

(Billing Cod



This document is scheduled to be published in the Federal Register on 08/19/2021 and available online at [federalregister.gov/d/2021-17777](https://www.federalregister.gov/d/2021-17777), and on [govinfo.gov](https://www.govinfo.gov)

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 Viravuth Yin, Ph.D. (Respondent), former Associate Professor, Mount Desert Island Biological Laboratory (MDIBL). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Institute of General Medical Sciences (NIGMS), National Institutes of Health (NIH), grants P20 GM104318 and P20 GM103423. The administrative actions, including supervision for a period of two (2) years, were implemented beginning on August 2, 2021, and are detailed below.

FOR FURTHER INFORMATION CONTACT:

Wanda K. Jones, Dr.P.H.
Acting Director
Office of Research Integrity
1101 Wootton Parkway, Suite 240
Rockville, MD 20852
(240) 453-8200

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

Viravuth Yin, Ph.D., Mount Desert Island Biological Laboratory: Based on the report of an investigation conducted by MDIBL and analysis conducted by ORI in its oversight review, ORI found that Dr. Viravuth Yin, former Associate Professor, MDIBL, engaged in research misconduct in research supported by PHS funds, specifically NIGMS, NIH, grants P20 GM104318 and P20 GM103423.

Respondent neither admits nor denies ORI's findings of research misconduct. The settlement is not an admission of liability on the part of the Respondent. The parties entered into a Voluntary Settlement Agreement to conclude this matter without further expenditure of time, finances, or other resources.

ORI found that Respondent engaged in research misconduct by knowingly, intentionally, and/or recklessly falsifying and/or fabricating data included in the following three (3) published papers and two (2) submitted manuscripts:

- Smith AM, Dykeman CA, King BL, Yin VP. Modulation of TNF α Activity by the microRNA Let-7 Coordinates Heart Regeneration. *iScience* 2019;15:1-15; doi: 10.1016/j.isci.2019.04.009 (hereafter referred to as "*iScience* 2019").
- Smith AM, Dykeman CA, King BL, Yin VP. Modulation of TNF α Activity by the microRNA Let-7 Coordinates Heart Regeneration. *iScience* 2019;17:225-29; doi: 10.1016/j.isci.2019.06.017 (hereafter referred to as "*iScience* Correction").

- Beauchemin M, Smith A, Yin VP. Dynamic microRNA-101a and Fosab expression controls zebrafish heart regeneration. *Development* 2015;142:4026-37; doi: 10.1242/dev.126649 (hereafter referred to as “*Development* 2015”).
- Smith AM, Dykeman CA, Yin VP. Modulation of epicardial TNF α Activity by the microRNA Let-7 Coordinates the Zebrafish Heart Regeneration. Manuscript submitted to *iScience* in 2018 (hereafter referred to as “*iScience* 2018 draft”).
- Smith AM, Dykeman CA, Yin VP. Modulation of epicardial TNF α Activity by the microRNA let-7 coordinates the zebrafish heart regeneration. Manuscript submitted to *PNAS* in 2018 (hereafter referred to as “*PNAS* 2018 draft”).

Specifically, Respondent intentionally, knowingly, and/or recklessly falsified and/or fabricated data by:

- reusing, relabeling, and reporting Phosphate Buffered Saline (PBS) controls as scrambled antisense Locked Nucleic Acids (LNAs) in the following experimental results:
 - RT-qPCR data representing the knockdown of let7 expression in Figure 2B of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019
 - images of tcf21:Dsred expression in LNA-let-7 treated hearts at 3, 14, and 21 days post-amputation (dpa) showing defects in wound closure in Figure 2C of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019

- quantification of *tcf21:Dsred* expression within the resection wound in LNA-let-7 treated hearts in Figure 2D of *iScience* 2019
- images exhibiting proliferating cardiac muscle (CM) in Figure 3A of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019
- suppression of CM proliferation indices in LNA-let-7 hearts at 3 and 7 dpa in Figure 3B of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019
- severity of the injured heart phenotype in Figure 3C of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019
- quantification of the severity of the injury heart phenotype in Figure 3D of *iScience* 2019
- electron microscopy images of remote and injury zones of resected 7-dpa hearts in Figure 4A of *PNAS* 2018 draft, *iScience* 2018 draft, *iScience* 2019, and *iScience* Correction
- images of Tg(*gata4:GFP*) expression in the primordial heart muscle layer in Figure 4B of *PNAS* 2018 draft, *iScience* 2018 draft, *iScience* 2019, and *iScience* Correction
- quantification of *gata4:GFP* expression in control and LNA-let-7 treated hearts in Figure 4C of *iScience* 2019 and *iScience* Correction
- RNA transcripts identifying differentially upregulated TNF α transcripts in Figure 5A of *PNAS* 2018 draft, *iScience* 2018 draft, *iScience* 2019, and their resultant qPCR results,

which identified increased TNF α expression in Figure 5C of *PNAS* 2018 draft, Figure 5B of *iScience* 2018 draft, *iScience* 2019, and Table S1 of *iScience* 2019

