Date: September 4, 2019

From: Lynn Pulliam, Ph.D., Research Microbiologist

Subj: Report of Research Misconduct Investigation – Joint Investigation Led by VA

To: Bonnie D. Graham, M.B.A. Director, San Francisco VA Medical Center

1. Preliminary Statement

A research Inquiry Committee reviewed 37 allegations of research misconduct related to 21 published papers involving 5 principal investigators (PIs). The Inquiry Committee reviewed and discussed each allegation and determined that 2 PIs warranted a formal investigation. This report covers Dr. Rajvir Dahiya, Senior Research Career Scientist, San Francisco VA Medical Center/ Professor of Urology, University of California, San Francisco (Respondent 1) as stated in the charge letter dated February 26, 2018 (Attachment 1). All papers reviewed here originated prior to the conclusion of the last investigation and do not reflect any changes in lab or investigator policies initiated since that last review.

The Research Integrity Officer (RIO) at the San Francisco VA Medical Center has determined that the allegations pertain to VA research funded by VA Merit Review, VA REAP, VA Program Project Award, National Institutes of Health grants R01CA111470, T32DK007790, R01CA101844, R01AG021418, R01CA108612, R01AG16870, R01CA130860, R01CA1018447, R01TW006215, Yamada Science Foundation, Grant-in-Aid 13220016 from the Ministry of Education, Science, Sports, Culture, and Technology, Japan. Therefore, the papers fall under the jurisdiction of VHA Handbook 1058.02.

The University of California, San Francisco (UCSF) has concurrent jurisdiction over one or more of the allegation(s) referenced above based on the facts that the Respondent is a UCSF faculty member (and was so during the period that the research in question was done) and that at least one of the grants that funded this work was administered by UCSF. UCSF will jointly participate in the investigation, with a UCSF faculty member as representative, but will be led by SFVAMC in accordance with the procedures of VHA Handbook 1058.02 (“Research Misconduct”).

The research misconduct investigation was convened for the purpose of investigating and making recommended findings about: (i) whether and to what extent research misconduct occurred; (ii) who is responsible; and (iii) what corrective actions are appropriate. The investigation consisted of a thorough review of the research misconduct allegations indicated in the charge letter; the Inquiry Memorandum, materials submitted by the Respondent, a forensic analysis of the figures in question, testimonial evidence, letter from the SFVAMC ACOS/R regarding journal articles authored by the respondent and a ‘best practices’ guide from ASBMB.

The Research Investigative Committee consisted of Dr. Lynn Pulliam, Chief, Microbiology, San Francisco VA Medical Center, and Professor of Laboratory Medicine, UCSF (Chair); Dr. Anthony Baker, Research Biologist, San Francisco VA Medical Center, and Professor of Medicine, UCSF (member and representative for UCSF); and Dr. Daniel Bikle, Staff Physician, San Francisco VA Medical Center, and Professor of Medicine, UCSF (member).

The Committee reviewed the allegations and interviewed the Respondent on June 19, 2018.

The Research Investigative Committee also interviewed 2 members of the Respondent's lab on June 19, 2018: [redacted]F; and [redacted]. They were on several publications and have been in the lab for many years.

Due to the complexity of the case, the SFVAMC Director sent memoranda dated June 19, 2018, September 20, 2018, December 14, 2018, March 6, 2019, and May 30, 2019 to ORO requesting extensions of the deadlines to complete the investigation. The requested extensions were granted by ORO on June 25, 2018, October 9, 2018, December 17, 2018, March 12, 2019, and May 30, 2019.

The allegations all include photographic images within figures. The allegations contend that the data reported was manipulated resulting in falsified research that was not accurate. Gradient Map software was used to overlay and color-compare blots and to create false color blots that reveal commonalities within internal characteristics of protein bands and the shape of bands. Images were enlarged and re-sized in Fuji/Image J and used to overlap and compare color blots.

