VA Department of Veterans Affairs

Memorandum

Date: March 21, 2024

From: Research Misconduct Investigation Committee (691/151)

Subject: Research Misconduct Investigation Report

To: Director, VA Greater Los Angeles Healthcare System (691/00)

The Research Misconduct Investigation Committee has completed its investigation as directed by your memorandum, dated October 6, 2023 (hereafter, "Charge Letter") (Attachment A). Capitalized terms shall have the meaning in VHA Directive 1058.02.

Preliminary Statement/Background Information

As indicated in the Charge Letter, the Investigation Committee was convened to conduct an investigation into Allegations that Alan Lichtenstein, MD, (hereafter, "**Respondent**"), a retired Staff Physician at the VA Greater Los Angeles Healthcare System (GLA) and Professor Emeritus in the University of California Los Angeles (UCLA) Department of Medicine, falsified Western blot data published in the following medical journals:

1. Yang Y, Bardeleben C, Frost P, Hoang B, Shi Y, Finn R, Gera J, Lichtenstein A. DEPTOR is linked to a TORC1-p21 survival proliferation pathway in multiple myeloma. *Genes & Cancer* 2014; 5:407-419.
2. Shi Y, Daniel-Wells TR, Frost P, Lee J, Finn RS, Bardeleben C, Penichet ML, Jung ME, Gera J, Lichtenstein A. Cytotoxic properties of a DEPTOR-mTOR inhibitor in multiple myeloma cells. *Cancer Research* 2016; 76:5822-5831.
3. Hsu J-H, Shi Y, Frost P, Yan H, Hoang B, Sharma S, Gera J, Lichtenstein A. Interleukin-6 activates phosphoinositol-3' kinase in multiple myeloma tumor cells by signaling through RAS-dependent and, separately, through p85-dependent pathways. *Oncogene* 2004; 23:3368-3375.
4. Shi Y, Frost P, Hoang B, Yang Y, Bardeleben C, Gera J, Lichtenstein A. MNK1-induced eIF-4E phosphorylation in myeloma cells: a pathway mediating IL-6-induced expansion and expression of genes involved in metabolic and proteotoxic responses. *PLoS One* 2014; 9:e94011.
5. Shi Y, Yan H, Frost P, Gera J, Lichtenstein A. Mammalian target of rapamycin inhibitors activate the AKT kinase in multiple myeloma cells by up-regulating the insulin-like growth factor receptor/insulin receptor substrate-1/phosphatidylinositol 3-kinase cascade. *Molecular Cancer Therapeutics* 2005; 4:1533-1540.
6. Cloninger C, Bernath A, Bashir T, Holmes B, Artinian N, Ruegg T, Anderson L, Masri J, Lichtenstein A, Gera J. Inhibition of SAPK2/p38 enhances sensitivity to

mTORC1 inhibition by blocking IRES-mediated translation initiation in glioblastoma. *Molecular Cancer Therapeutics* 2011; 10:2244-2256.
7. Benavides-Serrato A, Lee J, Holmes B, Landon KA, Bashir T, Jung ME, Lichtenstein A, Gera, J. Specific blockade of Rictor-mTOR association inhibits mTORC2 activity and is cytotoxic in glioblastoma. *PLoS One* 2017; 12:e0176599.
8. Shi Y, Frost P, Hoang B, Yang Y, Fukunaga R, Gera J, Lichtenstein A. MNK kinases facilitate c-myc IRES activity in rapamycin-treated multiple myeloma. *Oncogene* 2013; 32:190-197.
9. Hoang B, Benavides A, Shi Y, Yang Y, Frost P, Gera J, Lichtenstein A. The PP242 mammalian target of rapamycin (mTOR) inhibitor activates extracellular signal-regulated kinase (ERK) in multiple myeloma cells via a target of rapamycin complex 1 (TORC1)/eukaryotic translation initiation factor 4E (eIF-4E)/RAF pathway and activation is a mechanism of resistance. *Journal of Biological Chemistry* 2012; 287:21796-20805.
10. Shi Y, Yang Y, Hoang B, Bardeleben C, Holmes B, Gera J, Lichtenstein A. Therapeutic potential of targeting IRES-dependent c-myc translation in multiple myeloma cells during ER stress. *Oncogene* 2016; 35:1015-1024.
11. Hoang B, Shi Y, Frost PJ, Mysore V, Bardeleben C, Lichtenstein A. SGK kinase activity in multiple myeloma cells protects against ER stress apoptosis via a SEK-dependent mechanism. *Molecular Cancer Research* 2016; 14:397-407.
12. Vega MI, Shi Y, Frost P, Huerta-Yepez S, Antonio-Andres G, Hernandez-Pando R, Lee J, Jung ME, Gera JF, Lichtenstein A. A Novel therapeutic induces DEPTOR degradation in multiple myeloma cells with resulting tumor cytotoxicity. *Molecular Cancer Therapeutics* 2019; 18:1822-1831.
13. Hu L, Shi Y, Hsu J-H, Gera J, Van Ness B, Lichtenstein A. Downstream effectors of oncogenic ras in multiple myeloma cells. *Blood* 2003; 101:3126-3135.

The aforementioned Allegations were received in twelve separate emails by the GLA Research Integrity Officer (RIO) from an anonymous source, self-identified as “Anonymous PubPeer User” (Attachment B). The same Allegations were also sent by the anonymous source to UCLA and the Department of Health and Human Services’ Office of Research Integrity (ORI).

These Allegations pertain to VA and/or UCLA research funded by the following federal grants: I01BX002665, K01CA138559, P30A1028697, R01CA096920, R01CA109312, R01CA111448, R01CA132778, R01CA168700, R01CA196266, R01CA211562, R01CA217820, and R21CA168491. The Allegations also pertain to other grants from the Department of Veterans Affairs, Department of Defense, Multiple Myeloma Research Foundation, and the UCLA AIDS Institute.

The Respondent is a retired faculty member of GLA and UCLA. He was responsible as Principal Investigator for all aspects of the research referenced in the Allegations. All relevant research was conducted completely or in part in GLA laboratory space. Further, all research referenced in the Allegations was supported by grants administered by a GLA-affiliated non-profit corporation or UCLA. GLA and UCLA have concurrent and joint jurisdiction over all Allegations. UCLA jointly participated in this investigation, which was led by GLA. A representative from UCLA was appointed to, and served on, the Investigation Committee as a voting member. As such, this memorandum represents a joint GLA-UCLA Investigation Report.

The investigation was convened for the purpose of judging the accuracy of the allegations and making recommended findings about whether and to what extent Research Misconduct occurred; who is responsible; and what corrective actions are appropriate. The investigation consisted of a thorough review of the Allegations indicated in the Charge Letter; findings in the Inquiry Report (issued August 18, 2023; Attachment C), which determined that the Allegations had sufficient substance to warrant an investigation; and testimonial evidence.

