U.S. Department of Health and Human Services • Office of the Secretary • Office of Public Health and Science

Volume 18, No. 1 http://ori.hhs.gov December 2009

Office of Research Integrity

NEWSLETTER

IN THIS ISSUE

Director's Corner
The Costs of Research Misconduct 2

ORI Updates
2009 Annual Institutional Report on Misconduct Activities 3
Quest for Research Excellence 2010 Conference 4

RCR
Incorporating Ethics into RCR Courses 1
Proposed Study 4

International
A View from Europe on European Research Oversight 1
Health Canada Visits OPHS 6

Case Summaries 8

Save the Date
The 2nd World Conference on Research Integrity 12

The *ORI Newsletter* is published quarterly by the Office of Research Integrity, Office of the Secretary of Health and Human Services, and distributed to applicant or awardee institutions and PHS agencies to facilitate pursuit of a common interest in handling allegations of misconduct and promoting integrity in PHS-supported research. Please duplicate and circulate this newsletter freely. An electronic copy is available on the ORI home page.

Incorporating Ethics into RCR Courses

Sara Vollmer, Ph.D., University of Alabama at Birmingham, and Nancy J. Matchett, Ph.D., University of Northern Colorado

Philosophy departments have been expanding their offerings in applied ethics and ethical decision making for a number of years, yet relatively little attention has been paid to incorporating ethical thinking in the context of Responsible Conduct of Research (RCR) instruction. There has been a sense that the theories of philosophers like Aristotle, Kant, and Mill are too arcane, too complex, and too hard to apply to be of interest to the scientific community. So there has been concern that RCR students will be bored or confused and will gain little practical value.

Today, this situation is changing. A number of ethics instructors are using ethical theories in the context of group discussions, projects, and other assignments that require individuals to think in more principled ways. Rather than presenting the theories as objects of study themselves, the theories are used to inform concrete decision making about daily choices and actions. Aided by the availability of RCR video material, we have been teaching students to evaluate their own choices through the lens of three main ethical frameworks.

(See Incorporating Ethics, page 5)

A View from Europe on European Research Oversight

Xavier Bosch, Dept. of Internal Medicine, Hospital Clínic, Barcelona

Unlike the United States, research oversight in Europe appears fragmented and varies widely from nation to nation. With the exception of Scandinavia and, to a lesser degree, Germany, the United Kingdom (UK), Croatia, and France, there is little or no regulation governing scientific misconduct. Responses to instances of misconduct in Europe have varied greatly from country to country and, to date, the European Commission (EC), the European Union's executive body, has drawn no regulations addressing potential problems arising from its multibillion-dollar framework of research programs.

A 2000 European Science Foundation (ESF) policy paper supported developing transcontinental approaches to monitoring research integrity and misconduct, recommending national academies and research-funding agencies, universities, and research institutions employing scientists and the scientists themselves "to initiate discussions on the most appropriate national approach to procedures for investigating allegations of scientific misconduct" and urging funding agencies to make eligibility for research grants conditional on having adequate policies

(See A View from Europe, page 7)

Director's Corner

The Costs of Research Misconduct

John Dahlberg, Ph.D., Director, Division of Investigative Oversight (DIO)

ORI regularly receives queries asking for its assessment of the costs associated with research misconduct investigations and of the questioned research itself. First, there is the cost to taxpayers who support this office, which is responsible for overseeing both the reviews of misconduct cases, handled by the Division of Investigative Oversight (DIO), and the education and research efforts carried out by the Division of Education and Integrity (DEI). This cost is currently about $9 million per year.

There is also the cost to cash-strapped institutions of carrying out inquiries and investigations into allegations of research misconduct. ORI does not track this, but clearly the time and resources needed for major cases has on occasion reached into the millions.

