

SAN FRANCISCO VA AND UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

COMMITTEE ON SCIENTIFIC MISCONDUCT

RESPONDENT: Dr. Rajvir Dahiya, Ph.D.

FINAL Report

December 5, 2016

Committee Members: Paul M. Sullam, M.D. (chair); Clive Pullinger, Ph.D.;  
Stephen Massa, M.D., Ph.D; Paul Simpson, M.D.; Kewchang Lee, M.D.

The Investigation Committee has reviewed the allegations of research misconduct pertaining to eight publications co-authored by Dr. Rajvir Dahiya (hereafter, the Respondent), a Senior Research Career Scientist employed by the San Francisco VAMC (SFVAMC) and a Professor of Urology at the University of California, San Francisco (UCSF). UCSF has concurrent jurisdiction over one or more of the allegations referenced above, because the Respondent is a UCSF faculty member (and was so during the period that the research in question was done), and because at least one of the grants acknowledged in the above papers was administered by the university. UCSF jointly participated in the investigation, which was led by the SFVAMC, in accordance with the procedures of VHA Handbook 1058.02 ("Research Misconduct"). As such, this memorandum represents a joint SFVAMC and UCSF report.

All the allegations involve photographic images within the figures cited in the allegations. With the exception of the figure in allegation 8 (see below), the images in question show electrophoretic analyses of PCR products, or of proteins probed by immunoblotting (Western blotting). The allegations contend that the research reported in the figures was falsified, resulting in the research not being accurately represented. To address the validity of these charges, the committee has reviewed the figures in question, and interviewed the Respondent, as well as a number of past and current laboratory members. We have also examined all the sequestered laboratory notebooks and computers, as well as the available relevant applications for federal grants. Below is a summary of our analysis and recommendations for the allegations pertaining to each allegation.

### **Methods of analysis**

The Committee used the following resources and methods for assessing the merits of the allegations:

1. Review of allegations: The Investigation Committee first met on March 11, 2015, to review the allegations and the evidence for their basis. The members universally concurred with findings of the Inquiry Committee.
2. Interviews: We interviewed under oath the Respondent, on March 25, 2015. Prior to the interview and throughout the investigation, he was provided with extensive access to all sequestered material. Thus, he had ample opportunity to review his records and retrieve original data, for purposes of preparing his response to the allegations. We also interviewed nine current or past members of his laboratory, including all six current members of his laboratory who were co-authors on the papers in question. In addition, we interviewed Dr. Roger Erickson, the Respondent's lab manager and in-house editor for the past 28 years. We were unable to interview other first authors, because they had left the laboratory and could not be located. A list of the individuals interviewed is attached, as well as the corresponding transcripts or signed affidavits.

Despite considerable efforts, we were unable to interview some of the key potential witnesses for this investigation. We attempted to contact [REDACTED] via email, since each is a first author on one or more of the publications in question. We sent messages to the addresses on file with the Respondent, but these proved invalid in two cases, while no reply was received from the third. No email addresses for these individuals were on file within the VA Research Office, VA Human Resources, or the Northern California Institute for Research and Education. Extensive internet searches produced no leads for contacting [REDACTED] or [REDACTED]. We did find an email address for [REDACTED] that was linked to a 2015 online publication (PMCID:PMC4529429), but no response was obtained to our messages to him or the first author. Finally, we sent a message to the Japanese Urological Association, in hopes of reaching these individuals via a membership directory (none was available online), but we received no response.

3. Lab books and computers: All of the 66 lab books and 36 computers sequestered on August 6, 2014 from the respondent's laboratory were examined by at least one member of the research committee, for any data or files that might be relevant to this investigation. It should be noted, however, that neither the lab books nor the computers contained data that were clearly related to the publications, and in particular, we could not find any of the source data or images for the published figures in question. Indeed, it was difficult to find any laboratory data or records associated with the first authors of the eight publications. The Respondent was unable to provide any primary data (including original images) for review, and could not explain where such data might be located. He speculated that some notebooks may have been lost during one of the moves of his laboratory, but was uncertain. As far as we can discern, the respondent never reported to the SFVAMC, so there is no record or other evidence for such a loss.

4. Funded research: We reviewed all available VA and NIH funded projects that were cited by the Respondent in the publications under investigation, looking for any of the data or figures in question. None was found.

### **Allegations:**

**Allegation 1:** The Respondent falsified research data reported in Figures 2C, 3B and/or 5D in a Cancer Research journal article, titled "Regulation of minichromosome maintenance gene family by microRNA-1296 and genistein in prostate cancer" (vol. 70, pp. 2809-2818), published in 2010.

**Authors:** S. Majid, A.A. Dar, S. Saini, Y. Chen, V. Shahryari, J. Liu, M.S. Zaman, H. Hirata, S. Yamamura, K. Ueno, Y. Tanaka, and R. Dahiya.

**Grant funding:** NIH grants RO1CA 111470 and T32DK007790, Veterans Affairs Research Enhancement Award Program, and Merit Review.

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

The Investigation Committee reviewed the analytical methods and findings of the Inquiry Committee in detail. It unanimously agreed that in Figures 5D and 3B, there were similarities in the shapes and electrophoretic mobilities of the Western blot GAPDH bands shown in each figure, indicating possible data falsification. The three lanes in the upper panel (PC3 cells) of Figure 3B (labeled GAPDH) and the three left lanes (also labeled GAPDH) of the bottom panel in Figure 5D appear to be from the same blot (or a portion thereof). The high degree of similarity was more apparent when the relevant part of Figure 3B was stretched horizontally, compressed vertically and superimposed onto the left lanes of the bottom (GAPDH) panel in Figure 5D. The ORI Forensic Review used Gradient Map software to overlay and color-compare blots. Gradient Map was also used to create false color blots that revealed commonalities within the internal characteristics of the protein bands and the shape of protein bands in the GAPDH blots in Figs. 3B & 5D, with the two images appearing to originate from the same blot and to have been used in separate figures. Thus, the same image appears to have been used to depict two different blots, with different treatments, in two different figures.

The Investigation Committee performed an independent analysis of Figures 2C, 3B and 5D, and agreed that there were similarities in the shapes of the Western blot GAPDH bands shown in each figure, indicating data falsification. The three left lanes in the lowest panel of

Figure 2C (labeled GAPDH) and the three right lanes of the bottom panel (also labeled GAPDH) in Figure 5D appear to be from the same blot (or a portion thereof). The high degree of similarity matching was most apparent when the relevant part of Figure 2C was overlaid on top of the right 3 lanes of the bottom (GAPDH) panel in Figure 5D. Images were enlarged and re-sized in Fiji/ImageJ and used to overlay and compare color blots. False color blots using gradient mapping revealed commonalities in the shape and the internal characteristics of the protein bands, as well as the characteristics of their surrounding backgrounds. In lanes 1-3 for the GAPDH blot in Fig. 2C and lanes 4-6 for the GAPDH blot in Fig. 5D the two images appear to originate from the same blot and to have been duplicated in separate figures. Thus, it appears that the same image is used to depict two different blots, with different treatments, in two different figures.

We reviewed these findings with the Respondent, and two other authors (██████████ and ██████████) of this publication. In preliminary questioning, the Respondent indicated that in his laboratory, the first author was typically responsible for most of the experimentation, data collection, and manuscript preparation, including assembling the figures (Respondent Interview of 3/25/2015, transcript page 9, lines 3-4). As for the specific allegations, the Respondent initially defended the use of these images as scientifically appropriate. However, when it was pointed out that the same images were used to represent GAPDH levels under different experimental conditions, he seemed to acknowledge that this was not scientifically justified (transcript page 13, lines 21- 22). He could not explain how this had occurred.