The investigation was conducted in accordance with VHA Directive 1058.02 and VA Handbook 0700. For the purposes of this investigation, the provisions of VHA Directive 1058.02 took precedence over any contrary provisions of VA Handbook 0700. To establish a finding of Research Misconduct, the Allegations must be proven by a *preponderance of the evidence*.

In conducting the investigation, the Investigation Committee reviewed the readily available evidence. The members were unable to interview the individual(s) who submitted the Allegations since they were received anonymously. The Respondent was interviewed regarding the Allegations on August 10, 2023, by the Inquiry Committee. The Respondent turned down a request to be interviewed by the Investigation Committee (he can no longer be compelled to do so now that he is not an employee of either GLA or UCLA), but all members reviewed his previous recorded testimony as part of the investigation. [redacted] was interviewed as well (Attachment D).

Due to the large number of Allegations that needed to be reviewed and analyzed, the GLA Director requested an extension of the deadline for completing the investigation on December 6, 2023 (Attachment E). The requested extension was granted by the Office of Research Oversight's (ORO) Research Misconduct Office on December 7, 2023 (Attachment F).

With regard to all Allegations, the Investigation Committee's analysis of scientific images material to the investigation was limited to those images that were included in the published articles. The Inquiry Committee had requested that the Respondent provide the members with any original data or documentation of the experiments that were reported in the published articles. During a previous interview with the Inquiry Committee, the Respondent testified that all relevant original data had been destroyed or lost when his laboratory was closed. The GLA RIO conducted a review of electronic files on the network drives assigned to the Respondent; he was unable to identify any files that were material to the investigation. Therefore, the Committee was unable to obtain and analyze the original data for the underlying experiments that were the sources of the research related to the Allegations.

The following is a detailed list of the Allegations that were investigated. Superscript numbers in each refer to the publications listed above.

a. Reused p-4E-BP1-T37/46, p-4E-BP1-S65, and α-tubulin panels from Figure 3B of *Genes & Cancer* (2014)[1] to falsely represent p-4E-BP1, 4E-BPI, and tubulin expression, respectively, in cells exposed to different experimental conditions in

Figure 1F of *Cancer Research* (2016)[2] [related to Anonymous PubPeer User, Email 1].

b. Reused the P-AKT-S473 panel from Figure 3C of *Genes & Cancer* (2014)[1] with vertical compression to falsely represent DEPTOR expression in NSC126405 cells under different experimental conditions in lanes 1-4 of Figure 3C in *Cancer Research* (2016)[2] [related to Anonymous PubPeer User, Email 1].
c. Reused the p7056K1 panel from Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in Figure 4C of *Cancer Research* (2016)[2] [related to Anonymous PubPeer User, Email 1].
d. Reused a cropped image incorporating the parts or whole of lanes 1-4 in the P110 mu panel from Figure 5B to falsely represent the PI(3,4)P panel in Figure 4a, both from *Oncogene* (2004)[3] [related to Anonymous PubPeer User, Email 2].
e. Reused the actin bands (+/- OPM-2 expression) in Figure 1A to falsely represent actin bands (+/- IL-6 expression) under different experimental conditions in Figure 1C, both from *PLoS One* (2014)[4] [related to Anonymous PubPeer User, Email 3].
f. Reused lanes 1 and 2 of the FKHD-P and FKHD-T bands in Figure 1B of *Molecular Cancer Therapeutics* (2005)[5] to falsely represent P-MNK and T-MNK expression for PT#2 in cells exposed to different experimental conditions in Figure 1B of *PLoS One* (2014)[4] [related to Anonymous PubPeer User, Email 3].
g. Reused the actin and P-AKT(S473) $U87_{PTEN}$ western blot panel in Figure 2A of *Molecular Cancer Therapeutics* (2011)[6] that falsely represented S6K expression and was rotated horizontally to falsely represent AKT expression under different conditions in Figure 1F of *PLoS One* (2017)[7] [related to Anonymous PubPeer User, Email 4].
h. Reused lanes 1-2 of the T-HSP27 panel in Figure 2B of *Oncogene* (2013)[8] to falsely represent GAPDH expression in lanes 4 and 5 of the same figure [related to Anonymous PubPeer User, Email 5].
i. Reused lanes 1-3 of the p-erk panels and lanes 2-4 of the t-erk panels in Figure 3B to falsely represent erk (T202/Y204) and erk panels under different experimental conditions in Figure 4A, both from the *Journal of Biological Chemistry* (2012)[9] [related to Anonymous PubPeer User, Email 6].
j. Reused lanes 1-8 and a small portion of lane 9 of the α-tubulin panel in Figure 4E to falsely represent lanes 1-8 and a small portion of lane 9 in Fig. 4D under different experimental conditions of the α-tubulin control panel in *Genes & Cancer* (2014)[1] [related to Anonymous PubPeer User, Email 7].
k. Reused lanes 1-4 of the T p70 expression in in Figure 1B to falsely represent the C-myc panel in Figure 1E of *Oncogene* (2016)[10] [related to Anonymous PubPeer User, Email 8].
l. Reused lanes 1-4 of 4E-BP1 in OPM-2 cells in Supplemental Figure 2A to falsely represent expression of T-4E-BP1 in MM1.S cells in *Oncogene* (2016)[10] [related to Anonymous PubPeer User, Email 8].
m. Reused the T-S6 panel in Figure 1F of *Oncogene* (2016)[10] to falsely represent C-myc expression in the same figure [related to Anonymous PubPeer User, Email 8].
n. Reused lanes 2-5 of the MNK-P panel in Figure 3A to falsely represent ERK-T expression in Figure 4A of *Oncogene* (2016)[10] [related to Anonymous PubPeer User, Email 8].

