPDH blot in Figure 5A and in lanes 1-6 of the GAPDH blot in Figure 5B in Datta et al., Genes Cancer 2012.

### **Finding of Fact:**

- 1. Figure 5A shows Western blot analysis of DNMT1 and GAPDH from HCT116 cells treated with various PKCδ-specific inhibitors and then treated with decitabine. Figure 5B shows Western blot analysis of DNMT1 and GAPDH from HCT116 cells transfected with vector of PKCδ and treated with decitabine. Allegation #37 is the reuse of 6 lanes of GAPDH bands.
- 2. Adobe Photoshop overlay analysis demonstrated significantly overlapping bands when comparing lanes 4-9 of the GAPDH blot in Figure 5A with lanes 1-6 of the GAPDH blot in Figure 5B (see slide 142<sup>986</sup>).
- 3. The reuse of the lanes is made more evident by a visual inspection of the unique shapes of lanes 7, 8 and 9 of Figure 5A, which all have ridges and notches identical to those present on lanes 4, 5, and 6 of

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<sup>&</sup>lt;sup>986</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 142

Figure 5B.

- 4. No original data were available for this figure.
- 5. Figure inconsistencies in Datta et al., Genes & Cancer 2012 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017. 987 As of then, PubPeer had published 4 comments on Manuscript #13, corresponding to Allegations #36-37 & #39.
- 6. The Committee finds the forensic evidence and visual inspection demonstrated duplication of a series of six lanes in the GAPDH blots in Figures 5A and 5B, which the Committee concludes is indicative of falsification.
- 7. Dr. Datta was the co-first author of Genes Cancer 2012 and a Research Scientist (2006-2012) in the laboratory of Dr. Samson Jacob prior to the publication.
- 8. Dr. Kalpana Ghoshal was a co-first and co-corresponding author of Genes Cancer 2012 and an Associate Professor collaborating with Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Genes Cancer 2012.

### Respondent's Response:

- 1. Dr. Datta did not comment on this allegation in her interview with the CII other than stating that it was not a duplicate. However, Dr. Datta later stated that she could not remember who made this figure. 988
- 2. In her written response provided to ORC on May 18, 2018, <sup>989</sup> Dr. Datta indicated that the original data could not be found but that in case the lanes had been duplicated, it would have been an inadvertent and unintentional error as figures were made by multiple authors. From her recollection of repeated experiments, Dr. Datta stated that GAPDH lanes would appear very similar with equivalent amounts of protein in the same cell line.
- 3. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 4. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- 5. In her response to the CII report<sup>990</sup> and her appeal of their determination<sup>991</sup> Dr. Datta indicated the bands looked similar but not identical to her and further posited that "the care we took to ensure equal proteins may have resulted in very similar bands." <sup>992</sup>
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 8. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the co-corresponding authors have taken responsibility for generation of Figures 5A or 5B, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Ghoshal was considered a faculty member at the time of publication of this manuscript.

<sup>&</sup>lt;sup>987</sup> These data are reviewed elsewhere under DIO 6819.

<sup>988</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 81, lines 15-16

<sup>989</sup> Ex. 78 - OSU Response 1-JD, pages 3-4

<sup>&</sup>lt;sup>990</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7

<sup>&</sup>lt;sup>991</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>992</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7



- 2. Reuse of the same series of six GAPDH bands would not be scientifically valid as they represent different experimental conditions across the two figures. The expression levels for control proteins can be similar but not identical, making it very likely that a span of six bands representing a unique set of experimental conditions was reused to represent six different experimental conditions. The unique ridges and notches of bands in lanes 7-9 in Figure 5A would have been difficult to ignore if unintentionally replicated in Figure 5B, further indicating that the same data had been reused intentionally. Given the number of allegations within Figure 5, the preponderance of the evidence strongly points toward this duplication not being the result of honest error. In this manuscript, the authors conclude that PKCδ is involved in decitabineinduced degradation of DNMT1, that Rottlerin was as effective as MG-132, staurosporine, and Ro-318220 in blocking decitabine-induced degradation of DNMT1 in HCT116 cells, and that their observations suggest the probable involvement of PKCδ in drug-induced depletion of DNMT1 in human cancer cell lines. The manipulation of controls associated with the abovementioned inhibitors is highly significant to the hypotheses and conclusions of the manuscript, and taken together, the falsification of Figures 4, 5, and 6 (Allegations #36-37, 39, 61) negates the conclusion that PKCdelta is involved in decitabine induced DNMT1 degradation. Furthermore, when considered in the context of all the allegations within this and across all manuscripts, the Committee believes the falsification shows a lack of regard for the importance of control data and makes the falsification more significant.
- 3. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see previous discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 5A and 5B and that the actions of others caused the falsification within Figures 5A and 5B in Allegation #37, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figures 5A and 5B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified the GAPDH images in Figures 5A and 5B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #13, Allegation #39 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1, lane 3, and lane 4 of the DNMT1 blot in Figure 6E in Datta et al., Genes Cancer 2012.

#### **Finding of Fact:**

- 1. Figure 6E shows a Western blot of immuonprecipitated phosphorylated DNMT1 from HCT116 cells untreated or treated with rotterin (a PKCδ inhibitor) and decitabine. Total DNMT1 was used as a control.
- 2. Adobe Photoshop gradient mapping demonstrated identical bands in lanes 1, 3, and 4 of the DNMT blot in Figure 6E (see slide 143<sup>993</sup>). Furthermore, gradient mapping revealed two distinct coloration artifacts (i.e., purple dots) present in lanes 1, 3, and 4 providing further evidence that all three lanes come from the same source data.
- 3. Relevant data was offered by Dr. Datta as Exhibit 6, but original data corroborating the figure as presented were not available.
- 4. Figure inconsistencies in Datta et al., Genes Cancer 2012 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017.<sup>994</sup> As of then, PubPeer had published 4 comments on Manuscript #13, corresponding to Allegations #36-37 & #39.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in each of lanes 1, 3, and 4 of the DNMT1 blot in Figure 6E, which the Committee concludes is indicative of falsification.
- 6. Dr. Datta was the co-first author of Genes Cancer 2012 and a Research Scientist (2006-2012) in the laboratory of Dr. Samson Jacob prior to the publication.
- 7. Dr. Kalpana Ghoshal was a co-first and co-corresponding author of Genes Cancer 2012 and an Associate Professor collaborating with Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Genes Cancer 2012.

#### Respondent's Response:

- 1. In her interview with the CII, Dr. Datta stated she made Figure 6E, <sup>995</sup> that the DNMT1 antibody is not a good antibody to use for immunoprecipitation, and the antibody was also not good for phosphorylation determination, so they had to rerun several experiments where the exposure control was altered. They had to do this experiment several times since the antibody caused "blow-out". <sup>996</sup>
- 2. Dr. Jacob did not provide a response to this allegation during his interview with the CII.
- 3. In her written response provided to ORC on May 18, 2018, Dr. Datta expressed disagreement with the allegation and offered a rebuttal with original data from a 'relevant' experiment ("Exhibit 6")<sup>997</sup> and provided a new figure to demonstrate similarity and invalidate the claim that the DNMT1 lanes have been duplicated.<sup>998</sup> Additionally, in contrast to her statement during her interview with the CII, Dr. Datta stated that she does not remember who made the final figures for this manuscript.
- 4. In her response to the CII report<sup>999</sup> and her appeal of their determination,<sup>1000</sup> Dr. Datta disagreed that a duplication existed, argued that one should see splice lines in the presence of duplication, and indicated that though she believed she prepared the original Figure 6E, she did not cut and paste bands<sup>1001</sup>
- 5. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal exists from the Inquiry stage of the case.
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July

<sup>993</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 143

<sup>&</sup>lt;sup>994</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>995</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 87, lines 16-20

<sup>996</sup> Ex. 57 - 20180301-CII Interview + errata -Datta, page 85, lines 11-12

<sup>&</sup>lt;sup>997</sup> Ex. 79 - OSU response figures-Exhibit 1-6-JD, page 6

<sup>&</sup>lt;sup>998</sup> Ex. 78 - OSU Response 1-JD, pages 3-4

<sup>999</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7

<sup>&</sup>lt;sup>1000</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>1001</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-7



- 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 8. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.
- 2. Despite a reversal of accounts, Dr. Datta ultimately has taken responsibility for generation of Figure 6E.
- 3. Without original data, the COMIC is not able to determine the significance of the duplication and how it may have altered the interpretation and conclusions of the manuscript. Regardless, reuse of a single image to represent three different treatment conditions would not be scientifically valid, argues against the duplication occurring as a result of an honest error, and signifies to the Committee that the intention was to deceive the reader. The expression levels for control proteins can be similar but not identical, and the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error. In this manuscript, the authors conclude that PKCδ is involved in decitabine-induced degradation of DNMT1, that Rottlerin was as effective as MG-132, staurosporine, and Ro-318220 in blocking decitabine-induced degradation of DNMT1 in HCT116 cells, and their observations suggest the probable involvement of PKCδ in drug-induced depletion of DNMT1 in human cancer cell lines. Figure 6E shows that the phosphorylation of DNMT1 increased 3 fold after decitabine treatment without significant change in the protein level. Since the DNMT1 protein levels have been falsified, the conclusions stemming from this figure are not valid. The manipulation of controls associated with the abovementioned inhibitors is highly significant to the hypotheses and conclusions of the manuscript, and taken together, the falsification of Figures 4, 5, and 6 (Allegations #36-37, 39, 61) negates the conclusion that PKCdelta is involved in decitabine induced DNMT1 degradation. Furthermore, when considered in the context of all the allegations within this and across all manuscripts, the Committee believes the falsification shows a lack of regard for the importance of control data and makes the falsification more significant.
- 4. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see previous discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 5. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 6E and that the actions others caused the falsification within Figure 6E in Allegation #39, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 6. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT1 images in Figure 6E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT1 images in Figure 6E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #13, Allegation #61 -** S.T. Jacob reported falsified data by reuse of same data in lane 11 and in lane 12 (Rottlerin treatment) of the DNMT1 blot in Figure 5A in Datta et al., Genes Cancer 2012.

#### **Finding of Fact:**

- 1. Figure 5A shows Western blot analysis of DNMT1 and GAPDH from HCT116 cells treated with various PKCδ-specific inhibitors and then treated with decitabine.
- 2. Adobe Photoshop overlay analysis of lane 11 with lane 12 in Figure 5A of the Genes Cancer 2012 paper show significant overlap (see slide 144<sup>1002</sup>). This would not be scientifically valid as the two lanes represent different experimental conditions.
- 3. Both gradient mapping and visual inspection demonstrate a distinct background artifact (i.e., a small dot) on the far left bottom of the band, in both lanes 11 and 12.
- 4. No original data were available for this figure.
- 5. Figure inconsistencies in Datta et al., Genes Cancer 2012 were published on the web (i.e., PubPeer) and known at least to Dr. Ghoshal as early as September 2017.<sup>1003</sup> As of then, PubPeer had published 4 comments on Manuscript #13, corresponding to Allegations #36-37 & #39.
- 6. The Committee finds the forensic evidence and visual inspection of the band characteristics and background characteristics demonstrate reuse of the same data in Lanes 11 and 12, which the Committee concludes is indicative of falsification.
- 7. Dr. Datta was the co-first author of Genes Cancer 2012 and a Research Scientist (2006-2012) in the laboratory of Dr. Samson Jacob prior to the publication.
- 8. Dr. Kalpana Ghoshal was a co-first and co-corresponding author of Genes Cancer 2012 and an Associate Professor collaborating with Dr. Samson Jacob at the time of publication.
- 9. Dr. Samson Jacob was the laboratory PI and co-corresponding author of Genes Cancer 2012.

#### Respondent's Response:

- 1. In her written response provided to ORC on May 18, 2018, Dr. Datta indicated that though she was not able to find the original data for this figure, she strongly feels that there is no duplication. 1004
- 2. Dr. Jacob did not provide a response to this allegation during the Inquiry stage of the case.
- 3. As this allegation was added during the course of the investigation for Dr. Ghoshal, no response from Dr. Ghoshal exists from the inquiry stage of the case.
- 4. In her response to the CII report<sup>1005</sup> and her appeal of their determination,<sup>1006</sup> Dr. Datta indicated she could not agree to the duplication in the absence of original data, that the experiment was repeated several times, and, to her knowledge, the lanes were not duplicated.<sup>1007</sup>

<sup>&</sup>lt;sup>1002</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 144

<sup>&</sup>lt;sup>1003</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>1004</sup> Ex. 77 - 20180518 - Datta Response to New Allegation

<sup>&</sup>lt;sup>1005</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 6-8

<sup>&</sup>lt;sup>1006</sup> Ex. 247 - Appeal of Final Report of CII -JD-111218

<sup>&</sup>lt;sup>1007</sup> Ex. 211 - 20181022 - Jharna Datta Response to CII, page 8



- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 6. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. Neither the co-first nor the co-corresponding authors has taken responsibility for generation of Figure 5A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content. Dr. Ghoshal was considered a faculty member at the time of publication of this manuscript.
- 2. The expression levels for proteins can be similar but not identical, making it very likely that a single band was reused to represent two different experimental outcomes. Additionally, when considered with the evidence presented in Allegation #37 above, the number of manipulations to this figure leads the Committee to conclude that the manipulations were made intentionally with falsification as the goal. In this manuscript, the authors conclude that PKCδ is involved in decitabine-induced degradation of DNMT1, that Rottlerin was as effective as MG-132, staurosporine, and Ro-318220 in blocking decitabine-induced degradation of DNMT1 in HCT116 cells, and that their observations suggest the probable involvement of PKCδ in drug-induced depletion of DNMT1 in human cancer cell lines. The manipulation of controls associated with the abovementioned inhibitors is highly significant to the hypotheses and conclusions of the manuscript, and taken together, the falsification of Figures 4, 5, and 6 (Allegations #36-37, 39, 61) negates the conclusion that PKCdelta is involved in decitabine induced DNMT1 degradation. Furthermore, when considered in the context of all the allegations within this and across all manuscripts, the Committee believes the falsification shows a lack of regard for the importance of control data and makes the falsification more significant.
- 3. The fact that concerns already published on the web (i.e. PubPeer) regarding this manuscript were known at least to Dr. Ghoshal at the time of her initial notification of allegations by OSU, yet she failed to disclose this represents dishonesty in the opinion of the Committee and damages the credibility of arguments made by Dr. Ghoshal as a witness. Given the evidence that Dr. Ghoshal had corresponded with Dr. Datta about PubPeer comments for two additional manuscripts (see previous discussions of Manuscripts #5 and 10), the Committee believes that it is reasonable to conclude that Dr. Datta would have also been aware of the PubPeer concerns for this manuscript, and thus similarly questions the credibility of arguments made by Dr. Datta as a witness.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 5A and that the actions of others caused the falsification within Figure 5A in Allegation #61, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends retraction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT1 images in Figure 5A,

and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified DNMT1 images in Figure 5A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #14 under Review - Wang et al., Hepatology 2014 (1 Allegation)

Bo Wang, Shu-hao Hsu, Xinmei Wang, Huban Kutay, Hemant Kumar Bid, Jianhua Yu, Ramesh K. Ganju, Samson T. Jacob, Mariia Yuneva, Kalpana Ghoshal. "Reciprocal regulation of microRNA-122 and c-Myc in hepatocellular cancer: role of E2F1 and transcription factor dimerization partner 2." Hepatology (2014) 59 (2): 555–566.

**Manuscript #14, Allegation #40 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-4 of the GAPDH blot in Figure 1B and in lanes 2-5 of the GAPDH blot in Figure 1E in Wang et al., Hepatology 2014.