We subsequently interviewed ██████████ the first author on the publication. She stated that she was responsible for all the major aspects of the publication, including generating the data, assembling the figures, and writing the manuscript (witness interview of 4/29/2015, transcript page 6, lines 11 -20; page 19, line 8; page 14, line 14.). Despite extensive questioning, it remained unclear whether she fully understood the allegation. ██████████ was quite nervous during the interview, and seemed anxious to assure the Committee that she had not intentionally misrepresented her data. She defended the use of GAPDH as a control, stating that wherever it was used, the conditions were identical (page 10, line 18-22). However, when it was explicitly pointed out to ██████████ that in the above figures, it appeared that the same image was used to represent different experimental conditions (page 9, lines 9-13), her responses were lengthy, but did not clearly address this concern. She also stated that she has been unable to locate the original data and images for these figures (page 13, lines 5 – 11).

We also interviewed ██████████, another author on the paper. She stated that she was not involved in collecting the data or preparing the figures for the manuscript (transcript p. 9, lines 1-4), noting that this was likely to have been done primarily by ██████████ (p. 9, lines 22-23; p. 10, lines 7-9). She said that to her knowledge, the Respondent had no direct role in generating the data or preparing the figures, and indeed, it was not his usual role in the research. She also noted that the use of GAPDH controls in the above figures was scientifically inappropriate (page 15, lines 9-12).

Overall, the committee believes that although one or more of the GAPDH bands in the above figures have had a common source, the preponderance of evidence does not indicate research misconduct by the Respondent. Indeed, there is no evidence that he had any role in the preparation of the figures. For these reasons, the committee recommends that this allegation be dismissed. As for the role of ██████████ although it is likely that she prepared or edited the figures in question, the committee believes that there is insufficient evidence to indicate that she intentionally, knowingly or recklessly falsified the data. A more likely possibility is that ██████████ misunderstood the proper use of controls for these experiments or was sloppy in her work practices. During her interview she seemed slow to comprehend why the same image could not be used for experiments done under different condition, though this could have

been due to nervousness. Alternatively, the duplicate images could have resulted from the inadvertent use of the same image file. This also seems plausible, because the images do not appear to have undergone any alteration beyond resizing, or cropping. We did not find evidence of more active alterations, which would have indicated intentional manipulation for purposes of deception. For these reasons, we believe that [REDACTED] actions do not represent research misconduct, and thus she should not be named as a co-respondent.

**Allegation 2.** The Respondent falsified research data reported in Figures 2b, 4a, 4b and/or 4c in a journal article in *Oncogene*, titled "Knockdown of astrocyte-elevated gene-1 inhibits prostate cancer progression through upregulation of FOXO3a activity" (vol. 26, pp. 7647-7655), published in 2007.

**Authors:** N. Kikuno, H. Shiina, S. Urakami, K. Kawamoto, H. Hirata, Y. Tanaka, R.F. Place, D. Pookot, S. Majid, M. Igawa and R. Dahiya

**Grant funding:** This study was supported by grants RO1CA101844, RO1AG021418, RO1CA108612, RO1CA111470 and T32DK07790 from the NIH, VA REAP award, Merit Review grants and Yamada Science Foundation. The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

The Committee reviewed the analytical methods and findings of the Investigation Committee for this figure in detail. It unanimously agreed that there were numerous points of high similarity (defined as congruent points of morphology and/or patterns of intensity of bands and surrounding artifacts) between the images in Figure 2B. Furthermore, the Committee unanimously agreed that the images likely originated from the same blot and were apparently duplicated in separate locations to falsely represent data derived from different experimental conditions. Similarly, the Committee unanimously agreed that the above images in Figure 4 likely originated from the same blot and were apparently duplicated in separate locations to falsely represent data derived from different experimental conditions.

The allegations were reviewed with the Respondent on 3/25/15, and with co-author Dr. Y. Tanaka on 6/18/15. Both individuals stated that the first author, [REDACTED] was responsible for the producing the figures and the writing of this paper question (Tanaka interview, p. 18, lines 4 & 5). [REDACTED] was reported to have returned to Japan in the late 2000's. The Respondent initially indicated he had some contact with [REDACTED] (Respondent interview with Inquiry Committee transcript 9-17-14, p17-18 lines 25, 2-7; transcript of 3-25-15, p22, 23 lines 7-25, 1-7; p70-71, lines 13-25, 1). The Respondent did not provide any original data for analysis by the Committee. He did submit a densitometric analysis of the figures in question to the Inquiry Committee, which was performed on the same images that had been published, i.e., an analysis of the images that were alleged to be manipulated. This analysis found differences between the measured "densities" of bands in question, which was purported to show that bands were not derived from the same source. However, the Committee found this report unconvincing, since 1) given the apparent extent of manipulation, with changes in size, overall shape and intensity of the bands, an analysis performed on these images would not be expected to show the bands to be identical, 2) the Respondent's analysis did not account for the high degree of similarity of band morphology (overall shape, internal structure and placement of artifacts), and 3) densitometry is subject to variability depending on the placement of the region-of-interest relative to the bands, which may further contribute to observed differences.

We also found some of these manipulated images in a file entitled "Nobu\_CAN-06-4706\_1.pdf" (attached)," located on a laboratory computer drive assigned to Dr. Tanaka. It was unclear whether this manuscript (presumably authored by [REDACTED] had ever been submitted to a journal, and Dr. Tanaka did not recall it being on his drive. We could not find a similar publication by the Respondent, when searched on PubMed. This file did not contain a title page, but included an introduction, materials and methods, results, discussion, references, figure legends and figures, indicating it was a draft of a manuscript for publication. The topic was astrocyte-elevated gene-1 effects on NFkappaB, which was only briefly touched on in the paper that is the subject of this allegation. In this manuscript, Fig 3A, in the p50, IkappaBalpha, p-IkappaBalpha lanes contained numerous duplicated and mirrored bands, said to represent different experimental conditions. Many of these bands were identical to bands in the above published paper, and are said to represent different gene products. In addition, the EF1alpha lane contained numerous repeated bands, which were identical to those in the published paper.

Overall, the committee concluded that the above extensive manipulation and misrepresentation of data could not have occurred by accident, but instead, could have only been done intentionally. Thus, these figures contain clear evidence of data fabrication or falsification, and thus are instances of research misconduct. However, the preponderance of evidence did not indicate that the Respondent himself was responsible for this misconduct. The committee felt it was unlikely that he participated in, endorsed, or would have been aware of these manipulations. Given the testimonies of the Respondent and Dr. Tanaka indicating that the first author ([REDACTED] was responsible for the preparation of the manuscript and figures of this paper, and finding of similar manipulations in an ostensibly unpublished manuscript, the committee considered whether [REDACTED] could be held responsible for this misconduct. However, after substantial deliberation, the Committee found there was insufficient specific evidence to firmly establish the role of [REDACTED] in preparing the figures in question. With a view towards addressing these issues, the Committee made repeated attempts to reach [REDACTED] in Japan (as discussed above), but was unable to locate him. Thus, the Committee could not establish who was responsible for this research misconduct.

**Allegation 3:** The Respondent falsified research data reported in Figure 1B in a journal article in *Clinical Cancer Research*, titled "Polymorphisms of the CYP1B1 gene as risk factors for human renal cell cancer" (vol. 10, pp. 2015-2019), published in 2004, and/or Figure 1B in a *Cancer Research* journal article, titled "CYP1B1 gene polymorphisms have higher risk for endometrial cancer, and positive correlations with estrogen receptor  $\alpha$  and estrogen receptor  $\beta$  expressions" (vol. 63, pp. 3913-3918), published in 2003.