o. Reused lanes 2-5 of the MNK-T panel in Figure 3A to falsely represent Hsp-27-T expression in Figure 4A of *Oncogene* (2016)[10] [related to Anonymous PubPeer User, Email 8].
p. Reused the six western blot panels representing MNK1, MNK2, and GAPDH expression in ANBL-6 MM cells in Figure 3A of *PLoS One* (2014)[4] to falsely represent expression of the same proteins in 8226 cells in six panels of Figure 3e of *Oncogene* (2016)[10] [related to Anonymous PubPeer User, Email 8].
q. Reused the mTOR panel from Figure 8A in *Genes & Cancer* (2014)[1] with vertical compression to falsely represent ire1-total expression in Figure 5B of *Molecular Cancer Research* (2016)[11] [related to Anonymous PubPeer User, Email 9].
r. Reused lanes 4-9 of the actin control panel from Figure 2A to falsely represent the actin control for WT DEPTOR expression under different experimental conditions in Figure 2G of *Molecular Cancer Therapeutics* (2019)[12] [related to Anonymous PubPeer User, Email 10].
s. Reused the panel representing DEPTOR expression in MM15 cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in OPM2 cells in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [related to Anonymous PubPeer User, Email 10].
t. Reused the panel representing DEPTOR expression in RPMI8226 cells Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in RPM8226 cells under different experimental conditions in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [related to Anonymous PubPeer User, Email 10].
u. Reused the panel representing mTOR expression in MM1S cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent mTOR expression in OPM2 cells in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [related to Anonymous PubPeer User, Email 10].
v. Reused the panel representing mTOR expression in RPMI18226 cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent mTOR expression in RPM8226 cells under different experimental conditions in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [related to Anonymous PubPeer User, Email 10].
w. Reused the panel representing AKT expression in MM1.S cells exposed to rapamycin in Figure 1A to falsely represent IRS-1 expression in OPM-2 cells treated with PS-341 in Figure 6B of *Molecular Cancer Therapeutics* (2005)[5] [related to Anonymous PubPeer User, Email 11].
x. Reused lanes 1 and 2 of the panel representing IRS-1 expression in rapamycin-treated cells to falsely represent lanes 2 and 3 of the panel representing IRS-1 expression in PS-341-treated cells in Figure 6B of *Molecular Cancer Therapeutics* (2005)[5] [related to Anonymous PubPeer User, Email 11].
y. Used the same panel horizontally rotated 180 degrees to falsely represent the expression of both IGF-R and FLAG in the MUTANT IRS-1 cells in Figure 5B of *Molecular Cancer Therapeutics* (2005)[5] [related to Anonymous PubPeer User, Email 11].
z. Reused lanes 2 and 3 of the panel representing AKT-T expression in HS-S cells to falsely represent lanes 1 and 2 of the panel representing AKT-T expression in OPM-2 cells in Figure 1C of *Molecular Cancer Therapeutics* (2005)[5] [related to Anonymous PubPeer User, Email 11].
aa. Reused lanes 1 and 2 of the panel representing AKT-P expression in Patient 1 to falsely represent AKT-P expression in lanes 1 and 2 in Patient 3 of Figure 1E of *Molecular Cancer Therapeutics* (2005)[5] [related to Anonymous PubPeer User, Email 11].

bb. Reused the panel representing FKH-T expression on Day 0 to falsely represent FKH-T expression in lanes 2-4 of the Day +2/+3 panel in Figure 3C of *Blood* (2003)[13] [related to Anonymous PubPeer User, Email 12].
cc. Reused lane 1 of the panel representing TOTAL p70 expression in untreated wild type cells in Figure 4B to falsely represent Ser411 expression in N-ras cells treated with PD98059 (lane 4) in Figure 4C of *Blood* (2003)[13] [related to Anonymous PubPeer User, Email 12].
dd. Reused the panel representing Ser411 expression in wild-type cells in Figure 4B to falsely represent lanes 1-2 of Ser411 expression in N-ras cells in Figure 4C of *Blood* (2003)[13] [related to Anonymous PubPeer User, Email 12].
ee. Reused lane 1 of the ERK-P panel to falsely represent lane 2 of the ERK-T panel in both the N-ras and K-ras conditions in Figure 2C of *Blood* (2003)[13] [related to Anonymous PubPeer User, Email 12].

Findings of Fact

The Investigation Committee reviewed all figures identified in the Allegations, looking for similarities in the shapes, spatial orientations, distinguishing features, and electrophoretic mobilities of the bands shown in each figure. The members unanimously concluded that all bands alleged to be identical but labeled differently were indeed highly similar or identical in appearance, indicating that Falsification had taken place in each Allegation. Furthermore, many of the bands appear to have been altered: several have been stretched, one appears to have been horizontally flipped, and another appears to have been a colored molecular weight marker rather than GAPDH as labeled. Of course, without primary data, it was impossible for the members to determine which of the identical bands were accurately labeled (if either) and which were falsified.

After the inquiry phase and prior to this investigation, three of the publications involved in these Allegations (numbered above as 4, 7, and 10) were retracted by the respective journals as a result of the Allegations having been forwarded to the publishers by the same anonymous informant(s).

While the Respondent turned down a request to be interviewed by the Investigation Committee (and could not be compelled, as a non-employee), an in-person interview with the Respondent did take place during the inquiry stage on August 10, 2023. The interview was recorded in accordance with VHA Directive 1058.02 and reviewed by the Investigation Committee members.

In this August interview, the Respondent stated he had deleted all of the original electronic data files prior to retirement and had no knowledge of the present whereabouts of any of the gel images or other original data; he assumed everything had been discarded when he closed his laboratory. He further stated that the first author of the publications was always the person who cast and ran the gels in the laboratory. In earlier publications, the resultant bands were photographed with a film camera, printed, then scanned; in later publications, the gels were scanned with a digital gel scanner. The original images were sent via email from lab staff to the Respondent as PowerPoint files. The Respondent stated that he saved these files electronically according to the protein probe used and were formatted and arranged exclusively by the Respondent into the figures that were eventually published. The Respondent admitted to altering the contrast, brightness, and aspect ratio of the

images at times, claiming that he did not know this was possibly inappropriate. He stated that he may have inadequately or improperly labeled and organized the files, thereby increasing the probability that the images would be confused or misidentified, as an explanation for their consequent multiple use and mislabeling. The Respondent did not challenge the assertion that there were duplicate band pairs that occurred either in the same figure, in different figures within the same publication, or in another publication among those listed in the foregoing section. The Respondent attributed all of these alleged errors to "sloppiness" and not to any systematic or intentional modification of the data intended to alter their interpretation; indeed, he stands behind all of the conclusions in every publication in which he was senior author, contending that many of the conclusions drawn from his publications have been confirmed by data published by other groups. He also stated that the listed publications on which he was senior author represent a small fraction of the 60 or so publications published under his name within the same time period, for which no such duplications have been alleged. The Respondent expressed remorse regarding these data duplications and hoped that this matter could be resolved with minimal harm to the VA, the coauthors, the involved journals, and the funding agencies.

Given that the Respondent was not available, [redacted] was interviewed as a witness by the Investigation Committee on January 18, 2024. The interview was conducted in accordance with VHA Directive 1058.02—a transcript of the interview was drafted and approved by [redacted]. [redacted] is a VA- and NIH-funded investigator who worked with the Respondent [redacted]. He confirmed all aspects of the Respondent's August testimony, including that the Respondent was responsible for producing the falsified figures implicated in the Allegations.

Conclusions and Recommendations

Based on careful analysis of the bands alleged to be duplicated and mislabeled, the Investigation Committee finds all Allegations to be substantiated by a preponderance of the evidence as required by VHA Directive 1058.02. Based on testimony collected in interviews and by the Respondent's own admission, the Investigation Committee further finds that the Respondent is solely responsible for committing Research Misconduct through Falsification. By not carefully organizing or labeling image files, by manipulating images, and by not retaining the original data, the Respondent engaged in Reckless Research Misconduct, characterized by a conscious or willful disregard for ensuring the accurate representation of the research record that a member of the relevant research community would reasonably exercise in like circumstances. **Therefore, the Committee recommends that findings of Research Misconduct be made against the Respondent with regard to all Allegations.**

In consideration of a recommended corrective action, the Investigation Committee recognizes that the Respondent is retired both from academic and Federal employment, and no longer conducts research, so actions such as governmentwide debarment or prohibition from receiving future research funding would serve no meaningful purpose. **The Investigation Committee therefore recommends that the relevant editors be notified of these Research Misconduct findings with the**

intent of informing them of the alleged ethical violations specific to their journal. As noted above, three of these publications have already been retracted as of the date of this report (Attachment G).

