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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 Ya Wang, M.D., Ph.D. (Respondent), retired Professor and Director, Division of Experimental Radiation Oncology, Department of Radiation Oncology, Winship Cancer Institute, Emory University (EU). 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 P30 CA138292 and R01 CA186129 and National Institute of General Medical Sciences (NIGMS), NIH, grant R01 GM080771. The administrative actions, including debarment for a period of four (4) years, were implemented beginning on August 4, 2021, 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:

Ya Wang, M.D., Ph.D., Emory University: Based on the report of an inquiry conducted by EU and analysis conducted by ORI in its oversight review, ORI found that Dr. Ya Wang, retired Professor and Director, Division of Experimental Radiation Oncology, Department of Radiation Oncology, Winship Cancer Institute, EU, engaged in research misconduct in research supported by PHS funds, specifically NCI, NIH, grants P30 CA138292 and R01 CA186129 and NIGMS, NIH, grant R01 GM080771.

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 Exclusion 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 data that were included in the following one (1) PHS grant application and six (6) published papers:

- R21 HL154577-01, "GPRC5A Inhibits Error-Prone Repair to Maintain Lung Genomic Integrity," submitted to the National Heart, Lung, and Blood Institute (NHLBI), NIH, on December 13, 2019.

- miR-21-Mediated Radioresistance Occurs via Promoting Repair of DNA Double Strand Breaks. *J Biol Chem.* 2017 Feb 24;292(8):3531-40; doi: 10.1074/jbc.M116.772392 (hereafter

referred to as "*J Biol Chem*. 2017"). Retraction in: *J Biol Chem*. 2020 May 1;295(18):6250; doi: 10.1074/jbc.W120.013725.

- Distinct Roles of Ape1 Protein, an Enzyme Involved in DNA Repair, in High or Low Linear Energy Transfer Ionizing Radiation-Induced Cell Killing. *J Biol Chem*. 2014 Oct 31; 289(44):30635-44; doi: 10.1074/jbc.M114.604959 (hereafter referred to as "*J Biol Chem.* 2014"). Retraction in: *J Biol Chem.* 2020 May 1;295(18):6249; doi: 10.1074/jbc.W120.013724.

- OCT4 as a Target of miR-34a Stimulates p63 but Inhibits p53 to Promote Human Cell Transformation. *Cell Death Dis.* 2014 Jan 23;5(1):e1024; doi: 10.1038/cddis.2013.563 (hereafter referred to as "*Cell Death Dis.* 2014").

- MicroRNA-21 Modulates the Levels of Reactive Oxygen Species by Targeting SOD3 and TNFα. *Cancer Res.* 2012 Sep 15;72(18):4707-13; doi: 10.1158/0008-5472.CAN-12-0639 (hereafter referred to as "*Cancer Res.* 2012a").

- RNAi-Mediated Targeting of Noncoding and Coding Sequences in DNA Repair Gene Messages Efficiently Radiosensitizes Human Tumor Cells. *Cancer Res.* 2012 Mar 1; 72(5):1221-8; doi: 10.1158/0008-5472.CAN-11-2785 (hereafter referred to as "*Cancer Res.* 2012b").

- Over-Expression of miR-100 is Responsible for the Low-Expression of ATM in the Human Glioma Cell Line: M059J. *DNA Repair (Amst)*. 2010 Nov 10;9(11):1170-5; doi: 10.1016/j.dnarep.2010.08.007 (hereafter referred to as "*DNA Repair* 2010").

ORI found that respondent knowingly, intentionally, and/or recklessly falsified protein immunoblot data by reusing and relabeling the same images to represent different experimental conditions in mammalian tissue culture models of DNA damage and repair in eighteen (18) figure panels in eleven (11) figures in one (1) grant application and six (6) published papers. Specifically:

- western blot images for total protein expression in distinct transgenic mouse cell lines were falsified by reusing immunoblot bands and relabeling them to represent different experiments in eleven (11) figure panels in two (2) papers, including:

  - Figure 3D in *J Biol Chem.* 2017, representing β-actin expression (left side panel) in wildtype (WT), microRNA-21 (miR-21) knock-in, and miR-21$^{-/-}$ mouse embryonic fibroblast (MEF) cells exposed to irradiation

  - Figure 4C in *J Biol Chem.* 2017, representing DNA-PKcs expression in miR-21 knock-in MEF cells exposed to irradiation