**Authors:** M. Sasaki, Y. Tanaka, S.T. Okino, M. Nomoto, S. Yonezawa, M. Nakagawa, Seiichiro Fujimoto, N. Sakuragi, and R. Dahiya

**Grant funding:** NIH Grants RO1AG016870 and RO1AG21418, an award from the Veterans Affairs Research Enhancement Award Program, and Grant-in-Aid 13220016 from the Ministry of Education, Science, Sports, Culture, and Technology, Japan (S. Yonezawa).

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

The Investigation Committee reviewed in detail the analytical methods and findings of the Inquiry Committee. It unanimously agreed that there were numerous similarities between the figures in question, including the location and shape of streak and spot artifacts, as well as

band morphologies were noted. This was concluded by the Committee to support the allegation of data falsification or fabrication and research misconduct.

The Committee reviewed these allegations with the Respondent on 3/25/15, and with co-author Dr. Y. Tanaka on 6/18/15. The Respondent and Dr. Tanaka agreed that the first author, [REDACTED] was responsible for constructing the figures in question. (Respondent interview with Inquiry Committee transcript of 3-25-15, p. 28 lines 20-25; p. 29 lines 1-12; Tanaka interview of 6-18-15, p. 12 lines 8-17). The Respondent stated that he thought that [REDACTED] was "...not any more in the science business" and that he had "...made an attempt to get a hold of him...but couldn't..." (Respondent interview with Inquiry Committee transcript of 3-25-15, p. 30 lines 12-15). These same allegations were sent to the Journal editor, and the Respondent provided us with his correspondence with the editor. However, this correspondence did not contain any direct discussion or refutation of the allegations. The Respondent further stated: "These are all genotyping study. You can take from any part from any patients. You get the same. These are representative figures how the band pattern looks like. It just the same pictures, how they are polymorphic. ...and then when I respond to them, they -- they dropped the allegation (transcript of 3/25/15, p. 28, lines 4-9)."

It was determined by the Inquiry Committee that several of the figures in question, alleged to be manipulated images from the same source rearranged and relabeled in the two publications, were first published in a third publication, "Polymorphisms of the CYP1B1 gene have higher risk for prostate cancer", Biochemical and Biophysical Research Communications 296 (2002) 820–826, Authors, Y. Tanaka, M. Sasaki, M. Kaneuchi, H. Shiina, M. Igawa and R. Dahiya. Dr. Tanaka stated that, despite his position as first author on that paper, all of the figures were made by [REDACTED] ("I did not make those figures. ... [REDACTED] was...responsible -- he was the one that actually made the figures in all three"), while he (Tanaka) had done the principal write-up of the results (transcript p. 14, line 16-18). He had no explanation for the apparent manipulations and misrepresentative labeling. Although he described [REDACTED] as "sloppyish" in his work (p. 20, line 23), he stated that he did not think [REDACTED] would deliberately fabricate data (transcript p. 21, lines 7-12 and 20 - 21). It was also noted that while the 2002 paper, for which Dr. Tanaka was the first author, did not include a representation of 'Codon 453', which was apparently not present in the targeted population, the subsequent papers, which utilized the same population, included panels labeled 'codon 453'. Dr. Tanaka suggested the possibility that another population was used to generate this data, but was unsure whether this had been done. The committee considered this possibility less likely, as the codon 453 data appeared to have been replicated from bands carrying another label.

Overall, the committee concluded that there was clear evidence of intentional manipulation and misrepresentation of the data, even though the figures were meant only to be illustrative of genotyping results. The above figures contained evidence of intentional data fabrication or falsification, and that this constituted instances of research misconduct. The preponderance of evidence did not indicate that this misconduct was performed by the Respondent. Moreover, there is insufficient evidence to implicate Dr. Tanaka or other members of the Respondent's research group.

**Allegation 4:** The Respondent falsified research data reported in Figure 2D in a journal article in Proceedings of the National Academy of Sciences USA, titled "MicroRNA-373 induces expression of genes with complementary promoter sequence" (vol. 105, pp. 1608-1613), published in 2008.

**Authors:** R.F. Place, L-C. Li, D. Pookot, E.J. Noonan, and R. Dahiya

**Grant funding:** This work was supported by the Veterans Affairs Research Enhancement Award Program (REAP), a Veterans Affairs Merit Review grant, and National Institutes of Health Grants RO1CA101844, RO1CA111470, and T32DK007790 (to R.D.).

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

The Investigation Committee reviewed Figure 2D, (E-cadherin panel, lanes 5 and 6), which was said to represent different experimental samples, and concluded that these images were actually derived from the same source data. As part of this analysis, images were magnified and color-remapped to bring out detail. The committee concluded there were numerous points of high similarity between the images, supporting the allegation of falsification. In another panel of Fig. 2D, two lanes (GAPDH panel: lanes 2 and 5) representing differing experimental conditions also appeared to be derived from the same source data. In the ORI Forensic Review of this allegation images were magnified and color-remapped to bring out detail. The Committee concurred that the two bands appeared to be mirror images of one another, based on numerous areas of similarity of band morphology and surrounding artifacts. Further analysis by the Committee led to the finding of additional data falsification, wherein a portion of the Fig. 2D GAPDH panel encompassing approximately 1.5 lanes was mirrored and added to the panel and yet another portion of this was mirrored and added. Areas of overlap were identified by overlaying mirrored, inverted partially transparent images, suggesting two mirroring and appending events, consistent with falsification.

The Committee discussed these findings with the Respondent, as well as with three former lab members and authors on this paper (██████████). The Respondent stated that, as first author, ██████████ was responsible assembling the figures for the paper (p. 41, line 24). When pressed, he stated he was "pretty sure" about this (p. 25, line 1). He also mentioned ██████████ as contributing to the research, but not specifically to figures. When asked about how the above falsifications could have occurred, the Respondent's answers were often tangential, but eventually culminated in the statement, "I don't know what happened" (p. 44, line 8).

When interviewed under oath, ██████████ confirmed that he was largely responsible for writing the paper and assembling all the figures (transcript page 8, lines 21 – 25), but could not recall who provided the images that were assembled for figure 2D (p. 9, lines 6 – 11). He described the generation of data and figures, as well as the writing of the paper, as a collaborative process. He could not recall, however, who generated the image used in panel 2D. He did state that it was likely that he assembled the figure, using images collected either from his own work, or that of other lab members. He did not think the Respondent was involved in assembling this figure, though could not exclude that in the passing of the figures among lab members for review, someone could have made modifications.

The Committee also interviewed ██████████ co-author and spouse, ██████████. She also described the research as a collaborative process, where data was gathered from a number of people in the lab. She did not know who prepared Figure 2D, but was puzzled that the data in question was fabricated. She recalled that measuring GAPDH levels had not been technically difficult. Measuring E-cadherin had been initially technically challenging, but that the team had worked hard to resolve this problem, and had succeeded in doing so. Indeed, this had been a celebrated moment among members of the team (transcript of 9/14/2014, p. 17, lines 21 - 22). Thus, measuring these values should not have been problematic, thus obviating any need for data fabrication. As for the role of the Respondent, she could not recall any time



that he had personally made figures for manuscripts, nor had she at any time suspected him of fabricating images. She did think it was likely that the Respondent created figures for grant applications (p. 24, lines 19 – 24). She also described [REDACTED] as highly scrupulous about the accuracy of his data and as someone who was punctilious about data integrity (p. 19, lines 1-3).