If you have any questions about this report, please contact the Investigation Committee Chairperson.

[redacted] Investigation Committee Chairperson
Representing the VA Greater Los Angeles Healthcare System

[redacted]; Investigation Committee Member
Representing the VA Greater Los Angeles Healthcare System

[redacted]; Investigation Committee Member
Representing the University of California Los Angeles

cc: [redacted]

VA Department of Veterans Affairs

Memorandum

Date: October 6, 2023

From: Director, VA Greater Los Angeles Healthcare System (691/00)

Subject: Research Misconduct Investigation – Joint Investigation Led by VA

To: [redacted]

1. You are hereby appointed to an Investigation Committee regarding allegations of research misconduct against Alan Lichtenstein, MD (Respondent). [redacted] shall serve as Chair of the Investigation Committee.

2. An inquiry has determined that the following allegations of research misconduct have sufficient substance to warrant a formal investigation:

a. Reused p-4E-BP1-T37/46, p-4E-BP1-S65, and α-Tubulin panels from Figure 3B of *Genes & Cancer* (2014)[1] to falsely represent p-4E-BP1, 4E-BPI, and Tubulin expression, respectively, in cells exposed to different experimental conditions in Figure 1F of *Cancer Research* (2016)[2] [Anonymous PubPeer User, Email 1].
b. Reused the P-AKT-S473 panel from Figure 3C of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in NSC126405 cells under different experimental conditions in lanes 1-4 of Figure 3C in *Cancer Research* (2016)[2] [Anonymous PubPeer User, Email 1].
c. Reused the p7056K1 panel from Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in Figure 4C of *Cancer Research* (2016)[2] [Anonymous PubPeer User, Email 1].
d. Reused the PI(3,4)P panel from Figure 4A in *Oncogene* (2004)[3] to falsely represent the P110 mu panel of Figure 5B in *Oncogene* (2004)[3] [Anonymous PubPeer User, Email 2].
e. Reused the Actin control panel for OPM-2 expression in Figure 1A of *PLoS One* (2014)[4] to falsely represent the control for IL-6 expression under different experimental conditions in Figure 1C of *PLoS One* (2014)[4] [Anonymous PubPeer User, Email 3].
f. Reused lanes 1 and 2 of the FKHD-P and FKHD-T panels in Figure 1B of *Molecular Cancer Therapeutics* (2005)[5] to falsely represent P-MNK and T-MNK expression in cells exposed to different experimental conditions in Figure 1B of *PLoS One* (2014)[4] [Anonymous PubPeer User, Email 3].
g. Reused the P-AKT(S473) western blot panel in Figure 2A of *Molecular Cancer Therapeutics* (2011)[6] to falsely represent AKT expression under different expression in Figure 1F of *PLoS One* (2017)[7] [Anonymous PubPeer User, Email 4].
h. Reused lanes 1-2 of the T-HSP27 panel in Figure 2B of *Oncogene* (2013)[8] to falsely represent GAPDH expression in lanes 4 and 5 of the same figure [Anonymous PubPeer User, Email 5].
i. Reused p-erk and t-erk panels in Figure 3B of *Journal of Biological Chemistry* (2012)[9] to falsely represent erk(T202/Y204) and erk panels under different

experimental conditions in Figure 4A of the *Journal of Biological Chemistry* (2012)[9] [Anonymous PubPeer User, Email 6].

j. Reused the α-Tubulin control panel in Figure 4D of *Genes & Cancer* (2014)[1] to falsely represent lanes 1-8 of the α -Tubulin panel under different experimental conditions in Figure 4E of *Genes & Cancer* (2014)[1] [Anonymous PubPeer User, Email 7].
k. Reused the C-myc panel in Figure 1B of *Oncogene* (2016)[10] to falsely represent T p70 expression in lanes 1-4 in Figure 1E of *Oncogene* (2016)[10] [Anonymous PubPeer User, Email 8].
l. Reused the T-4E-BP1 panel representing expression in MM1.S cells in Supplemental Figure 2A of *Oncogene* (2016)[10] to falsely represent lanes 1-4 of 4E-BP1 expression in OPM-2 cells in Supplemental Figure 2A of *Oncogene* (2016)[10] [Anonymous PubPeer User, Email 8].
m. Reused the T-S6 panel in Figure 1F of *Oncogene* (2016)[10] to falsely represent C-myc expression in the same figure [Anonymous PubPeer User, Email 8].
n. Reused lanes 2-5 of the MNK-P panel in Figure 3A of *Oncogene* (2016)[10] to falsely represent ERK-T expression in Figure 4A of *Oncogene* (2016)[10] [Anonymous PubPeer User, Email 8].
o. Reused lanes 2-5 of the MNK-T panel in Figure 3A of *Oncogene* (2016)[10] to falsely represent Hsp-27-T expression in Figure 4A of *Oncogene* (2016)[10] [Anonymous PubPeer User, Email 8].
p. Reused the western blot panels representing MNK1, MNK23, and GAPDH expression in ANBL-6 MM cells in Figure 3A of *PLoS One* (2014)[4] to represent falsely expression of the same proteins in 8226 cells in Figure 3E of *Oncogene* (2016)[10] [Anonymous PubPeer User, Email 8].
q. Reused the mTOR panel from Figure 8A in *Genes & Cancer* (2014)[1] to falsely represent ire1-total expression in Figure 5B of *Molecular Cancer Research* (2016)[11] [Anonymous PubPeer User, Email 9].
r. Reused lanes 6-9 of the Actin control panel from Figure 2A in *Molecular Cancer Therapeutics* (2019)[12] to falsely represent the Actin control for protein expression under different experimental conditions in Figure 2G of *Molecular Cancer Therapeutics* (2019)[12] [Anonymous PubPeer User, Email 10].
s. Reused the panel representing DEPTOR expression in MM15 cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in OPM2 cells in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [Anonymous PubPeer User, Email 10].
t. Reused the panel representing DEPTOR expression in RPMI8226 cells Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent DEPTOR expression in RPM8226 cells under different experimental conditions in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [Anonymous PubPeer User, Email 10].
u. Reused the panel representing mTOR expression in MM1S cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent mTOR expression in OPM2 cells in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [Anonymous PubPeer User, Email 10].
v. Reused the panel representing mTOR expression in RPMI18226 cells in Figure 1A of *Genes & Cancer* (2014)[1] to falsely represent mTOR expression in RPM8226 cells under different experimental conditions in Figure 6A of *Molecular Cancer Therapeutics* (2019)[12] [Anonymous PubPeer User, Email 10].
w. Reused the panel representing AKT expression in MM1.S cells exposed to rapamycin in Figure 1A of *Molecular Cancer Therapeutics* (2005)[5] to falsely represent IRS-1 expression in OPM-2 cells treated with PS-341 in Figure 6B

of *Molecular Cancer Therapeutics* (2005)[5] [Anonymous PubPeer User, Email 11].