The Office of Research Integrity, who has concurrent jurisdiction over the NIH funded research, requested that the additional papers and grant applications that are covered by the time limitations in 42 CFR § 93.105 be analyzed for additional possible instances of research misconduct. This analysis was performed by the research misconduct officer at the Office of Research Oversight and no additional allegations of research misconduct were found.

There were several factors that made analysis of the allegations difficult. Some of the allegations go back many years; however, even for the recent allegations, the data retention practices in this lab have been lacking, so the Committee was unable to obtain and analyze the underlying data for figures that are the subject of the allegations. Additionally, the first authors of the papers in question, the individuals who did the experiments (and presumably made the figures) are no longer at the VA and were unavailable for direct interviews by the Investigation Committee, although they did provide some material directly to the Respondent.

2. Findings of Fact for Respondent 1

Allegation a. Respondent falsified data reported in Figure 4b *Oncogene* (2007) 26:7647-7655 by using the same band(s):

i. Flipped vertically and stretched, to represent LNCaP cells in the AEG-1 panel in Figure 1D and control PMO treated PC-3 cells in the AEG-1 panel in Figure 2b.

ii. Flipped over a horizontal axis to represent LNCaP cells in the Anti-PTEN panel in Figure 4a and CE of LNCaP cells in the Anti-phospho-FOXO3a panel of Figure 4c.

iii. To represent (1) lanes 2-6 of the Anti-p-FOXO3a and (2) lanes 1-5 in the Anti-p27KIP1 panel in Figure 4b.

iv. To represent untreated DU145 cells in the Anti-AKT panel in Figure 4a and untreated CE from DU145 cells in the Anti-phospho-FOXO3a panel in Figure 4c.

v. To represent both CE from PC-3 cells in the Anti-FOXO3a panel and NE from DU145 cells in the Anti-phospho-FOXO3a panel in Figure 4C.

vi. To represent (1) NF-κB binding in AEG-1 PMO treated PC-3 cells, (2) NF-κB binding in AEG-1 PMO treated DU145 cells, (3) AP-1 binding in AEG-1 PMO treated PC-3 cells and (4) AP-1 binding in AEG-1 PMO treated DU145 cells in Figures 5A and 5C.

Evidence analyzed to come to a conclusion:

1) The forensic analyses (Exhibit 1, pp 1 (bottom slide) 2 (top slide) 3 (top slide) were not conclusive for a.i (analysis of background was inconclusive) a.ii (low resolution and absence of background) and a.iv (overall similarity but not definitive) and these subparts were not considered for further evaluation.
2) The Investigative Committee evaluated forensic analyses for a.iii, a.v and a.vi (Exhibit 1, pp. 2 (bottom slide), 3 bottom slide), 4 (top slide) of this allegation and concluded that falsification occurred because the same bands were used to represent different experimental conditions. The fact that non-overlapping strips of bands, representing different proteins wind up in different panels of the figures (a.iii), makes it unlikely to have occurred by honest error. Additionally, entire strips have not been copied, but sections of strips of bands have been cut out and pasted into different panels or parts of the same panel (a.v and a.vi).
3) The nature of this manipulation makes it unlikely to have occurred by error because the bands are in separate strips of bands.
4) Testimony from the Respondent (Exhibit 2, Dahiya transcript p.17, lines 1-6 and 18-22) stated that the first author was the corresponding author who was communicating with the journal and was responsible for generating the data and figures.
5) The Respondent stated that the raw data are unavailable in his lab, and the first author is in Japan and while he responded with an analysis, it was not with the original data (Exhibit 2, Dahiya transcript, p. 14, line 25 and p.15, lines 1- 4; p.17, lines 16-25; p. 18, line 1).
6) The Respondent provided line scans of the analysis given to him by the first author of the published figures (Exhibit 3, pp. 5, 6, 7). Line scans can be manipulated to get a different result and are not as definitive as whole morphometry as presented in Exhibit 1 and the Respondent agreed that is one interpretation (Exhibit 2, Dahiya transcript p. 21, lines 4-8).
7) The Investigation Committee does not accept the densitometry as valid but rather finds the forensic analyses (Exhibit 1, pp. 2, 3) more compelling. The densitometry analysis was performed on the published figure and not the original data. It does not take into account any adjustment made during the final editing for publication. Additionally, using a line scan analysis is very dependent on being able to match the area around the bands; therefore, it is easy to have a result showing bands are different even if they are the same.

