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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.

ACTION: Notice.

SUMMARY: Findings of research misconduct have been made against Yiorgos (Georgios) I. Laliotis, M.D. (Respondent), who was a Postdoctoral Fellow, Department of Cancer Biology and Genetics, College of Medicine, The Ohio State University (OSU), and Postdoctoral Fellow, Department of Oncology, Johns Hopkins University (JHU). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Cancer Institute (NCI), National Institutes of Health (NIH), grants R01 CA186729, R01 CA198117, P30 CA016058, K22 CA245487, and R21 CA252530 and included in grant applications submitted for PHS funds, specifically R01 CA186729-07 and R01 CA198117-05 submitted to NCI, NIH. The administrative actions, including supervision for a period of three (3) years, were implemented beginning on June 12, 2023, and are detailed below.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Yiorgos (Georgios) I. Laliotis, M.D., The Ohio State University and Johns Hopkins University: Based on the reports of inquiries conducted by OSU and JHU, admissions by Respondent, and analysis conducted by ORI in its oversight review, ORI found that Yiorgos (Georgios) I. Laliotis,

M.D., former Postdoctoral Fellow, Department of Cancer Biology and Genetics, College of Medicine, OSU, and former Postdoctoral Fellow, Department of Oncology, JHU, engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically NCI, NIH, grants R01 CA186729, R01 CA198117, P30 CA016058, K22 CA245487, and R21 CA252530 and included in grant applications submitted for PHS funds, specifically R01 CA186729-07 and R01 CA198117-05 submitted to NCI, NIH.

ORI found that Respondent engaged in research misconduct by intentionally and knowingly falsifying and/or fabricating data, methods, results, and conclusions by representing a fabricated Exon 2 splice variant of *U2AF2,* which would translate as a Serine-Arginine-Rich deficient U2AF65 isoform, leading to the repression of lung adenocarcinomas and by enhancing the role of splicing in mutant *PIK3CA* breast cancer cell lines in the following three (3) published papers, two (2) NIH grant applications, and two (2) unpublished manuscripts:

- AKT3-mediated IWS1 phosphorylation promotes the proliferation of EGFR-mutant lung adenocarcinomas through cell cycle-regulated *U2AF2* RNA splicing. *Nat. Commun.* 2021 Jul 30; 12(1):4624. doi: 10.1038/s41467-021-24795-1 (hereafter referred to as "*Nat. Commun.* 2021"). Retraction in: *Nat. Commun.* 2022 Jun 28;13(1):3711. doi: 10.1038/s41467-022-31445-7.
- Phosphor-IWS1-dependent *U2AF2* splicing regulates trafficking of CAR-E-positive intronless gene mRNAs and sensitivity to viral infection. *Commun. Biol.* 2021 Oct 11; 4(1):1179. doi: 10.1038/s42003-021-02668-z (hereafter referred to as "*Commun. Biol.* 2021"). Retraction in: *Commun. Biol.* 2021 Dec 15;4(1):1419. doi: 10.1038/s42003-021-02941-1.
- Overexpression of the SETD2 WW domain inhibits the phosphor-IWS1/SETD2 interaction and the oncogenic AKT/IWS1 RNA splicing program. *bioRxiv* 2021.08.12.454141. doi: 10.1101/2021.08.12.454141 (hereafter referred to as "*bioRxiv* 2021"). Withdrawn. The manuscript also was submitted to *Commun. Biol*. in 2021 but was withdrawn prior to completion of peer review.

- R01 CA186729-07, "The role of IWS1-dependent alternative RNA splicing in lung cancer," submitted to NCI, NIH, on November 5, 2020.
- R01 CA198117-05, "The role of IWS1 in development and tumorigenesis," submitted to NCI, NIH, on June 3, 2019.
- The transcriptomic landscape of oncogenic P13K reveals key functions in splicing and gene expression regulation. Manuscript submitted to *Cancer Res.* (hereafter referred to as the "*Cancer Res.* manuscript").
- Interpretable deep learning for chromatin-informed inference of transcriptional programs driven by somatic alterations across cancers. Manuscript in preparation (hereafter referred to as "Manuscript 2021").