x. Reused lanes 1 and 2 of the panel representing IRS-1 expression in rapamycin-treated cells to falsely represent lanes 2 and 3 of the panel representing IRS-1 expression in PS-341-treated cells in Figure 6B of *Molecular Cancer Therapeutics* (2005)[5] [Anonymous PubPeer User, Email 11].
y. Used the same panel horizontally rotated 180 degrees to falsely represent the expression of both IGF-R and FLAG in the MUTANT IRS-1 cells in Figure 5B of *Molecular Cancer Therapeutics* (2005)[5] [Anonymous PubPeer User, Email 11].
z. Reused lanes 2 and 3 of the panel representing AKT-T expression in HS-S cells to falsely represent lanes 1 and 2 of the panel representing AKT-T expression in OPM-2 cells in Figure 1C of *Molecular Cancer Therapeutics* (2005)[5] [Anonymous PubPeer User, Email 11].
aa. Reused lanes 1 and 2 of the panel representing AKT-P expression in Patient 1 to falsely represent AKT-P expression in Patient 3 of Figure 1E of *Molecular Cancer Therapeutics* (2005)[5] [Anonymous PubPeer User, Email 11].
bb. Reused the panel representing FKH-T expression on Day 0 to falsely represent FKH-T expression in lanes 2-4 of the Day +2/+3 panel in Figure 3C of *Blood* (2003)[13] [Anonymous PubPeer User, Email 12].
cc. Reused lane 1 of the panel representing TOTAL p70 expression in untreated wild type cells in Figure 4B to falsely represent Ser411 expression in N-ras cells treated with PD98059 (lane 4) in Figure 4C of *Blood* (2003)[13] [Anonymous PubPeer User, Email 12].
dd. Reused the panel representing Ser411 expression in wild type cells in Figure 4B to falsely represent lanes 1-2 of Ser411 expression in N-ras cells in Figure 4C of *Blood* (2003)[13] [Anonymous PubPeer User, Email 12].
ee. Reused lane 1 of the ERK-P panel to falsely represent lane 2 of the ERK-T panel in both the N-ras and K-ras conditions in Figure 2C of *Blood* (2003)[13] [Anonymous PubPeer User, Email 12].

3. The Research Integrity Officer (RIO) has determined that these allegations pertain to VA and/or UCLA research funded by the following federal grants: I01BX002665, K01CA138559, P30A1028697, R01CA096920, R01CA109312, R01CA111448, R01CA132778, R01CA168700, R01CA196266, R01CA211562, R01CA217820, R21CA168491. The allegations also pertain to other grants from the Department of Veterans Affairs, Department of Defense, Multiple Myeloma Research Foundation, and the UCLA AIDS Institute.

4. The University of California Los Angeles (UCLA) has concurrent jurisdiction over one or more of the allegations and will jointly participate in the investigation, which will be led by VA. The investigation shall be conducted in accordance with VHA Directive 1058.02 ("Research Misconduct"). [redacted] shall serve as UCLA's representative to the investigation.

5. The research misconduct investigation is being convened for the purpose of making recommended findings about whether and to what extent research misconduct has occurred, who is responsible, and what corrective actions are appropriate. The investigation consists of a thorough review of the research misconduct allegations indicated in this Charge Letter; any other potential instances of related research misconduct not specified in the allegations, provided any new allegations are added to the Investigation Committee's charge and the Respondent is notified of the new allegations; the Inquiry Report; sequestered and submitted

materials; and any other relevant evidence that can be obtained. To establish a finding of research misconduct, the allegations must be proven by a *preponderance of the evidence*. A higher burden of proof, such as "by clear and convincing evidence" or "beyond a reasonable doubt", is not required to establish a finding of research misconduct.

6. The investigation must adhere to the following requirements:

   a. The investigation shall be conducted in accordance with VHA Directive 1058.02 and VA Handbook 0700 ("Administrative Investigations"). For the purposes of this investigation, the provisions of VHA Directive 1058.02 take precedence over any contrary provision of VA Handbook 0700.

   b. The investigation (including issuance of the final Investigation Report) must be completed within 120 days of the date of this memorandum unless an extension has been granted by ORO.

   c. The Investigation Committee must produce an Investigation Report.

      i. The report must indicate the name and position of the respondent(s); a detailed summary of the allegation(s); the research and funding involved; that the report represents a joint report of VA and UCLA; the basis for UCLA's joint procedural jurisdiction over the allegation; and that VA led the joint investigation under the procedures of VHA Directive 1058.02.

      ii. The report must be in standard format in accordance with VA Handbook 0700. An index identifying the evidentiary exhibits cited in the report must be prepared in accordance with VA Handbook 0700.

      iii. For each allegation, the report must indicate:

         1. the basis for why the allegation falls within the scope of VHA Directive 1058.02;

         2. recommended findings about whether and to what extent research misconduct has occurred and who is responsible;

         3. the evidence reviewed;

         4. how the *preponderance of the evidence* supports a recommended finding of research misconduct, or that the committee determined that there was not a preponderance of the evidence to support a finding of research misconduct;

         5. a response to any contrary evidence, including but not limited to, the respondent's affirmative defenses; and

         6. what corrective actions, if any, are appropriate.

7. This memorandum authorizes you to require VA employees to cooperate with you; to require all employees having any knowledge of the allegations to furnish testimony under oath or affirmation without a pledge of confidentiality; to obtain voluntary sworn testimony from other individuals; to administer oaths and affirmations; and to gather other evidence that you determine is necessary and

relevant. These authorities are delegated for the purposes and duration of this investigation only.

8. The privacy of all participants and the confidentiality of information gathered in a research misconduct proceeding are to be preserved by all persons to the extent possible and as allowed by law. Any person who receives information pertaining to a VA research misconduct proceeding is obligated to keep that information confidential until otherwise made public or as required by law.

9. Please let me express my appreciation of your time and effort in serving in this capacity.

[redacted]

cc: [redacted]

[1] Yang Y, Bardeleben C, Frost P, Hoang B, Shi Y, Finn R, Gera J, Lichtenstein A. DEPTOR is linked to a TORC1-p21 survival proliferation pathway in multiple myeloma. *Genes & Cancer* 2014; 5:407-19.

[2] Shi Y, Daniel-Wells TR, Frost P, Lee J, Finn RS, Bardeleben C, Penichet ML, Jung ME, Gera J, Lichtenstein A. Cytotoxic properties of a DEPTOR-mTOR inhibitor in multiple myeloma cells. *Cancer Research* 2016; 76:5822-5831.

