

Memorandum

Date: January 4, 2021
From: Research Misconduct Inquiry Committee
Subj: Inquiry into an Allegation of Research Misconduct
To: Bonnie S. Graham, Director, San Francisco VA Health Care System (Facility #662)

1. The San Francisco VA Medical Center (SFVAMC) Research Misconduct Inquiry Committee has completed its inquiry as directed by your memorandum, dated October 5, 2020 (hereafter, “**appointment letter**”) (Attachment A).

2. **Preliminary Statement/Background Information**

- a. As indicated in the appointment letter (Attachment A), the Inquiry Committee was convened to conduct an inquiry into an allegation of research misconduct in connection with research carried out by [REDACTED] (Assistant Professor of Urology, University of California, San Francisco and WOC employee, San Francisco VA Health Care System) and Dr. Rajvir Dahiya (Professor of Urology, University of California, San Francisco and Research Career Scientist at the San Francisco VA Health Care System) (hereafter, “**Respondents**”), both members of the SFVAMC Urology Research Unit. The specific allegation arises in connection with a paper they published in *Cellular Physiology and Biochemistry* (2020) 54:53-70, where an anonymous complainant discovered and reported that partially overlapping duplicate images were presented in Figure 1C that were falsely purported to represent two different cell lines. Based on this duplication, it was alleged that the authors presented falsified data (hereafter, “**allegation #1**”).
- b. The aforementioned allegation was received by the SFVAMC Research Integrity Officer (RIO; Dr. Robert Nissenson) on August 28, 2020 from an anonymous source. The allegation was subsequently forwarded to the VHA Office of Research Oversight (ORO). As indicated in a memorandum, dated September 23, 2020, the RIO determined that the allegation met the requirements of VHA Directive 1058.02 (“Research Misconduct”) Appendix A §4.d.(1) for opening a research misconduct inquiry (Attachment B).
- c. The research referenced in allegation #1 was supported by VA Research funded by the Department of Veterans Affairs (Program Project Award BX001604 and Merit Review Awards); by the NIH (grants RO1CA196848, RO1CA138642, RO1CA160079, RO1CA199694 and UO1CA184966); and by the Astellas Foundation for Research on Metabolic Disorders fellowship funded by Astellas Pharma, Inc., and was conducted in SFVAMC research laboratory space assigned to the Respondents. The research was reported, in part, by the Respondents in their capacity as VA employees as evidenced by the reference in the *Cellular Physiology and Biochemistry* journal article to the Respondent’s affiliation with SFVAMC. Therefore, allegation #1 falls within the scope of VHA Directive 1058.02.
- d. The University of California, San Francisco (UCSF) has concurrent jurisdiction over allegation #1 referenced above based on the fact that the Respondents are UCSF faculty

members and at least one of the grants supporting the work in question was administered by UCSF. UCSF jointly participated in the inquiry, which was led by SFVAMC in accordance with the procedures of VHA Directive 1058.02. A representative from UCSF, Dr. Stephen Massa, a Professor of Neurology at UCSF, was appointed to, and served on, the Inquiry Committee. As such, this report represents a joint Inquiry Report of SFVAMC and UCSF.

- e. The research misconduct inquiry was conducted in accordance with VHA Directive 1058.02, and convened for the sole purpose of determining whether the allegation referenced above has sufficient substance to warrant opening a formal investigation. As indicated in the Directive, a research misconduct allegation is deemed to have “sufficient substance” if the inquiry determines that the readily available evidence would raise a reasonable suspicion of research misconduct.
- f. In conducting the inquiry, the committee reviewed the readily available evidence (see Index of Evidentiary Exhibits) and interviewed the Respondents. The committee was unable to interview the individual(s) who submitted the allegation because the allegation was submitted anonymously.

Due to difficulties in accommodating the schedules of the Respondent and the Inquiry Committee members, as well as the amount of documentary evidence that needed to be reviewed and analyzed, the SFVAMC Director sent a memorandum, dated December 1, 2020, to ORO requesting an extension of the 60-day time limit for conducting the inquiry (Attachment C). The requested extension was granted by ORO on December 8, 2020 (Attachment D).

3. Based on a review of the evidence, including testimonial evidence provided by the Respondents, the Inquiry Committee’s recommendations for the allegation and the basis for said recommendations are as follows:

- a. **Allegation #1:** The Respondents falsified cell line data published in Figures 1c in a *Cellular Physiology and Biochemistry* journal article, titled “Genistein Represses HOTAIR/Chromatin Remodeling Pathways to Suppress Kidney Cancer” (vol 54(1): pages 53-70), which was published in 2020.