### **Finding of Fact:**

- 1. Figure 1B shows Western blot analysis of c-Myc and GAPDH control from liver tissue of normal (N) and tumors (T) from Myc-on mice with or without deoxycycline treatment. Figure 1E shows Western blot analysis of miR-122 targets and GAPDH control in FBVN parental mouse liver (L), begin liver (N) and tumor (T) tissue. Allegation #40 is reuse of GAPHD bands in Figure 1B and 1E for N1/T1/N2/T2.
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap of bands when comparing lanes 1-4 GAPDH bands in Figure 1B to lanes 2-5 of the GAPDH band in Figure 1E (see slide 146<sup>1008</sup>). This would not be scientifically valid as it has the same data being used to represent different experimental conditions.
- 3. The original source data for the blots represented in the published Figure 1B and 1E were located by Dr. Ghoshal. 1009 However, the review of the original source data led to further issues/concerns as the published Figure 1E did not correspond to the protein concentrations that were handwritten on the original source data films.
- 4. There are two (2) GAPDH blots in published Figure 1E, which was not explained in the published figure legend.
- 5. Figure inconsistencies in Wang et al., Hepatology 2014 were published on the web (i.e., PubPeer), known at least to Dr. Ghoshal as early as September 2017, and apparently addressed by Dr. Ghoshal via a pseudonymynous PubPeer comment in September 2017. This activity occurred approximately three (3) weeks prior to Drs. Jacob and Ghoshal being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry.
- 6. The Committee finds the forensic evidence and visual inspection demonstrates reuse of a series of four GAPDH lanes in Figures 1B and 1E, which the Committee concludes could be indicative of falsification.
- 7. Dr. Ghoshal was final and corresponding author of Wang et al., Hepatology 2014 and an Associate Professor collaborating with Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and a senior author of Hepatology 2014.

#### Respondent's Response:

1. Following her notification of this allegation, Dr. Ghoshal provided original data (14 Western blot films), scans of the original data, and a PowerPoint highlighting the differences between the original figures and

<sup>&</sup>lt;sup>1008</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 146

<sup>&</sup>lt;sup>1009</sup> Ex. 128 - Hepatology 2014 Fig. 1BE western scans 01252018

<sup>&</sup>lt;sup>1010</sup> These data are reviewed elsewhere under DIO 6819.

her proposed corrected figure. 1011, 1012, 1013 Previously, Dr. Ghoshal had provided an explanation to former RIO Dr. Julia Behnfeldt that the GAPDH blots should actually be the same because Figures 1E and 1B were the same experiment but that different exposures were required to visualize c-Myc in the normal samples (low expressing) compared to the tumor samples (high expressing). However, after reviewing the original data, Dr. Ghoshal stated to Dr. Behnfeldt that her earlier explanation was incorrect and provided a proposed corrected figure that Dr. Ghoshal had put together in PowerPoint. The corrected figure contained scans of the original data Dr. Ghoshal provided to ORC on January 25, 2018. 1014

- 2. During her interview with the CII on March 5, 2018, Dr. Ghoshal stated that her previous explanation to Dr. Behnfeldt (above) was incorrect. Dr. Ghoshal stated that Figure 1B and Figure 1E should actually have different GAPDH blots since they loaded different amounts of protein in each experiment (100/200 micrograms versus 50/100 micrograms). Dr. Ghoshal further indicated that Figure 1E was also incorrect in that two different protein concentrations were used and some of the panels were incorrectly assigned to the wrong GAPDH control panel. Dr. Ghoshal stated that they had the GAPDH blots for both sets of experiments so the duplication occurred based on human error and that she would like to correct the figure using the films Dr. Ghoshal had previously provided to ORC. 1015
- 3. Dr. Ghoshal provided new proposed corrected figures for both Figure 1B and 1E. 1016, 1017
- 4. In her response to the CII's preliminary report<sup>1018</sup> and her appeal of their determination,<sup>1019</sup> Dr. Ghoshal reaffirmed her previous explanation that Figures 1B and 1E should actually have different GAPDH blots since they loaded different amounts of protein in each experiment (100/200 micrograms versus 50/100 micrograms) and that since they had the GAPDH blots for both sets of experiments they could demonstrate that the duplication occurred based on human error and would like to pursue a correction. Dr. Ghoshal further indicated,

"The legends in the published paper are not totally incorrect. In fact, we used 100 µg protein for one panel in both B and E. We will provide the protein amounts used in each panel in the corrected figure legends. (See attached Exhibit B.) I believe that original data shows that we had no reason to falsify data, and the conclusions of Figs 1B and 1E remain the same irrespective of the corrections to the GAPDH blots…Nevertheless, an inadvertent error did occur here, and it is completely correctable." 1020

- 5. Dr. Jacob did not provide a response to this allegation during the Inquiry stage of the case.
- 6. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 7. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.

#### Respondent's Responsibility and Intent:

1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation

<sup>&</sup>lt;sup>1011</sup> Ex. 126 - 20180125- Ghoshal Sequestration Data Sheet

<sup>&</sup>lt;sup>1012</sup> Ex. 127 - 20180126 Email RIO to CII- New data for Wang Hepatology 2014

<sup>&</sup>lt;sup>1013</sup> Ex. 128 - Hepatology 2014 Fig. 1BE western scans 01252018

<sup>&</sup>lt;sup>1014</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 147

<sup>&</sup>lt;sup>1015</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 144

<sup>&</sup>lt;sup>1016</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 147

<sup>&</sup>lt;sup>1017</sup> Ex. 128 - Hepatology 2014 Fig. 1BE western scans 01252018

<sup>&</sup>lt;sup>1018</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits

<sup>&</sup>lt;sup>1019</sup> Ex. 251 - Appeal to Dr. Zadnik - Ghoshal

<sup>&</sup>lt;sup>1020</sup> Ex. 213 - 20181022 - Ghoshal Response to CII with Exhibits, page 12 & 15

that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation.

- 2. Dr. Ghoshal has taken responsibility for the duplications found in the manuscript.
- 3. The Committee finds the corrected figure <sup>1021</sup> and explanation provided by Dr. Ghoshal to be convincing and supports that honest error may have occurred. Given the relatively recent publication of the paper in comparison to the others in this case, the availability of the original data, and the authors' ability and willingness to issue a complete correction, the Committee finds that this duplication may have occurred as the result of honest error with no intent to mislead and that the scientific literature can be corrected.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 1 and that the actions of others caused the duplication within Figure 1 in Allegation #40, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. The Committee recommends correction of the manuscript to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified GAPDH images in Figures 1B and 1E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified GAPDH images in Figures 1B and 1E, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #15 under Review - Motiwala et al., JBC 2009 (1 Allegation)

Motiwala T\*, Majumder S\*, Ghoshal K, Kutay H, Datta J, Roy S, Lucas DM, and Jacob ST. "PTPROt inactivates the oncogenic fusion protein BCR/ABL and suppresses transformation of K562 cells." J Biol Chem. 2009 Jan 2; 284(1): 455-64. RETRACTED 02/13/18<sup>1022</sup> \*co-first authors

**Manuscript #15, Allegation #63 -** S.T. Jacob reported falsified data by splicing between lane 2 and lane 3, PTPROt-flag blot in Figure 1A in Motiwala et al., JBC 2009.

#### **Finding of Fact:**

- 1. Figure 1A shows Western blot analysis of PTPROt and Ku70 in K562 cells (myelogenous leukemia cells) transfected with vector, PTPROt-WT or PTPROt-CS (catalytic site).
- 2. Adobe Photoshop gradient map analysis, performed and provided by JBC and ORC, shows clear demarcation around the band in lane 3 of Figure 1 PTPROt-flag blot, indicative of a cut/paste action rather than mere splicing (see slide 149-150<sup>1023</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 1A) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr.

<sup>&</sup>lt;sup>1021</sup> Ex. 373 - Ghoshal Image Forensics\_COMIC Final, slide 47

<sup>&</sup>lt;sup>1022</sup> Ex. 26 - 20180309- Retraction- J. Biol. Chem.-2018-Motiwala-3589

<sup>&</sup>lt;sup>1023</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 149-150

<sup>&</sup>lt;sup>1024</sup> Ex. 277 - 20170630- Email JBC to Jacob

Majumder on July 2, 2017<sup>1025</sup> and Dr. Motiwala on July 20, 2017.<sup>1026</sup> All authors were notified in follow-up directly by JBC on July 31, 2017.<sup>1027</sup> As such, Drs. Jacob, Majumder, and Motiwala knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry.

- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection demonstrate clear and distinct lines between lanes 2 and 3 of the PTPROt-flag blot in Figure 1A as well as sharp lines and changes in background around the lane 3 band itself, which the Committee concludes represents cutting and pasting of that band and indicative of falsification.
- 6. Dr. Sarmila Majumder was a co-first author of JBC 2009 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Tasneem Motiwala was a co-first author of JBC 2009 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2009.

#### Respondent's Response:

- 1. In her written response to the allegation, Dr. Motiwala wrote that they were not able to find the original data from which this figure was created, but they had created other blots confirming the ectopic expression of PTPROt in K562 cells. Dr. Motiwala also wrote, "We are not certain why gel splices were used to create the image for the paper," indicating she was in agreement that there are splice lines present. 1029
- 2. Dr. Jacob's written response to the allegation was the same as Dr. Motiwala's, similarly agreeing to the presence of splice lines and including a corrected figure, 1030 and was the same response he'd provided to JBC. 1031
- 3. In her response to the CII's preliminary report<sup>1032</sup> and her appeal of their determination, <sup>1033</sup> Dr. Motiwala reiterated that she could not recall who prepared the figure or why splice lines were present and indicated that the findings of the figure are replicated (i.e. in Figure 3<sup>1034</sup>).
- 4. As this allegation was added late in the course of the Inquiry, the CII could not address the allegation with Dr. Jacob or Dr. Motiwala during Inquiry interviews.
- 5. In her interview with the COMIC on June 12, 2019<sup>1035</sup>, Dr. Motiwala indicated that as first author she would have performed experiments and drafted the manuscript, she doesn't remember performing the experiment in question, but acknowledged the presence of splicing and could not explain why it would have been done. When questioned why the splice did not extend through the entirety of the figure, which would be expected in circumstances of permissible splicing to remove extraneous data, Dr. Majumder could not offer an explanation. See also Dr. Motiwala's General Respondent/Witness statements #1-6 above.
- 6. In her interview with the COMIC on June 12, 2019, 1037 Dr. Majumder was not fully prepared to discuss the allegation having just been notified the day before, but did indicate that she could not recall performing

<sup>&</sup>lt;sup>1025</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>1026</sup> Ex. 332 - 20170720 - Email Jacob to Motiwala - FW JBC articles

<sup>&</sup>lt;sup>1027</sup> Ex. 486 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles Motiwala

<sup>&</sup>lt;sup>1028</sup> Ex. 116 - New Allegations-response-041918, page 3

 $<sup>^{1029}</sup>$  Ex. 116 - New Allegations-response-041918, page 3

<sup>&</sup>lt;sup>1030</sup> Ex. 152 - JBC M802840200 Motiwala-10172017, page 1

<sup>&</sup>lt;sup>1031</sup> Ex. 333 - 20171019 - Email Jacob to JBC - JBC response \_Motiwala 2009

<sup>&</sup>lt;sup>1032</sup> Ex. 217 - 20181022 - Response to Preliminary CII Report-102218, page 5

<sup>&</sup>lt;sup>1033</sup> Ex. 253 - Motiwala Appeal - Final CII Report-111318

<sup>&</sup>lt;sup>1034</sup> Ex. 116 - New Allegations-response-041918, page 3

<sup>&</sup>lt;sup>1035</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 59-65

<sup>&</sup>lt;sup>1036</sup> Ex. 304a - 20190612 - COMIC Interview + errata - Motiwala Redaction 1, page 62 line 1 to page 63 line 2

<sup>1037</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 88-89

the experiment or preparing the figure. Upon seeing the forensic analysis, Dr. Majumder agreed that she could see the splicing and that the figure appeared manipulated, 1038 but could not remember who performed the experiment or constructed the figure, was not convinced that a duplication had occurred, and could not rely on the software showing such. 1039 See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors have taken responsibility for generation of Figure 1A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content (or at least the first author's responsibility, in the opinion of Dr. Majumder<sup>1040</sup>).
- 2. Without original data, the COMIC is not able to determine if the splicing was performed to remove extraneous noncontiguous data (and not properly documented with a demarcation) or if the splicing was performed to remove non-ideal experimental results so that the published figure no longer represents the true experimental outcome. Another blot in the paper showed that the laboratory was able to express this particular construct (i.e. Figure 6A shows same result in 6.15 cells, a murine myeloid 32D cell line).
- 3. The Committee believes the allegation of simple splicing does not fully reflect what they believe to be an intentional cut/paste falsification of the PTPROt-flag band in Figure 1A, lane 3. Were this to be merely a permitted instance of splicing, the splice line would be expected to run all the way down through the complete set of blots, which is not the case in Figure 1A.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 1A and that the actions others caused the falsification of Figure 1A in Allegation #63, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified PTPROt-flag images in Figure 1A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified PTPROt-flag images in Figure 1A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>1038</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 89 line 2-9

<sup>1039</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 78 line 8 to page 79 line 1; page 81 line 3-12

<sup>&</sup>lt;sup>1040</sup> Ex. 303 - 20190612 - COMIC Interview + errata - Majumder, page 23, lines 13-23; page 36, lines 6-10

### Manuscript #16 under Review - Bai et al., JBC 2006 (1 Allegation)

Bai S, Ghoshal K, and Jacob ST. "Identification of T-cadherin as a novel target of DNA methyltransferase 3B and its role in the suppression of nerve growth factor-mediated neurite outgrowth in PC12 cells." J Biol Chem. 2006 May 12; 281 (19): 13604-11. **RETRACTED 02/13/18** 

**Manuscript #16, Allegation #66 -** S.T. Jacob reported falsified data by the reuse of the same data in lane 1 and in lane 5 of the T-cad gel image in Figure 3B in Bai et al., JBC 2006.

### **Finding of Fact:**

- Figure 3B shows a ChIP-ChOP assay to identify the association of DNMT3b with unmethylated or methylated DNA. Primers for the T-Cad promoter or GAPDH control were used to amplify the DNA. PCR product generated with the methylation sensitive enzyme, HpaII (H) indicates methylation. MspI (M) is a methylation insensitive enzyme. Figure 3B is the ethidium bromide staining of an agarose gel for amplified DNA.
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC, demonstrates clear evidence of the same internal structures and overall shape of the bands for lanes 1 and 5 of the T-cad gel images, which indicates that the same data had been reused to represent two different experimental conditions (see slide 152<sup>1041</sup>).
- 3. Adobe Photoshop overlay analysis, performed by ORC, demonstrates significant similarity and overlap of lanes 1 and 5 of the T-cad gel images (see slide 153<sup>1042</sup>).
- 4. Original data was offered by Dr. Jacob in his response to JBC<sup>1043</sup>, but original data corroborating the figure as published were not available. Notably, the "H" lane for the input panel shows a greater expression/concentration than the "H" lane that was published.
- 5. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same T-cad gel image data in lanes 1 and 5 of Figure 3B, which the Committee concludes is indicative of falsification.
- 6. Dr. Jacob received formal notice of concerns with figures (including Figure 3B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. As such, Dr. Jacob knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017. 1045, 1046
- 7. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2006.

### Respondent's Response:

- 1. In a written response provided to ORC on April 19, 2018, Dr. Jacob provided "raw data that shows we used separate data for each experimental condition" and a repeat of the experiment where a gap was left to denote the DNA samples were run on different gels. This response was the same as that provided to JBC. 1048, 1049
- 2. As this allegation was added late in the course of the Inquiry, the CII could not address the allegation with Dr. Jacob during his Inquiry interview.
- 3. First author, Dr. Shoumei Bai, provided witness statements via written communication with the

<sup>&</sup>lt;sup>1041</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 152

<sup>&</sup>lt;sup>1042</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 153

<sup>&</sup>lt;sup>1043</sup> Ex. 150 - JBC M513278200 Bai 2006- 10172017, page 1 and 3

<sup>&</sup>lt;sup>1044</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1045</sup> Ex. 334 - 20171019 - Email Jacob to JBC - JBC response \_Bai 2006

<sup>&</sup>lt;sup>1046</sup> Ex. 150 - JBC M513278200 Bai 2006-1012017

<sup>&</sup>lt;sup>1047</sup> Ex. 150 - JBC M513278200 Bai 2006-1012017, page 1 and 3

<sup>&</sup>lt;sup>1048</sup> Ex. 334 - 20171019 - Email Jacob to JBC - JBC response Bai 2006

<sup>&</sup>lt;sup>1049</sup> Ex. 150 - JBC M513278200 Bai 2006-1012017

COMIC.<sup>1050</sup> She generally maintains that she has no access to any original data and does not have a memory from which she can answer specific questions relating to the research,<sup>1051</sup>

Regarding duplication, Dr. Bai indicated:

"Because I do not have access to any original data for the papers you mention, I cannot affirm that the images have been duplicated. I believe that bands of normalizers can look very, very similar, especially when equal amounts of protein/PCR product are run on the same gel. Further, in the absence of splicing, duplication is technically not possible.