[3] Hsu J-H, Shi Y, Frost P, Yan H, Hoang B, Sharma S, Gera J, Lichtenstein A. Interleukin-6 activates phosphoinositol-3' kinase in multiple myeloma tumor cells by signaling through RAS-dependent and, separately, through p85-dependent pathways. *Oncogene* 2004; 23:3368-337.

[4] Shi Y, Frost P, Hoang B, Yang Y, Bardeleben C, Gera J, Lichtenstein A. MNK1-induced eIF-4E phosphorylation in myeloma cells: a pathway mediating IL-6-induced expansion and expression of genes involved in metabolic and proteotoxic responses. *PLoS One* 2014; 9:e94011.

[5] Shi Y, Yan H, Frost P, Gera J, Lichtenstein A. Mammalian target of rapamycin inhibitors activate the AKT kinase in multiple myeloma cells by up-regulating the insulin-like growth factor receptor/insulin receptor substrate-1/phosphatidylinositol 3-kinase cascade. *Molecular Cancer Therapeutics* 2005; 4:1533-1540.

[6] Cloninger C, Bernath A, Bashir T, Holmes B, Artinian N, Ruegg T, Anderson L, Masri J, Lichtenstein A, Gera J. Inhibition of SAPK2/p38 enhances sensitivity to mTORC1 inhibition by blocking IRES-mediated translation initiation in glioblastoma. *Molecular Cancer Therapeutics* 2011; 10:2244-2256.

[7] Benavides-Serrato A, Lee J, Holmes B, Landon KA, Bashir T, Jung ME, Lichtenstein A. Specific blockade of Rictor-mTOR association inhibits mTORC2 activity and is cytotoxic in glioblastoma. *PLoS One* 2017; 12:e0176599.

[8] Shi Y, Frost P, Hoang B, Yang Y, Fukunaga R, Gera J, Lichtenstein A. MNK kinases facilitate c-myc IRES activity in rapamycin-treated multiple myeloma. *Oncogene* 2013; 32:190-197.

[9] Hoang B, Benavides A, Shi Y, Yang Y, Frost P, Gera J, Lichtenstein A. The PP242 mammalian target of rapamycin (mTOR) inhibitor activates extracellular signal-regulated kinase (ERK) in multiple myeloma cells via a target of rapamycin complex 1 (TORC1)/eukaryotic translation initiation factor 4E (eIF-4E)/RAF pathway and activation is a mechanism of resistance. *Journal of Biological Chemistry* 2012; 287:21796-20805.

[10] Shi Y, Yang Y, Hoang B, Bardeleben C, Holmes B, Gera J, Lichtenstein A. Therapeutic potential of targeting IRES-dependent c-myc translation in multiple myeloma cells during ER stress. *Oncogene* 2016; 35:1015-1024.

[11] Hoang B, Shi Y, Frost PJ, Mysore V, Bardeleben C, Lichtenstein A. SGK kinase activity in multiple myeloma cells protects against ER stress apoptosis via a SEK-dependent mechanism. *Molecular Cancer Research* 2016; 14:397-407.

[12] Vega MI, Shi Y, Frost P, Huerta-Yepez S, Antonio-Andres G, Hernandez-Pando R, Lee J, Jung ME, Gera JF, Lichtenstein A. A Novel therapeutic induces DEPTOR degradation in multiple myeloma cells with resulting tumor cytotoxicity. *Molecular Cancer Therapeutics* 2019; 18:1822-1831.

[13] Hu L, Shi Y, Hsu J-H, Gera J, Van Ness B, Lichtenstein A. Downstream effectors of oncogenic ras in multiple myeloma cells. *Blood* 2003; 101:3126-3135.

VA Department of Veterans Affairs

Memorandum

Date: August 18, 2023

From: Research Misconduct Inquiry Committee (691/151)

Subject: Inquiry Report Regarding Allegations of Research Misconduct

To: Director, VA Greater Los Angeles Healthcare System (691/00)

The joint VA Greater Los Angeles Healthcare System (GLA) and University of California Los Angeles (UCLA) Research Misconduct Inquiry Committee has completed its inquiry as directed by your appointment letter, dated June 28, 2023 (Attachment A).

Preliminary Statement/Background Information

As indicated in the appointment letter, the Inquiry Committee was convened to conduct an inquiry into Allegations that Alan Lichtenstein, MD, (hereafter, "**Respondent**"), a retired Staff Physician at GLA and current WOC employee, and Professor Emeritus in the UCLA Department of Medicine, falsified Western blot data published in the following medical journals:

1. Yang Y, Bardeleben C, Frost P, Hoang B, Shi Y, Finn R, Gera J, Lichtenstein A. DEPTOR is linked to a TORC1-p21 survival proliferation pathway in multiple myeloma. *Genes & Cancer* 2014; 5:407-419.
2. Shi Y, Daniel-Wells TR, Frost P, Lee J, Finn RS, Bardeleben C, Penichet ML, Jung ME, Gera J, Lichtenstein A. Cytotoxic properties of a DEPTOR-mTOR inhibitor in multiple myeloma cells. *Cancer Research* 2016; 76:5822-5831.
3. Hsu J-H, Shi Y, Frost P, Yan H, Hoang B, Sharma S, Gera J, Lichtenstein A. Interleukin-6 activates phosphoinositol-3' kinase in multiple myeloma tumor cells by signaling through RAS-dependent and, separately, through p85-dependent pathways. *Oncogene* 2004; 23:3368-3375.
4. Shi Y, Frost P, Hoang B, Yang Y, Bardeleben C, Gera J, Lichtenstein A. MNK1-induced eIF-4E phosphorylation in myeloma cells: a pathway mediating IL-6-induced expansion and expression of genes involved in metabolic and proteotoxic responses. *PLoS One* 2014; 9:e94011.
5. Shi Y, Yan H, Frost P, Gera J, Lichtenstein A. Mammalian target of rapamycin inhibitors activate the AKT kinase in multiple myeloma cells by up-regulating the insulin-like growth factor receptor/insulin receptor substrate-1/phosphatidylinositol 3-kinase cascade. *Molecular Cancer Therapeutics* 2005; 4:1533-1540.
6. Cloninger C, Bernath A, Bashir T, Holmes B, Artinian N, Ruegg T, Anderson L, Masri J, Lichtenstein A, Gera J. Inhibition of SAPK2/p38 enhances sensitivity to mTORC1 inhibition by blocking IRES-mediated translation initiation in glioblastoma. *Molecular Cancer Therapeutics* 2011; 10:2244-2256.

