DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Research Integrity
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CONFIDENTIAL/SENSITIVE

October 18, 2022

Belinda Adamson, B.S., M.Ed., CIP, CCRC
Research Integrity Officer
Director, Office of Research Compliance
Central Michigan University
1200 S. Franklin Street
Mount Pleasant, MI 48859

TRANSMITTED VIA EMAIL TO: adams1bs@cmich.edu

RE: DIO 7758

Dear Ms. Adamson:

The Division of Investigative Oversight (DIO), Office of Research Integrity (ORI), has received allegations of possible research misconduct against Panchanan Maiti, Ph.D., Adjunct Faculty, Central Michigan University (CMU), and Gary L. Dunbar, Ph.D., Director, Program in Neuroscience, CMU. The respondents allegedly falsified data included in a published paper (cited below). The questioned research was supported in part by U.S. Public Health Service (PHS) funds, specifically National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), grant K22 HL113045.[1]

The allegations involve apparent reuse and relabeling of histological images in the following PHS-supported published paper:

- Maiti P, Manna J, Burch ZN, Flaherty DB, Larkin JD, Dunbar GL. Ameliorative Properties of Boronic Compounds in In Vitro and In Vivo Models of Alzheimer's Disease. *Int J Mol Sci.* 2020 Sep 11;21(18):6664. doi: 10.3390/ijms21186664 (hereafter referred to as "*Int J Mol Sci*. 2020").

[1]K22 HL113045, "Multi-scale Simulations of Bronic Acids in Proteasome Inhibition and Saccharide," Joseph D. Larkin, Ph.D., Principal Investigator (P.I.), Funded Project Dates: April 10, 2014-January 31, 2019.

The respondents allegedly falsified data in *Int J Mol Sci*. 2020 by reusing and relabeling images of histological and immunofluorescent staining of mouse cortex and hippocampal sections to represent different tissues and conditions.[2] Specifically:

- a subfield of an image representing hippocampal tissue from 6-month-old 5xFAD mice without treatment (column 2, row 2) also was used to represent hippocampal tissue from 12-month-old wildtype (WT) mice treated with trans-beta-styryl-boronic acid (TBSA) (column 8, row 3) in Figure 4A

- a subfield of an image representing the cortex of 6-month-old WT mice (column 1, row 1) also was used to represent the cortex of 12-month-old WT mice (column 5, row 1) in Figure 5A

- an image representing hippocampal tissue from 6-month-old 5xFAD mice treated with TBSA (column 3, row 2) also was used to represent hippocampal tissue from 12-month-old 5xFAD mice treated with TBSA (column 7, row 2) in Figure 5A

- a subfield of an image representing microglial activation in hippocampal tissue from 6-month-old 5xFAD mice treated with TBSA (column 2, row 3) also was used to represent hippocampal tissue from 12-month-old 5XFAD mice treated with TBSA (column 6, row 3) in Figure 6A

Since the questioned data concern a published paper that was supported by PHS funds, ORI has jurisdiction in this matter. There is no presumption of wrongdoing. However, the allegations require a prompt and thorough assessment to determine whether further action is necessary. Therefore, DIO requests that CMU conduct an inquiry, in accordance with § 93.307.

DIO notes that the respondents are authors on seven (7) additional papers with data concerns.[3] CMU should review these additional concerns and establish whether the questioned research was conducted at CMU and utilized PHS funds. If so, CMU should include these allegations as part of its inquiry. If CMU determines that the questioned research was conducted at another institution(s), CMU should refer the allegations concerning those papers to the appropriate institution(s) for assessment.

In an attempt to help you and the inquiry committee review the issues in a way that will be fully compliant with ORI's requirements for oversight review, DIO has listed some of the specific issues relevant to the PHS interest in this case. Specifically:

1. As required by § 93.305(a), institutions must sequester evidence either **before** or when the institution notifies the respondent of the allegation, inquiry or investigation. ORI emphasizes that this timing of the sequestration process prior to notification of the respondent is critical for ensuring the integrity of the research record and other relevant evidence.

[2] https://pubpeer.com/publications/F3E5381765723A129BEB2093A4C7B2

[3] https://pubpeer.com/search?q=Panchanan+Maiti+Gary+Dunbar

As required by § 93.307(b) and § 93.310(d), CMU must take all reasonable and practical steps to obtain custody of all of the research records and evidence needed to conduct the research misconduct proceeding during the inquiry, inventory the records and evidence, and sequester them in a secure manner. If additional items become known or relevant to the inquiry or subsequent investigation, please take appropriate steps to properly sequester and obtain the evidence. Instructions for Submitting Electronic Records to ORI are enclosed with this letter for your convenience.