With regard to Figure 1c (Exhibit #1, *Cellular Physiology and Biochemistry* journal article), it was alleged that the micrographs showing experimental effects of genistein on two purportedly distinct renal cancer cell lines (786-O and ACHN) were images sampled from partially overlapping area. Figure 1c shows cell line 786-O on the left, and cell line ACHN on the right, yet the micrographs shown for each of these distinct cell lines contain substantial areas where the images are identical, suggesting that they were derived from a single parent micrograph.

The committee reviewed Figure 1c, and with the aid of image stitching software (Hugin), confirmed that the micrographs purporting to represent experimental effects in two distinct cell lines were in fact overlapping sub-section images taken from a single larger micrographic field.

The committee was unable to obtain the original data for the underlying experiments that were purportedly the source of the research reported in the figure. However, the committee did have access to the folders containing the micrographic images taken by the first author (██████████) organized by cell line and treatment conditions. Data from two folders from the Respondent’s computer were reviewed, again with the aid of image stitching software (Hugin), the committee determined that most of the images in the folder labeled as containing ACHN cell line data were duplicates of those in a folder

labeled as containing 786-O cell line data, suggesting possible mislabeling of images at the time images were acquired.

Prior to meeting with each of the Respondents for interviews, the committee received notice from [REDACTED] that they had discovered a labeling error leading to inclusion of the incorrect micrographic image in Figure 1c, and that he had notified the journal editors and published an Erratum (Exhibit #3: Cellular Physiology and Biochemistry (2020): Erratum). The Erratum states:

“In the original article by [REDACTED] et al., entitled “Genistein Represses HOTAIR/Chromatin Remodeling Pathways to Suppress Kidney Cancer” [Cell Physiol Biochem 2020;54(1):53-70, DOI: 10.33594/000000205], a mistake has been made during the compilation of the data for the representative images of migrated cells in Figure 1C. The authors confirm that all of the results and conclusions of the article remain unchanged, as well as the figure legend. The authors sincerely apologize for this mistake.

Additionally, there has been a change in authorship; Rajvir Dahiya is no longer co-author. All authors agree with this change.

The corrected title section of the paper and the corrected Fig. 1 are displayed below.”

The committee met with [REDACTED]. He clarified in the interview that the research supporting the publication was done in his laboratory at the SFVAMC, principally by the first author [REDACTED] and himself, with collaborative roles for others on the author list. He confirmed that both cell 786-O and ACHN cell lines were used in the study, and that while there was a mislabeling of micrographic images chosen to illustrate representative effects, there was no mislabeling of the data used in the quantitative analyses, and that the scientific results and conclusions remain valid. This was simply an honest error in mislabeling of the micrographic images chosen to represent the cell lines and effects. [REDACTED] further explained that the camera used at the time to capture images of cell line micrographs did not have a way to automate or systematize the naming of image files as they were captured. Cameras now used in the lab do not suffer from this limitation, allowing labeling of the images at the time they are taken. [REDACTED] explained that the first author would have kept a list of the images in a separate text document or notepad as they were being taken to keep track of their numeric order and the conditions to which they corresponded.

The committee asked [REDACTED] to contact the first author [REDACTED] to provide the original images, as well as notes from [REDACTED] indicating how the numeric labeling of the micrograph images was mapped onto cell line and experimental condition. These were received and reviewed by the committee, and it was concluded that the documentation of the micrograph image capture order looked reasonable. Furthermore, using image stitching software as before, the committee confirmed that the ACHN cell line images lined up with prior images, whereas the newly provided 786-O images did not overlap with any of the prior images nor amongst themselves, consistent with their origin in a separate group of 786-O images.

The committee asked [REDACTED] to provide a complete list of all of the published study's co-authors and their specific roles on the projects. [REDACTED] supplied this list and, after review by the committee, was deemed reasonable. When asked, [REDACTED] did not know why Dr. Dahiya had requested to be removed from the author

list of the published paper, which was instantiated at the time the journal published the Erratum.