"1052

4. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

#### Respondent's Responsibility and Intent:

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The first author, Dr. Shoumei Bai, has neither specifically commented on nor taken responsibility for generation of Figure 3B;
- 3. The data were reused to support conclusion that Dnmt3b is associated with both methylated and unmethylated T-Cad promoter. Reused band represents unmethylated T-Cad promoter for comparison to bands under lanes H. This reuse of the band raises questions as to which of the two experimental conditions the duplicated band actually represents and as a result, raises doubts about the validity of the quantitation (79%:21% ratio) presented in Figure 3C. Given the duplication the data are invalid as they do not represent actual findings.
- 4. Without original data, the COMIC is not able to determine exactly how the duplication may have altered the interpretation and conclusions of the manuscript. Regardless, reuse of a single image to represent two different treatment conditions would not be scientifically valid, and argues against the duplication occurring as a result of an honest error. The change in data used in the publication for the same experimental conditions suggests to the Committee that data were intentionally manipulated with the intention to deceive the reader. The expression levels for control proteins can be similar but not identical, and the preponderance of the evidence points toward this duplication being an intentional act not the result of honest error.
- 5. The Committee has determined that Dr. Jacob failed in his role as graduate student mentor and corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 3B and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 3B in Allegation #66, as described above. The Committee finds Dr. Jacob failed in his duties as principal

<sup>&</sup>lt;sup>1050</sup> Ex. 296 - 20190630 - Email response Bai to COMIC

<sup>1051</sup> Ex. 294 - 20190618 - Memo to Bai from COMIC Chair

<sup>&</sup>lt;sup>1052</sup> Ex. 296 - 20190630 - Email response Bai to COMIC, page 2

investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified T-cad gel images in Figure 3B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified T-cad gel images in Figure 3B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #17 under Review - Nasser et al., JBC 2008 (1 Allegation)

Nasser MW\*, Datta J\*, Nuovo G, Kutay H, Motiwala T, Majumder S, Wang B, Suster S, Jacob ST\*\*, and Ghoshal K\*\*. "Down-regulation of Micro-RNA-1 (miR-1) in Lung Cancer." J Biol Chem. 2008 Nov 28; 283(48):33394-405. <u>RETRACTED 07/19/18</u><sup>1054</sup> \* co-first authors \*\* co-corresponding authors

**Manuscript #17, Allegation #69 -** S.T. Jacob reported falsified data by the reuse of the same data in lanes 12-19 (samples 17-20) 18S rRNA (upper blot) and in lanes 2-9 (samples 22-25) of the 18S rRNA (lower blot) in Figure 8A in Nasser et al., JBC 2008.

#### **Finding of Fact:**

- 1. Figure 8A shows RT-PCR analysis of MET, FoxP1 and 18S rRNA control in different samples of human primary lung cancers (T) and matching normal lung tissue (N).
- 2. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing between lanes 12-19 (upper 18S rRNA blot) and lanes 2-9 (lower 18S rRNA blot) in Figure 8A (see slide 155<sup>1055</sup>). This would not be scientifically valid as it has the same data being used to represent different experimental conditions. Of additional concern for samples 22-30, there are fourteen (14) MET bands, twelve (12) FoxP1 bands and thirteen (13) 18S rRNA bands (see slide 156<sup>1056</sup>).
- 3. Additional Adobe Photoshop gradient mapping analysis, performed and provided by JBC, also indicates these data were reused in lanes 12-19 (samples 17-20) of the upper 18S rRNA blot in Figure S1 and in lanes 2-9 (samples 22-25) of the lower 18S rRNA blot in Figure S1 (see light blue boxes, slide 157). Furthermore, the same data was used in lanes 10-12 of the lower 18S rRNA blot of Figure 8A and in lanes 14-16 of the lower 18S rRNA blot in Figure S1 (see purple boxes, slide 158). Finally, the same data was used in lanes 13-14 (sample 30) of the lower 18S rRNA blot of Figure 8A and in lanes 18-19 (H792 and N417, respectively) of the lower 18S rRNA blot in Figure S1 (see yellow boxes, slide 158). Adobe Photoshop overlay analysis performed by ORC demonstrated corresponding overlap and consistency of shape, intensity and spacing (see slide 157-158<sup>1057</sup>).

<sup>&</sup>lt;sup>1054</sup> Ex. 32 - 20180817-Retraction-J. Biol. Chem.-2018-Nasser-12945

<sup>&</sup>lt;sup>1055</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 155

<sup>&</sup>lt;sup>1056</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 156

<sup>&</sup>lt;sup>1057</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 157-158

- 4. Original data 1058 were offered by Dr. Ghoshal, but do not completely match Figure 8A as published. Adobe Photoshop overlay analysis demonstrated consistency of shape, intensity, and spacing of samples 4, 6, 8, 13, 16-20 when comparing Dr. Ghoshal's original data to both published figures, 8A and S1. However, samples 26, 28, and 30 do not appear consistent with those published in Figure 8A. See slide 159 1059). The original data show thirty-two (32) bands representing sixteen (16) samples, while the published data show thirty-one (31) bands representing the same sixteen (16) samples.
- 5. The original data 1060 offered by Dr. Ghoshal do appear, in part, to match Figure S1 as published. Adobe Photoshop overlay analysis demonstrated consistency of shape, intensity, and spacing of samples 4, 6, 8, 13, 16-20 when comparing Dr. Ghoshal's original data to the published figure. However, source data samples 4, 6, 8, 13, 16-20, 22-26 also appear to be reused as the entire bottom 18S rRNA panel of Figure S1. See slide 160. 1061
- 6. Upon careful review of Figure 8A, the COMIC noted that for samples 22 30, purportedly representing 7 pairs of normal and tumor samples, the protein expression levels showed 14 lanes for MET, 12 lanes for FoxP1, and 13 lanes for 18S RNA, proving that these panels misrepresent the pairs of normal/tumor samples as claimed.
- 7. Dr. Jacob received formal notice of concerns with figures (including Figure 8A) within this manuscript from the Journal of Biological Chemistry on June 30, 2017, 1062 Dr. Jacob subsequently notified Dr. Ghoshal the same day. 1063, 1064 All authors, including Dr. Datta, were notified in follow-up directly by JBC on July 31, 2017. 1065 As such, the co-first and corresponding authors knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry.
- 8. Dr. Jacob sent a formal response to JBC on October 19, 2017. 1066, 1067
- 9. The Committee finds the forensic evidence and visual inspection demonstrates reuse of the same data in lanes 12-19 as in lanes 2-9 of the 18S rRNA blots as well as a different number of lanes/samples in the lower MET vs. FoxP1 vs. 18S rRNA blots (14 vs.12 vs. 13, respectively). Reuse of lanes is indicative of falsification.
- 10. Dr. Jharna Datta was a co-first author of Nasser et al., JBC 2008 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of publication.
- 11. Dr. Kalpana Ghoshal was final and co-corresponding author of Nasser et al., JBC 2008 and a Research Assistant Professor (2007-2010) in the laboratory of Dr. Samson Jacob at the time of publication.
- 12. Dr. Samson Jacob was the laboratory PI and co-corresponding author of JBC 2008.

## Respondent's Response:

1. In her written response provided to ORC on April 19, 2018, Dr. Ghoshal provided what she believed were scans of the original data used for the figure 1068 and stated:

"When we went back to find the original data, we did see that errors occurred in the construction of the 18S panel of Fig. 8A. It appears the gene-specific (MET and FoxP1) RT-PCR products were separated on agarose gels with wider wells (20 wells/gel) whereas the 18S rRNA PCR products were separated on agarose gels with narrower wells (30 wells/gel). An inadvertent error

 $<sup>^{1058}\</sup> Ex.\ 130$  - New Allegations Ghoshal, page 3

<sup>&</sup>lt;sup>1059</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 159

<sup>&</sup>lt;sup>1060</sup> Ex. 130 - New Allegations Ghoshal, page 3

<sup>&</sup>lt;sup>1061</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slides 160

<sup>&</sup>lt;sup>1062</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1063</sup> Ex. 306 - 20170630 - Email Jacob to Ghoshal - FW JBC articles

<sup>&</sup>lt;sup>1064</sup> Ex. 307 - 20170630 - Email Jacob to Ghoshal #2 - FW JBC articles

<sup>&</sup>lt;sup>1065</sup> Ex. 485 - 20170731 - Email - JBC Editor to Authors - FW JBC Articles Nasser

<sup>&</sup>lt;sup>1066</sup> Ex. 335 - 20171019 - Email Jacob to JBC - JBC response Nasser 2008

<sup>&</sup>lt;sup>1067</sup> Ex. 336 - JBC\_Nasser M804788200\_2008

<sup>&</sup>lt;sup>1068</sup> Ex. 130 - New Allegations Ghoshal, page 3

in selecting the correct set of 18S rRNA bands while trying to separate these into two different panels corresponding to the gene-specific PCR seems to have occurred 1069

- 2. Dr. Jacob did not provide a specific response to this allegation during the Inquiry phase of the case.
- 3. As this allegation was added late in the course of the Inquiry, the CII could not address the allegation with Dr. Jacob or Dr. Ghoshal during Inquiry interviews.
- 4. Co-first author Dr. Jharna Datta was not identified as co-first author during the Inquiry phase of the case and therefore was not questioned about this allegation in her interview.
- 5. In her interview with the COMIC on June 28, 2019, Dr. Datta did not specifically address this allegation, in the interest of time. See also Dr. Datta's General Respondent/Witness statements #1-4 above.
- 6. In her interview with the COMIC on June 28, 2019, Dr. Ghoshal did not specifically address this allegation, in the interest of time. See also Dr. Ghoshal's General Respondent/Witness statements #1-5 above.
- 7. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 8. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 19, 2017 letter, 1070, 1071 the authors touted the manuscript as highly cited, with findings repeated and confirmed by other laboratories and in different cancers. They go on to explain that the same panels were used for Figures 8A and S1 because the same cDNA stocks were used to generate the data and thus both data share the same normalizer and that inadvertent errors occurred in the selection and construction of the panels, and provided corrected figures. Raw data is provided.
- 9. The explanation provided by Dr. Ghoshal in her April 19, 2018 response to new allegations borrows heavily from the October 19, 2017 response to JBC, however only addresses the duplications internal to Figure 8A and not the duplications across Figure 8A and S1. The raw data provided by Dr. Ghoshal appears to be the same as that provided to JBC in the October 19, 2017 response to JBC, 1072 however appears to have been transferred into an editable format where the color has been inverted and lane/sample delineations added.

#### Respondent's Responsibility and Intent:

- 1. It has been clearly and consistently maintained by all witnesses during both the Inquiry and Investigation that Dr. Jacob did not personally create figures for publication and that the first author(s) were responsible for figure generation and integrity of any submitted/published manuscripts. None of the co-first authors nor corresponding author has taken responsibility for generation of Figure 8A, but espouse the view that all authors on a publication are responsible for its scientific integrity and content.
- 2. Figure 8A as published demonstrates that expression is upregulated in tumor tissues as compared to normal tissue and is significant to the mechanistic conclusions of the manuscript. The scans of the data provided by Dr. Ghoshal show unequal expression levels between the N and T lanes for sample set 25, and smears and background artifacts in the lanes for sample sets 22 and 23. This may have provided a motive for Dr. Ghoshal to reuse lanes 12-19 (sample sets 17-20) in place of lanes 2-9 (sample sets 22-25) as overall they look nicer and more significantly they show equal expression levels of 18S rRNA, which is important as the 18s rRNA serves as a control for this experiment. The lack of a verified loading controls invalidate the stated impact of the expression levels of the genes, as this is dependent on a valid loading control, which is now not available. Drs. Jacob and Ghoshal admit that "errors" occurred in the figure preparation; however, the Committee does not find the explanation that those errors were due to different gels/well size plausible nor scientifically valid. Given the number of allegations within and across

<sup>&</sup>lt;sup>1069</sup> Ex. 130 - New Allegations Ghoshal, page 3

<sup>&</sup>lt;sup>1070</sup> Ex. 335 - 20171019 - Email Jacob to JBC - JBC response Nasser 2008

<sup>&</sup>lt;sup>1071</sup> Ex. 336 - JBC\_Nasser M804788200\_2008

<sup>&</sup>lt;sup>1072</sup> Ex. 336 - JBC\_Nasser M804788200\_2008

Figures 8A and S1, the Committee believes it is more likely than not that the duplications are not the result of honest error. Furthermore, either extreme sloppiness or incomplete manipulation in samples 22-30 was also evinced by the presence of fourteen (14) MET bands, twelve (12) FoxP1 bands and thirteen (13) 18s rRNA bands.

- 3. Different lanes of the same raw data, purportedly representing 18S rRNA PCR products of lung cancer tissues and cell lines, were used to compose Figures 8A and S1.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 8A and that the actions of others caused the falsification within Figure 8A in Allegation #69, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified 18S rRNA images in Figure 8A and S1, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified 18S rRNA images in Figure 8A and S1, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #18 under Review - Dong et al., JBC 2002 (4 Allegations)

Dong, X., Ghoshal, K., Majumder, S., Yadav, S. P., & Jacob, S. T. (2002). Mitochondrial transcription factor A and its downstream targets are up-regulated in a rat hepatoma. *The Journal of biological chemistry*, 277(45), 43309-18. **RETRACTED-07/19/18**<sup>1073</sup>

**Manuscript #18, Allegation #70 –** S.T. Jacob reported falsified data by the reuse of the same data in lanes 1-2 of the NS blot in Figure 1B and in lanes 1-2 of the NS blot in Figure 6B in Dong et al., JBC 2002

#### **Finding of Fact:**

- 1. Figure 1B is a Western blot analysis of Tfam and NS (as a control) in mitochondrial extracts from normal rat liver (L) and hepatoma (H). Figure 6B is a Western blot analysis of Tfam, COX I and NS from normal rat liver (rLiver) and hepatoma (H4) and normal mouse liver (mLiver) and hepatoma (Hepa).
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC, demonstrates evidence of the same overall shape of the bands for lanes 1-2 of the NS blots in Figures 1B and 6B, which suggests that the same data had been reused to represent two different experimental conditions (see slide 163<sup>1074</sup>).
- 3. Adobe Photoshop overlay analysis, performed by ORC, demonstrates significant similarity and clear overlap of lanes 1-2 of the NS blot in Figure 1B with lanes 1-2 of the NS blot in Figure 6B (see slide 164 1075).
- 4. The reuse of the bands is made more evident by the presence of a dot beneath the left side of lane 2 of

<sup>&</sup>lt;sup>1073</sup> Ex. 30 - 20180817-Retraction-J.Biol Chem.-2018-Dong-12947

<sup>&</sup>lt;sup>1074</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 163

<sup>&</sup>lt;sup>1075</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 164

the NS blot in Figure 1B which reappears in lane 2 of the NS blot in Figure 6B. Additionally a small area of darkening extending from the middle of the band in lane 1 into the background beneath the band appears both in the NS blot in Figure 1B and the lane 1 of NS blot in Figure 6B. While these features are visible to the naked eye, the Adobe Photoshop embossing feature demonstrates these artifacts more clearly (see slide 164 1076).

- 5. Dr. Jacob received formal notice of concerns with figures (including Figure 6B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017.<sup>1077</sup> As such, Dr. Jacob knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.<sup>1078, 1079</sup>
- 6. No original data were available for this figure.
- 7. The Committee finds the forensic evidence and visual inspection of the allegedly reused lanes indicative of falsification.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Dr. Jacob was not questioned about this allegation during the Inquiry phase of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, 1080 Dr. Jacob indicated,

"The inclusion of the NS (non-specific) blot in Fig. 1B was an error as the Coomassie staining gel was the intended loading control and the NS blot data should have been deleted in the final version of the manuscript. The difference in the level of Tfam in L and H was drawn based on Coomassie and not on the non-specific band."