The Committee chair spoke by phone on two occasions with [REDACTED] who was the second author on this paper. In a signed affidavit (attached), he specifically stated that, “I was second author on the paper by RF Place *et al.*, “MicroRNA-373 Induces Expression of Genes With Complementary Promoter Sequences”, published in the *Proceedings of the National Academy of Sciences*, Feb 5, 2008. I had no direct role in preparing the published figures. I believe that Dr. (R.) Place was responsible for the content and appearance of the final figures and manuscript. However, I do not know who provided the images or made any of the figures in this paper, including figure 2D, and I do not know Dr. Dahiya’s role in preparing this manuscript.”

No other witness provided testimony relevant to this publication. After reviewing all the available evidence, the Committee has concluded that the extensive manipulation of some of images in figure 2D could only have occurred intentionally, and that these fabricated or falsified, data represent instances of scientific misconduct. There is no evidence, however, directly linking this misconduct to the Respondent, and to the contrary, the testimony of several witnesses indicate the he did not have any direct role in the physical or electronic preparation of the images. As to who else may have been responsible for this misconduct, there is no clear suspect. Given his central role as first author, [REDACTED] would had the most control over the assembling of the figures for the manuscript. However, it is not certain who generated the images used in figure 2D, especially in view of the collaborative nature of the preparation of this paper. Thus, there is no direct evidence that [REDACTED] fabricated or falsified the data. Moreover, the Committee found [REDACTED] to be a credible witness, who seemed genuinely surprised and distressed by discovering that some aspects of the work were possibly falsified, thereby jeopardizing a publication that he thought was a significant contribution to science. For these reasons, the Committee does not believe [REDACTED] should be named as a co-respondent.

**Allegation 5.** The Respondent falsified research data reported in Figures 6A and/or 6B in a journal article in *Molecular Cancer Therapeutics*, titled “Oncogenic functions of secreted Frizzled-related protein 2 in human renal cancer” (vol. 9, pp. 1680-1687), published in 2010.

**Authors:** S. Yamaura, K. Kawakami, H. Hirata, K. Ueno, S. Saini, S. Majid, and R. Dahiya.

**Grant funding:** NIH grants RO1CA130860 (S. Yamamura, K. Kawakami, H. Hirata, K. Ueno, and R. Dahiya) and T32DK007790 (S. Saini, S. Majid, and R. Dahiya), Veterans Affairs Research Enhancement Award Program (R. Dahiya), and Veterans Affairs Merit Review (R. Dahiya).

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent’s affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

We reviewed the findings of the Inquiry Committee regarding this allegation in detail. Two panels, one from Fig 6A (GAPDH panel) and the other from 6B (GAPDH panel) (each containing 3 bands) are said to represent different experimental conditions, but in reality are derived from the same source data. The images were overlain and color remapped to bring out background detail allowing comparison based on shape and relative intensities of bands and surrounding artifacts. The Investigation Committee unanimously agreed there were there were

numerous points of high similarity between the images.

In written comments received by the Committee and dated 11/21/2014, the Respondent stated "As I responded to the committee during my interview that GAPDH for Fig 6A and 6B are the same since these experiments were run at the same time and GAPDH represents only the loading control." In his interview with the Investigation Committee (3/25/2015), the Respondent agreed that the experimental conditions were different in Fig 6A versus 6B (before and after UV irradiation) and that each separate treatment should have its own internal GAPDH control (transcript page 50, lines 9-25 and page 51, lines 1-3). He agreed the images in the publication were the same and that they should have been different. The Respondent also stated that [REDACTED] prepared these figures (transcript page 51, lines 22-25). When the respondent was asked if he had the original GAPDH images for this paper he stated, "No, I don't have it" (page 53, lines 16-20). When asked whether [REDACTED] had admitted to the Respondent to duplicating the GAPDH bands in Fig 6A and 6B the Respondent indicated that [REDACTED] had done so (transcript page 53, lines 22-25 and page 54 lines 1-3). When another coauthor of this paper, [REDACTED] was asked about this paper she told the Committee that in the Respondent's lab it was always the primary author who makes the figures (Majid transcript page 23 lines 14-25, and page 24 lines 1-21). This witness also stated that neither the Respondent nor [REDACTED] would have changed the composition of a figure (transcript page 31 lines 22-25, and page 32 lines 1-3). In her testimony about this paper, coauthor Dr. [REDACTED] Saini reiterated that it was the custom in the Respondent's lab for the primary author to put together all the figures, and that neither the Respondent nor [REDACTED] would have changed a figure (transcript page 11, lines 12-25 and page 12, line1).

The first author on this paper, [REDACTED] was interviewed by the Committee on 4/29/2015, and his statements corroborated the above testimony. This witness admitted that he had made an error in creating the figure and had duplicated the GAPDH bands by mistake (transcript page 10 lines 15-25 and page 11 lines 1-12). This witness said he had been careless (transcript page 11 line 17).

The Committee concluded, by a preponderance of the evidence, that the numerous points of high similarity between the images indicate that these panels were derived from a common source. By his own admission, [REDACTED] was responsible for producing this figure and not the Respondent. The Committee believes that [REDACTED] did not intentionally falsify the figure, but rather, his actions were a simple mistake. We therefore believe that neither the actions of the Respondent nor [REDACTED] rise to the level of research misconduct.

**Allegation 6:** The respondent falsified research data reported in Figure 6a in a journal article in *Oncogene*, titled "Promoter CpG hypomethylation and transcription factor EGR1 hyperactivate heparanase expression in bladder cancer" (vol. 24, pp. 6765-6772), published in 2005.

**Authors:** Ogishima T, Shiina H, Breault JE, Terashima M, Honda S, Enokida H, Urakami S, Tokizane T, Kawakami T, Ribeiro-Filho LA, Fujime M, Kane CJ, Carroll PR, Igawa M, Dahiya R.

**Grant funding:** This work was supported by grants RO1AG21418, T32DK07790, RO1CA1018447 and RO1TW006215 from NIH, and the VA REAP award and Merit Review grants.

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent, in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, this allegation falls within the scope of VHA Handbook 1058.02.

In figure 6a, two panels (EGR1 and heparanase panels each containing 5 lanes), representing different experimental conditions, appear to be derived from the same experimental source. When the images were magnified and compared as overlays by the Inquiry Committee, the sample DNA bands were found to be highly similar in shape and morphology. It was also noted that the bands representing PCR products of the EGR1 and heparanase transcripts should have been of different sizes (130 bp and 206 bp respectively), but instead have highly similar sizes of about 200 bps in this figure. It is not stated in the paper what primer pairs were used for these experiments, but the control G3PDH1 (376bp) can clearly be seen to migrate differently from the above PCR products. In his initial interview with the Inquiry Committee the Respondent did not address the issue of the similarity of the appearance of the gels, but stated that the observed sizes of the above transcripts reflected the limited resolving power of the gel. In written comments the Inquiry Committee received dated 11/21/2014 the Respondent stated *“EGFI and heparanase have closer MWs ranging from 130 to 206 bp that did not get well resolved on the gels. It is common that if protein does not resolve properly on gel, the closer MWs do not get much differentiated.”* The Inquiry Committee found these comments to be an inadequate explanation, because the relevant size standards used in this figure were well separated. Thus, the gel should have been able to clearly demonstrate differences in the sizes of EGFI and heparanase PCR products.