Response: Dr. Dahiya has corresponded with first author, [redacted] and claims he has forwarded the densitometry readings of the published blots, not the original data and is convinced that the bands are different.

Conclusions: The committee finds that the preponderance of the evidence supports a finding of intentional research misconduct for allegations a.iii, a.v and a.vi because the misrepresentations are falsifications that could not have occurred by honest error. The Committee concluded that this activity constitutes a significant departure from accepted research practices. The 2 bands in a.vi (a) appear to be the same and the 2 bands in (b) appear to be the same although we could not conclude that all 4 bands are identical to each other. However, because of a lack of primary data and an inability to interview the first author, we cannot say with a preponderance of evidence

who is responsible. The numerous misrepresentations are sufficiently serious as to reduce confidence in the overall conclusions of the publication.

Action for this paper: With regard to Oncogene (2007) 26:7647-7655, 1) in the absence of the original data and the densitometry analysis which the committee finds inconclusive, we find retraction is more appropriate than a correction and 2) even though the journal has been notified after the last investigation and not taken action, they should be notified again because additional research misconduct has been found (also see allegation b below). As of the date of this report, this retraction has not occurred.

Allegation b. Respondent falsified results reported in *Intl J of Cancer* (2008) 123:552-560 (*IJC*) by using the same panels/bands to represent:

i. PC-3 cells in the p65 panel of Figure 2C of *IJC* and PC-3 cells in the Anti-IL-6 panel of Figure 5e of Oncogene (2007) 26:7647-7655 (*ONC*).

ii. Lanes 5-8 of the p50 panel in Figure 2C and lanes 1-4 of the Anti-MMP-9 panel in Figure 5e of *ONC*.

iii. (1) NE from PC-3 cells in the Phospho-FOXO3a panel in Figure 1e of *IJC*, (2) NE from LNCaP cells in the p65 panel of Figure 2C of *IJC*, (3) LNCaP cells in the Anti-IL-6 panel of Figure 5e of *ONC* and (4) DU145 cells in the Anti-MMP-9 panel of Figure 5e in *ONC.*

Evidence analyzed to come to a conclusion:

1) The Investigative Committee evaluated forensic analysis (Exhibit 1, pp. 4 (bottom slide) and 5) of this allegation and concluded that falsification occurred based on an analysis of overlaying the bands and comparing them. Bands labelled to represent different proteins in different figures appear to be the same when the contrast is enhanced in one of the figures to match the contrast in the other.
2) The nature of this manipulation makes it unlikely to have occurred by error because the same bands purported to represent different proteins are only sections of complete panels and are found in in separate experiments in different journals, *INJ* and *ONC* (b.i and b.ii) and different figures of the same article (b.iii).
3) The Respondent provided a linear densitometry analysis given to him by [redacted] first author of the published figures (Exhibit 3, p.7) demonstrating that the bands are different. The Committee does not consider that a line drawing of a published band is equivalent to densitometry of original data as described in Allegation a, 6 above.
4) The Investigation Committee finds the forensic analysis in Exhibit 1 more compelling.

Response: First author of this paper, [redacted] left the lab almost 11 years ago. The same paper was in the last investigation in 2014 and [redacted] corresponded with the journal for correction or retraction in March, 2017 (Exhibit 4).