- This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 19, 2017 letter, an explanation was not provided for the duplication, but rather it was referred to as "confusion" and a corrected figure removing the NS blot was provided. 1081

#### Respondent's Responsibility and Intent:

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The COMIC could not determine who generated the original data or who produced the figure for the manuscript,

<sup>&</sup>lt;sup>1076</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 164

<sup>&</sup>lt;sup>1077</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>1078</sup> Ex. 337 - 20171019 - Email Jacob to JBC - JBC response \_Dong 2002

<sup>&</sup>lt;sup>1079</sup> Ex. 338 - JBC\_M206958200\_Dong 10172017

<sup>&</sup>lt;sup>1080</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 25-26

<sup>&</sup>lt;sup>1081</sup> Ex. 338 - JBC M206958200 Dong 10172017, page 1-2

- 3. It is the Committee's understanding that the standards in the field are that Dr. Jacob, as the corresponding author, should review all figures and all text in the manuscript. The experiments in this manuscript were conducted when Dr. Jacob was a PI with staff under his guidance.
- 4. The NS data in Figures 1B and 6B represent data purportedly from different experimental conditions that are mutually exclusive. The reuse of the same NS bands for both experiments is scientifically invalid and is a difficult and actually impossible error to make, because the bands would otherwise correctly be produced in two different lanes acquired from two different experimental protocols. The lack of a verified loading controls invalidate the stated impact of the expression levels of the proteins, as this is dependent on a valid loading control, which is now not available.
- 5. The Committee does not find Dr. Jacob's explanation regarding the inclusion of the NS data vs. the intended loading control (Coomassie) as being an error with the NS blot mistakenly not being deleted in the final version of the manuscript plausible nor relevant to the apparent reuse. The Committee does not find Dr. Jacob's justification that the difference in the level of Tfam in L and H that was reported was based on Coomassie and not on the non-specific band plausible, relevant, or scientifically valid.
- 6. The Committee has determined that Dr. Jacob failed in his role as graduate student mentor and corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 1B and 6B and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figures 1B and 6B in Allegation #70, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 2 in favor (reckless) and 5 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS images in Figures 1B and 6B, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified NS images in Figures 1B and 6B, and therefore this act <u>does not</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #18, Allegation #71** – S.T. Jacob reported falsified data by the reuse of the same β-actin blot for Figure 1D, Figure 2A, Figure 5 and Figure 6A in Dong et al., JBC 2002.

#### Finding of Fact:

1. Figure 1D, 2A, 5 and 6A show RT-PCR analysis using β-actin as a control. Figures 1D, 2A, 5 and 6A

- (lanes 1-2) show expression of different proteins with the  $\beta$ -actin control for rat liver (L) and hepatoma (H).
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC, demonstrates evidence of the same overall shape of the bands for lanes 1-2 of the  $\beta$ -actin blots in Figures 1D, 2A, 5, and 6A, which suggests that the same data had been reused (see slide  $166^{1085}$ ).
- 3. Adobe Photoshop overlay analysis, performed by ORC, demonstrates significant similarity and clear overlap of lanes 1-2 when the various figures are overlaid on one another (e.g., Figure 5 on Figure 1D, Figure 2A on Figure 5, and Figure 2A on Figure 6A). The β-actin bands as presented in Figures 1D, 2A, 5 had to be stretched vertically to match those used as Figure 6A. See slide 167.<sup>1086</sup>
- 4. Dr. Jacob received formal notice of concerns with figures (including Figure 1D, Figure 2A, Figure 5 and Figure 6A) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. As such, Dr. Jacob knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017. 1088, 1089
- 5. No original data were available for this figure.
- 6. The Committee finds the forensic evidence and visual inspection of the allegedly reused lanes demonstrates their reuse across four figures. However, all four of these figures are demonstrating the same experimental conditions per the figure legends and text (20 ng poly A+ RNA was reverse transcribed to cDNA then amplified with different gene specific primers). This would be a scientifically valid reuse of an internal control for PCR reactions in the same hepatoma cell line, Morris hepatoma 3924A. However, Figure 6A uses a different hepatoma cell line: rat H4-II-E-C3.<sup>1090</sup>
- 7. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Dr. Jacob was not questioned about this allegation during the Inquiry phase of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019<sup>1091</sup>, Dr. Jacob merely indicated, "These were gel images of RT-PCR products for the loading control beta-actin for the L, H, and H4 RNA samples. They were collected from independent gels of PCR products."
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 19, 2017 letter, the authors provided no explanation for the β-actin image in Figure 6A, but indicated:

"Regarding β-actin loading control for Fig. 1D, Fig. 2A and Fig. 5, the L and H samples were the same for those PCR experiments. For that reason, β-actin data was intentionally duplicated". 1092

#### Respondent's Responsibility:

<sup>&</sup>lt;sup>1085</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 166

<sup>&</sup>lt;sup>1086</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 167

<sup>&</sup>lt;sup>1087</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1088</sup> Ex. 337 - 20171019 - Email Jacob to JBC - JBC response \_Dong 2002

<sup>&</sup>lt;sup>1089</sup> Ex. 338 - JBC M206958200 Dong 10172017

<sup>&</sup>lt;sup>1090</sup> Ex. 33 - Dong et al., JBC 2002, page 43315

<sup>&</sup>lt;sup>1091</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 26

<sup>&</sup>lt;sup>1092</sup> Ex. 338 - JBC\_M206958200\_Dong 10172017, page 1



- 1. Dr. Jacob has consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- The Committee cannot determine who generated the original data or who produced the figure for the manuscript,
- 3. Figures 1D, 2A, and 5 come from experiments in the rat H
- 3. Figures 1D, 2A, and 5 come from experiments in the Morris hepatoma 3924A. However, Figure 6A comes from experiments in the rat H4-II-E-C3 cell line. Furthermore, if the reuse of the β-actin bands would have been scientifically correct, then Tfam should also be the same in Figure 1D and 6A, which it is not. Given this and the fact that the same blot was duplicated across cell lines, the Committee finds falsification of Figure 1D, 2A, 5, and/or 6A and intention to deceive as the only logical explanation. Because no original data exists, the Committee is unable to determine which figure may have been the source and therefore must conclude that all four figures are erroneous.
- 4. The falsified data potentially changed the reported results because the levels of Tfam and other proteins that are known to interact with Tfam cannot be related to the β-actin loading control, and cannot be interpreted unambiguously. The lack of a verified loading controls invalidate the stated impact of the expression levels of the proteins, as this is dependent on a valid loading control, which is now not available.
- 5. The Committee has determined that Dr. Jacob failed in his role as graduate student mentor and corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figures 1D, 2A, 5, or 6A themselves and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 6A in Allegation #71, as described above. The Committee, however, finds Dr. Jacob was reckless in executing his duties as a graduate student advisor and corresponding author to ensure appropriate training of junior researchers and to ensure the validity of data submitted for publication, given the reuse of the same data four times and their significance to the results reported in the manuscript (i.e., Tfam and its regulatory factors are upregulated in rat hepatoma), and that these reckless actions caused the inclusion and reporting of falsified data within Figure 1D, Figure 2A, Figure 5 and Figure 6A as described above.
- 6. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor and 0 against, that the Respondent recklessly reported falsified beta-actin images in Figures 1D, 2A, 5, and 6A, and therefore this act <u>does</u> constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified beta-actin images in Figures 1D, 2A, 5, and 6A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #18, Allegation #72 – S.T. Jacob reported falsified data with the cut and paste of lane 2 (Liver/V) of "UPPER STRAND" blot and cut and paste of lane 1 (Liver/N) of "LOWER STRAND" blot in Figure 4B in Dong et al., JBC 2002.

#### **Finding of Fact:**

- 1. Figure 4B shows in vitro (N) and in vivo (V) genomic footprinting assays of the rat Tfam gene promoter to identify interactions between DNA-binding proteins and specific DNA sites. The Sp1 sites and NRF2 sites are indicated with vertical lines. Protected G residues are marked with arrows; hypersensitive G residues are marked with asterisks.
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC as well as ORC, demonstrates evidence of sharp lines at the edges of the top portion of the gel for lanes 2 and 4 of the Upper Strand and sharp lines and boxes around the Sp1-A portion of the gel for lanes 1 and 3 of the Lower Strand suggesting that data have been superimposed onto the figure (see slide 168-169<sup>1094</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 4B) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. As such, Dr. Jacob knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017. 1096, 1097
- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection suggests cutting and pasting of data into the figure, which the Committee concludes is indicative of falsification.
- 6. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Dr. Jacob was not questioned about this allegation during the Inquiry phase of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, 1098 Dr. Jacob denied any cutting/pasting and offered the low resolution of the sequencing gels as a possible explanation.
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 4. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 19, 2017 letter, the authors appealed to low resolution to account for the issues and provided a corrected figure using "additional data for the genomic footprinting of the upper strand that was generated independently." 1099 The alleged cut/paste in the lower strand is not addressed.

### Respondent's Responsibility and Intent:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The Committee cannot determine who generated the original data or who produced the figure for the manuscript,

<sup>&</sup>lt;sup>1094</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 168-169

<sup>&</sup>lt;sup>1095</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1096</sup> Ex. 337 - 20171019 - Email Jacob to JBC - JBC response Dong 2002

<sup>&</sup>lt;sup>1097</sup> Ex. 338 - JBC M206958200 Dong 10172017

<sup>&</sup>lt;sup>1098</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 26

<sup>&</sup>lt;sup>1099</sup> Ex. 338 - JBC M206958200 Dong 10172017, page 1, 3-4

- 3. Figure 4B supports the role of NRF2 and SP1 in rat Tfam expression. The genomic footprinting is a significant component of this finding because it shows that they are functional binding sites in the rat. In addition it highlights a difference between the rat and human Tfam because it shows no involvement of NRF1. The falsification of the genomic footprinting significantly detracts from the conclusions of the manuscript.
- 4. It is the Committee's understanding that the standards in the field are that Dr. Jacob, as the corresponding author, should review all figures and all text in the manuscript. The experiments in this manuscript were conducted when Dr. Jacob was a PI with staff under his guidance.
- 5. The Committee has determined that Dr. Jacob failed in his role as graduate student mentor and corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 4B and that the intentional, knowing, and/or reckless actions of others caused the falsification of Figure 4B in Allegation #72, as described above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 2 in favor (reckless) and 5 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 4B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 4B, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

**Manuscript #18**, **Allegation #73** – S.T. Jacob reported falsified data such that COX1 and ND1 seem to be stretched horizontally and vertically with respect to the rest of Figure 5 in Dong et al., JBC 2002.

### Finding of Fact:

- 1. Figure 5 shows RT-PCR analysis of different genes and the β-actin control for rat liver (L) and hepatoma (H).
- Adobe Photoshop gradient mapping analysis demonstrates a difference in the spacing of the COX1 and ND1 bands with respect to the other pairs presented in the figure (see slide 170<sup>1100</sup>). The COX I and ND1 blots appear that they may have been horizontally and vertically expanded vs. other blots, which are all otherwise proportional.
- 3. Dr. Jacob received formal notice of concerns with figures (including Figure 5) within this manuscript from the Journal of Biological Chemistry on June 30, 2017. 1101 As such, Dr. Jacob knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the

<sup>&</sup>lt;sup>1100</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 170

<sup>&</sup>lt;sup>1101</sup> Ex. 277 - 20170630- Email JBC to Jacob



initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 19, 2017.1102, 1103

- 4. No original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection of Figure 5 as presented in the manuscript non-conclusive and not compelling enough to suggest malfeasance.
- 6. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2002.

#### Respondent's Response:

- 1. This allegation was identified and added during the course of the Investigation, and as such Dr. Jacob was not questioned about this allegation during the Inquiry phase of the case.
- 2. In written documentation provided to OSU via his legal counsel on July 15, 2019, 1104 Dr. Jacob explained that the COX1 and ND1 samples may look different because the comb used for the gels might not be identical, that there was no inappropriate manipulation, and that he was surprised anyone would raise concern about the way a gel ran.
- 3. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

### Respondent's Responsibility and Intent:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. Though the COX I and ND1 blots appear to have been horizontally and vertically expanded vs. other blots in the figure (which are all otherwise proportional), the preponderance of the evidence does not suggest an intent to deceive the reader or misrepresent the data.
- 4. Given the inconclusive nature of the analysis, the COMIC believes that this allegation should be dismissed.

#### Committee Conclusion:

3.

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified COX1 and ND1 images in Figure 5, and therefore this act does not constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified COX1 and ND1 images in Figure 5, and therefore this act does not constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

#### Manuscript #19 under Review – Majumder et al., JBC 2004 (2 Allegations)

Majumder S\*, Varadharaj S\*, Ghoshal K, Monani U, Burghes AHM, Jacob ST. "Identification of a Novel Cyclic AMP-response Element (CRE-II) and the Role of CREB-1 in the cAMP-induced Expression of the Survival Motor Neuron (SMN) Gene." The Journal of Biological Chemistry. 2004; 279(15):14803-14811.

<sup>&</sup>lt;sup>1102</sup> Ex. 337 - 20171019 - Email Jacob to JBC - JBC response Dong 2002

<sup>&</sup>lt;sup>1103</sup> Ex. 338 - JBC\_M206958200\_Dong 10172017

<sup>1104</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 26

doi:10.1074/jbc.M308225200. RETRACTED-07/19/18<sup>1105</sup> \* co-first authors

Manuscript #19 (Majumder JBC 2004) was included as an attachment to the progress report and referenced on page 2 of funded grant R01 NS041649-04. Arthur Burghes is PI, Samson Jacob is Co-PI, and Sarmila Majumder is Key Personnel.

**Manuscript #19, Allegation #74 –** S.T. Jacob reported falsified data by the cut and paste of lane 2 and lane 3 in Figure 2A in Majumder et al., JBC 2004.

#### **Finding of Fact:**

- 1. Figure 2A shows a genomic footprinting assay of nuclei from brain and liver cells of Smn<sup>-/-</sup> mice with naked DNA (N) or DNA from control cells (C).
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC as well as ORC, demonstrates evidence of sharp lines at the edges and/or boxes around portions of the gel at the top in lanes 2 and 3, as well as a third portion of the gel near the bottom of lane 3 in Figure 2A, suggesting that data have been superimposed into the figure (see slide 172-173<sup>1106</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript (including Figure 2A) from the Journal of Biological Chemistry on June 30, 2017. Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017. As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the initial Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 31, 2017. 1109, 1110
- 4. No original data were available for this figure. The authors, however, proposed a corrected figure to JBC, merely deleting the contested portions of the figure (see also slide 172<sup>1111</sup>). 1112
- 5. The Committee finds the forensic evidence and visual inspection suggests cutting and pasting of data into the figure, which the Committee concludes is indicative of falsification.
- 6. Dr. Sarmila Majumder was co-first author of JBC 2004 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2004.

### Respondent's Response:

- 1. As this allegation was added during the course of the Investigation, no response from Dr. Majumder or Jacob exists from the Inquiry stage of the case.
- 2. In written documentation provided to OSU via her legal counsel on June 7, 2019, 1113, 1114 Dr. Majumder indicated that she was unable to find any raw data to refute the allegation and that JBC's review of the figure did not draw any conclusions or determine the alleged cut/paste of lanes 2 and 3 in Figure 2A.
- 3. In her interview with the COMIC on June 12, 2019, 1115 Dr. Majumder indicated that she performed the experiment and made the figure but couldn't comment definitively without the original data. Dr. Majumder denied having any motive for falsification and stated she did not remember modifying the figure, but did

<sup>&</sup>lt;sup>1105</sup> Ex. 29 - 20180817-Retraction-J.Biol Chem.-2018-Majumder-12946

<sup>&</sup>lt;sup>1106</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 172-173

<sup>&</sup>lt;sup>1107</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1108</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>1109</sup> Ex. 340 - 20171031 - Email Jacob to JBC - JBC response Majumder 2004

<sup>&</sup>lt;sup>1110</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917

<sup>&</sup>lt;sup>1111</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 172

<sup>&</sup>lt;sup>1112</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917, page 5

<sup>&</sup>lt;sup>1113</sup> Ex. 350a - 2019-06-07 Pre-Interview Submision Majumder, pages 6-7, 9-10; see page 10

<sup>&</sup>lt;sup>1114</sup> Ex. 434 - 20200601 - Email Counsel to LA - 2019-06-07 Attachments

<sup>1115</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 88-89

concede that there was something not natural about the figure. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.