Equally important are the costs resulting from the misconduct itself. Some of the relevant cost elements were carefully considered by ORI, the National Institutes of Health (NIH), and court officials when it became necessary for the Federal Court in Burlington, Vermont, to calculate the damages resulting from the research misconduct of Dr. Eric Poehlman prior to his sentencing hearing. Dr. Poehlman had pled guilty to criminal and civil charges arising from a major scientific misconduct case at the University of Vermont, and ORI was asked to assist in evaluating the costs to the injured party, in this case the funding agency, NIH, and to other parties. NIH officials took the lead in evaluating how falsified data in funded grant applications would have deprived more worthy applicants of the opportunity to obtain funding and testified to that effect during the sentencing hearing. ORI noted that Dr. Poehlman's misconduct had led to a number of costs that were significant but could not easily be calculated, if at all.

For example, the University of Vermont, despite having done an exemplary job of investigating a case of misconduct involving an internationally recognized scientist and having cooperated fully with ORI and the Department of Justice, was unfairly linked with the misconduct. The hundreds of volunteers from the Burlington area who had participated in the rather extensive procedures carried out in Dr. Poehlman's research protocols were dismayed to hear that his research results had been falsified, thereby undermining the university's ability to continue to attract volunteers for its clinical studies. Also significant was the impact of the misconduct on the many collaborators and co-authors on the more than 200 published papers authored by Dr. Poehlman, but not directly involved in Dr. Poehlman's scientific misconduct. A number of young scientists and physicians had Dr. Poehlman as a co-author on all or nearly all of their own publications, leading inevitably to concern and mistrust by others of their scientific output and to serious obstacles in finding new research positions.

Last, there is the cost associated with falsified publications. It would be virtually impossible to estimate how many laboratories attempt to reproduce falsified and fabricated results and how much such efforts cost scientists in time and resources. Often, these costs are borne by graduate students and postdoctoral fellows who can ill-afford the time wasted on chasing after irreproducible results.

ORI recently received a perceptive letter from Professor Eliane S. Azevêdo, Emeritus Professor of Medicine, Nucleus of Bioethics, Faculty of Medicine of Bahia, Federal University of Bahia, Brazil, who commented on secondary adverse consequences of a large body of research carried out at the University of Alabama at Birmingham that has led to 16 retractions of papers by Drs. Judith Thomas and Juan Contreras. ORI recently made findings against both researchers, leading to a 10-year debarment for Dr. Thomas and a three-year debarment for Dr. Contreras.

Professor Azevêdo was particularly concerned about how review articles and meta-analyses can perpetuate fraudulent scientific claims even after the original papers have been retracted. For example, she notes (with minor edits by ORI): "...*ORI Newsletter*, Vol. 17, No. 4, entitled 'A Major Case of Misconduct Involving Non-human Primates,' ... left the reader with a disturbing question regarding the unrecoverable echo of its bad effect on medical practice. The

(See Costs, page 3)

ORI Updates

2009 Annual Institutional Report on Misconduct Activities

Robin Parker, ORI, Division of Education and Integrity

In December 2009, ORI will send e-mail messages (with a password and an IPF number) to officials responsible for submitting the 2010 Annual Report. **In order to assure continuous Public Health Service support, the report must be submitted between January 1, 2010, and March 1, 2010.** You may obtain further information from Robin Parker at robin.parker@hhs.gov or (240) 453-8400.

ORI will automatically acknowledge receipt of the Annual Report. ORI uses the contact information provided by institutions for mailing the *ORI Newsletter*, the ORI Annual Report, and other publications; for sending e-mail messages with updates on conferences, programs, and other announcements; and for referring research misconduct allegations to appropriate officials. **Please be sure your mailing address is up-to-date.**

The research misconduct activity data are reported in the aggregate to the research community in the *ORI Newsletter*, the ORI Annual Report, presentations at scientific meetings, special reports, and the ORI web site.

PRIM&R Honors Albert Jonsen

At the 2009 Public Responsibility in Medicine and Research (PRIM&R) Annual Meeting, Albert Jonsen received the **Lifetime Achievement Award for Excellence in Research Ethics**. This award is intended to recognize and honor individuals who have made a major and sustained contribution to the development or dissemination of the ethical principles that govern research. Al Jonsen is widely considered to be one of the pioneers in the research ethics field and was one of the drafters of the Belmont Report.

Costs *(from page 2)*

retracted publications, dated from 1997 through 2005, add up to 16. So, there was plenty of time to construct a school of false ideas in medical science either through teaching, medical practice, and review papers or through meta-analysis data."