Conclusions: The Committee finds by a preponderance of evidence that research misconduct occurred and concludes that this activity constitutes a significant departure from accepted research practices. Since the primary first author and raw data are not available, it is not possible to determine who collected and analyzed the data. While a particular individual cannot be held responsible for the misconduct, it is intentional as the committee concluded that the manipulations could not have been due to honest error.

Action for this paper: With regard to *Intl J of Cancer* (2008) 123:552-560 (*IJC),* the Committee determined that additional figures than those evaluated in a previous Investigation constitute research misconduct as they were intentionally duplicated to represent different experimental conditions. This paper was retracted so no further action is required regarding the publication.

Allegation c. Respondent falsified results reported in *Clin Cancer Re*s (2004) 10:2015-2019 (*CCR*) and *Cancer Res (2003)* 15:3913-3918 (*CR*) by using the same bands to represent both:

i. The genotyping for codon 119 in the Common Allele from renal carcinoma patients in Figure 1B of *CCR* and the genotyping for codon 119 in the Common Allele from endometrial cancer patients in Figure 1B of *CR*.

ii. The genotyping for codon 119 in the Rare Allele from renal carcinoma patients and the genotyping for codon 119 in the Rare Allele from endometrial cancer patients in Figure 1B of *CR*.

iii. The genotyping for codon 432 in the Common Allele from renal carcinoma patients in Figure 1B of *CCR* and the genotyping for codon 432 in the Common Allele from endometrial cancer patients in Figure 1B of *CR*.

Evidence analyzed to come to a conclusion:

1) The Investigative Committee evaluated forensic analysis (Exhibit 1, p. 6) of this allegation and concluded that falsification occurred by overlaying the bands and comparing them and the background.
2) The nature of this manipulation makes it impossible to have occurred by honest error because the same bands are from patients with different diseases, separate experiments and reported in 2 different journals.
3) The Respondent agreed that the genotyping in the paper allegedly from 2 different subjects are actually the same subject and the 2 papers were retracted.

Response: The Respondent agrees that the genotyping for the two different conditions is the same and doesn't change and while he does not say it was deliberately used over and over, he does say the genotyping is the same but states that the overall result is not affected and does not think any further explanation is required since the papers have already been retracted (Exhibit 2, Dahiya transcript p. 30, lines 2-3).

Conclusion: The Committee finds that research misconduct occurred and concludes that this activity constitutes a significant departure from accepted research practices. Since the first author and the original data are not available, it is not possible to determine who collected and analyzed the data and determine who is responsible. However, the Respondent admits that the codon bands in different papers were the same bands. It is intentional because it is unlikely that a duplication like this (sample from patients with different diseases, appearing in two separate publications) could occur by honest error. Therefore, the research misconduct was intentional.

Action for this paper: The Committee determined that the genotyping bands representing different cancer patients were all the same and there was intentional falsification of data. Both papers were retracted in 2014 (Exhibit 3) so no additional action is required at this point.

Allegation d. Respondent falsified results reported in *Clin Can Res* (2007) 13:2541-2548 by using a blank panel to represent a negative result for:

i. AcH4 modification of the RASSF1A gene in LNCaP cells in Figure 5A.

ii. AcH4 modification of the RASSF1A gene in cells untreated for 5-aza-dC and TSA in Figure 6.

Evidence analyzed to come to a conclusion:

1) The Investigative Committee evaluated forensic analysis (Exhibit 1, p. 7) of this allegation and concluded that falsification occurred by using blank lanes instead of data. Experiments are properly controlled if a person, group, antibody is used as a constant and unchanging standard of comparison in scientific experimentation. Even in a panel that represents a negative result, normal experimental data has background and irregularities simply from the procedure. A completely blank lane as demonstrated by the single pixilation peak is not representative of a true control or is an image that has been excessively digitally adjusted.
2) The nature of this manipulation makes it impossible to have occurred by honest error because the area used for the negative result was not taken from an area with data. The Respondent agreed that there are no bands in the lanes in question.
3) It is not standard practice to use blank lanes to represent what may be negative data. This misrepresentation is considered falsification of data. Although there may be no bands in the negative control panels, it is falsification to use a blank space to represent a lack of bands. The point of a controlled experiment is to demonstrate that samples undergoing the same conditions do not produce bands; this is not true if blank panels are used.