4. In written documentation provided to OSU via his legal counsel on July 15, 2019, Dr. Jacob stated,

"Although we were unable to locate the raw data for this paper published 15 years ago, I would like to point out that the most significant experiment that validated the finding in Fig 2A was the DNase I foot printing assay. There is no obvious reason or motive to cut and paste anything in lanes 2 and 3 in Fig. 2A." 1116

- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.
- 6. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 31, 2017 letter, an explanation was not provided for the apparent cut/paste, only that it "might have been an inadvertent error," that the conclusions were supported by other areas of the figure as well as Figure 3, and a corrected figure was provided.<sup>1117</sup>

### Respondent's Responsibility:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Sarmila Majumder has taken responsibility for generation of Figure 2A but denies any falsification.
- 3. Without original data, the COMIC is not able to determine if the published figure represents the true experimental outcome, nor what impact the apparent manipulation might have on the reported results.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 2A and that the actions of others caused the falsification of Figure 2A, as described in Allegation #74 above. The Committee finds Dr. Jacob failed in his duties as principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified Figure 2A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

<sup>&</sup>lt;sup>1116</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 26

<sup>&</sup>lt;sup>1117</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917, page 1-3

**Manuscript #19, Allegation #75 –** S.T. Jacob reported falsified data by the cut and paste of lane 3 (FI.SMN band) in Figure 7A in Majumder et al., JBC 2004.

#### **Finding of Fact:**

- 1. Figure 7A is a sequencing gel for multiplex PCR, a technique used to amplify multiple targets in a single PCR experiment, from primary hepatocytes isolated from 2 Smn<sup>-/-</sup> mice expressing human SMN2 gene.
- 2. Adobe Photoshop gradient mapping analysis, performed and provided by JBC as well as ORC, demonstrates evidence of horizontal lines at the upper and lower edges of the Lane 3 FI.SMN band in Figure 7A suggesting that data have been superimposed into the figure (see slide 174-175<sup>1118</sup>).
- 3. Dr. Jacob received formal notice of concerns with figures within this manuscript (including Figure 7A) from the Journal of Biological Chemistry on June 30, 2017.<sup>1119</sup> Dr. Jacob subsequently notified Dr. Majumder on July 2, 2017.<sup>1120</sup> As such, Drs. Jacob and Majumder knew of potential issues with the research for at least three (3) months prior to being notified by OSU on October 18, 2017 of the Research Misconduct allegations requiring inquiry. Dr. Jacob sent a formal response to JBC on October 31, 2017.<sup>1121, 1122</sup>
- 4. The authors proposed a corrected figure to JBC, which was purportedly assembled from a higher exposure of the original data (see also slide 176<sup>1123</sup>). The validity of this source data cannot be confirmed, and no other original data were available for this figure.
- 5. The Committee finds the forensic evidence and visual inspection of the figure inconclusive: the sharp line could be explained by cutting and pasting of data into the figure or a PDF compression artifact.
- 6. Dr. Sarmila Majumder was co-first author of JBC 2004 and a Research Scientist in the laboratory of Dr. Samson Jacob at the time of the publication.
- 7. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2004.

### Respondent's Response:

- 1. As this allegation was added during the course of the Investigation, no response from Dr. Majumder or Jacob exists from the Inquiry stage of the case.
- 2. In written documentation provided to OSU via her legal counsel on June 7, 2019, 1125, 1126 Dr. Majumder disagreed with the allegation and provided an original image of the experiment at higher exposure (not that as published). She argued that the original conclusions drawn from the figure as published remain the same and that there would be no motive for falsification based on "clear evidence of altered expression in lane 3." 1127
- 3. In her interview with the COMIC on June 12, 2019,<sup>1128</sup> Dr. Majumder disagreed with the allegation, but took responsibility for performing the experiment and generating the figure. See also Dr. Majumder's General Respondent/Witness statements #1-4 above.
- 4. In written documentation provided to OSU via his legal counsel on July 15, 2019, 1129 Dr. Jacob indicated that he did not see any cutting and pasting of lane 3 in Figure 7A.
- 5. This allegation was not specifically discussed with Dr. Jacob during his interview with the COMIC on July 17, 2019. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above regarding

<sup>&</sup>lt;sup>1118</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 174-175

<sup>&</sup>lt;sup>1119</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1120</sup> Ex. 308 - 20170702 - Email Jacob to Majumder - FW JBC articles

<sup>&</sup>lt;sup>1121</sup> Ex. 340 - 20171031 - Email Jacob to JBC - JBC response Majumder 2004

<sup>&</sup>lt;sup>1122</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917

<sup>&</sup>lt;sup>1123</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 176

<sup>&</sup>lt;sup>1124</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917, page 5

<sup>&</sup>lt;sup>1125</sup> Ex. 350a - 2019-06-07 Pre-Interview Submision Majumder, pages 6-7, 9-10; see page 10

<sup>&</sup>lt;sup>1126</sup> Ex. 434 - 20200601 - Email Counsel to LA - 2019-06-07 Attachments

<sup>&</sup>lt;sup>1127</sup> Ex. 350a - 2019-06-07 Pre-Interview Submision Majumder, pages 6-7, 9-10; see page 10

<sup>&</sup>lt;sup>1128</sup> Ex. 303a - 20190612 - COMIC Interview + errata - Majumder\_Redaction 1, page 88-89

<sup>1129</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 26



laboratory practices, oversight, construction of figures, application of the subsequent use exception, and responsibility of authors.

6. A review of selected and pertinent email records revealed Dr. Jacob's formal response submitted to JBC. In this October 31, 2017 letter, an explanation was not provided for the apparent cut/paste, but indicated that they were able to retrieve an original image and a corrected figure was provided. 1130

### Respondent's Responsibility and Intent:

- 1. Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. The first author, Dr. Sarmila Majumder has taken responsibility for generation of Figure 7A but denies any falsification.
- 3. Without verifiable original data, the COMIC is neither able to determine if the published figure represents the true experimental outcome nor what impact the apparent manipulation might have on the reported results.
- 4. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 7A and that the actions of others caused the falsification of Figure 7A, as described in Allegation #75 above. The Committee finds Dr. Jacob failed in his duties as corresponding author to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that he was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 5. As the manuscript has already been retracted, no further action is necessary to correct the scientific record.

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 7A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### Manuscript #20 under Review - Ghoshal et al., PLoS One 2010 (1 Allegation)

Ghoshal K\*, Motiwala T, Claus R, Yan P, Kutay H, Datta J, Majumder S, Bai S, Majumder A, Huang T, Plass C, and Jacob S\*. (2010) "HOXB13, a Target of DNMT3B, Is Methylated at an Upstream CpG Island, and Functions as a Tumor Suppressor in Primary Colorectal Tumors." PLoS ONE 5(4): e10338. doi:10.1371/journal.pone.0010338. \*\*Co-corresponding authors\*

**Manuscript #20, Allegation #84 –** S.T. Jacob reported falsified data in the DNMT3B Western blot in Figure 1A, PLoS One 2010, for WT and DNMT1-/- in HCT cells, for RKO cells, and for the ladder by:

• using the bands present in Ghoshal data file, "HCT-RKO-DNMT3B.tiff" labeled for WT and DNMT1-/-, but flipped horizontally in Figure 1A to give the desired result.

<sup>&</sup>lt;sup>1130</sup> Ex. 341 - Response-Majumder-JBC-M308225200- 102917, page 2, 4-5

- using the ladder present in Ghoshal data file "Marker.tiff," which is an unrelated experiment labeled with a date prior to the date on the original data file "HCT-RKO-DNMT3B" used for Figure 1A.
- using an unidentified source for the RKO bands in Figure 1A, when the original data file "HCT-RKO-DNMT3B.Tiff" showed no RKO expression.

#### **Finding of Fact:**

- Figure 1A shows a Western blot analysis of whole cell extracts from human colon cancer cell lines RKO and HCT (wild type and mutant) with antibodies specific for DNMTs and demonstrates that expression of DNMT3B is higher in RKO cells.
- 2. The file "HCT-RKO-DNMT3B.psd" found in sequestered computer files from the laboratory appears to be a composite figure in an intermediate stage of manipulation, made from various lanes taken from two other files found on her computer (see slide 179<sup>1131</sup>):
  - a. the 100ug HCT DNMT1 +/+ and DNMT1-/- lanes (and likely empty DNMT3b -/- lane) from the right side of "HCT-RKO-DNMT3B.tiff," and lane 10 (49-hr, 5um 17-DMAG treatment in Huh-7 cells) from the left side of "HCT-RKO-DNMT3B.tiff,"
  - b. the ladder from "Marker.tiff" (which shows what appears to be 8- and 10-week genotyping samples from various cre/lox transgenic animals).
- 3. This series of three image files was identified by ORC from a folder titled "Photoshop" in Dr. Ghoshal's sequestered computer files (see also slide 180<sup>1132</sup>):
  - a. "HCT-RKO-DNMT3B.psd"1133 with a last modified date of 03/11/2010 7:13PM
  - b. "HCT-RKO-DNMT3B.tiff"<sup>1134</sup> with a last modified date of 03/11/2010 7:46PM. The film has a handwritten date of 3/7/2010 on it.
  - c. "Marker.tiff" with a last modified date of 03/12/2010 6:44PM. The film has a handwritten date of "10.23.09" on it.
- 4. The composite "HCT-RKO-DNMT3B.psd" image appears with marked similarity to Figure 1A of Ghoshal et al., PLoS One 2010 with the exception of lanes 1 and 2 now being reversed in their orientation (see slide 181<sup>1136</sup>). The rightmost lane of "HCT-RKO-DNMT3B.psd" (corresponding to 49-hr, 5um 17-DMAG in Huh-7 cells on the left side of "HCT-RKO-DNMT3B.tiff"), however, does not match the data presented in the RKO lane of Figure 1A of Ghoshal et al., PLoS One 2010 (see slide 181<sup>1137</sup>). Comparing Figure 1A of Ghoshal et al., PLoS One 2010 with the original source data in "HCT-RKO-DNMT3B.tiff" reveals the same discrepancies (see slide 182<sup>1138</sup>). Source data for the RKO lane of Figure 1A of Ghoshal et al., PLoS One 2010 has not been identified.
- 5. Adobe Photoshop overlay analysis demonstrated significant similarity and overlap when comparing the Photoshop files with the published image:
  - a. The 100ug HCT DNMT1 +/+ and DNMT1-/- lanes from the file "HCT-RKO-DNMT3B.tiff" overlay perfectly when used in reversed orientation (by a horizontal flip) as lanes 1 and 2 (WT and DNMT1 -/-) in Figure 1A (see slide 183<sup>1139</sup>) and appears to be the source data for these lanes. This would not be scientifically valid as it has the wrong (opposite) data being used to represent certain experimental conditions.

<sup>&</sup>lt;sup>1131</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 179

<sup>&</sup>lt;sup>1132</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 180

<sup>1133</sup> Ex. 342 - HCT-RKO-DNMT3B.psd

<sup>1134</sup> Ex. 343 - HCT-RKO-DNMT3B.tiff

<sup>&</sup>lt;sup>1135</sup> Ex. 344 - Marker.tiff

<sup>&</sup>lt;sup>1136</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 181

<sup>1137</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 181

<sup>&</sup>lt;sup>1138</sup> Ex. 305 - Jacob Image Forensics\_COMIC Final, slide 182

<sup>&</sup>lt;sup>1139</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 183

- b. The ladder lane from the file "Marker.tiff" overlays perfectly with the ladder in Figure 1A (see slide 184-185<sup>1140</sup>) and appears to be the source data for the lane. While this is not a true experimental sample, this would not be scientifically valid nor accepted practice to paste in a marker lane that didn't run on the same gel as the experimental samples.
- 6. The Committee finds the forensic evidence and visual inspection demonstrates merging and reorientation of data from multiple different experiments, performed months apart, to create a composite figure not accurately representing the experimental conditions to be indicative of falsification.
- 7. Dr. Kalpana Ghoshal was first and co-first corresponding author of PLoS One 2010 and a Research Assistant Professor in the laboratory of Dr. Samson Jacob at the time of the publication.
- 8. Dr. Samson Jacob was the laboratory PI and corresponding author of JBC 2004.

### Respondent's Response:

- 1. As this allegation was added during the course of the Investigation, no response from Dr. Ghoshal or Jacob exists from the Inquiry stage of the case.
- 2. In written documentation provided to OSU via her legal counsel on November 15, 2019:1141
  - a. Dr. Ghoshal indicated with respect to the WT and DNMT1 -/- being flipped between the original data and the published figure that there was no reason to do so "as DNMT3B is supposed to be expressed in both WT and DNMT1-/- cells at comparable levels, and no claim about any differential expression" was made. 1142
  - b. Regarding the use of a ladder from an unrelated experiment, Dr. Ghoshal commented that the original gel included a hand-written marker not an ECL marker, but that regardless of the marker used, "it was not essential as the only conclusion of this figure is that the antibody we raised is specific for DNMT3B." 1143
- 3. With respect to the use of unidentified source of data showing expression in the RKO lane of Figure 1A, Dr. Ghoshal stated that the expression of DNMT3B was show quantitatively in Figure 1B of PLoS One 2010 as well as in a previously published manuscript (Figure 3A of Datta et al., Cancer Res 2009, Manuscript #10 above, for which retraction has been recommended). Dr. Ghoshal posits that the protein may have been degraded in the batch run on the "HCT-RKO-DNMT3B.tiff" blot, but that another blot run at the same time (3/11/2010) shows expression of DNMT3B in HCT cells. Thus, Dr. Ghoshal argued that the allegation as phrased "no RKO expression" is not true. 1145 Dr. Ghoshal provided this RKO positive blot as "Figure A" on page 3 (see slide 1861146, 1147). See also Dr. Ghoshal's General Respondent/ Witness statements #1-2, #4-6 above.
- 4. In written documentation provided to OSU via his legal counsel on November 15, 2019, 1148 Dr. Jacob objected to OSU's application of the subsequent use exception and indicated that he did not prepare the sub-figure in question or know who did, but would have reviewed the manuscript's figures at the time and noted their consistency with results he'd observed in the laboratory. It is noted that he concurs with the points raised by Dr. Ghoshal in her response, that he disagrees with the allegation, and that the purpose of the experiment and figure was to determine the specificity of the lab's DNMT3B antibody with no claim to differential expression. Regarding the use of a ladder from an unrelated experiment, Dr. Jacob acknowledged that it was possible, reiterated the purpose of the sub-figure and that the conclusions

<sup>&</sup>lt;sup>1140</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 184-185

<sup>&</sup>lt;sup>1141</sup> Ex. 345a - 2019-11-15 Dr. Ghoshal Response to New Allegations\_Redacted

<sup>&</sup>lt;sup>1142</sup> Ex. 345a - 2019-11-15 Dr. Ghoshal Response to New Allegations Redacted, page 3

<sup>&</sup>lt;sup>1143</sup> Ex. 345a - 2019-11-15 Dr. Ghoshal Response to New Allegations Redacted, page 3

<sup>&</sup>lt;sup>1144</sup> Ex. 343 - HCT-RKO-DNMT3B.tiff

<sup>&</sup>lt;sup>1145</sup> Ex. 345a - 2019-11-15 Dr. Ghoshal Response to New Allegations\_Redacted, page 3

<sup>&</sup>lt;sup>1146</sup> Ex. 305 - Jacob Image Forensics COMIC Final, slide 186

<sup>&</sup>lt;sup>1147</sup> These data are also reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>1148</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob

<sup>&</sup>lt;sup>1149</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob, Page 1-2

drawn from it are not changed, and that there would be nothing to be gained from such a "mix-up."<sup>1150</sup> Finally, Dr. Jacob provides the exact same argument as Dr. Ghoshal with respect to the use of unidentified source of data showing expression in the RKO lane of Figure 1 and stands by the conclusions of the figure. See Dr. Jacob's General Respondent/Witness statements #1-2, #4-7 above.

