(Billing Code: 4150-31)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.

ACTION: Notice.

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

Dong Xiao, Ph.D., University of Pittsburgh: Based on the report of an inquiry conducted by the University of Pittsburgh (UP), additional analysis conducted by ORI in its oversight review, and an admission by the Respondent that he had "intentionally fabricated data contained in a paper entitled 'Guggulsterone inhibits prostate cancer growth via inactivation of Akt regulated by ATP citrate signaling,' specifically Figure 6G," ORI found that Dr. Dong Xiao, former Research Assistant Professor, Department of Urology, UP, engaged in research misconduct in research supported by National Cancer Institute (NCI), National Institutes of Health (NIH), grant R01 CA157477.

ORI found that Respondent engaged in research misconduct by reporting falsified data in Figures 1, 4, 5, S2, and S3 in the following paper published online:

- Gao, Y., Zeng, Y., Tian, J., Kslam, M.S., Jiang, G., & Xiao, D., "Gugglesterone inhibits prostate cancer growth via inactivation of Akt regulated by ATP citrate signaling." *Oncotarget*, June 26, 2014 [Epub ahead of print], PMID: 24980815; hereafter referred to as the "*Oncotarget* paper."

Specifically, in the *Oncotarget* paper, Respondent:

- falsely stated that 10 mice per group were used to obtain data for tumor volume (Figure 1A) and tumor weight (Figure 1B) when data for only four mice per group were available

- falsified the results for C-caspase 3 and phosphorylated Akt in the Western blots presented in Figure 1D to claim that treatment of tumor bearing mice with Z-Gug significantly enhanced C-capase 3 activity and significantly inhibited Akt phorphorylation, while the original data showed no significant effect for either activity

- falsified Figure 4C by manipulating p-Akt bands to show that Z-Gug alone and in combination with PHTM significantly inhibited Akt phosphorylation in PC3 and LNCaP human prostate cancer cell lines; the numbers above each band representing the fold change human prostate cancer cell lines; the numbers above each band representing the fold change in expression relative to the DMSO control also were falsified for p-ACLY

(LNCaP cell line) and p-Akt (PC3 and LNCaP cell lines) compared to the values provided to the Respondent

- falsified Figure 4D by substituting bands for p-ACLY for those provided to him to allow Respondent to claim that Z-Gug significantly inhibited phosphorylation of ACLY in lysates of prostate tumors obtained from mice, when the original data showed no effect

- falsified Figures 5C and 5D to show that treatment of PC3 and LNCaP cells with Z-Gug alone and with Z-Gug plus si-RNA targets to ACLY stimulated Caspase 3/7 activity, when the original data provided to him showed no significant effect of either treatment in PC3 cells and no effect of Z-Gug alone in LNCaP cells

- falsified Figures 6G and 6H; these figures purported to show that N-acetyl-L-cysteine (NAC), an inhibitor of reactive oxygen species (ROS), reversed the inhibition of Akt phosphorylation caused by Z-Gug in PC3 cells (Figure 6G) and LNCaP cells (Figure 6G) when no Akt data for this protocol was available to the Respondent; Respondent admitted to falsifying Figure 6G

- falsified Figures S2B and S3B by altering data provided to him; these experiments are complementary to those shown in Figures 5C and 5D, except that the effect of Z-Gug and Z-gug plus si-RNA on Caspase 3/7 activity utilized on si-RNA was directed to Akt activity. The original data showed no significant effect of either treatment in PC3 cells and no effect

of Z-Gug on LNCaP cells, while both treatments were claimed to be significant inducers of caspase activity in both cell lines in the published figures.

Dr. Xiao has entered into a Voluntary Settlement Agreement (Agreement) and has voluntarily agreed for a period of three (3) years, beginning on December 23, 2014:

(1) to have his research supervised; Respondent agreed to ensure that prior to the submission of an application for U.S. Public Health Service (PHS) support for a research project on which the Respondent's participation is proposed and prior to Respondent's participation in any capacity on PHS-supported research, the institution employing him must submit a plan for supervision of his duties to ORI for approval; the plan for supervision must be designed to ensure the scientific integrity of Respondent's research contribution; Respondent agreed that he will 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 plan for supervision;

(2) that any institution employing him must submit, 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 in the application, report, manuscript, or abstract; and

(3) 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 FURTHER INFORMATION CONTACT:

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Donald Wright,
Acting Director,
Office of Research Integrity.

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