Response: The Respondent shows gels in Exhibit 3, p.8-14 that do not address where the blank lanes in question came from. He states in the transcript that there is no band in the publication and he does not know why (Exhibit 2, Dahiya transcript p. 34, lines 9-10, 13-14, p. 40, lines 5-8). The data in Exhibit 3, pp. 9 and 12 from Figure 6 looks like the appropriate negative control for allegation d.i. It is unclear why he did not provide the original data for the gel in allegation d.ii. The Respondent produced original data to demonstrate that the appropriate negative controls were done for one of the sub allegations. However, it is not clear how or why the blank panels made it into the final figure despite having the correct original data for one of the figures in question.

Conclusion: The Committee finds that intentional research misconduct occurred and concludes that this activity constitutes a significant departure from accepted research practices. The panels were intentionally manipulated to appear negative. We were unable to determine who was responsible.

Action for this paper: The Committee concluded that the insertion of blank lanes in Figures 5A and 6 constitutes research misconduct. The blank lanes do not represent controls, as the Respondent stated in his letter to the Editor. The committee recommends that there be a follow-up email to the journal stating that additional instances of research misconduct have been discovered.

Allegation e. Respondent falsified results reported in *Br J Cancer* (2014) 110:1645-1654 by:

i. Using the same panel to represent a wound healing assay for both PC-3 cells transfected with miR-NC and PC-3 cells transfected with miR-1260b in the top row (the zero-time point) in Figure 4D.

Evidence analyzed to come to a conclusion:

1) The Investigative Committee evaluated forensic analysis (Exhibit 1, p. 8, top slide) of this allegation and concluded that falsification occurred by using the same panel to represent 2 different experiments transfected with different miRs.
2) The nature of this manipulation makes it unlikely to be an error because different frames of the same image were used to reflect 2 different experiments. The Respondent notified the journal of the mistake without providing a reason (Exhibit 3, p.15).

Response: There was a discussion about this replacement data being part of the original experiment. The Respondent stated that the original data was on the R drive and that it was sent to the journal. The Committee requested to see the replacement data to establish that the date of the corrective data corresponds to the data of the original set of experiments (Exhibit 2, Dahiya transcript, p.47, lines 17-24, p.48, lines1-5). As of this report, the Committee has not seen that data.

Conclusion: Although a correction was published in this journal for Figure 4D (Exhibit 3, p. 15), without original data showing pictures (negative and positive) taken at the same time, we conclude intentional research misconduct occurred because the reuse of different frames of the same data to represent 2 conditions is research misconduct and this activity constitutes a significant departure from accepted research practices. We are unable to determine who is responsible.

ii. Representing Beta-tubulin sFRP1 and Smad4 as all being from 1 gel when the sFRP1 and Smad4 panels are discontinuous in Figure 5D.

Evidence analyzed to come to a conclusion:
1) The Investigative Committee evaluated forensic analysis (Exhibit 1, p. 8, bottom slide) of this allegation and concluded that the 2 panels, sFRP1 and Smad4 demonstrate discontinuity raising the possibility that the results come from different blots and the beta tubulin is a continuous blot.
2) The Respondent provided the original data in Exhibit 3, pp. 17. The Respondent stated that he routinely runs gels and then cuts off the beta tubulin at the bottom which the committee agreed is acceptable. However, he than cuts the blots vertically to run the same antibody although it was not clear why blots would be cut vertically if they are to be blotted with the same antibody. Cutting blots so it is unclear if they come from a single experiment is not considered acceptable unless a vertical line is drawn at the splice site and it is described in the text and/or figure legend.
3) We cannot say if research misconduct occurred since the original blots are not available and there are certain conditions where cutting blots would be acceptable. However, there was a lengthy discussion about the use of a continuous beta tubulin lane and the vertical cuts for the PC3 and DU-145 using the same antibody as not standard scientific practice (Exhibit 5).