### Respondent's Responsibility and Intent:

- Dr. Jacob and other witnesses have consistently indicated that he did not generate of any figures for publication, and that primary responsibility for any manuscript usually rested with the first and/or second author(s).
- 2. Dr. Ghoshal, first author and co-corresponding author has not taken responsibility for generation of Figure 1A, but has espoused the view that all authors on a publication are responsible for its scientific integrity and content.
- 3. The file "HCT-RKO-DNMT3B.psd" that appears to show the wholesale construction of a figure from related and unrelated source data calls strongly suggests to the Committee that the falsification was intentional, but also that the data were not associated with Dr. Jacob and that Dr. Jacob was likely not responsible for the data manipulation in Figure 1A.
- 4. The following three discrepancies between the source data identified and the published figure provide clear and convincing evidence to the Committee that the figure was fabricated/falsified with the goal of misleading the scientific community.
  - a. The file "HCT-RKO-DNMT3B.tiff" contains the source data for the WT and DNMT1-/- lanes in published Figure 1A, however the data is flipped in the published figure with WT reported as DNMT1-/- and DNMT1-/- reported as WT for DNMT3B expression. The correct orientation/lane labeling of these two bands of data was observed in conversion of the source data to the Photoshop file ("HCT-RKO-DNMT3B.psd"). The flipping of bands in the published figure signifies to the Committee an attempt to mask their duplication/reuse.
  - b. The molecular weight ladder lane in published Figure 1A was taken from the file "Marker.tiff" containing a completely unrelated experiment performed 10/23/09 and pasted into the figure.
  - c. The file "HCT-RKO-DNMT3B.tiff" shows no expression of DNMT3B in the RKO lane but the published Figure 1 shows equal expression for the RKO lane as for WT HCT and DNMT1-/- lanes.
- 5. When comparing the remaining data presented in Figure 1A to additional data found amidst the sequestered data from the laboratory, the rest of the published findings in Figure 1A appear valid. 1151
- 6. When initially confronted with the information that files appearing to demonstrate image manipulation had been located, Dr. Ghoshal purposely obfuscated and lied to the Inquiry committee, explaining away the files as irrelevant, having not been generated for the purpose of using or publishing them, and stating that "as far as anyone can tell, these images were never published or used in any way." 1152 Such statements epitomize dishonesty in the opinion of the Committee and damage the credibility of arguments made by Dr. Ghoshal as a witness.
- 7. The Committee has determined that Dr. Jacob failed in his role as corresponding author to ensure the validity of data submitted for publication. The Committee believes, based on witness testimony, that Dr. Jacob was not responsible for the creation of Figure 1A and that the actions of others caused the falsification within Figure 1A in Allegation #84, as described above. The Committee finds Dr. Jacob failed in his duties as laboratory principal investigator to ensure the validity of data submitted for publication, although the COMIC failed to identify a preponderance of evidence that this represented recklessness (i.e., that Dr. Jacob was on notice of the significantly increased risk of falsified information being generated/used) as described in the Policy III. A and 42 C.F.R. § 93.103 (b).
- 8. The Committee recommends retraction of the manuscript to correct the scientific record.

<sup>&</sup>lt;sup>1150</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 2

<sup>&</sup>lt;sup>1151</sup> These data are reviewed elsewhere in DIO 6819.

<sup>1152</sup> Ex. 213 - 20181022 - Ghoshal Response CII with Exhibits, page 7

#### **Committee Conclusion:**

By a preponderance of the evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 1A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 0 in favor and 7 against, that the Respondent intentionally, knowingly, and/or recklessly reported falsified images in Figure 1A, and therefore this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

### **Summary of Investigation Committee Conclusions**

As defined under the University's Policy and Procedures Concerning Research Misconduct, Research Misconduct means Fabrication, Falsification or Plagiarism in proposing, performing, or reviewing research, or in reporting research results, and "Falsification" is "manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in research record." Further, a finding of Research Misconduct requires that there is a significant departure from accepted practices of the relevant research community, that the misconduct be committed intentionally, knowingly, or recklessly, and that the allegation be proved by a "Preponderance of the Evidence" under the federal regulations, and by "Clear and Convincing Evidence" under the University Rule 3335-5-04 regarding complaints made against faculty members.

Based on the Preponderance of the Evidence standard, the COMIC determined for four (4) allegations (Allegations #17, 23, 25, 71) in Manuscripts #4, #8, and #18 that Dr. Jacob committed Research Misconduct by deviating from the accepted practices of image handling and figure review and intentionally, knowingly, and/or recklessly reported falsified research data or including falsified data in performing or reviewing research, or in reporting research results.

The COMIC determined at both the Preponderance of the Evidence and Clear and Convincing Evidence standards that for ten (10) allegations (Allegations #8-11, 44-45, 47, 50-51, , 76) in Manuscripts #3, #7, and #8 that Dr. Jacob committed Research Misconduct by deviating from the accepted practices of image handling, figure review and/or manuscript correction and intentionally, knowingly, and/or recklessly reported falsified research data.

A summary of the COMIC's final findings of Research Misconduct are listed below, along with an explanation of the COMIC's reckless determination:

- 1. Dr. Jacob recklessly reported falsified data in Figures 1A, 1B, 3D, 6C-1, 6C-2, of Ghoshal et al., Mol Cell Biol. 2005; 25(11):4727-41 (Manuscript #3). By failing to execute his duties to perform a complete review of the data after he was aware of potential errors in this published manuscript and issuing an erratum without addressing or reviewing all of these other falsifications, Dr. Jacob acted recklessly and allowed the following falsified data to remain uncorrected in the published literature:
  - The reuse of the same data in lanes 1-5 and in lanes 6-10 (flipped 180 degrees) of the NS blot in Figure 3D
  - b. The reuse of the same data in lanes 1-3 and in lanes 7-9 of the GFP blot in Figure 6C-1
  - c. The reuse of the same data in lane 2 and in lane 4 of the Dnmt1 blot in Figure 6C-2
  - d. The reuse of the same data in
    - i. lanes 1-3 and lanes 7-9 of the GFP blot in Figure 6C-1 (internal duplication)
    - ii. lanes 1-8 (of a 9 lane blot representing GFP) in Figure 6C-1 of MCB 2005 and in lanes 1-8 (representing β-tubulin) in Figure 2 of J Nutr. 2006 (cross-publication duplication).

- e. The reuse of the same data in lane 1 and in lane 7; and the reuse of same data in lane 5 and in lane 6 (horizontal flip of image) in Dnmt3a blot in Figure 1A
- f. The reuse of same data in lanes 1, 2 and in lanes 4, 5 in Ku70 blot in Figure 1B
- g. The reuse of the lower bands in lanes 1-2 and 5-6 in the DNMT3B blot of Figure 1B
- 2. Dr Jacob committed reckless research misconduct by attempting to correct the falsified data in Figure 6C, JBC 2006 Aug 4; 281 (31): 22062-72 (Manuscript #7), by using data included in other publications under investigation (Manuscripts #4 and #16) that contained falsified data, when he already knew that the data from those other publications were in question. One publication (Manuscripts #16) has since been retracted. The specific falsification of multiple bands in Figure 6C that would have been obvious to a typical researcher upon careful review of the figure against source data is:
  - a. the reuse of same data (upper band) in lane 2, lane 3, and lane 6 in Figure 6C and reuse of the same data in the lower band in lane 2 as the lower band in lane 3 (when rotated 180°) in Figure 6C
- 3. Dr. Jacob recklessly reported falsified data in Figure 8C of Bai et al., Mol Cell Biol. 2005; 25(2):751-66 (Manuscript #4). By failing to execute his duties as graduate student mentor and corresponding author, Dr. Jacob deviated from accepted practices and failed to identify the following duplications of multiple bands and backgrounds that would have been obvious to a typical researcher upon careful review of figures proposed for publication against the original source data:
  - a. The reuse of the same data in sample 3 and sample 4 (with possible erasure of the band) in the Hdac2 blot
  - b. The reuse of the same blank background image in samples 15-16 and 17-18 in the Hdac2 blot
  - c. The reuse of the same data in samples 7-8 and 9-10 (with possible erasure of the bands) in the Dnmt3a blot
  - d. The reuse of the same blank background image in sample 16 and sample18 (with possible erasure of background artifact) in the Dnmt3a blot
- 4. Dr. Jacob intentionally, knowingly, or recklessly reported falsified data in Figure 2C, 3E, 6B, and 7D of Bai et al., J Biol Chem. 2007; 282 (37): 27171-80 (Manuscript #8), by reusing the same data to represent different experimental results. Specifically Dr. Jacob:
  - a. Recklessly allowed the reuse of the same data in lanes 1-4 and in lanes 5-8 of the GAPDH blot in Figure 2C by deviating from accepted practices in his failure identify the duplications of multiple bands that would have been obvious to a typical researcher upon careful review of figures proposed for publication. Dr. Jacob failed to execute his duties as a graduate student mentor and corresponding author to ensure the validity of data submitted for publication.
  - b. Recklessly allowed the reuse of the same data in lanes 1-3 and in lanes 6-8 of the NS blot in Figure 3E by deviating from accepted practices in his failure identify the duplications of multiple bands that would have been obvious to a typical researcher upon careful review of figures proposed for publication. Dr. Jacob failed to execute his duties as a graduate student mentor and corresponding author to ensure the validity of data submitted for publication.
  - c. Intentionally or knowingly reported a falsified Figure 6B by the reuse of the same data in lane 4 and in lane 5, and in lane 6 (0, 2 and 4 hours) in the  $\Delta$ CD2-5 sample +NGF (lower panel).
  - d. Intentionally or knowingly reported a falsified Figure 6B by the reuse of the same data in lanes 1-3 in the top panel (-NGF) in Figure 6B and in lanes 1-3 of the Tcadflag blot in Figure 7D; and also by the reuse of same data in lanes 1-3 in the bottom panel (+NGF) in Figure 6B, and in lanes 7-9, Tcadflag blot in Figure 7D.
  - e. Intentionally or knowingly reported a falsified expression patterns for +NGF ΔCD2-5 and for +NGF ΔCD3-5 in Figure 6B, which both show the desired results to match the hypothesis of the paper, but neither match the expression patterns of the purported raw data for +NGF ΔCD2-5 or +NGF ΔCD3-5 that were provided as a proposed correction of Figure 6B.
- 5. Dr. Jacob recklessly reported falsified data in Figure 1D, 2A, 5, and/or 6A of Dong et al., J Biol. Chem. 2002; 277(45), 43309-18 (Manuscript #18). By failing to execute his duties as graduate student mentor and corresponding author, Dr. Jacob deviated from accepted practices and failed to identify the following

duplications of control bands that would have been obvious to a typical researcher upon careful review of figures proposed for publication against the original source data and methodology:

a. The reuse of the same in the  $\beta$ -actin blot for Figure 1D, Figure 2A, Figure 5 and Figure 6A

The COMIC determined at the Preponderance of the Evidence standard that fifty-three (53) allegations (Allegations #1-7, 12-16, 18-20, 24, 26-37, 39-40, 43, 48, 55-57, 60-61, 63, 66, 69-70, 72-75, 77-84) do not constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b) and should be dismissed.

- 1. Though the COMIC determined that Research Misconduct was committed in the following manuscripts as alleged, they concluded that the falsification was committed by someone other than Dr. Jacob.
  - a. Manuscript #1: Allegation #4
  - b. Manuscript #2: Allegation #5, #6, #43
  - c. Manuscript #5: Allegation #18
  - d. Manuscript #6: Allegation #19, #20
  - e. Manuscript #7: Allegation # #79
  - f. Manuscript #8: Allegation #24, #26, #27, #48
  - g. Manuscript #9: Allegation #28, #29, #80
  - h. Manuscript #10: Allegation #30, #81, #82, #83
  - i. Manuscript #11: Allegation #31, #32, #33
  - j. Manuscript #12: Allegation #35, #56, #57
  - k. Manuscript #13: Allegation #36, #37, #39, #61
  - I. Manuscript #15: Allegation #63
  - m. Manuscript #17: Allegation #69
  - n. Manuscript #19: Allegation #74, #75
  - o. Manuscript #20: Allegation #84
- For the following manuscripts and allegations, the COMIC determined that falsifications were present, but that the allegations did not meet the threshold or it was unclear who committed the Research Misconduct.
  - a. Manuscript #4: Allegation #12, #13, #14, #15, #16, #77
  - b. Manuscript #16: Allegation #66
  - c. Manuscript #18: Allegation #70, #72
- 3. For the following manuscripts and allegations, the COMIC determined that no falsifications were evident and that the associated allegations should be dismissed.
  - a. Manuscript #1: Allegation #1, #2, #3
  - b. Manuscript #3: Allegation #7
  - c. Manuscript #7: Allegation #78
  - d. Manuscript #12: Allegation #34, #55, #60
  - e. Manuscript #14: Allegation #40
  - f. Manuscript #18: Allegation #73

The COMIC finds that generally speaking, Dr. Jacob maintained a large laboratory with 12-15 undergraduate students, graduate students, post-doctoral researchers, and senior staff, which published frequently. With his graduate students or new staff, Dr. Jacob indicated that he would spend the first one or two months with them on a one-on-one basis, after which time he would rarely meet with them individually, but that he had structured his lab with one or two senior people who the students or trainees would report to for routine day-to-day questions. Dr. Jacob stated that the senior people were honest and dedicated, and he had no reason to doubt them, specifically naming Dr. Kalpana Ghoshal and Dr. Sarmila Majumder as the most senior researchers in his laboratory. All witnesses stated that Dr. Jacob led a weekly lab meeting to review results. However, in terms of the generation of a final figure, Dr. Jacob did not perform this task personally and appears

to have relied on his many students, staff, and co-authors to generate all the figures within the publications. While Dr. Jacob described that he carefully read and reviewed every paper and figure, he acknowledged that months or years could have passed between his initial comparison of a figure to the original data and even then that he only reviewed the data within the figure for being consistent with his memory of results he'd previously seen obtained. 1153, 1154, 1155 The COMIC believes that such actions are wholly inconsistent with longstanding data review practices, fail to meet long held standards of laboratory and trainee mentoring and oversight, and generate the risk for data manipulation so obvious that a typical researcher in the relevant research community should have known and could not have ignored.

The COMIC, as the CII before it, does not believe Dr. Jacob created any of the final figures for publication or generated any of the alleged falsified figures. However, the definition of Research Misconduct accounts for the reviewing of research, and the allegations against Dr. Jacob involve the *reporting* of falsified data. The COMIC believes that it was arguably irresponsible, and at times reckless for someone at Dr. Jacob's level to assume, and not take any action to verify, that figures placed in publications where he was listed as a last/senior author were reliable and accurately represented the experimental results.

The Committee members further believe that when accepting graduate students, principal investigators assume the responsibility of being active advisors and are completely responsible for the review of student work, which should include comparison of publication-ready figures with the original source data. Regardless of how comfortable Dr. Jacob was with the data, or how many times he believes he had seen similar results, the Committee believes that the standards of the field remain that graduate student advisors must provide the highest levels of training and oversight so as to prevent errors or deliberate falsifications being reported from student-generated data. Dr. Jacob has frequently touted his long, illustrious research career, but has also made the statement that he may have taken on too many responsibilities at the University in addition to his role as a PI. This statement suggests that Dr. Jacob was potentially aware of his short-comings as a PI, his inability to spend the necessary time required with his trainees and researchers, and should have known that this created a risk that falsified data could be generated.

Furthermore, Dr. Jacob has categorically stated that he has never submitted a manuscript via upload to a journal and has never checked the online assurance statement that many journals require for submission, deferring instead to lab and secretarial staff. In not even knowing that such statements existed and that as corresponding author he would be attesting to a manuscript's validity and his responsibility as the steward of the data, Dr. Jacob further demonstrated that he has departed from and not kept pace with the publishing standards and typical practices of the scientific community.

During the course of this Investigation, Dr. Jacob has placed all responsibility for any irregularities or data manipulation onto, as he states, the first and second authors of any questioned publication. By commonly accepted scientific publishing standards, the first and/or second authors are generally deemed to be responsible for generating the majority of the experimental data, generating figures, and the overall validity of manuscripts. But the COMIC believes that as senior and/or corresponding author, Dr. Jacob also bears some responsibility for the validity of the data in his published papers, particularly when graduate students or junior staff are involved. The COMIC has found that by the first authors' own accounts, as well as those of Dr. Jacob, the first authors have been largely unable to provide satisfactory explanations or affirmative defenses for any of the allegations. The continued argument of Dr. Jacob and other witnesses that in the absence of original data they cannot verify that an image has been falsified is not valid nor persuasive.

<sup>1153</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 6

<sup>1154</sup> Ex. 300 - 2019.11.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 1

<sup>&</sup>lt;sup>1155</sup> Ex. 298 - 2019.07.15 - Letter to Emily Schriver on behalf of Dr. Jacob, page 6

<sup>1156</sup> Ex. 56 - 20180305-CII Interview + errata - Jacob, page 20, lines 16-24

This Committee, made up of a panel of experienced research scientists, has concluded that the preponderance of evidence supports the conclusion that data have been inappropriately manipulated and falsified. The Committee's conclusions are based on very clear forensic analyses as well as on the standards of practice for data management and presentation over the past twenty years. While original data is very helpful in many cases to understand the impact of a specific falsification on the reported results, in most cases original data are not needed to verify that falsification has occurred.