  - Figure 5A in *J Biol Chem.* 2017, representing CDC25A and β-actin expression in WT, GSK3B$^{-/-}$, and Cyclin D1$^{-/-}$ MEF cells transfected with control or gene-specific silencing RNA (siRNA)

  - Figure 1 in *J Biol Chem.* 2014, representing β-actin expression in Ku80$^{-/-}$ (Figure 1A) and Ogg1$^{-/-}$ (Figure 1C) MEF cells transfected with expression or control vectors

  - Figure 3 in *J Biol Chem.* 2014, representing H2A expression in WT MEF (Figure 3A), Ku80$^{-/-}$ MEF (Figure 3B), Ogg1$^{-/-}$ MEF (Figure 3C), and Ogg1^{+} (rescue) MEF (Figure

3D) cells transfected with expression or control vectors and in the absence or presence of radiation exposure

- Figure 3D in *J Biol Chem.* 2014, representing Mre11 (left panel) expression in $Ogg1^{+}$ (rescue) MEF cells transfected with expression or control vectors in the absence or presence of radiation exposure

- Figure 4B in *J Biol Chem.* 2014, representing Mre11 expression in $Ogg1^{-/-}$ MEF cells with control or Ape1 expression vector in the presence of low or high linear energy transfer (LET) irradiation

- Figure 5C in *J Biol Chem.* 2014, representing Ape1 and β-actin expression in WT MEF cells with or without gene depletion and transfected with control or various Ape1 expression vectors

- western blot images for total protein expression in human cell lines subject to gene depletion and/or overexpression were falsified by reusing immunoblot bands and relabeling them to represent different experiments in seven (7) figure panels in five (5) papers and one (1) grant application, including:

  - Figure 4A in NIH grant application R21 HL154577-01, representing GPRC5A levels in different patient-derived cell lines with gene suppression or depletion

  - Figure 4D in *J Biol Chem.* 2017, representing total DNA-PKcs, phosphorylated DNA-PKcs, CDC25A, and GSK3B levels in human embryonic kidney cells transfected with controls or various expression vectors and/or miR-21 mimics

- Figure 5C in *J Biol Chem.* 2017, representing CDC25A, GSK3B, Cyclin D1, and β-actin expression in human embryonic kidney cells with or without gene depletion and transfected with controls or miR-21 mimics

- Figure 5B in *Cell Death Dis.* 2014, representing p53 and p63 levels in human lung epithelial cells with or without gene depletion

- Figure 3A in *Cancer Res.* 2012a, representing TNFα levels in control and miR-21 overexpressing human lung epithelial cells at different time points following irradiation

- Figure 5A in *Cancer Res.* 2012b, representing XRCC4 levels in both human lung and brain epithelial cells with gene depletion at multiple time points and treated with or without an artificial microRNA

- Figure 3A in *DNA Repair* 2010, representing ATM and Ku70 levels in human glioblastoma-derived cells with or without gene depletion

- western blot images for proteins from chromatin DNA complexes in mouse cell lines transfected with control or expression vectors and in the absence or presence of irradiation were falsified by reusing immunoblot bands and relabeling them to represent different experiments in three (3) figure panels in one (1) paper, including:

  - Figure 3 in *J Biol Chem*. 2014, representing chromatin-bound γ-H2AX levels in WT MEF (Figure 3A), Ogg1$^{-/-}$ MEF (Figure 3C), and Ogg1^{+} (rescue) MEF (Figure 3D) cells

transfected with a control or expression vector and in the absence or presence of irradiation

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

(1) Respondent agreed to exclude herself voluntarily for a period of four (4) years beginning on August 4, 2021, from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 C.F.R. Part 376) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension, 2 C.F.R. Part 180 (collectively the "Debarment Regulations").

(2) Respondent agreed to exclude herself 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 four (4) years, beginning on August 4, 2021.

(3) As a condition of the Agreement, Respondent will request that the following papers be corrected or retracted in accordance with 42 C.F.R. § 93.407(a)(1) and § 93.411(b):

- *Cell Death Dis.* 2014 Jan;5(1):e1024
- *Cancer Res.* 2012 Sep 15;72(18):4707-13
- *Cancer Res.* 2012 Mar 1;72(5):1221-8
- *DNA Repair (Amst).* 2010 Nov 10;9(11):1170-5

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

Dated: September 15, 2021

Wanda K. Jones,

Acting Director, Office of Research Integrity,

Office of the Assistant Secretary for Health.

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