

and the Assistant Secretary for Health have taken final action in the following case:

*Timothy R. Smith, Ph.D., Michigan State University:* Based on the findings of Michigan State University, the respondent's admission, and analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Timothy R. Smith, Ph.D., former Postdoctoral Fellow, Department of Biochemistry and Molecular Biology at Michigan State University, engaged in scientific misconduct in research supported by National Institute of General Medical Sciences (NIGMS), National Institutes of Health (NIH) grant P01 GM57323, entitled "Oxygen utilizing membrane heme proteins."

Specifically, PHS found that Dr. Smith falsified and fabricated data involving research into the physical interaction of prostaglandin endoperoxide synthase-2 (PGHS-2) with cell membranes, and the effects of arachidonate and nonsteroidal anti-inflammatory drugs (NSAIDs) on PGHS-2 structure.

Dr. Smith committed scientific misconduct by falsifying and fabricating data for the following tables and figures in his 2000 doctoral dissertation and in a paper in the *Journal of Biological Chemistry* (275:40407-40415, 2000) entitled "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H<sub>2</sub> Synthase-2 (Cyclooxygenase-2)" (*JBC* paper):

I. *JBC* paper Table II, entitled "Comparison of inter-residue distances as determined by EPR spectroscopy and as calculated from the x-ray crystal structures" (and corresponding Dissertation Table 6 entitled "EPR determined and X-ray crystal modeled inter-nitroxide distances of PGHS-2 MBD mutants");

II. *JBC* paper Table III entitled "Changes in inter-nitroxide differences between PGHS-2 holoenzyme and the apoenzyme, and the arachidonate, flurbiprofen, and SC58125 complexes" (and corresponding Dissertation Table 7), entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme";

III. *JBC* paper Figure 4 (binding curves) (and corresponding Dissertation Figure 20 entitled "Binding curves for the association of heme, flurbiprofen and arachidonic acid with PGHS-2 double mutants");

IV. Dissertation Table 8 entitled "EPR determined inter-nitroxide distances for

NSAID and arachidonate complexes of PGHS-2 MBD mutants;"

V. Dissertation Table 9 entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme;"

VI. Dissertation Table 10 entitled "Kinetic properties and NSAID sensitivities of PGHS-2 active site mutants;"

VII. Dissertation Table 12 entitled "Relative PGHS-2 protein incorporation of PGHS-2 into liposomes of varying composition;"

IX. Dissertation Table 13 entitled "EPR determined inter-nitroxide distances for detergent solubilized and liposome reconstituted PGHS-2 mutants;" and

X. Dissertation Figure 27 entitled "Lipid and activity profile of sucrose gradient fractions."

The research misconduct was significant for several reasons. First, the *JBC* paper was novel in that it reported that binding of arachidonate and NSAIDs induced structural changes in PHS-2. For the naturally occurring fatty acid arachidonate, this had not previously been shown. These results could be interpreted as having important implications for understanding the catalytic mechanism of this enzyme. In addition, a considerable expenditure of other researchers' time and resources was prompted by using results generated from the falsified and fabricated data in the *JBC* paper.

Dr. Smith has entered into a Voluntary Exclusion Agreement (Agreement) in which he has voluntarily agreed:

(1) to exclude himself 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 three (3) years, beginning on October 27, 2003;

(2) to exclude himself voluntarily from any contracting or subcontracting with any agency of the United States Government and from eligibility or involvement in nonprocurement programs of the United States Government defined as "covered transactions" in the debarment regulations at 45 CFR part 76 for a period of three (3) years, beginning on October 27, 2003. During the three (3) year period of voluntary exclusion, PHS grant funds may be used to pay for page charges for any written work currently being prepared for submission and/or publication on which Dr. Smith is listed as an author only if (i) such written work is unrelated to the misconduct

findings described in the Agreement, (ii) Dr. Smith is not listed as first author, and (iii) the publication does not state that Dr. Smith was supported by a PHS grant. Dr. Smith must certify that all data supporting such written work is true and accurate to the best of his knowledge; and

(3) to submit a letter within 30 days of notification of this action to *JBC* requesting retraction of the following paper: Smith, T., McCracken, J., Shin, Y.K., & DeWitt, D. "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H<sub>2</sub> Synthase-2 (Cyclooxygenase-3)." *J. Biol. Chem.* 275:40407-40415, 2000. Dr. Smith agreed that the retraction will state that he alone was responsible for the falsification and fabrication of the results and will specifically list the falsified figures delineated on page 1 of the Agreement (Findings I, II, and III). Dr. Smith must submit a draft of the retraction letter for ORI approval prior to sending it to *JBC*. This requirement for retraction will be noted on the ALERT System until Dr. Smith sends a copy of the retraction letter to ORI.

**FOR FURTHER INFORMATION CONTACT:**  
Director, Division of Investigative Oversight, Office of Research Integrity, 1101 Wootton Parkway, Suite 750, Rockville, MD 20852, (301) 443-5330.

**Chris B. Pascal,**

*Director, Office of Research Integrity.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Administration for Children and Families

#### Head Start Survey Under Emergency Review by the Office of Management and Budget (OMB)

*Title:* Survey of Salaries and Other Compensation of Head Start Grantees and Delegate Agencies Nationwide.

*OMB No.* New request.

*Description:* A committee of the U.S. House of Representatives requested that the Secretary of Health and Human Services conduct a review of the financial management of Head Start grantees nationwide. The House Education and the Workforce Committee is interested in knowing the salaries and benefits of the top 25 Head Start executives and the amount of their salary and benefits financed using Federal Head Start dollars. To be responsive to the House of