Response: The beta tubulin comes from the same blot and the PC3 and DU-145 are from different blots (Exhibit 3, p. 17).

Conclusion: This technique is used in the Dahiya lab and considered to be permissible whereas the committee does not agree this is standard practice and can be misleading if not disclosed properly. While there is not a preponderance of evidence to demonstrate that research misconduct occurred, the Committee considers this a bad research practice. Because there was no description in the text or figure legend that the gel was spliced, the authors deliberately wanted the reader to believe the gel staining results were performed at the same time. Without original data, there is no way to show that the strips of gel came from the same experiment, so the figure

is not trustworthy, but at the same time it cannot be ruled out that the strips did not come from the same experiment.

Action for this paper: A correction has already been published for Figure 4D (Exhibit 3, p.15). The Committee recommends that the splicing the gel in Figure 5D be referred to the ACOS/ R&D to determine if the journal should be notified.

Allegation f. Respondent falsified data reported in in *Br J Cancer* (2013) 108:2070-2080 by:

i. representing beta-tubulin, Smad4, sFRP1 and Dkk2 as all being from one gel when there is a possible splice site in the sFRP1 panel in Figure 5C, but no splice sites in the corresponding Dkk2, Smad4 and tubulin panels in Figure 5c.
ii. representing tubulin and the corresponding sFRP1, Dkk2 and Smad 4 blots as all being from one gel when there are possible splice sites in the sFRP1 and Smad4 panels, but no corresponding splice sites in the corresponding Tubulin panels in Figure 6B.

Evidence analyzed to come to a conclusion:

1) The Investigative Committee evaluated forensic analysis (Exhibit 1, p. 9) of Figures 5C (f.i) and 6B (f.ii) to determine if there is a splice site in the sFRP1 panel coupled with a continuous beta tubulin in Figure 5C and possible splice sites in the sFRP1 and Smad4 panels in Figure 6B. A forensic analysis of Figure 5C shows a definitive splice site in the middle of the sFRP1 panel that is acknowledged in Exhibit 3, p.19, where 2 panels are shown that were represented as 1 panel in the publication.
2) For sub allegation f.i., the committee concludes that it is inappropriate to show data in this manner unless justified or acknowledged in the text. Although the respondent provided original data, it is unclear when the blot was cut and there is no way to determine if it is acceptable to have the splice sites.
3) It is appropriate to cut parts of a Western blot in certain situations; however, it is necessary to disclose when splicing is done and why so as not to raise questions about manipulation of the data presentation.

Response: The original blots from the Respondent in Exhibit 3, p. 19, shows that in Figure 5C there are 2 panels (786-0 and A-498) that were spliced for the sFRP-1 lane. The original gels shown in Exhibit 3, p. 20 show no splicing in Figure 6B.

Conclusions: For f.i, there was undisclosed splicing and although the committee does not have confidence in the data. without the original gel (pre-blot) there is not a preponderance of evidence that research misconduct occurred. For allegation f.ii, the preponderance of the evidence does not support a finding of research misconduct as the original data were provided and corroborate the forensic analysis that they do not appear to be spliced.

Action for this paper: The committee finds a prevailing problem of Western blots that are arbitrarily spliced and therefore manipulated. This seems to be a common practice of the former PI and first author in the Dahiya lab, [redacted] The Committee notes that this practice of splicing gels for some experiments can be research misconduct in certain situations but it could not be proven here. The journal should be notified.