The Committee was not swayed by Dr. Jacob's responses. Dr. Jacob's attempts to discredit the allegations of duplication/reuse of data based on the lack of splice lines has been clearly refuted by evidence and testimony that splicing had been performed to remove unwanted lanes yet was not visible in the final figure (see <u>Allegation #5</u>, <u>Allegation #28</u>, and <u>Allegation #29</u> above). Additionally, the Committee finds Dr. Jacob's arguments that his publications have been frequently cited or replicated, that no reviewer or journal has previously brought forth concerns, that the questioned figures represent only a small percentage of all figures and subpanels in his manuscripts, and that there have been no allegations of plagiarism to be completely irrelevant and inconsequential to the allegations being brought against him.

Dr. Jacob has claimed that no one has previously brought up concerns regarding any of his publications, specifically stating in his response to the CII's preliminary report, "The first time I ever knew that anyone had alleged that any figure in any of my papers was not accurately reported was on October 18, 2017."1157 The Committee finds this claim to be disingenuous. As early as March 23, 2017 and June 30, 2017, Dr. Jacob had received formal notifications from Proceedings of the National Academy of Sciences 1158 and the Journal of Biological Chemistry, 1159 respectively, that there were concerns with data in a number of publications (i.e. Manuscripts #1 (JBC 2002), #2 (PNAS 2004), #7 (JBC 2006), #8 (JBC 2007), #12 (JBC 2011), #15 (JBC 2009), #16 (JBC 2006), #17 (JBC 2008), #18 (JBC 2002), #19 (JBC 2004)). Additionally, inconsistencies identified in Manuscripts #3 (MCB 2005), #5 (Cancer Res 2005), #8 (JBC 2007), #10 (Cancer Res 2009), #13 (Genes Cancer 2012), and #14 (Hepatology 2014) were published on the web (i.e., PubPeer) and known in detail at least to Dr. Ghoshal and Dr. Datta by September 2017. The general existence of PubPeer concerns with multiple manuscripts was specifically mentioned to Dr. Jacob via email on September 19, 2017. Though Dr. Ghoshal appeared to respond to the concerns raised on PubPeer for Manuscript #14 with her own commentary, 1162 the COMIC is skeptical that information about these manuscripts was known only to Dr. Ghoshal and Dr. Datta based on the history of communication amongst members of the Jacob lab. At minimum there is evidence that during the investigation Dr. Ghoshal provided PubPeer search results to Dr. Jacob 1163 and Dr. Majumder. 1164 It remains unknown when and to what extent all members of the laboratory were performing PubPeer searches or receiving and reading notifications of concern from PubPeer. 1165

Nonetheless, after he was made aware of these concerns, no further actions were taken by Dr. Jacob. Dr. Jacob also disavowed knowledge of any concerns with the data or any other ongoing investigations. The

<sup>&</sup>lt;sup>1157</sup> Ex. 209 - 20181022 - Jacob Response CII with Exhibits, page 4

<sup>&</sup>lt;sup>1158</sup> Ex. 276 - 20180313 - Email PNAS to Jacob - PNAS Motiwala et al. 2004

<sup>&</sup>lt;sup>1159</sup> Ex. 277 - 20170630- Email JBC to Jacob

<sup>&</sup>lt;sup>1160</sup> These data are reviewed elsewhere under DIO 6819 and 6822.

<sup>&</sup>lt;sup>1161</sup> Ex. 297 - 20170919 - Email - JBC Editor to Jacob - Re Response JBC articles

<sup>&</sup>lt;sup>1162</sup> These data are reviewed elsewhere under DIO 6819.

<sup>&</sup>lt;sup>1163</sup> Ex. 349 - 20180305 - Email Ghoshal to Jacob - sakabe's papers in pubpeer (attached)

These data are reviewed elsewhere under DIO 6819 and 6820.

<sup>&</sup>lt;sup>1165</sup> It is the practice of PubPeer to attempt contact with the corresponding author of a manuscript for which a comment is posted. Based on a limited review of Dr. Ghoshal's and Jacob's email records that were routinely put on hold upon receipt of initial allegations, both Dr. Ghoshal and Dr. Jacob received numerous "New Comment" emails from PubPeer. As many of these were initially quarantined by the OSU Medical Center email system as potential spam emails, it remains unknown if and to what extent Drs. Ghoshal and Jacob viewed or opened these emails (with the exception of two cases relating to Manuscripts #5 and #10 previously mentioned) or whether they proceeded directly to PubPeer's website without opening the email.

Committee believes that standard practice would be to expect any reputable scientist to address any concerns by correcting the published literature. The Committee also believes that if a concern is raised regarding a single figure in a paper, a typical researcher would meticulously review the entire publication for any errors, experiments to rerun, corrections to submit, and he or she would do whatever was necessary to address the concern. This was not done by Dr. Jacob or the members of his lab: in fact, in at least one case (Manuscript #3), an erratum was submitted for only one figure when there were many other problematic figures in the manuscript. It should be reiterated that during the course of the Inquiry, nine papers (Manuscripts #1, #7, #8, #12, #15-19) were retracted and one manuscript (Manuscript #3) corrected and that the university was not informed of this until after the fact.

Finally, the Committee notes that initially Dr. Jacob staunchly objected to any and all allegations; however, as the evidence mounted against the laboratory, Dr. Jacob vacillated between positioning himself as a victim of the dubious actions of members of his laboratory and aligning himself with them and relying on their responses to the allegations. The Committee finds that these opposing positions over time weaken Dr. Jacob's credibility.

### Response to the Preliminary Report

Dr. Jacob was provided a copy of the Preliminary Investigation Report on October 29, 2020. 1166, 1167 As per the Policy, Dr. Jacob was given thirty (30) days to file a written response 1168 and a 30-day extension. 1169, 1170, 1171 A second extension was granted, bringing the deadline to January 20, 2021. 1172, 1173, 1174 Dr. Jacob provided a response to the Preliminary Investigation Report on January 20, 2021. 1175, 1176 The COMIC carefully reviewed Dr. Jacob's response and the supporting documentation.

In his response, Dr. Jacob again touts his background and achievements, maintaining that his integrity has never been questioned and that he has never been accused of research misconduct previously. Dr. Jacob reiterates his objections to OSU's subsequent use process and argues that as applied it violates OSU's own policies, federal regulations, and due process. The Policy<sup>1177</sup> and subsequent use exception process<sup>1178</sup> employed throughout the preliminary assessment, inquiry, and investigation of this case are in concert with each other as well as the federal regulations. Dr. Jacob's continued use and citation of the manuscripts published greater than six years before the university's receipt of allegations was certainly for his potential benefit per the federal regulations and has been well established in the documentation supporting this report. Dr. Jacob's claim that his due process was violated because the subsequent use exception process employed by the university was expansive and he was not specifically made aware of it prior to his notification of allegations is without merit. The COMIC believes that ignorance of or disagreement with university policies and procedures does not render them inapplicable. Further claims that the revision and implementation of the university's Policy and associated process documents are evidence of a flawed application of the subsequent use process are equally unmerited. The revised research misconduct policy has not yet gone into effect and further would not apply to this research

<sup>&</sup>lt;sup>1166</sup> Ex. 491 - 20201029 - Preliminary Investigation Report - Jacob

<sup>&</sup>lt;sup>1167</sup> Ex. 493 - 20201029 - Email RIO to Jacob - COMIC PR

<sup>&</sup>lt;sup>1168</sup> Ex. 492 - 20201029 - Letter RIO to Jacob - COMIC PR

<sup>1169</sup> Ex. 509a - 20201106 - Email RIO to SVPR - Extension request\_Redacted

<sup>&</sup>lt;sup>1170</sup> Ex. 510 - 20201106 - Email SVPR to RIO - Extension approved

<sup>1171</sup> Ex. 511 - 20201106 - Email RIO to Jacob - Deadline extended

<sup>&</sup>lt;sup>1172</sup> Ex. 535 - 20201217 - Email RIO to SVPR - 2nd Extension request

<sup>&</sup>lt;sup>1173</sup> Ex. 536 - 20201217 - Email SVPR to RIO - 2nd Extension approved

<sup>1174</sup> Ex. 537 - 20201217 - Email RIO to Jacob - 2nd Extension Granted

<sup>&</sup>lt;sup>1175</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021)

<sup>&</sup>lt;sup>1176</sup> Ex. 543 - 20210120 - Email - Counsel to LA - Jacob Response

<sup>&</sup>lt;sup>1177</sup> Ex. 1 - University Policy and Procedures Concerning Research Misconduct

<sup>&</sup>lt;sup>1178</sup> Ex. 2 - Subsequent Use Exception Process-V1

misconduct case since it would be executed to its completion under the policies, procedures, and laws in effect at its initiation. The fact that the duration of this case has been protracted by the number of allegations, the number of respondent responses and requests for extensions, and a thorough vetting of the vast amount of evidence by the inquiry and investigation committees, has afforded the time for the university to modify and improve its research misconduct policy and the equity of its application as well as the affiliated procedures.

Dr. Jacob's January 20, 2021 response included an attestation that he was actively engaged in meeting with and training his students, but confirmed that he did not "go back, prior to publication, and compare each and every figure in every paper to the raw data on which each such figure was based." 1179 Findings made by the COMIC were not predicated upon a lack of engagement, but rather their belief as experts in the field that graduate students are known to require an additional level of oversight based on the inherent risk posed from their positions and lack of expertise as students and that Dr. Jacob's engagement didn't include the verification of figures with the raw data that would be necessary for such graduate student oversight. Furthermore, in claiming unsubstantiated assertions of recklessness by the Committee (regarding M#4, A#17 and M#18, A#71 1180), Dr. Jacob erroneously appealed to a statement in the federal Office of Research Integrity's response to the notice of investigation indicating that "ORI will need evidence that Dr. Jacobs (sic) was truly disengaged from the laboratory's work" 1181 This statement has been removed from its original context, which actually stated that if Dr. Jacob were disengaged in his oversight, then it could be argued that he was reckless. Again, the Committee is not arguing that Dr. Jacob was disengaged, but rather that his engagement did not include the verification of figures with raw data requisite of graduate student oversight.

Despite Dr. Jacob's objections that a finding of recklessness cannot be based on his actions post publication, 1182 the Committee contends that the 2018 correction of Manuscript #3 is an amendment/supplement to the original publication and that both relate to the allegations under investigation. The Committee was charged with pursuing all significant issues and relevant leads, including any evidence of additional instances of possible research misconduct and not precluding a potential expansion of scope or limitation by the phrasing of an allegation itself. Presumption of innocence or fully adjudicated findings of research misconduct are irrelevant to the need to correct the scientific record. The OSU Research Data Policy, as well as the policies of journals, presume that the research record is accurate: "As per national practice, the PI has the right and responsibility to ensure that research is accurately reported to the scientific and academic community..." The Committee found that the misconduct related to Manuscript #3, perhaps initiated with the original publication in 2005, was reiterated in 2018 when Dr. Jacob was on notice of a multitude of concerns with the publication and proceeded to act recklessly, attesting to the accuracy of the manuscript and allowing the falsified data to remain uncorrected.

Dr. Jacob's response included additional arguments that the committee employed an improper reliance on forensic analyses and applied an improper definition of research misconduct because original data is not available, but also because, in Dr. Jacob's opinion, the validity and reproducibility of each manuscript's conclusions and his general body of work still stands. These arguments merit little response by the committee other than to note that Photoshop forensic analysis is a reliable tool used by the federal research misconduct oversight agencies, US universities and scientific journals. Furthermore, the definition of research misconduct remains silent on the validity/reproducibility of a manuscript's conclusions or a respondent's body of work, rather only defining research misconduct as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. The validity/reproducibility of the conclusions in a manuscript has no bearing on whether research misconduct occurred regarding a specific figure in the manuscript, and in this case was not a mitigating factor in the acts of falsification themselves. Furthermore,

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<sup>&</sup>lt;sup>1179</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), page 10-12.

<sup>&</sup>lt;sup>1180</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), page 22-23

<sup>&</sup>lt;sup>1181</sup> Ex. 377 - 20190125 - Letter ORI to RIO - Response to Investigation Notice, page 2

<sup>&</sup>lt;sup>1182</sup> Ex. 542 - Response of Dr. Jacob to Preliminary Report of Investigation (Jan 20 2021), page 15-16

<sup>&</sup>lt;sup>1183</sup> Ex. 555 - Research Data Policy

reliability and reproducibility of the manuscripts' general findings are distinctly different from validity of specific results and figures reported therein.

The COMIC found that no new evidence or explanation was presented by the respondent in defense of the allegations and findings. As such, the COMIC remained focused on the scientific quality of the evidence presented in the published data, the subsequent analytics, and respondent/witness responses, and maintains the key findings of the report. The COMIC strongly disagrees with Dr. Jacob's claim that if any irregularities occurred, they were "inadvertent errors". Any suggestion that Dr. Jacob was held to an unfair standard, that his credibility was improperly assessed, that the committee was inequitable, or that the committee went beyond the scope of its charge is an unfounded and unwarranted attempt to present the findings of the committee as biased and prejudicial. The COMIC executed its investigation per 42 C.F. R. § 93.310 and "pursue[d] diligently all significant issues and leads discovered that [were] determined relevant to the investigation, including any evidence of additional instances of possible research misconduct, and continue[d] the investigation to completion," which resulted in affirmation of its earlier conclusion, by a preponderance of the evidence and/or by clear and convincing evidence, that fourteen (14) allegations (Allegations 8-11, 17, 23, 25, 44-45, 47, 50-51, 71, 76) do constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b) and that fiftythree (53) allegations (Allegations 1-7, 12-16, 18-20, 24, 26-37, 39-40, 43, 48, 55-57, 60-61, 63, 66, 69-70, 72-75, 77-84) do not constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b) and should be dismissed.

### **Recommended Actions**

Under the University Policy and Procedures Concerning Research Misconduct, section IV.F.5, the Committee shall include recommended sanctions in cases where allegations of Research Misconduct are substantiated. Given the pattern, scope, and gravity of the Research Misconduct findings against Dr. Jacob, the COMIC believes that Dr. Jacob should be prohibited from conducting research activities, overseeing graduate student research, or submitting applications for federally funded research for a period of three (3) years. Therefore the COMIC strongly recommends that the following sanctions be imposed:

- 1. Permanent revocation of Dr. Jacob's Emeritus Faculty status
- 2. Permanent revocation of Dr. Jacob's Distinguished Faculty title
- 3. Revocation of Dr. Jacob's PI/Co-PI status for a period of three (3) years from the date of the final Investigation report
- 4. Prohibition from overseeing graduate students or other trainees
- 5. RETRACTIONS The COMIC recommends that Dr. Jacob be required to work with the Institution and the other co-authors in contacting the following journals to request the immediate retraction of the following manuscripts:

Manuscript #2 - Motiwala et al., PNAS 2004; 101(38):13844-9

Manuscript #3 – Ghoshal et al., Mol Cell Biol. 2005; 25(11):4727-41.

Manuscript #4 – Bai et al., Mol Cell Biol. 2005; 25(2):751-66.

Manuscript #5 – Datta et al., Cancer Res. 2005; 65(23):10891-900.

Manuscript #6 – Ghoshal et al., J Nutr. 2006; 136(6):1522-7.

Manuscript #9 - Datta et al., Cancer Res. 2008; 68(13):5049-58

Manuscript #10 - Datta et al., Cancer Res. 2009; 69(10):4277-85.

Manuscript #11 - Ramaswamy et al., Mol Endocrinol. 2009; 23(2):176-87.

Manuscript #13 – Datta et al., Genes Cancer. 2012; 3(1):71-81.

Manuscript #20 – Ghoshal et al., PLoS ONE 2010; 5(4): e10338.

In the event that Dr. Jacob does not immediately retract these publications, the COMIC recommends that the Institution take whatever actions are needed to contact the journals and effect retraction of these publications.

6. CORRECTIONS - The COMIC recommends that Dr. Jacob be required to work with the Institution and the other co-authors in contacting the following journal to process a correction for the following manuscript. In the event that the manuscript cannot be corrected with verified original research records, then retraction will be required:

Manuscript #14 – Wang et al., Hepatology 2014; 59(2): 555–566. Correction of Figure 3B

In the event that Dr. Jacob does not immediately take steps to correct this publication, the COMIC recommends that the Institution take whatever actions are needed to effect retraction of the publication.