7. Benavides-Serrato A, Lee J, Holmes B, Landon KA, Bashir T, Jung ME, Lichtenstein A, Gera, J. Specific blockade of Rictor-mTOR association inhibits mTORC2 activity and is cytotoxic in glioblastoma. *PLoS One* 2017; 12:e0176599.
8. Shi Y, Frost P, Hoang B, Yang Y, Fukunaga R, Gera J, Lichtenstein A. MNK kinases facilitate c-myc IRES activity in rapamycin-treated multiple myeloma. *Oncogene* 2013; 32:190-197.
9. Hoang B, Benavides A, Shi Y, Yang Y, Frost P, Gera J, Lichtenstein A. The PP242 mammalian target of rapamycin (mTOR) inhibitor activates extracellular signal-regulated kinase (ERK) in multiple myeloma cells via a target of rapamycin complex 1 (TORC1)/eukaryotic translation initiation factor 4E (eIF-4E)/RAF pathway and activation is a mechanism of resistance. *Journal of Biological Chemistry* 2012; 287:21796-20805.
10. Shi Y, Yang Y, Hoang B, Bardeleben C, Holmes B, Gera J, Lichtenstein A. Therapeutic potential of targeting IRES-dependent c-myc translation in multiple myeloma cells during ER stress. *Oncogene* 2016; 35:1015-1024.
11. Hoang B, Shi Y, Frost PJ, Mysore V, Bardeleben C, Lichtenstein A. SGK kinase activity in multiple myeloma cells protects against ER stress apoptosis via a SEK-dependent mechanism. *Molecular Cancer Research* 2016; 14:397-407.
12. Vega MI, Shi Y, Frost P, Huerta-Yepez S, Antonio-Andres G, Hernandez-Pando R, Lee J, Jung ME, Gera JF, Lichtenstein A. A Novel therapeutic induces DEPTOR degradation in multiple myeloma cells with resulting tumor cytotoxicity. *Molecular Cancer Therapeutics* 2019; 18:1822-1831.

The aforementioned Allegations were received in ten separate emails by the GLA Research Integrity Officer (RIO) on April 21–25, 2023, from an anonymous source, self-identified as “Anonymous PubPeer User” (Attachment B). As indicated in an email to you, dated April 26, 2023, the RIO determined that the Allegations met the requirements of VHA Directive 1058.02 Appendix A §4.d for opening a research misconduct inquiry and were subsequently forwarded to the VHA Office of Research Oversight’s (ORO) Office of Research Misconduct and the UCLA RIO. The U.S. Department of Health & Human Services’ Office of Research Integrity (ORI) also received these allegations and requested that GLA and UCLA initiate an inquiry in a letter dated May 3, 2023 (Attachment C).

The research referenced in the Allegations was supported by one or more of the following National Institutes of Health (NIH) awards: K01CA138559, P30A1028697, R01CA096920, R01CA109312, R01CA111448, R01CA132778, R01CA168700, R01CA196266, R01CA211562, R01CA217820, and R21CA168491. Funding from the U.S. Department of Veterans Affairs was also implicated in several Allegations: I01BX002665. The Allegations also pertain to funding provided by the U.S. Department of Defense, the Multiple Myeloma Research Foundation, and the UCLA AIDS Institute.

The Respondent is a retired faculty member of the UCLA Department of Medicine and GLA (currently a WOC employee). He was responsible as Principal Investigator for all aspects of the research referenced in all Allegations. All research was conducted completely or in part in GLA laboratory space. Further, all research referenced in the Allegations was supported by grants administered by a GLA-affiliated non-profit corporation or UCLA. Therefore, GLA and UCLA have concurrent and joint jurisdiction over all Allegations. UCLA jointly participated in the inquiry, which was led by GLA. A representative from UCLA was appointed to, and served

on, the Inquiry Committee. As such, this memorandum represents a joint GLA-UCLA Inquiry Report.

The inquiry was conducted in accordance with VHA Directive 1058.02 and convened for the sole purpose of determining whether the Allegations referenced above have sufficient substance to warrant opening a formal investigation. As indicated in the Directive, an allegation of research misconduct is deemed to have "sufficient substance" if the inquiry determines that the readily available evidence would raise a reasonable suspicion of research misconduct.

In conducting the inquiry, the committee reviewed the readily available evidence. The committee was unable to interview the individual(s) who submitted the Allegations since the Allegations were received anonymously. The Respondent was interviewed regarding the Allegations on August 10, 2023.

Allegations

Please note that the letter beside each Allegation listed below is identical to that listed in Attachment A. The reader is referred to Attachment D for the identification of the specific bands implicated in each Allegation. Numbers in brackets correspond to the list of references in the previous section. Comments have been added, where needed, to illustrate unique salient features of each Allegation.

a. Portions of Figure 3B from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently in portions of Figure 1F from Cancer Research (2016)[2], suggesting data falsification (Anonymous PubPeer User, Email 1).
b. Portions of Figure 3C from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently in portions of Figure 3C from Cancer Research (2016)[2], suggesting data falsification (Anonymous PubPeer User, Email 1). Note that the band labeled "P-AKT-S473" in Fig. 3C, Ref. 1, appeared to have an altered aspect ratio that when compressed vertically matched that of the leftmost 4 bands of Fig. 3C, Ref. 2, labeled "DEPTOR".
c. Portions of Figure 1A from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently in portions of Figure 4C from Cancer Research (2016)[2], suggesting data falsification (Anonymous PubPeer User, Email 1). Note that the band labeled "DEPTOR" in Fig. 4C, Ref. 2, appeared to have an altered aspect ratio that when expanded vertically matched that of the band labeled ""P7056K1"of Fig. 1A, Ref. 1.
d. Portions of Figures 4A and 5B from Oncogene (2004)[3] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 2). Note that the band labeled "P110mu" from Fig. 5b, Ref. 3, when cropped and vertically expanded resembled the band labeled "PI(3,4)P" from, Fig. 4A, Ref. 3.
e. Portions of Figures 1A and 1C from PLoS ONE (2014)[4] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 3).
f. Portions of Figure 1B from Molecular Cancer Therapeutics (2005)[5] appear to have been duplicated and labeled differently in portions of Figure 1C from PLoS ONE (2014)[4], suggesting data falsification (Anonymous PubPeer User, Email 3).
g. Portions of Figure 2A from Molecular Cancer Therapeutics (2011)[6] appear to have been duplicated and labeled differently in portions of Figure 1F from PLoS ONE (2017)[7], suggesting data falsification (Anonymous PubPeer User, Email 4).