Dr. Azevêdo continues to point out, "It is generally accepted that modern medicine must mostly be rooted in evidence produced by scientific publications. Medical professors, students, and clinicians are constantly seeking new findings in medicine aiming to offer the best for the patients. Thus, review articles on specific subject and data from meta-analysis are preferable sources for updating medical knowledge. However, if this precious source of scientific information happens to be based on publications that become retracted, the harm on science will not be dismissed. The retracted publications made by single journals will have not reached review papers and meta-analysis data already published.

"As an example, a review by Knechtle SJ, published in the *Philos Trans R Soc Lond B Biol Sci*, 2001, May 29;356(1409):681-9, entitled 'Treatment with immunotoxin,' cites four publications from the Thomas Laboratory that have been retracted because of false claims: Contreras, J.L., et al., 1998, *Transplantation* **65**,1159-1169; Contreas, J.L., et al., 1999, *Transplantation* **68**, 215-219; Thomas, J.M., et al., 1997, *Transplantation* **64**, 124-135; and Thomas, J.M., et al., 1997, *Transplantation* **68**, 1660-1673. Not only were the misleading papers cited, but the reviewer seemed, at the time, impressed by the Thomas work, so page 686 states, 'Studies by J M Thomas and others, also in collaboration with the Neville Laboratory, initially focused on combining the IT with donor bone marrow infusion (Thomas et al., 1997). This laboratory, with extensive experience in donor bone marrow infusion as an adjunct to tolerance induction....' Unfortunately, the 1997 Thomas et al. has now been retracted."

Professor Azevêdo certainly makes an important note, to which it could be added that when papers providing results on clinical studies are plagiarized wholesale, as happens with some regularity, the risk to having the duplicated data be overrepresented in meta-analyses is very real and possibly significant, thus posing a possible additional cost to the scientific enterprise and possibly even having an adverse impact on how patients are treated.

ORI Updates

Quest for Research Excellence Conference / Oct. 31-Nov. 4, 2010, Washington, DC

Cynthia Ricard, Ph.D., ORI, Division of Education and Integrity

This conference will explore ways for all members of the research community to build collaborative and innovative research teams relevant for both bench scientists and social scientists. There will be diverse tracks that will appeal to scientists but also to journal editors, research administrators, and research partners.

Learn from Nobel laureates and researchers who are innovative and collaborative in conducting research in times of crisis.

Collaborations between industry and academia are burgeoning. Research often is driven by the needs of industry or the needs of the government. Such multiple directives can be daunting and stressful for research groups. Translational research, in fact, expects scientists to move beyond their own expertise and work with different types of scientists. True advising and mentoring require skills beyond our usual scientific expertise. We depend increasingly on research teams to solve complex issues.

At this conference, you will discover how to form and maintain successful collaborations. The conference planners hope that you will leave the conference inspired and enriched with additional research skills and that your team will work more effectively and innovatively. Speakers and agenda will be made available on the ORI web site at *http://ori.hhs.gov/*

If you have suggestions or recommendations for dynamic speakers please contact Cynthia.ricard@hhs.gov.

RCR

Abstract: What Do Researchers Do When They Observe or Learn about Irresponsible Science?

Patricia Keith-Spiegel and Gerald P. Koocher, Simmons College, and Joan Sieber, California State University

A number of surveys reveal that scientists and advanced students know first-hand of scientific misconduct and other research wrongdoings. Yet we know little about what researchers themselves actually do, if anything, to prevent or correct purposeful or unintentional actions that corrupt or misrepresent data. Do they ignore what they know (or think they know)? Or do they make some attempt to intervene, either formally or informally?

We have responses to our on-line survey from 2,599 researchers from the 8,000 Principal Investigators who were randomly selected from the CRISP database. Our paper will focus on the following questions:

- What kinds of interventions are attempted, and do differences exist depending on the type of transgression?
- Which intervention strategies work best and which result in unsuccessful or difficult outcomes?
- Does the social or physical proximity of a suspected violator play a role in a decision to take action?
- What role does the relative status of the suspected violator play in the decision to confront or ignore possible instances of misconduct?
- Under what conditions do researchers not intervene? Do they experience any regrets?
- Do researchers who intervene face negative consequences afterward? If so, what forms do these take?
- Do researchers perceive that their institutions will proactively handle incidents reported to them? Do perceptions of institutional responsibility affect intervention rate?