### **Previous Corrections/Retractions**

Manuscript #1: Majumder S, Ghoshal K, Datta J, Bai S, Dong X, Quan N, Plass C, and Jacob ST. "Role of de novo DNA methyltransferases and methyl CpG-binding proteins in gene silencing in a rat hepatoma." J Biol Chem. 2002 May 3; 277(18):16048-58. Epub 2002 Feb 13. [Supported by: NIH ES10874 and CA81024] RETRACTED 07/19/18

Manuscript #3: Ghoshal K, Datta J, Majumder S, Bai S, Kutay H, Motiwala T, and Jacob ST."5-Azadeoxycytidine induces selective degradation of DNA methyltransferase 1 by a proteasomal pathway that requires the KEN box, bromo-adjacent homology domain, and nuclear localization signal." Mol Cell Biol. 2005 Jun; 25(11):4727-41. [Supported by: NIH ES10874, CA81024, and CA86978] **CORRECTED 04/30/18** 

Manuscript #7: Majumder S, Ghoshal K, Datta J, Smith DS, Bai S, and Jacob ST." Role of DNA methyltransferases in regulation of human ribosomal RNA gene transcription." J Biol Chem. 2006 Aug 4; 281(31):22062-72. Epub 2006 May 30. [Supported by: NIH ES10874 and CA86978] **RETRACTED 02/13/18** 

Manuscript #8: Bai S, Datta J, Jacob ST, and Ghoshal K "Treatment of PC12 cells with nerve growth factor induces proteasomal degradation of T-cadherin that requires tyrosine phosphorylation of its cadherin domain. J Biol Chem. 2007 Sep 14; 282(37):27171-80. Epub 2007 Jul 13. [Supported by: NIH CA86978 and CA10195] **RETRACTED 02/13/18** 

Manuscript #12: Lu Y, Roy S, Nuovo G, Ramaswamy B, Miller T, Shapiro C, Jacob ST, and Majumder S. "Anti-microRNA-222 (anti-miR-222) and -181B suppress growth of tamoxifen-resistant xenografts in mouse by targeting TIMP3 protein and modulating mitogenic signal. J Biol Chem. 2011 Dec 9; 286(49):42292-302. Epub 2011 Oct 18. [Supported by: NIH CA137567] **RETRACTED 02/13/18** 

Manuscript #15: Motiwala T, Majumder S, Ghoshal K, Kutay H, Datta J, Roy S, Lucas DM, and Jacob ST. "PTPROt inactivates the oncogenic fusion protein BCR/ABL and suppresses transformation of K562 cells." J Biol Chem. 2009 Jan 2; 284(1):455-64. [Supported by: NIH CA122695, CA101956, and CA086978] RETRACTED 02/13/18

Manuscript #16: Bai S, Ghoshal K, Jacob ST. "Identification of T-cadherin as a novel target of DNA methyltransferase 3B and its role in the suppression of nerve growth factor-mediated neurite outgrowth in

PC12 cells." J Biol Chem. 2006 May 12; 281(19):13604-11. [Supported by: NIH ES 10874 and CA86978] **RETRACTED 02/13/18** 

Manuscript #17: Nasser MW, Datta J, Nuovo G, Kutay H, Motiwala T, Majumder S, Wang B, Suster S, Jacob ST, and Ghoshal K. "Down-regulation of Micro-RNA-1 (miR-1) in Lung Cancer." J Biol Chem. 2008 Nov 28; 283(48):33394-405. [Supported by: NIH CA122695, and P01CA101956] **RETRACTED 07/19/18** 

Manuscript #18: Dong, X., Ghoshal, K., Majumder, S., Yadav, S. P., & Jacob, S. T. (2002). Mitochondrial transcription factor A and its downstream targets are up-regulated in a rat hepatoma. *The Journal of biological chemistry*, 277(45), 43309-18. [Supported by: NIH CA 81024 and ES 10874] **RETRACTED 07/19/18** 

Manuscript #19: Majumder S, Varadharaj S, Ghoshal K, Monani U, Burghes AHM, Jacob ST. "Identification of a Novel Cyclic AMP-response Element (CRE-II) and the Role of CREB-1 in the cAMP-induced Expression of the Survival Motor Neuron (SMN) Gene." The Journal of Biological Chemistry. 2004; 279(15):14803-14811. doi:10.1074/jbc.M308225200. [Supported by: NIH NS 41649] **RETRACTED 07/19/18** 

### **Length of Proceedings**

The proceedings have taken longer than the regulatory allotted one hundred and twenty (120) days to complete due to the extensive nature and scope of the allegations, the large number of manuscripts involved each containing many questioned figures, the number of witnesses involved, and the COVID-19 pandemic. The Ohio State University Office of Research Compliance did obtain all necessary and appropriate extensions to the deadline from the Office of Research Integrity during this process. 1184, 1185, 1186, 1187, 1188, 1189, 1190, 1191, 1192, 1193, 1194, 1195, 1196, 1197, 1198, 1199, 1200, 1201

<sup>&</sup>lt;sup>1184</sup> Ex. 447 - 20190524 - ORI Extension Request Redacted Jacob

<sup>&</sup>lt;sup>1185</sup> Ex. 448 - 20190524 - Email RIO to ORI - Extension Request Redacted Jacob

<sup>&</sup>lt;sup>1186</sup> Ex. 449 - 20190529 - Email ORI to ORC - Extension Granted\_Redacted

<sup>&</sup>lt;sup>1187</sup> Ex. 450 - 20190927 - ORI Extension Request Redacted

<sup>&</sup>lt;sup>1188</sup> Ex. 451 - 20190927 - Email RIO to ORI - Extension Request Redacted

<sup>&</sup>lt;sup>1189</sup> Ex. 452 - 20191001 - Email ORI to ORC - Extension Granted Redacted

<sup>&</sup>lt;sup>1190</sup> Ex. 453 - 20200124 - ORI Extension Request\_Redacted

<sup>&</sup>lt;sup>1191</sup> Ex. 454 - 20200124 - Email RIO to ORI - Extension Request Redacted

<sup>&</sup>lt;sup>1192</sup> Ex. 455 - 20200129 - Email ORI to ORC - Extension Granted Redacted

<sup>&</sup>lt;sup>1193</sup> Ex. 456 - 20200528 - ORI Extension Request\_Redacted

<sup>&</sup>lt;sup>1194</sup> Ex. 457 - 20200528 - Email RIO to ORI - Extension Request Redacted

<sup>1195</sup> Ex. 458 - 20200528 - Email ORI to ORC - Extension Granted Redacted

<sup>&</sup>lt;sup>1196</sup> Ex. 488 - 20201002 - ORI Extension Request Redacted

<sup>1197</sup> Ex. 489 - 20201002 - Email RIO to ORI - Extension Request Redacted

<sup>&</sup>lt;sup>1198</sup> Ex. 490 - 20201002 - Email ORI to ORC - Extension Granted Redacted

<sup>&</sup>lt;sup>1199</sup> Ex. 552 - 20210129 - ORI Extension Request Redacted

<sup>&</sup>lt;sup>1200</sup> Ex. 553 - 20210129- Email RIO to ORI - Extension Request\_Redacted

<sup>1201</sup> Ex. 554 - 20210129- Email ORI to ORC - Extension Granted Redacted

### **Appendix**

### Complainant:

Claire Francis

#### **Respondent:**

Samson Jacob, OSU Professor Emeritus, Department of Cancer Biology and Genetics, College of Medicine

#### **Respondent Counsel:**

Loriann E. Fuhrer, Kegler Brown Ritter + Hill Co. LPA

#### **Known PHS Federal Support:**

NIH ES10874 (Manuscript #1, 2, 3, 4, 5, 7, 16, 18)

NIH CA81024 (Manuscript #1, 2, 3, 4, 5, 18)

NIH CA86978 (Manuscript #2, 3, 4, 5, 6, 7, 8, 9, 11, 13, 14, 15, 16, 20)

NIH CA101956 (Manuscript #8)1202

NIH CA122695 (Manuscript #9, 15, 17)

NIH CA101956 (Manuscript #9, 10, 11, 13, 15, 17, 20)

NIH CA122523 (Manuscript #11)

NIH CA137567 and -01A11203 (Manuscript #12)

NIH DK088076 (Manuscript #14)

NIH NS41649 and -04 (Manuscript #19)

#### **Committee Members**

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**Lakshmi (Prasad) Dasi, Ph.D. (non-COM representative)**, Associate Professor, Biomedical Engineering; Associate Professor, Department of Surgery (until 12/31/2019). Professor, Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University (1/1/2020 onward). **Colleen Rupp,** Senior Employee and Labor Relations Consultant, College of Medicine Human Resources

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Dr. Jen Yucel, Former Associate Vice President for Research Compliance

Dr. Julia Behnfeldt, Former Associate Director/RIO

<sup>&</sup>lt;sup>1202</sup> The publication itself references support by NIH CA10195

<sup>&</sup>lt;sup>1203</sup> Figure 6B in the R21 CA137567-01A1 grant proposal is similar to Figure 5C in Manuscript #12, Lu et al. J Biol. Chem. 2011 except the lanes for 10 ng/ml EGF are omitted from the published Figure 5C.

#### **OSU Office of Legal Affairs Staff**

Ms. Emily Schriver, Assistant Vice President and Senior Associate General Counsel

Ms. Nilukshie Ekanayake, Associate General Counsel

Mr. Brandon Lester, Associate General Counsel

#### **Correspondence and Documentary Evidence**

- Ex. 245 20181105 Email RIO to DO- Final Reports 1204
- Ex. 254 20181114 RIO to DO- Appeals to Final Reports 1205
- Ex. 256 20181206- Email DO to RIO-Concur with CII<sup>1206</sup>
- Ex. 258 20181210-Email RIO to Jacob-DO Decision 1207
- Ex. 459 20190206- Email RIO to Jacob COMIC Composition 1208
- Ex. 460 20190607 Email Jacob counsel request interview docs 1209
- Ex. 461 20190607 Email RIO to Jacob interview docs 1210
- Ex. 462 20190610 Email Counsel to LA postpone interview 1211
- Ex. 463 20190611 Email RIO to Jacob Postpone interview 1212
- Ex. 464 20190712 Letter RIO to Jacob re. interview Materials 1213
- Ex. 465 20190712 Shipping label Jacob 1214
- Ex. 466 20190715 UPS Proof of Delivery 1215
- Ex. 467 20190821 Email Jacob to ORC Transcript errata<sup>1216</sup>
- Ex. 468 20191022 Notification of new allegations-Jacob 1217
- Ex. 469 20191022 Notice of Allegations Jacob Figure 1218
- Ex. 470 20191022 Email RIO to Jacob Notification of new allegations 1219
- Ex. 471 20191029 Email Jacob to RIO Extension request 1220
- Ex. 472 20191029 Email RIO to Jacob Extension approved 1221
- Ex. 473 20191115 Email Counsel to LA Jacob response to new allegations 1222
- Ex. 481 20181212- Email RIO to Jacob Referral 1223
- Ex. 482 20190220 Email RIO to COMIC Letter from Dr. Jacob, Feb 14, 20191224
- Ex. 483 20190220 Email RIO to Jacob communication with COMIC 1225
- Ex. 516 20201111 Email Jacob BuckeyeBox access to counsel 1226

- <sup>1206</sup> Ex. 256 20181206- Email DO to RIO-Concur with CII
- <sup>1207</sup> Ex. 258 20181210-Email RIO to Jacob-DO Decision
- 1208 Ex. 459 20190206- Email RIO to Jacob COMIC Composition
- 1209 Ex. 460 20190607 Email Jacob counsel request interview docs
- <sup>1210</sup> Ex. 461 20190607 Email RIO to Jacob interview docs
- 1211 Ex. 462 20190610 Email Counsel to LA postpone interview
- 1212 Ex. 463 20190611 Email RIO to Jacob Postpone interview
- <sup>1213</sup> Ex. 464 20190712 Letter RIO to Jacob re. interview Materials
- <sup>1214</sup> Ex. 465 20190712 Shipping label Jacob
- <sup>1215</sup> Ex. 466 20190715 UPS Proof of Delivery
- <sup>1216</sup> Ex. 467 20190821 Email Jacob to ORC Transcript errata
- <sup>1217</sup> Ex. 468 20191022 Notification of new allegations-Jacob
- <sup>1218</sup> Ex. 469 20191022 Notice of Allegations Jacob Figure
- <sup>1219</sup> Ex. 470 20191022 Email RIO to Jacob Notification of new allegations
- <sup>1220</sup> Ex. 471 20191029 Email Jacob to RIO Extension request
- 1221 Ex. 472 20191029 Email RIO to Jacob Extension approved
- 1222 Ex. 473 20191115 Email Counsel to LA Jacob response to new allegations
- <sup>1223</sup> Ex. 481 20181212- Email RIO to Jacob Referral
- <sup>1224</sup> Ex. 482 20190220 Email RIO to COMIC Letter from Dr. Jacob, Feb 14, 2019
- 1225 Ex. 483 20190220 Email RIO to Jacob communication with COMIC
- <sup>1226</sup> Ex. 516 20201111 Email Jacob BuckeyeBox access to counsel

<sup>&</sup>lt;sup>1204</sup> Ex. 245 - 20181105 Email RIO to DO- Final Reports

<sup>&</sup>lt;sup>1205</sup> Ex. 254 - 20181114 RIO to DO- Appeals to Final Reports



- Ex. 517 20201130 Email Jacob to RIO document requests 1227
- Ex. 518 20201201 Email Jacob to RIO document requests 1228
- Ex. 519 20201201 Email RIO to Jacob email received 1229
- Ex. 520 20201201 Email Counsel to LA document requests 1230
- Ex. 521 20201203 Email RIO to Jacob + Counsel grant documents 1231
- Ex. 522 Jacob Progress Report 20070730 5 P01 CA101956-021232
- Ex. 523 Jacob Grant Proposals 2 P01 CA101956-06 & 06A1 1233
- Ex. 524 20201203 Email Counsel to RIO add'l document request 1234
- Ex. 525 20201203 Email RIO to Jacob + Counsel add'l grant documents 1235
- Ex. 526 2 R01 CA086978-11A submitted 20131236
- Ex. 527 20201204 Email Counsel to RIO issues with documents 1237
- Ex. 528 20201204 Email RIO to Counsel issues with documents 1238
- Ex. 529 20201207 Email Jacob to RIO only need slides 1239
- Ex. 530 20201207 Email RIO to Jacob Forensic slides set #11240
- Ex. 531 20201207 Email RIO to Jacob Forensic slides set #21241
- Ex. 532 20201211 Email RIO to Counsel Grants as Ex. 5231242

<sup>1227</sup> Ex. 517 - 20201130 - Email Jacob to RIO - document requests

<sup>1228</sup> Ex. 518 - 20201201 - Email Jacob to RIO - document requests

<sup>&</sup>lt;sup>1229</sup> Ex. 519 - 20201201 - Email RIO to Jacob - email received

<sup>1230</sup> Ex. 520 - 20201201 - Email Counsel to LA - document requests

<sup>1231</sup> Ex. 521 - 20201203 - Email RIO to Jacob + Counsel - grant documents

<sup>&</sup>lt;sup>1232</sup> Ex. 522 - Jacob Progress Report 20070730 5 P01 CA101956-02

<sup>&</sup>lt;sup>1233</sup> Ex. 523 - Jacob Grant Proposals 2 P01 CA101956-06 & 06A1

<sup>1234</sup> Ex. 524 - 20201203 - Email Counsel to RIO - add'l document request

<sup>1235</sup> Ex. 525 - 20201203 - Email RIO to Jacob + Counsel - add'l grant documents

<sup>1236</sup> Ex. 526 - 2 R01 CA086978-11A submitted 2013

<sup>1237</sup> Ex. 527 - 20201204 - Email Counsel to RIO - issues with documents

<sup>1238</sup> Ex. 528 - 20201204 - Email RIO to Counsel - issues with documents

<sup>&</sup>lt;sup>1239</sup> Ex. 529 - 20201207 - Email Jacob to RIO - only need slides

<sup>&</sup>lt;sup>1240</sup> Ex. 530 - 20201207 - Email RIO to Jacob - Forensic slides set #1

<sup>&</sup>lt;sup>1241</sup> Ex. 531 - 20201207 - Email RIO to Jacob - Forensic slides set #2

<sup>&</sup>lt;sup>1242</sup> Ex. 532 - 20201211 - Email RIO to Counsel - Grants as Ex. 523