During his interview with the Investigation Committee (3/25/2015), it was pointed out to the Respondent that in Figure 6a, in addition to the morphologic similarity of the heparanase and EGR1 PCR bands, these bands should have been of different sizes, but instead, had identical electrophoretic mobilities (transcript page 55 lines 19-24). This indicated that identical or replicated sample sets were used to represent different data. The Respondent answered that if the gel had been run for a longer time there would have been a better resolution of the bands (transcript page 56 lines 2-7). The Committee pointed out that there was a separation between the 100 and 200 base pair standard marker bands, and thus there should have been a comparable separation between the heparanase and EGR1 bands. However, this was not observed. The Respondent then mentioned that the other numerous authors of this paper were no longer in his lab. He also stated that he had not been in touch with the first author [REDACTED] who left 10 or 11 years previously (transcript page 57 lines 19-22). The Respondent did not have any comment as to what may have happened to explain the anomalies with Figure 6a (transcript page 57 line 25 and page 58 lines 1-4). When questioned further the Respondent stated that the figure had been assembled in Powerpoint and shown at a lab meeting prior to publication, but that for the journal a format with better resolution would have been used (transcript page 58 lines 15-25 and page 59 lines 1-16). He was not clear as to the format or application used, and said the primary author would have assembled the figure. He was asked whether he had tried to find the original data for Figure 6. He stated that he had contacted [REDACTED] who didn't have the data or figure (transcript page 60 lines 12-22). This seems to contradict the statement above that he had not been in touch with the first author [REDACTED]. However, the Committee felt his initial answer may have been the result of the anxiety the Respondent may have felt during the interview. His answer to a question as to where [REDACTED] was now was unclear. The Respondent was asked if people working in his lab left their notebooks behind when they left the lab. He answered that they did and that the relevant notebook should still be in his possession, but that it is now lost (transcript page 61 lines 12-25 and page 62 lines 1-12). He also stated that all information in his lab is held digitally now and that he should have a digital copy of the primary data in this case, and said that those responsible for each paper would have a digital copy (transcript page 62 lines 14-25). However, the respondent could not produce any of original data for the committee, despite repeated requests. He also stated that there was no key person in his lab who was responsible for data management.

The Committee concluded, after close examination of Figure 6a, and taking into account the testimony of the Respondent and other witnesses, that the two panels in Figure 6a are nearly identical, and are likely to represent duplicate images, or two images derived from a common source. In addition, the bands identified as EGR1-related PCR products are instead likely to be PCR products of heparanase transcripts. However, the Committee could not determine whether these misrepresentations of data were done inadvertently or intentionally. It is possible that a duplicate image could have been used in error, and it is also possible that whoever assembled the figure failed to recognize that the PCR products should have migrated differently. However, it is equally possible that someone willfully misrepresented the data, for unknown reasons. Unlike some of the figures examined in other allegations, there are no features of Figure 6a that could only exist by intentional manipulation of the data. Therefore, the Committee concluded that the preponderance of evidence does not indicate that these findings are indicative of data fabrication or falsification, nor that the Respondent committed research misconduct

**Allegation 7.** The Respondent falsified research data reported in Figures 3a, 4a, 4b, 4e, and/or 5b in a journal article in the International Journal of Cancer, titled “Genistein mediated histone acetylation and demethylation activates tumor suppressor genes in prostate cancer cells” (vol. 123, pp. 552-560), published in 2008.

**Authors:** Nobuyuki Kikuno, Hiroaki Shiina, Shinji Urakami, Ken Kawamoto, Hiroshi Hirata, Yuichiro Tanaka, [REDACTED] Majid, Mikio Igawa and Rajvir Dahiya

**Grant funding:** NIH, VA REAP award, Merit Review grants; Grant numbers: RO1CA111470, T32DK007790.

The research referenced in these allegations was supported by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent’s affiliation with SFVAMC. Therefore, these allegations fall within the scope of VHA Handbook 1058.02.

The Committee examined the figures directly and using Fiji-ImageJ. In Fig 3A, showing RT-PCR results, it appeared that mirror images of the first and second lanes in the PC3 panel (CYLD treatment) were used to represent lanes 3 and 4 in that panel. Similarly it appeared that mirror images of the first and second lanes in the LNCaP panel (PTEN treatment) were used to represent lanes 3 and 4 in that panel. For the row labeled GAPDH, the same image appeared to have been used to represent two different cell lines (LNCaP and PC-3). Further image analysis of the CYLD row, PC-3 panel, in which bands were grayscale inverted, flipped horizontally and overlaid on the original image, found that the two images were entirely superimposable, indicating that that data from two experimental conditions with PC-3 cells had been used to represent data from two additional conditions. In addition, the Committee noted that the image for the PTEN treatment (LNCaP cells) appeared to be similar to the image in the CYLD row, PC-3 panel. Image analytic examination of with grayscale inversion and overlaying on the original image for the PTEN treatment (LNCaP cells) found again that the images were superimposable, indicating that data from two experimental conditions with different cell lines had been used to represent data from two additional conditions. The Committee also reviewed four lanes in GAPDH row LNCaP cells; by overlaying the relevant image panels it was concluded that different exposures of the same GAPDH blot were likely used to represent two different cell lines. Regarding figures 4a and 4b, using Image J, the Committee examined an inverted image of the SIRT1 PC-3 panel (Fig. 4a) overlain on both the SIRT1 image LNCaP panel (Fig. 4b) and the SIRT1 image PC-3 panel (Fig 4b). This provided good evidence that the three images were derived from the same blot and thus did not represent different experimental origins. In review of figure 4e, the same image appeared to have been used to represent experiments from two

different cell lines (PC-3 and LNCaP). Enlargement and false colorization of the images revealed striking commonalities, such as the shape of the protein bands and features of the surrounding backgrounds in the two pairs of bands in question; lanes 3 and 4 eIF1 $\alpha$  blot, left panel (PC-3 cell line) appear to have been duplicated as lanes 1 and 2 of the eIF1 $\alpha$  blot, right panel (LNCaP cell line). Regarding figure 5b the Committee examined enlarged and false colored versions of the PTEN and CYLD images, revealing multiple striking similarities in the shapes and internal characteristics of the DNA bands and backgrounds. The Committee concluded that the PTEN and CYLD promoter panels in the INP column are likely to have been derived from a single source.

Based on these findings, the Committee unanimously agreed that these figures contain clear evidence of manipulation and misrepresentation of the data. Given the number of such events, as well as their type (e.g., the flipping of bands), the evidence strongly indicates that these manipulations were done intentionally. In his interview with the Investigation Committee, the Respondent indicated that he had been contacted by the "International Journal of Cancer" regarding these same allegations and that "... after we provide them the data, they submit this letter that they are satisfied with the response" (Respondent interview 9-17-14 p. 32, lines 24-25, p. 33 line 1). He again noted that the first author, ██████████ was responsible for preparing the figures. He also indicated that he had contacted ██████████ who "...said he didn't have doesn't have original data. But...did not explain the allegation." (Respondent interview 3-25-15 p. 70, lines 24-25, p. 71, line 1). ██████████ could not be reached for interview.

Overall, the Investigation Committee concluded that the above figures contained multiple examples of intentional data fabrication and falsification, and thus represent instances of research misconduct. The preponderance of evidence, however, does not indicate that the Respondent committed the research misconduct, and it was unlikely that he participated in, endorsed or would have been aware of the data manipulations. Furthermore, although the testimony implicates that the first author ██████████ would have been responsible for preparing the figures, the committee found there was insufficient evidence to establish the responsibility of that individual, or to implicate other members of the Respondent's research group.

**Allegation 8:** The Respondent falsified research data reported in Figure 3A in a pre-print publication article in the Journal of Biological Chemistry, titled "Long non-coding RNA HOTAIR is targeted and regulated by miR-141 in human cancer cells," published electronically on March 10, 2014.