2. CMU should pursue diligently all significant issues and leads discovered that are determined relevant to the inquiry or subsequent investigation (per § 93.310(h)), including any evidence of additional instances of possible research misconduct, such as in other papers published or manuscripts submitted but not accepted for publication by the respondents, submitted or awarded PHS grant applications, progress reports, posters, presentations, and other research records, subject to the time limitations stated in § 93.105. ORI has issued a notice of information about the scope of research misconduct in institutional proceedings[4] and provided several hypothetical case examples for reference.[5] In accordance with § 93.310(c), an institution must give the respondent written notice of any new allegations of research misconduct within a reasonable amount of time of deciding to pursue allegations not addressed during the inquiry or in the initial notice of investigation.

3. The allegations should be re-framed to ensure that there is sufficient information to identify the issues that concern PHS under its definition of research misconduct and CMU's analysis conducted during the inquiry and/or subsequent investigation to support a finding of research misconduct. The re-framed allegations should address who (one specific respondent), did what (falsified/fabricated/plagiarized), where (publications, grant applications, research records), and specifically how (duplicated, cut and pasted, altered, etc.). For example:

    - Allegation 1: Respondent (falsified/fabricated/plagiarized) Figure (#) in (publication/grant application/document) by doing "X."

      "X" should describe the specific falsification/fabrication, such as "by using the same data panel in Figure # of publication X, when the figure represented results from different experiments." If the false figure was used in another figure, state the figure number and the publication or grant application number involved.

4. The prospect of more than one researcher being responsible for the alleged should be considered. Notably, the P.I., laboratory members, and coauthors who were involved in generating the primary data or creating the figures in the published paper should be considered as respondents in the inquiry. If any additional respondent(s) are identified throughout the research misconduct proceedings, including an investigation, they are to be notified of the allegations, in accordance with § 93.307(b), § 93.308(a), and § 93.310(c).

[4] https://ori.hhs.gov/blog/notice-information-about-scope-research-misconduct-institutional-proceedings

[5] https://ori.hhs.gov/sites/default/files/2021-05/Scope%20of%20Research%20Misconduct%2005-27-2021.pdf

5. In accordance with § 93.307(d), the inquiry's purpose is to decide if the allegation(s) warrant an investigation. An investigation is warranted if:

    a. there is a reasonable basis for concluding that the allegation(s) falls within the definition of research misconduct under this part and involves PHS-supported biomedical or behavioral research, research training, or activities related to that research or research training, as provided in § 93.102

    b. preliminary information-gathering and preliminary fact-finding from the inquiry indicate that the allegation(s) may have substance

6. The research in the published paper was supported by PHS funds as well as funds from other funding institutions, including the National Science Foundation.[6] If not already done, CMU also should provide notice to the other funding institutions about the research misconduct allegations and inquiry.

As you know, an inquiry should be completed within the 60 days specified in the PHS regulations. Therefore, ORI would expect to receive your inquiry report on or about December 19, 2022. An institution may submit a written request via email to Tracy.Sumner@hhs.gov if an extension is needed for completion of its inquiry. Please provide an explanation of the circumstances or reasons that warrant a longer period for completion of the inquiry, in accordance with §93.307(g). In addition, ORI has issued an update for institutions on the submissions of files and documents to ORI.[7]

Enclosed for your convenience are an Inquiry Report Checklist for documents that should be provided with the inquiry report and an Outline for an Inquiry Report as well as the previously referenced Submitting Files and Evidence to ORI.

Finally, ORI's mission in protecting PHS funds complements that of NIH. Both NIH and recipient institutions are stewards of those funds, as explained in the NIH Grants Policy Statement (https://grants.nih.gov/policy/index.htm). Consistent with § 93.401, ORI works closely with NIH to share relevant information related to research misconduct proceedings. To ensure that NIH has the information it needs to work with the applicant/grantee institution to protect the funds and research, CMU also should communicate directly with NIH, if necessary. Specifically, if the allegations in this matter rise to a level that involves the health and safety of the public, including the misuse of NIH grant or contract funds, foreign influence, animal welfare concerns, or if there are other considerations under § 93.309(d), CMU should directly contact Dr. Patricia Valdez, NIH Extramural Research Integrity Officer, at patricia.valdez@nih.gov or at 301-451-2160. To protect the confidentiality of the matter(s) between NIH and your institution, please do not contact any other NIH program officials or scientific review officers and solely communicate with Dr. Valdez.

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[6] *Int J Mol Sci.* 2020 acknowledges NSF grant CHE-1531590

[7] https://ori.hhs.gov/blog/update-ori-file-submission-process

If you have any questions regarding the handling of this case, or questions about technical matters, please contact me at 240-453-8800 or via email at alexander.runko@hhs.gov.

Sincerely,

Alexander P. Runko -S

Digitally signed by Alexander P. Runko -S
Date: 2022.10.18 17:11:13 -04'00'

Alexander Runko, Ph.D.
Director
Division of Investigative Oversight
Office of Research Integrity

Enclosures