- CM proliferation analyses results in Figures S4B and S4C of *PNAS* 2018 draft and *iScience* 2018 draft, and Figures S5B and S5C of *iScience* 2019
- images representing the function of let-7 in Figure 2C of *iScience* Correction and reusing and relabeling images from an unrelated experiment, such that let-7 function is not represented in the image
- images reporting the function of let-7 in Figure 3A of *iScience* Correction
- images representing differences in the effects of miR-101a depletion on Met2 and PNA expression and the quantification of cardiomyocyte proliferation in uninjured control and *Tg(hs:miR-101a-sp)* heat exposed hearts (CM proliferation analysis) in Figures 2A, 2B, 2C, and 2D, and results in Figure 2E of *Development* 2015
- muscle, fibrin, and collagen staining images representing increased scar tissue presence in *Tg(hs:miR-101a-sp)* heat-treated hearts, as compared to wild type hearts in Figures 3A, 3B, 3C, 3D, 3E, and 3F of *Development* 2015
- scarring indices and the size of the injured area in wild type versus *Tg(hs:miR-101a-sp)* heat-treated hearts in Figures 3G and 3H of *Development* 2015
- differences in (1) the amount of scarring, as represented by AFOG staining in control and *Tg(hs:miR-101a-sp)* ventricles from resected and heat-treated hearts in Figures 4B and

4C; (2) the amount of scar tissue in the presence of suppressed miR-101a expression in *Tg(hs:miR-101a-sp)* hearts, compared to control hearts in Figures 4H and 4I; and (3) the quantification of the scarring indices in control versus *Tg(hs:miR-101a-sp)* hearts in Figure 4J of *Development* 2015

- differences in (1) the amount of scarring, as represented by comparing AFOG staining in control and *Tg(hs:miR-101a-sp)* and *Tg(hs:miR-133a1-pre)* hearts exposed to long term heat therapy in Figures 5A, 5B and 5C, or Tropomyosin staining in Figures 5D, 5E, and 5F; and (2) the quantification of the scarring indices, tropomyosin expression, and injury area in Figures 5G, 5H, and 5I of *Development* 2015
- increased Fosab expression in *Tg(hs:miR-101a-sp)* ventricles relative to controls in Figures 6A and 6B, RNA *in situ* hybridization studies in control and regenerating hearts detecting miR-101a expression in Figures 6C, 6D, 6E, and 6E', and Fosab expression in Figures 6F, 6G, 6H, and 6H' of *Development* 2015
- images reporting significant differences in Dsred expression, cardiomyocyte proliferation, collagen and fibrin staining, and scar tissue removal in ventricles from zebrafish treated with *lna-Let-7*, as compared to scrambled control, to support the importance of miR-101a in scar tissue removal/ventricular regeneration in Figures 6H, 6I, 6J, 7C, 7D, and 7E of *Development* 2015
- reporting research methods and statistics that were not performed in the following experimental results:

- PCR data in the graph represented in Figure 2B of *PNAS* 2018 draft, *iScience* 2018 draft, and *iScience* 2019, by representing the data from two (2) remote PCR experiments as being from the same experiment

- PCR data in the graph represented in Figure 2B of *iScience* Correction by reusing and relabeling a graph containing data that were the result of different experimental conditions (exposure to heat shock), to include scrambled control data

- control data and statistical differences between control and experimental data represented in *PNAS* 2018 draft, *iScience* 2018 draft, *iScience* 2019, and *iScience* Correction, by falsely reporting the use of both antisense scrambled and LNA oligonucleotides that were designed and administered to adult animals via intraperitoneal injection at 10ug/g body weight

- representing the “n” of one biological replicate or one experiment as being multiple independent samples or experiments in *iScience* 2019 and *iScience* Correction

- control data and statistical differences between control and experimental data and the reported methods in *Development* 2015, concluding that miR-101a controls both CM proliferation and scar tissue removal, by falsely reporting the use of LNA oligonucleotides to modulate miR-101 activity *in vivo* to elucidate its contributions during adult heart regeneration

Dr. Yin entered into a Voluntary Settlement Agreement (Agreement) and voluntarily agreed to the following:

- (1) Respondent agreed to have his research supervised for a period of two (2) years beginning on August 2, 2021. Respondent agreed that prior to 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 on PHS-supported research, Respondent shall ensure that a plan for supervision of Respondent's duties is submitted to ORI for approval. The supervision plan must be designed to ensure the scientific integrity of Respondent's research contribution. Respondent agreed that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and approved by ORI. Respondent agreed to maintain responsibility for compliance 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 two (2) 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 any PHS grant applications (including supplements, resubmissions, etc.), manuscripts reporting PHS-funded research submitted for publication, and abstracts. 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/publication is supported by the research record.

- (3) Respondent agreed that for a period of two (2) years beginning on August 2, 2021, any institution employing him shall submit, in conjunction with each application of 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 in the application, report, manuscript or abstract.
- (4) If no supervisory plan is provided to ORI, Respondent agreed to provide certification to ORI at the conclusion of the supervision period that he has not engaged in, applied for, or had his name included on any application, proposal, or other request for PHS funds without prior notification to ORI.
- (5) Respondent agreed to exclude himself voluntarily from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of two (2) years, beginning on August 2, 2021.
- (6) As a condition of the Agreement, Respondent will request that the following papers be retracted in accordance with 42 C.F.R. § 93.407(a)(1) and § 93.411(b):

- *Development* 2015 Dec 1;142(23):4026-37
- *iScience* 2019 May 31;15:1-15
- *iScience* 2019 Jul 26;17:225-29

Respondent will copy ORI and the Research Integrity Officer at MDIBL on the correspondence.

Dated: August 16, 2021

Wanda K. Jones,

Acting Director, Office of Research Integrity,

Office of the Assistant Secretary for Health.

[FR Doc. 2021-17777 Filed: 8/18/2021 8:45 am; Publication Date: 8/19/2021]