**Authors:** T. Chiyomaru, S. Fukuhara, S Saini, S. Majid, G. Deng, V. Shaharyary, I. Chang, Y. Tanaka, H. Enokida, M. Nakakgawa, R. Dahiya, and S. Yamamura.

**Grant funding:** NIH RO1CA130860, a Veterans Affairs Program Project and Veterans Affairs Merit Review grants.

The research referenced in these allegations was supported, in part, by the VA. Further, the research was reported, in part, by the Respondent in his capacity as a VA employee as evidenced by the reference in the article to the Respondent's affiliation with SFVAMC. Therefore, this allegation falls within the scope of VHA Handbook 1058.02.

In Figure 3A, the image in the panel labeled "HOTAIR siRNA-2" of the pre-print is identical to the image labeled "ACHN HOTAIR siRNA-1." In the final version of the paper, the latter image has been replaced.

The Inquiry Committee reviewed both the online preprint version and the final printed form, and indeed, the images appeared identical in the former. The respondent acknowledged this difference and stated that the error originated with the journal. However, this seemed to the Inquiry Committee implausible, since the figure is complex, containing multiple images, and thus

was most likely assembled by the Respondent or other members of the research group. The Inquiry Committee requested that the Respondent provide copies of his correspondence with the JBC corroborating his statement, or otherwise clarifying the circumstances by which the above duplication was detected. However, this information was not provided to the Inquiry Committee. The Investigation Committee has examined this allegation further. In written comments the Committee received dated 11/21/2014 the Respondent stated. *"This error was noticed in pre-print publication. We have already provided the committee with all the e-mails exchanged we had with the J Biol Chem publication department prior to publication of this manuscript. This error was corrected by the journal and now there are no issues in the final publication version of this manuscript."*

The Investigation Committee asked the Respondent how the error in Figure 3 had occurred (transcript page 75, lines 20-25). He stated that the JBC had made a mistake at the level of production of the galley proofs, that the Journal was contacted, leading to correction of the error (transcript page 76 lines 6-20). However, when further questioned, the Respondent said he didn't know whether the figure was sent to the Journal as separate images or whether it was assembled before being submitted. He said he would talk to [REDACTED] about this issue, and that in general, each primary author uploaded figures to a journal (transcript page 77 lines 6-23). The Respondent seemed confused as to who the first author was, stating that it was [REDACTED]. When corrected by the Committee, the Respondent said Dr. Takeshi Chiyomara (the first author) wrote and submitted the manuscript, and [REDACTED] was the senior corresponding author who picked up the mistake (transcript page 80 lines 4-16). The Committee pointed out to the Respondent that the correspondence (email) with the Journal he had forwarded to the Committee did not, in fact, discuss the error in question.

The Committee interviewed five other coauthors of this paper and questioned them about this allegation. On Guoren Deng told the Committee that he did not remember the mistake happening, was not involved in the relevant cell culture experiments, and did not remember any discussion of the error in the lab (transcript of 5/18/2015, page 10, lines 23-25 and page 11, lines 3-9). In her interview with the committee, [REDACTED] Majid stated in reply to a question about this paper that in the Respondent's lab, it was always the primary author who was involved with the preparation of the figures (transcript page 30 lines 13-22). Saini [REDACTED] when interviewed on 4/29/2015 and asked about this allegation, stated that until approached by the Committee she did not know about the corrected error. However, she said she had talked to [REDACTED] on the morning of the interview and that [REDACTED] had told her it was an error on his part that he rectified (transcript page 21 lines 6-22). Dr. Varahram Shahryari was interviewed on 5/18/2015 and told the Committee that he was not directly involved with this paper and that he did not know that Figure 3 had to be corrected for the final version (transcript page 12 lines 6-25). He stated that whenever a paper is submitted *"the first author is the one who is responsible for all these things"*. The Committee on 4/29/2015 interviewed [REDACTED]. When asked who made the mistake he stated that it was the first author, and he also said the first author detected and then fixed the mistake (transcript page 13 lines 6-23).

Despite the statements made by the Respondent that the error in the initial online version of Figure 3 was the fault of the Journal, and despite inconsistencies in other verbal evidence, the Committee concluded, by a preponderance of the evidence, that this was in all probability an honest mistake by Dr. Chiyomara or [REDACTED] and was subsequently corrected by one of these authors. The Committee believes that Dr. Dahiya was not responsible for the mistake, even though he may have misled the Committee as to who was responsible in his evidence. The Committee does not believe that Dr. Chiyomara or [REDACTED] acted

intentionally, knowingly or willfully, and that this allegation should not be considered research misconduct.

### **Summary of findings and analysis**

The Investigation Committee has concluded the following:

**Allegation 1:** The images described in the allegation are likely derived from a common source. These anomalies most likely represent either simple mistakes, or errors of experimental design, and do not represent instances of research misconduct by the Respondent, or members of his research group.

**Allegation 2:** The preponderance of evidence indicates that intentional data fabrication or falsification had occurred, thus representing instances of research misconduct. However, there is no evidence indicating that the Respondent committed research misconduct. Moreover, it is unknown who was responsible for the misconduct.

**Allegation 3:** The preponderance of evidence indicates that intentional data fabrication or falsification had occurred, thus representing instances of research misconduct. However, there is no evidence indicating that the Respondent committed research misconduct. Moreover, it is unknown who was responsible for the misconduct.

**Allegation 4:** The preponderance of evidence indicates that intentional data fabrication or falsification had occurred, thus representing instances of research misconduct. However, there is no evidence indicating that the Respondent committed research misconduct. Moreover, it is unknown who was responsible for the misconduct.

**Allegation 5:** The images in question were derived from a common source, but this duplication of images was due to an error by [REDACTED]. There is no evidence that the Respondent committed research misconduct. In addition, there is no evidence that [REDACTED] intentionally, knowingly, or recklessly duplicated the above images, and thus, did not commit research misconduct.

**Allegation 6:** The two panels in question are nearly identical, and are likely to represent images derived from a common source. However, the Committee could not determine whether these misrepresentations of data were done inadvertently or intentionally. The Committee concluded that the preponderance of evidence does not indicate that these findings are indicative of data fabrication or falsification, and that the Respondent had not committed research misconduct.

**Allegation 7:** The preponderance of evidence indicates that intentional data fabrication or falsification had occurred, thus representing instances of research misconduct. However, there is insufficient evidence that the Respondent was responsible for this misconduct. Moreover, it is unknown who was responsible for the misconduct.

**Allegation 8:** The images in question were derived from a common source, but this was done unintentionally by [REDACTED]. There is no evidence that the Respondent committed research misconduct.

## **Analysis and Recommendations**

In assessing these allegations, the Committee faced several limitations. To begin with, we were unable to interview some of the first authors of the publications under investigation, because they were no longer in the United States and could not be reached, despite our concerted and repeated efforts to do so, as discussed above (“Methods of analysis”). These individuals may have been informative witnesses, in view of their likely central role in data collection and analysis, as well as in manuscript preparation. Second, much of the research was done five or more years ago, so in some instances, witnesses were unable to recall the roles of various lab members in the research. Third, no original experimental data were available as evidence. Such information would potentially have been useful in determining how the images were generated. It was puzzling how little raw data (including images), or other relevant material (e.g., drafts of manuscripts or figures for publication) were available, especially since the Respondent stated that digital copies of data were collected beginning in 2005 (transcript page 62 lines 14-25). With few exceptions, however, we found no notebooks or files whatsoever by the first authors of these papers among the books and computers sequestered from his office and laboratory by the VA Research Service. Although the Respondent speculated in our interviews and communications that these items were lost during laboratory moves, there is no direct evidence for this occurring, and neither the former nor current ACOS for Research at the San Francisco VAMC has any record or recollection of such a loss. This absence of original data greatly limited our ability to determine whether the published images accurately represented their source data, and raised the issue for the Committee as to whether such information had been intentionally destroyed to avoid auditing. We ultimately decided that since there was a global loss of data by the laboratory, consistent with a chronic, general laxity of data management, and not a selective loss of information related to this investigation, we could not conclude that data had been deliberately destroyed. For that reason, we did not believe that the loss of data per se constituted evidence of scientific misconduct.

