



(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:

Takao Takahashi, M.D., Ph.D., University of Texas Southwestern Medical Center: Based on the report of an investigation conducted by the University of Texas Southwestern Medical Center (UT Southwestern) and analysis conducted by ORI in its oversight review, ORI found that Dr. Takao Takahashi, currently a faculty member in the Department of Surgical Oncology, Gifu University, Graduate School of Medicine, Gifu, Japan, and formerly a Visiting Scientist in the Hamon Center for Therapeutic Oncology Research, UT Southwestern, engaged in research misconduct in research supported by National Cancer Institute (NCI), National Institutes of Health (NIH), grant U01 CA084971.

ORI found that Respondent knowingly, intentionally, and recklessly falsified data reported in four (4) publications:

- Takahashi, T., Shivapurkar, N., Reddy, J., Shigematsu, H., Miyajima, K., Suzuki, M., Toyooka, S., Zöchbauer-Müeller, S., Drach, J., Parikh, G., Zheng, Y., Feng, Z., Kroft, S.H., Timmons, C., McKenna, R.W., & Gazdar, A.F. “DNA methylation profiles of lymphoid and hematopoietic malignancies.” *Clin Cancer Res.* 10(9):2928-35, 2004 May 1 (hereafter referred to as “*CCR 2004*”); Retraction in: *Clin Cancer Res.* 19(1):307, 2013 Jan 1
- Takahashi, T., Suzuki, M., Shigematsu, H., Shivapurkar, N., Echebiri, C., Nomura, M., Stastny, V., Augustus, M., Wu, C.W., Wistuba, I.I., Meltzer, S.J., & Gazdar, A.F. “Aberrant methylation of Reprimo n human malignancies.” *Int J Cancer* 115(4):503-10, 2005 Jul 1 (hereafter referred to as “*IJC 2005*”); Retraction in: *Int J. Cancer* 132(2):498, 2013, Jan 15
- Takahashi, T., Shigematsu, H., Shivapurkar, N., Reddy, J., Zheng, Y., Feng, Z., Suzuki, M., Noomura, M., Augustus, M., Yin, J., Meltzer, S.J., & Gazdar, A.F. “Aberrant promoter methylation of multiple genes during multistep pathogenesis of colorectal cancers.” *Int J Cancer* 118(4):924-31, 2006 Feb 15 (hereafter referred to as “*IJC 2006*”); Retraction in: *Int J Cancer* 132(2):499, 2013 Jan 15
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- Tokuyama, Y., Takahashi, T., Okumura, N., Nonaka, K., Kawaguchi, Y., Yamaguchi, K., Osada, S., Gazdar, A., & Yoshida, K., “Aberrant methylation of heparan sulfate

glucosamine 3-O-sulfotransferase 2 genes as a biomarker in colorectal cancer.” *Anticancer Res.* 30(12):4811-8, 2010 Dec (hereafter referred to as “AR 2010”); Retraction in: *Anticancer Res.* 32(11):5138, 2012 Nov.

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Respondent falsified data representing glyceraldehyde 3-phosphate dehydrogenase (GAPDH) loading controls and methylated/unmethylated polymerase chain reaction (PCR) in reverse transcription-PCR (RT-PCR) gel panels.

Specifically, ORI found by a preponderance of the evidence that Respondent engaged in research misconduct by knowingly, intentionally, and recklessly falsely reporting the results of RT-PCR experiments by:

1. reusing and relabeling an image and claiming it represents different experiments of human tumor cell lines subjected to different treatments; specifically, an identical image was used to represent the:
  - (a) GAPDH RT-PCR panels of several lymphoma, leukemia, multiple myeloma, and colorectal cancer cell lines in *CCR* 2004, Figures 1A and 1B, *IJC* 2005, Figure 1A, *IJC* 2006, Figures 1A and 2A, and AR 2010, Figure 1A
  - (b) GAPDH RT-PCR panels of the lymphoma cell lines BC-1 and Raji in *CCR* 2004, Figure 1B, lanes 1-3, and the colorectal cancer cell lines HCT116 and COLO201 in AR 2010, Figure 1C, lanes 4-6



- (c) unmethylated form of p16 (p16UM) controls in the methylation-specific PCR (MSP) panels for the leukemia (Le) and multiple myeloma (MM) samples in *CCR* 2004, Figure 2
  - (d) p16UM MSP panels for the lymphoma (Ly) and Le samples in *CCR* 2004, Figure 2, and the unmethylated (UM) bands MSP panel for the colorectal cancer (CRC) cell line in *IJC* 2005, Figure 5.
2. manipulating an image and claiming it represents a gel with contiguous lanes; specifically, the RT-PCR products in the lanes of gels were cropped, spliced, and pasted together to form a single image for the MSP panels in *IJC* 2006, Figure 3.

Dr. Takahashi has entered into a Voluntary Settlement Agreement (Agreement) and has voluntarily agreed for a period of three (3) years, beginning on August 26, 2014:

- (1) to have his research supervised; Respondent agrees 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, 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; Respondent agrees that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and

approved by ORI; Respondent agrees to maintain responsibility for compliance with the agreed upon supervision plan;

- (2) that any institution employing him shall 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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