Specifically, ORI finds that Respondent knowingly and intentionally:

- falsified the sequencing data in Figure 1g of *Nat. Commun*. 2021 by splicing two sequencing chromatograms together to falsely represent a novel identification of a previously undescribed *U2AF2* RNA transcript lacking Exon 2
- falsified conclusions about the fabricated *U2AF2* splice variant in RT-PCR results in Figures 1f, 2a, 2b, 2c, 3d, 4a, 4b, 4c, 4e, 5h, 6f, 6i, and 7c of *Nat. Commun.* 2021
- falsified conclusions about the fabricated *U2AF2* splice variant as the source of two endogenous protein isoforms in immunoblot panels in Figures 5c and 5g of *Nat. Commun.* 2021 and Figure 2 of R01 CA186729-07
- falsified the experimental conditions of p-ERK1/2 (Y202/T204), p-CDK1 (Y15), CDK1, and Cyclin B1 immunoblot panels in Figure 5g of *Nat. Commun.* 2021 and Figure 2 of R01 CA186729-07 by using shControl or shIWS1 instead of the samples as reported in the figure labels to falsely represent the immunoblots as the result of *U2AF2* containing spliced Exon 2
- falsified the experimental conditions of the α-actinin immunoblot panel in Figure 1e of *Commun. Biol.* 2021 by using shIWS1 instead of shISWS1/U2AF65β-V5 as reported in the figure label

- in *Commun. Biol.* 2021, *bioRxiv* 2021, R01 CA186729-07, and R01 CA198117-05, reported falsified conclusions highlighting the role of the fabricated *U2AF2* RNA transcript lacking Exon 2 from *Nat. Commun.* 2021
- fabricated and/or falsified the dose response curves in Figures 3k and S5N of the *Cancer Res.* manuscript by treating the MCF7 and T47D cells lines with DMSO or Alpelisib instead of treating with the presence or absence of splicing inhibitors H3B-8800 or E7070 as reported in the figure legend
- fabricated and/or falsified the quantitative RNA immunoprecipitation qPCR data in Figures S4c and S4d of the *Cancer Res.* Manuscript
- fabricated and/or falsified the qPCR data in Figure 6 of Manuscript 2021 to show changes in gene expression between control and inhibitor treatment
- fabricated and/or falsified the experimental methods described in the legend of Figure 6 of Manuscript 2021 by using CREB1 as a control gene instead of ACTIN as reported in the figure legend

Respondent entered into a Voluntary Settlement Agreement (Agreement) and voluntarily agreed to the following:

(1) Respondent will have his research supervised for a period of three (3) years beginning on June 12, 2023 (the "Supervision Period"). Prior to the submission of an application for PHS support for a research project on which Respondent's participation is proposed and prior to Respondent's participation in any capacity in PHS-supported research, Respondent will submit a plan for supervision of Respondent's duties to ORI for approval. The supervision plan must be designed to ensure the integrity of Respondent's research. Respondent will not participate in any PHS-supported research until such a supervision plan is approved by ORI. Respondent will comply with the agreed-upon supervision plan.

(2) The requirements for Respondent's supervision plan are as follows:

i. A committee of 2-3 senior faculty members at the institution who are familiar with Respondent's field of research, but not including Respondent's supervisor or collaborators, will provide oversight and guidance for a period of three (3) years from the effective date of the Agreement. The committee will review primary data from Respondent's laboratory on a quarterly basis and submit a report to ORI at six (6)-month intervals setting forth the committee meeting dates and Respondent's compliance with appropriate research standards and confirming the integrity of Respondent's research.

ii. The committee will conduct an advance review of each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved. The review will include a discussion with Respondent of the primary data represented in those documents and will include a certification to ORI that the data presented in the proposed application, report, manuscript, or abstract are supported by the research record.

(3) During the Supervision Period, Respondent will ensure that any institution employing him submits, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved, a certification to ORI that the data provided by Respondent are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported and not plagiarized in the application, report, manuscript, or abstract.

(4) If no supervision plan is provided to ORI, Respondent will provide certification to ORI at the conclusion of the Supervision Period that his participation was not proposed on a research project for which an application for PHS support was submitted and that he has not participated in any capacity in PHS-supported research.

(5) During the Supervision Period, Respondent will exclude himself voluntarily from serving in any advisory or consultant capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee.

Dated: June 26, 2023.

Sheila Garrity,

Director, Office of Research Integrity,

Office of the Assistant Secretary for Health.

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