Notwithstanding these limitations, the Committee has extensively reviewed all the available evidence, and has interviewed all available witnesses that were likely to provide insights into the genesis of the figures in question, as well as to the research practices of the Respondent. In particular, we interviewed almost half of the first authors, at least one coauthor for seven of the eight publications, as well as the Respondent, who was senior author on every paper under investigation. In addition, we studied the forensic evidence in detail. The Committee has concluded that four of the eight allegations in question are clear instances of research misconduct. In none of these instances, however, does the preponderance of evidence indicate that the Respondent himself intentionally, knowingly, or recklessly falsified or fabricated data. As discussed above, there is no evidence that the respondent intentionally, knowingly, or recklessly, either personally or through a surrogate, manipulated the figures in question, thereby committing scientific misconduct. The Committee also specifically discussed whether the Respondent’s failure to maintain records constituted reckless misconduct. We believe that the Respondent’s behavior clearly falls below accepted practices of the research community, and that he was negligent in his duties as a laboratory director. However, there is no clear evidence that his failure to maintain research records was done with the intention or knowledge that his behavior incurred the risk of data fabrication or falsification, i.e., scientific misconduct by members of his research group. Thus, while the Respondent was careless or negligent, his actions did not meet the criteria for recklessness. In assessing the Respondent’s role, the Committee felt that the Respondent was not entirely credible in some of his testimony or response to our requests for information. For example, his explanation for the loss of data varied somewhat, and the email correspondence he provided with journals regarding possible falsified images was incomplete. However, we do not believe that these gaps in information significantly hindered our ability to analyze the evidence, nor do we believe these shortcomings



on the part of the respondent clearly reflect attempts to obstruct the investigation. Overall, while we believe there is definite evidence of research misconduct, there is insufficient evidence to conclude that he Respondent was responsible for this misconduct.

In addition, there is insufficient evidence to conclude who else was responsible for these falsifications. Aside from the Respondent, ██████████ was the most frequent individual associated with the publications (6 out of 8 papers) that are under investigation. Although he was not an author on the papers, he is uniformly acknowledged for his support and assistance with the preparation of the above six publications. When the Committee interviewed ██████████ on 5/18/2015 he stated that he routinely edited hard copies of the manuscripts, and to do this he used a red pen (transcript page 7 lines 3-8). He stated he didn't see raw data (transcript page 7 lines 15-16) and worked only on a hard copy and not on electronic files (transcript page 7 lines 21-24). ██████████ said that he looked at figures and made suggestions to improve papers (transcript page 8 lines 21-25 and page 9 lines 1-3). He said that he was fairly sure that Dr. Dahiya "would make the final decision on the paper" and he also stated that the Respondent knows how to create figures using software like Illustrator or PowerPoint, and indicated that the Respondent generated figures for research grants (transcript page 9 lines 17-25). The testimony given by ██████████ and others leads the Committee to believe that the preponderance of evidence does not show that ██████████ is responsible for any of the misconduct. ██████████ states that he was unclear as to Dr. Erickson's exact role but that "Everything kind of went through him, like your reports, your data or your manuscripts or your drafts and your figure drafts or whatever. (interview transcript p. 21, lines 7 – 12)." However, ██████████ does not recall any instance where ██████████ personally modified a figure. ██████████ described his role as strictly that of an editor, and definitely not someone who would edit figures (interview transcript p. 31, lines 1 – 25). ██████████ similarly described his role as that of an editor (Saini transcript p. 9, lines 9 – 15). Thus, the committee believes it is unlikely ██████████ would have personally altered the figures and there is no evidence from the testimony that he instructed others to falsify or fabricate data.

██████████ was first author on two of the four publications found to have evidence of scientific misconduct. A third unpublished manuscript presumably by him contained the some of the same altered images associated with the paper in allegation #2. These findings certainly link ██████████ with the misconduct under investigation. Moreover, as first author on two papers, he presumably would have been responsible for the accuracy of the publication. However, there is no direct evidence that he personally altered the figures, instructed others to do so, or was aware that the figures had been improperly modified. A number of the witnesses were directly asked about ██████████ his role in preparing figures, and whether they had any reason to suspect that he had committed scientific misconduct, while in the Respondent's lab. None of the witnesses could recall who specifically prepared the figures in the above papers, nor did any witness ever suspect ██████████ of misconduct. It is unfortunate that the committee has been unable to communicate with ██████████ despite repeated efforts to do so, since he may well have been able to provide useful information. In the absence of more direct evidence regarding ██████████ role in preparing the above publications, the committee believes that there is insufficient evidence to conclude he committed scientific misconduct.

As for the other two publications and their associated allegations, there is no direct evidence linking any of the first authors to the misconduct, beyond the central role of the first author in preparing manuscripts, as practiced in the Respondent's research group.. Unfortunately, we were unable to reach ██████████ who both moved to Japan after leaving the Respondent's lab. Given the relatively minor and often specialized roles of other authors within this research group, and the fact that many of these secondary authors were no longer in this country, the committee felt that it was unlikely these potential witnesses would offer significant

insights. We were able to interview four of the five authors associated with the 2008 PNAS paper (allegation 4). Although [REDACTED] (the first author) acknowledged that he was responsible for assembling the figures, neither he nor the other authors interviewed could recall who generated the images that were subsequently inserted in the figures. Notwithstanding his role as first author, the committee felt that [REDACTED] was a credible witness, and thus concluded that it could not determine who was responsible for the data falsification or fabrication in this paper.

In summary, the Investigation Committee has concluded that the preponderance of evidence indicates that scientific misconduct has occurred in the research described in allegations 2, 3, 4, and 7. There is insufficient evidence to conclude that the Respondent was responsible for this misconduct. Although it is highly likely that one or more members of his research group committed the above research misconduct, there is not sufficient evidence to implicate specific individuals. The Investigation Committee does recommend the following corrective actions:

1. The editorial offices for papers 2, 3, 4, and 7 should be notified that these publications contain instances of data fabrication or falsification, and should thus be assessed for correction or retraction.
2. The Respondent should develop a systematic, comprehensive approach for data storage, including the archiving of original data, images, and laboratory notebooks. This should meet or exceed current VA standards for data integrity.
3. The Respondent should implement formal training in scientific integrity for the members of his research group, under the guidance of the local Research Integrity Officer (RIO). Since no single individual was clearly responsible for this misconduct, it is likely that the instances of misconduct described in the four allegations represent the actions of multiple individuals over a period of years. This suggests that the research environment in the Respondent's lab does not adequately foster or oversee ethically sound scientific practices.
4. The Respondent should also implement a plan for periodically auditing the scientific integrity of the work done in his laboratory, under the guidance of the local RIO.

The Committee believes these actions will be important both for correcting the scientific record, and for reducing the likelihood of future misconduct in the Respondent's laboratory.

**From:** [Dahiya, Rajvir](#)  
**To:** [Holleran, Walter M.](#)  
**Cc:** [Nissenson, Robert A.](#)  
**Subject:** RE: Correspondence - Confidential  
**Date:** Monday, November 14, 2016 11:37:39 AM

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Hi Walter and Bob:

I have nothing to add to this report.