Allegation g. Respondent falsified results reported in Figure 1 of *J Urology* (2000) 163:1339-1342 by:

i. using the same band to represent lane 6 and 10 of the BPY2 panel.
ii. using the same band to represent lane 7 and lane 11 of the BPY2 panel.

Evidence analyzed to come to a conclusion:

1. The Investigative Committee concluded that the forensic analysis (Exhibit 1, p. 10) was not definitive because the low resolution and bland background made the forensic analysis inconclusive.

Conclusion: There is not a preponderance of evidence to support a finding of research misconduct for this allegation.

Action for this paper: The Committee recommends no further action for this paper.

Allegation h. Respondent falsified research results reported in Figure 6 of *Mol Carcinogenesis* (2001) 32:19-27by using the same band five times to represent the PCR product of the (1) the E-cadherin gene in caki-2 cells treated with 5-AZA, (2) the E-cadherin gene in HRCE cells treated with 5-AZA, (3) the β-actin gene in 786 cells treated with 5-AZA, (4) the β-actin gene in caki-2 cells treated with AZA-5 and (5) the β-actin gene in HRCE cells treated with 5-AZA.

Evidence analyzed to come to a conclusion:

1. The Investigative Committee concluded that the forensic analysis (Exhibit 1, p. 11, top slide) was not definitive. Although the shapes look very similar, there are not other identifying characteristics that could demonstrate in a forensic analysis that they were more likely than not identical.

Conclusion: There is not a preponderance of evidence to support a finding of research misconduct for this allegation.

Action for this paper: The Committee recommends no further action for this paper.

Allegation i. Respondent falsified results reported in Figure 1 of *BBRC* (2002) 297:558-564 by using the same image to represent genotyping at codon10 (bottom left panel) and genotyping at codon 87 (bottom middle panel).

Evidence analyzed to come to a conclusion:

1. The Investigative Committee evaluated the forensic analysis (Exhibit 1, p.11) and concluded that in Figure 1, the same image is used to represent genotyping at codon 10 and codon 87 because the shapes of the bands and background halo of the gel appear identical.
2. The committee was not convinced by the densitometry analysis provided by the Respondent (Exhibit 3 p. 21) that the bands were different because the overlay in Exhibit 1 was more convincing than the densitometry provided by the Respondent.
3. The nature of the manipulation makes it unlikely to have occurred by error since the bands represent either the same gene in different cells or a different gene in different cells and the shape and size appear identical. Some variability in band shape or intensity would be expected in these different experiments.

Response: The Respondent provided a linear densitometry (Exhibit 3, p. 21) from the published figure (not raw data). The Respondent argued that the bands were distinct and not duplicated

(transcript p.59 11-13). The Respondent stated that he would go to the original data and then get back to the Committee (Dahiya transcript p.62, lines 15 and 16). He has not done this.

Conclusion: The Committee finds that the preponderance of the evidence supports a finding that research misconduct occurred, and that the same band(s) was used in different experiments. It is unlikely that the bands are different. This activity constitutes a significant departure from accepted research practices; it is unclear who is responsible.

Action for this paper: The Committee finds that the same pair of bands is used to represent genotyping at both codons 10 and 87 in Figure 1 and that this was intentional. The Committee concluded that the journal be contacted for possible retraction.

Allegation j. Respondent falsified results reported in Figure 2C of *Carcinogenesis* (2012) 33:501-508 by representing β-tubulin MEK1, Survivin and CTNB1 panels as all being from one gel when the Survivin and CTNB1 panels are discontinuous.

Evidence analyzed to come to a conclusion:

1. The Investigative Committee evaluated the forensic analysis (Exhibit 1, p. 12, top slide) and concluded that in Figure 2C, the CTNNB1 and Survivin panels appear to be from different blots because of the splice sites.
2. The splicing of gels may be considered research misconduct if it does not represent the results accurately. There are justifiable reasons for splicing and this is normally disclosed; however, this was not noted and explained in the paper. Not disclosing the splicing of gels can lead to inappropriate manipulation of data when comparing concentration of proteins. The same author, [redacted] has the pattern of doing this in all the papers he is on (Exhibit 2, Dahiya transcript p. 63, 3-6).
3. The original data is not available making it impossible to know if the bands came from the same gel or experiment.