On a separate occasion, the committee interviewed Dr. Dahiya. He denied any detailed knowledge of the labeling errors that led to duplicate images being labeled as distinct cell lines in Figure 1c of the paper on which he was listed as a co-author. The work was done in [REDACTED] lab, not his lab. Although he'd helped to design the study, he chose to have his name removed from the paper because he did not want his name associated with any further controversy (he acknowledged that he'd been subjected to a prior inquiry at the SFVAMC) and did not need this publication at this point in his career. He is not questioning the scientific accuracy of the results presented in the paper.

Based on a review of the images and interviews with the Respondents, the committee believes that an honest error in labeling the image files during the preparation of Figure 1 led to inclusion of partially duplicate images. No evidence of deliberate falsification of data was found. The Respondent [REDACTED] has now published an Erratum acknowledging the error, apologized for it, and provided an updated corrected figure (Exhibit 2). Accordingly, **the Inquiry Committee believes that allegation #1 does not have sufficient substance to warrant an investigation.**

4. **In summary, the Inquiry Committee recommends that allegation #1 be dismissed.**

If you have any questions about this report, please contact the Inquiry Committee Chairperson, Daniel H. Mathalon, Ph.D., M.D., by telephone or by email at your earliest convenience.

<Please see attached Signature page(s)>

Daniel H. Mathalon, Ph.D., M.D.; Inquiry Committee Chairperson

<Please see attached Signature page(s)>

Gary Cecchini, Ph.D.; Inquiry Committee Member

<Please see attached Signature page(s)>

Stephen Massa, M.D., Ph.D.; Inquiry Committee Member

cc: Research Integrity Officer, SFVAMC (123/151)
Research Integrity Officer, UCSF
Research Misconduct Officer, ORO (10R)

INDEX OF EVIDENTIARY EXHIBITS

Exhibit Number	Description	Source
1	<i>Cellular Physiology and Biochemistry</i> journal article, titled “Genistein Represses HOTAIR/Chromatin Remodeling Pathways to Suppress Kidney Cancer” (vol 54(1): pages 53-70), which was published in 2020	<i>Cellular Physiology and Biochemistry</i> journal website (https://www.cellphysiolbiochem.com/Articles/000205/)
2	Figures generated using Hugin image stitching software documenting overlap between sections of micrographic images labeled as belonging to different cell lines.	Dr. Massa from the Inquiry Committee generated these figures from his analysis of the micrographic image files stored on ██████████ research drive folder.
3	Erratum for <i>Cellular Physiology and Biochemistry</i> journal article, titled “Genistein Represses HOTAIR/Chromatin Remodeling Pathways to Suppress Kidney Cancer” (vol 54(1): pages 53-70), which was published in 2020	<i>Cellular Physiology and Biochemistry</i> journal website (https://www.cellphysiolbiochem.com)
4	Notes from ██████████ showing records of image files acquired during microscopic imaging of cell-line slides.	Provided to Interview committee by Respondent, ██████████

INDEX OF ADMINISTRATIVE ATTACHMENTS

Attachment	Description	Source
A	Inquiry Committee Appointment Letter, dated October 5, 2020	SFVAMC Director
B	RIO-issued memorandum, dated September 23, 2020, indicating that the submitted allegation met the requirements for convening a research misconduct inquiry	SFVAMC RIO
C	Memorandum, dated December 1, 2020, requesting an extension of the deadline for completing the inquiry	ORO
D	Memorandum, dated December 8, 2020, approving the SFVAMC Director's December 1, 2020, request for an extension of the deadline for completing the inquiry	SFVAMC Director

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

Dan Mathalon, PhD, MD

Daniel H.
Mathalon 262972

Digitally signed by Daniel
H. Mathalon 262972
Date: 2021.01.04
16:06:30 -08'00'

Signature

January 4, 2021

Date

Stephen Massa, MD, PhD

Signature

Date

Gary Cecchini, PhD

Signature

Date

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

Dan Mathalon, PhD, MD

Signature

Date

Stephen Massa, MD, PhD



Digitally signed by Stephen
M. Massa 347002
Date: 2021.01.04 14:13:13
-08'00'

Signature

January 4, 2021

Date

Gary Cecchini, PhD

Signature

Date

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

Dan Mathalon, PhD, MD

Signature

Date

Stephen Massa, MD, PhD

Signature

Date

Gary Cecchini, PhD

Gary L. Cecchini
507553



Digitally signed by Gary
L. Cecchini 507553
Date: 2021.01.04
15:26:57 -08'00'

Signature

January 4, 2021

Date