Thank you  
Raj Dahiya

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**From:** Holleran, Walter M.  
**Sent:** Monday, November 14, 2016 10:01 AM  
**To:** Dahiya, Rajvir  
**Cc:** Nissenson, Robert A.  
**Subject:** RE: Correspondence - Confidential

Hi Raj,  
Please note that you have until Nov 23 to respond in writing to the draft initial report that was provided to you on Oct 24.  
Thanks very much,  
Walt

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**From:** Dahiya, Rajvir  
**Sent:** Monday, October 24, 2016 5:28 PM  
**To:** Holleran, Walter M.  
**Cc:** Nissenson, Robert A.  
**Subject:** RE: Correspondence - Confidential

Hi Walter

Thank you so much for your information

Raj Dahiya

---

**From:** Holleran, Walter M.  
**Sent:** Monday, October 24, 2016 5:26 PM  
**To:** Dahiya, Rajvir  
**Cc:** Nissenson, Robert A.  
**Subject:** RE: Correspondence - Confidential

Thanks Raj.  
Please note any response will be due on or before November 23 so that it can be included into the Final report provided to ORO.  
Walt

---

**From:** Dahiya, Rajvir  
**Sent:** Monday, October 24, 2016 5:20 PM  
**To:** Holleran, Walter M.  
**Cc:** Nissenson, Robert A.  
**Subject:** RE: Correspondence - Confidential

Hi Walter:

I received the folder and I will let Bob know if I have any question.  
Thank you

Raj Dahiya

---

**From:** Holleran, Walter M.  
**Sent:** Monday, October 24, 2016 4:43 PM  
**To:** Dahiya, Rajvir  
**Subject:** RE: Correspondence - Confidential

Hi Raj,  
Were you able to access the folder and documents? Please confirm by reply email.  
Thanks,  
Walt

---

**From:** Holleran, Walter M.  
**Sent:** Monday, October 24, 2016 11:20 AM  
**To:** Dahiya, Rajvir  
**Cc:** Nissenson, Robert A.  
**Subject:** Correspondence - Confidential  
**Importance:** High

Dear Dr. Dahiya,

With respect to the ongoing Research Misconduct Investigation, as we discussed earlier today, you can find the draft Investigation Report in a secure folder (named "RD Secure") on the VA Research R-drive located here ([RD Secure](#)). Please open this folder to insure that you can access all of the files contained therein, including the Investigation Committee Report, as well multiple Attachments (3) and Exhibits (16), as well as lists of these Attachments and Exhibits.

According to the VA process governing this investigation, you now will have 30 calendar days to provide a response to this draft report in the form of a letter to the Research Integrity Officer (RIO), Dr. Nissenson. Any response that you provide will become part of the official final Investigation Report that will be forwarded to the VA Office of Research Oversight (ORO).

If you find that you have no response to the report, please inform Dr. Nissenson of this. If Dr. Nissenson does not receive a response from you within 30 calendar days, he will conclude that you do not wish to provide a response to the Investigation Committee Report.

Please acknowledge your receipt of this message, as well as your ability to access the files noted above, by return email.

Thank you for your understanding and cooperation.

Sincerely,

Walt

\*\*\*\*\*

**Walter M. Holleran, M.A., Pharm.D.**

Director of Research Operations

Research & Development, San Francisco VA Health Care System

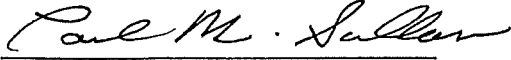
Professor, Dermatology & Pharm Chem, UCSF

Office: (415) 221-4810 ext. 2-2118

VA Cell: (415) 559-9517

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

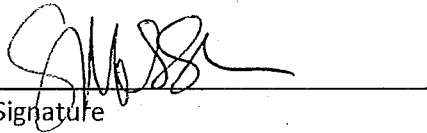
**Paul Sullam, MD**



Signature

12-1-2016  
Date

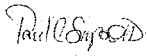
**Stephen Massa, MD**



Signature

12-5-2016  
Date

**Paul Simpson, MD**



Digitally signed by Paul C Simpson Jr MD  
DN: cn=Paul C Simpson Jr MD, o, ou=San Francisco WAMC and UCSF,  
email=paul.simpson@ucsf.edu, c=US  
Date: 2016.12.05 11:21:15 -08'07

Signature

12-5-16  
Date

**Kewchang Lee, MD**

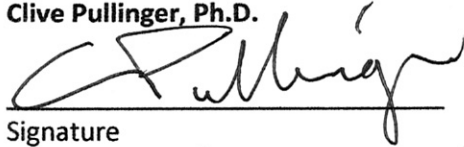


Signature

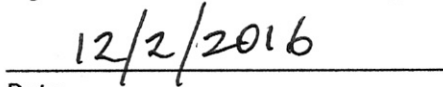
12/1/16  
Date

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

**Clive Pullinger, Ph.D.**

A handwritten signature in black ink, appearing to read 'Clive Pullinger', written over a horizontal line.

Signature

A handwritten date '12/2/2016' written in black ink over a horizontal line.

Date

## SFHCS Director's Certification Statement

**Date:** December 20, 2016

**Summary:** The Research Misconduct Investigation Committee concluded that “the preponderance of evidence indicates that scientific misconduct occurred in the research described in allegations 2, 3, 4, and 7.” Importantly, the Committee indicated that “there is insufficient evidence to conclude that the Respondent was responsible for this misconduct.” In addition, the Committee indicated that “Although it is highly likely” that one or more members of the Respondent’s research group committed the above research misconduct, there was “not sufficient evidence to implicate specific individuals”.

**Recommendations:** The Investigation Committee recommended the following four (4) corrective actions to be important both for correcting the scientific record, and for reducing the likelihood of future misconduct in the Respondent’s laboratory:

1. The editorial offices for papers 2, 3, 4, and 7 should be notified that these publications contain instances of data fabrication or falsification, and should thus be assessed for correction or retraction.
2. The Respondent should develop a systematic, comprehensive approach for data storage, including the archiving of original data, images, and laboratory notebooks. This should meet or exceed current VA standards for data integrity.
3. The Respondent should implement formal training in scientific integrity for the members of his research group, under the guidance of the local Research Integrity Officer (RIO). Since no single individual was clearly responsible for this misconduct, it is likely that the instances of misconduct described in the four allegations represent the actions of multiple individuals over a period of years. This suggests that the research environment in the Respondent’s lab does not adequately foster or oversee ethically sound scientific practices.
4. The Respondent should also implement a plan for periodically auditing the scientific integrity of the work done in his laboratory, under the guidance of the local RIO.

### Certification:

- *As Director of the San Francisco Health Care System, I hereby certify the Final Report of this Investigation Committee (dated 12.05.2016).*
- *I concur with each of the four corrective actions recommended by the Investigation Committee (as above).*
- *As it has been determined that there was research misconduct, I would recommend the following additional actions:*
  - a. Report to Journals and funding agencies the erroneous figures in publications.
  - b. Require laboratory members to take Scientific Integrity Training.
  - c. Require laboratory involved to save experimental data as is standard practice.
  - d. Inform Chair of Urology at UCSF of the issues.
  - e. Look into issue of destruction of prior data.
  - f. Review the suitability of the Respondent to function as a PI and/or to supervise research at the VA.

BONNIE S  
GRAHAM 132060

Digitally signed by BONNIE S GRAHAM 132060  
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**Bonnie S. Graham, M.B.A.**

Director, San Francisco VA Health Care System (662)