This project was funded by both the National Institute of Neurological Disorders and Stroke and the Office of Research Integrity, Grant No. R01 NS049573, awarded to Simmons College, Boston.

RCR

Incorporating Ethics *(from page 1)*

While viewing a video case study, students are repeatedly asked how they would respond to the situations. A series of prompts inserted between key scenes encourage students to reflect on the reasons behind each character's choices, as well as on the actions that they themselves might choose if placed in a similar situation. Do they (1) try to produce "the greatest good for the greatest number" of people affected by the situation, viewing themselves as simply one person among many (Mill)? Or do they (2) adhere to one or more duties that apply to the situation, viewing themselves as an individual agent who is obligated to do the right thing regardless of the consequences to self and others (Kant)? Or perhaps they choose to (3) act in ways that exemplify the best or most admirable character traits, traits that are shaped by the communities in which they grew up and currently participate (Aristotle)?

As the video plays out, students learn to recognize subtly different patterns of thought and motivation and develop a deeper awareness of the pattern(s) that govern their own choices and actions. The videos also provide opportunities to practice coordinating individual goals and decisions in a context in which each person's success or failure is inextricably linked to that of a larger group. Since the ethics lessons are brief and presented in the context of ongoing scientific research, students can see the immediate personal relevance, and at the same time, they are being encouraged to think about their own choices from a broader social and ethical perspective.

Improving ethical thinking has obvious implications for the integrity of the research group. We have found that group discussions can help students understand how the benefit of the individual relates to the benefit of the whole group and how this requires conceptualizing the situation in a way that does not place the individual and the group in essential conflict.

In our experience, the process of comparing and contrasting their various beliefs and responses enables students to consider alternate behaviors and learn new solutions to old problems. This heightens their awareness of their own ethical outlooks while also broadening their understanding of the cultures and norms applied by members of other social groups. This leads to discussions on the place of specific rules and values within their research group. When combined with good mentoring practices that exemplify research integrity and affirm the value of students as members of a research community, ethics learning can be fully integrated with scientific training.

That cultivating research integrity requires teaching students how to achieve individual goals in the group context is something RCR educators have known for at least a decade, during which time they have been developing and sharing their cases at sites like *www.OnLineEthics.org* and *www.uab.edu/graduate/rcr* (the latter also contains video content). New teaching methods at the intersection of RCR and ethical theory now promise to enrich this instruction. The result will be practical lessons in how mentoring and other forms of interpersonal cooperation can help individuals achieve their research goals—while at the same time enhance the research integrity of the scientific communities in which they work.

Research Funding Announcement Specifies Focus

"Research on Integrity in Collaborative Research"

The format for 2010 researchers who are interested in conducting Research on Research Integrity (RRI) will use the R21 mechanism. The R21 directs researchers to focus on questions in the context of research collaborations.

Partnering with ORI this year will be the National Center for Research Resources (NCRR), Fogarty International Center, National Institute of Biomedical Imaging and Bioengineering (NIBIB), and Office for Human Research Protections (OHRP). NCRR also will provide administration at all stages of the grant process, including the review process.

Deadline for applications is April 7, 2010. The announcement can be found at *http://grants.nih.gov/grants/guide/rfa-files/RFA-RR-09-004.html*

International

Health Canada Visits the Office of Public Health and Science (OPHS)

Susan Garfinkel, Ph.D., Scientist Investigator, ORI, Division of Investigative Oversight

On October 14, 2009, representatives from Health Canada (HC) visited the Office of Research Integrity (ORI) to discuss the development of HC's *Scientific Integrity Policy and Procedure for Addressing Allegations of Scientific Misconduct*. Dr. Zubin Master, Senior Policy Analyst, and Dr. Basanti Ghosh, Manager, Research Policy, both of the Science Policy Directorate, HC, met with members of ORI, Office for Human Research Protections (OHRP), and the Office of the General Counsel, Public Health Division, to draw on the many years of experience from our Offices.