Note that the band labeled “P-AKT(S473)” in the “U87” lane from Fig. 2A, Ref. 6, appears similar to the band labeled “AKT” from Fig. 1F., Ref. 7, when flipped horizontally.

h. Portions of Figure 2B from Oncogene (2013)[8] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 5).
i. Portions of Figures 3B and 4A from the Journal of Biological Chemistry (2012)[9] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 6). Note that unlike the lanes as designated by the red box, the first 3 lanes from Fig. 3B labeled “t-erk” from Ref. 9 resemble the band labeled “erk” from Fig. 4A, Ref. 9.
j. Portions of Figures 4D and 4E from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 7).
k. Portions of Figures 1B and 1E from Oncogene (2016)[10] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 8).
l. Portions of Supplemental Figure 2A from Oncogene (2016)[10] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 8).
m. Portions of Figure 1F from Oncogene (2016)[10] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 8).
n. Portions of Figures 3A and 4A from Oncogene (2016)[10] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 8).
o. Portions of Figure 3A from PLoS ONE (2014)[4] appear to have been duplicated and labeled differently in portions of Figure 3E from Oncogene (2016)[10], suggesting data falsification (Anonymous PubPeer User, Email 8). Note that that the bands labeled “GAPDH” in the lane marked “shRNA MNK2” from Fig. 3e, Ref. 10, and Fig. 3A, Ref. 4, have a reddish color indicating that these bands actually contained a molecular weight marker and not GAPDH as labeled.
p. Portions of Figure 8A from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently in portions of Figure 5B from Molecular Cancer Research (2016)[11], suggesting data falsification (Anonymous PubPeer User, Email 9). Note that the band labeled “ire1-total” from the right panel of Fig. 5B, Ref. 11, and the band labeled “mTOR” from Fig. 8A, Ref. 1, are similar after the vertical aspect is adjusted.
q. Portions of Figures 2A and 2G from Molecular Cancer Therapeutics (2019)[12] appear to have been duplicated and labeled differently, suggesting data falsification (Anonymous PubPeer User, Email 10).
r. Portions of Figure 1A from Genes & Cancer (2014)[1] appear to have been duplicated and labeled differently in portions of Figure 6A from Molecular Cancer Therapeutics (2019)[12], suggesting data falsification (Anonymous PubPeer User, Email 10).

Summary and Recommendations

The Inquiry Committee reviewed all listed figures, looking for similarities in the shapes, spatial orientations, distinguishing features, and electrophoretic mobilities of the bands shown in each figure. They conclude that all bands alleged to be similar according to the anonymous informant were indeed highly similar or identical in

appearance. Furthermore, as indicated under “Allegations” above, many of the bands appear to have been altered, one appears to have been horizontally flipped, and another appears to have been a colored molecular weight marker rather than GAPDH as labeled.

The committee was unable to obtain the original data for the underlying experiments that were purportedly the source of the research reported in the figures. In his interview, the Respondent stated that the original data (e.g., photos of the original gels) or documentation of the experiments (e.g., written lab notebook entries) were no longer available, having been discarded when his laboratory was closed upon his retirement.

As senior author of References 1-5 and 8-12 and the PI of nearly all of grants that supported this work, the Respondent is primarily responsible for addressing the Allegations listed above.

The Inquiry Committee and RIO conducted an in-person interview with the Respondent on August 10, 2023, at 1:00-2:30 PM PDT in Building 114, Room 125, to discuss these Allegations. The interview was recorded in accordance with VHA Directive 1058.02.

The Respondent stated he had deleted all of the original electronic data files on retirement and had no knowledge of the present whereabouts of any of the gel images or other original data. He further stated that the first author of the publications was always the person who cast and ran the gels in the laboratory. In earlier publications, the resultant bands were photographed with a film camera, printed, then scanned; in later publications, the gels were scanned with a digital gel scanner. The images were sent via email from lab staff to the Respondent as PowerPoint files. The Respondent stated that the images were filed electronically according to the protein probe used and were formatted and arranged into the figures that were eventually published. The Respondent admitted to altering the contrast, brightness, and aspect ratio of the images at times, claiming that he did not know this was inappropriate. He admitted that since many of the files may have been inadequately or improperly labeled, there is a chance that some of the files may have been confused or misidentified, with consequent multiple use and mislabeling. The Respondent did not challenge the assertion that there were 32 duplicate band pairs that occurred either in the same figure, in different figures in the same publication, or in another publication among the ten listed publications that contained images allegedly copied from the same or prior publications. The Respondent attributed all of these alleged errors to “sloppiness” and not to any systematic modification of the data intended to alter their interpretation; indeed, he stands behind all of the conclusions stated in every publication in which he was senior author and further states that many of the conclusions drawn from his publications have been confirmed by other publications. He also stated that the ten listed publications on which he was senior author represent a small fraction of the 60 or so publications published under his name within the same time period, for which no such duplications have been alleged. The Respondent expressed remorse with regard to these alleged data duplications and hopes that this matter can be resolved with minimal harm to the VA, the coauthors, the involved journals, or the funding agencies.

While the committee agreed that honest error was a possibility for the mislabeling identified in the Allegations, the respondent provided no evidence to substantiate this claim.

Based on the similarities in the bands depicted in all listed figures and the Respondent's inability to provide original images and documentation of the experiments, ***the Inquiry Committee believes that all Allegations have sufficient substance to warrant the opening of a formal investigation***.

If you have any questions about this report, please contact the Inquiry Committee Chairperson, [redacted], by telephone or by email.

[redacted]; Inquiry Committee Chairperson
Representing the VA Greater Los Angeles Healthcare System

[redacted]; Inquiry Committee Member
Representing the University of California Los Angeles

cc: [redacted]

VA Department of Veterans Affairs

Memorandum

Date: December 6, 2023

From: Director, VA Greater Los Angeles Healthcare System (691/00)

Subject: Request for Extension – Research Misconduct Investigation

To: Research Misconduct Officer, Office of Research Oversight (10RO)

1. I am writing to request an extension to the 120-day time limit to complete our ongoing joint investigation.

2. Progress has been made, including formation of a joint inquiry team, training of the team members, and scheduling of major milestones in the conduct of the investigation.

3. Additional time is required because of the requirement to meet interim draft deadlines and to provide the Respondent and others time to read and comment on the draft report.

4. An extension of the current deadline will be needed to allow the Investigation Committee sufficient time to complete the draft investigation report. We therefore request a 60-day extension.

5. Thank you for your consideration of this request.

[redacted]

cc: [redacted]

VA | U.S. Department of Veterans Affairs
Veterans Health Administration
Office of Research Oversight

Memorandum

Date: October 7, 2023

From: Research Misconduct Officer, Office of Research Oversight (ORO) (10RO)

Subj: Research Misconduct Investigation Deadline Extension Request

To: Director, VA Greater Los Angeles Healthcare System (691/00)

1. The VHA Office of Research Oversight (ORO) acknowledges receipt of your memorandum, dated December 6, 2023, requesting that the deadline for completing an ongoing research misconduct investigation at the VA Greater Los Angeles Healthcare System be extended by 60 days to April 8, 2024. ORO understands that this request is being made to complete the draft report by the required deadline.

2. As permitted by VHA Directive 1058.02 ("Research Misconduct") Appendix C §3.b.(3)(c), ***ORO grants the requested extension of the deadline for completing the Investigation***.

3. If this office can be of any further assistance, please contact me by telephone at 202-253-1375 or by email at [redacted]@va.gov.

[redacted]

cc: [redacted]