Response: The Respondent provided a diagram (Exhibit 3, p.22) of how the gel was spliced but it was not clear to the Committee why the gel was cut and splices made.

Conclusion: The Committee does not have confidence in the data based on the splice sites since there is no original data available. Splicing/cutting gels is a practice widely practiced in the Dahiya lab and is not standard practice in research labs. While the Committee does not have confidence in the data, the Committee does not believe there is a preponderance of evidence to support the allegation of research misconduct in the absence of the original data.

Action for this paper: With regard to Figure 2C in Carcinogenesis, the PI was not able to present the original gel to the Committee. Without this, there is no confidence the blots are coming from the same gel. While the Committee cannot say that it did not come from the same gel, there needs to be an explanation for why the splicing was done or the original gel must be presented. The Committee recommends this be referred to the ACOS/R&D to determine if the journal should be notified.

Allegation k. Respondent falsified results reported in Figure 3C of *PLoS ONE* (2012) 7:e51056 by representing β-tubulin, RECK and Smad4 panels as all being from the same gel when the Smad4 panel is discontinuous.

Evidence analyzed to come to a conclusion:

1. The Investigative Committee evaluated the forensic analysis (Exhibit 1, p. 12, bottom slide) and concluded that in Figure 3C, the $Smad_4$ blot has been spliced while the other 2 panels are continuous.

Response: Same concern as above with the one PI formerly in the Dahiya lab.

Conclusion: The practice of splicing gels may be considered research misconduct if not stipulated in the Methods with an explanation why it was spliced. While the Committee does not have confidence in the data based on the splice sites since there is no original data available, the Committee does not believe there is a preponderance of evidence to support the allegation of research misconduct because of the lack of original data.

Action for this paper: The PI was not able to present the original gel to the Committee. Without this, there is no confidence the blots are coming from the same gel. The Committee recommends that this be referred to the ACOS/R&D to determine if the journal should be notified.

Summary of findings: The committee finds that the preponderance of the evidence supports findings of research misconduct for allegations a.iii, a.v, a.vi, b.i, b.ii, b.iii, ci, cii, ciii, d.i, and d.ii, e.i and i. The manipulation of Western blot gels and splicing of gels have been pervasive in the Dahiya lab. While the first authors have all left the lab, Dr. Dahiya was senior/last author on all these publications and therefore responsible for the results. In many cases, the original data that should be kept in the Dahiya lab was not available. There are numerous examples of manipulation of data to make the results fit what was expected, for example, a blank space on a gel to represent a negative control that was not run.

Corrective actions for research misconduct:
1) In cases where research misconduct was found to have occurred as stipulated above, the journal should be notified.
2) All members of the laboratory will undergo training as to best practices for publishing figures that contain gels, blots or images, including that a negative control does not mean a blank lane. This requires documentation.
3) The head of the laboratory must audit data to be published from his laboratory and document that published figures are accurate until no longer determined necessary by the ACOS/R&D.
4) The head of the laboratory may not apply for external funding until these Corrective Actions are in place and documented.

Non research misconduct concerns uncovered by the committee that should be referred to the ACOS/R&D:
1) In cases where research misconduct was not found to have occurred, but the Investigation Committee did not have confidence in the data as published, the publications should be referred to the ACOS/R&D for review to determine if any action is required, which could possibly include notification of the journal.

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As members of the Investigation Committee we each agree to the contents of this Final Report.

Lynn Pulliam, PhD

Signature

1/8/20

Date

Daniel Bikle, MD, PhD

Signature

1/10/20

Date

Anthony Baker, PhD

Signature

1-8-20

Date