HC is the federal department responsible for helping the people of Canada maintain and improve their health. HC has five core roles: leader and partner, regulator, funder, service provider, and information provider in order to realize its vision.

As a regulator, HC is involved in protecting Canadians and facilitating the provision of products vital to the health and well-being of Canadians. HC regulates and approves the use of health products including biologics, pharmaceuticals, medical devices, and natural health products. In this regard, HC's responsibilities are similar to those of the U.S. Food and Drug Administration. In addition, HC is also responsible for delivering a variety of programs and services in environmental health and protection, substance abuse, tobacco policy, workplace health, and the safe use of consumer products. HC also oversees the safety of consumer goods, foods, pesticides, and toxic substances.

In 2006, under the leadership of HC, the Canadian Research Integrity Committee was formed with the objective of strengthening the research integrity system in Canada. The committee concluded that a pan-Canadian approach for governing research integrity was necessary. Hence, several ongoing initiatives were developed to promote research integrity; one focus is an assessment by the Council of Canadian Academies to determine the key research integrity principles, procedural mechanisms, and practices, appropriate in the Canadian context, that could be applied across research disciplines at institutions receiving funds from the federal granting councils *(http://www.scienceadvice.ca/research_integrity.html)*.

In addition, efforts are underway to improve the current research integrity framework, in part through *The Tri-Council Policy Statement: Integrity in Research and Scholarship (http://www.nserc-crsng.gc.ca/NSERC-CRSNG/Policies-Politiques/tpsintegrity-picintegritie_eng.asp)*.

HC realizes that integrity within its federal science-based departments and agencies is crucial to deliver its mandate of both helping to ensure the health and safety of Canadians and increasing public trust while maintaining the credibility and reputation of the Department and the Minister of Health. To continue to foster a culture of integrity and to address immediate organizational needs, the Science Policy Directorate is developing a Scientific Integrity Framework for the Department.

The scientific integrity framework when completed will include: (1) a policy on the ethical conduct of science, (2) a procedure to address allegations of scientific misconduct, and (3) an education and training component.

Work on the policy is focused on building from existing policies and delineating what is considered ethical conduct of research and the use of science in decision making. It also will address the need for a harmonized procedure for addressing allegations of scientific misconduct. The education and training component will address the training needs of the departmental scientific community on scientific integrity and the procedures to follow for resolving ethical issues that may be encountered at work.

Two OPHS Offices, ORI and OHRP, are pleased to continue to collaborate with HC as it models its scientific integrity framework. Because science is now a global enterprise, it is more important now, than ever before, for concurrence of international research misconduct policies and for the international scientific community to foster responsible conduct in research.

International

A View from Europe *(from page 1)*

for good scientific practice and procedures for investigating allegations of misconduct *(http://www.esf.org/publications/policy-briefings.html)*.

Seven years have elapsed without consensus for harmonizing policies on research misconduct in Europe. Another ESF report in May 2008, commissioned for the First World Conference on Research Integrity, intended to "provide a systematic review of various approaches to promote research integrity and handle allegations of research misconduct." The information-collection process for this report concentrated on public-funding research agencies and learned societies.

Since there is a consensus that research institutions are the main guarantors of integrity, it was surprising that universities, research institutions, and private research-supporting agencies (e.g., the UK Welcome Trust) were excluded. Although the report stated that countries surveyed used a wide range of approaches to deal with research integrity and misconduct, there was no discussion of the variability of standards and no mention of the number of investigations submitted to existing panels. Nevertheless, the report contains useful information about countries' recent efforts to promote research integrity guidelines. For instance, in 2004, the Slovak Research and Development Agency pragmatically adopted the rigorous recommendations of the Deutsche Forschungsgemeinschaft, Germany's main research-funding agency, for safeguarding good scientific practice *(http://www.codex.vr.se/texts/StewardsOfIntegrity.pdf)*.

From 1990 to 2005, the number of international collaborations, measured by co-authorship of refereed papers, grew linearly, but the number of international addresses grew exponentially. The rise in multiple authorships reflects the multidisciplinary, collaborative character of modern research. Yet a lack of homogeneity in research monitoring means that when misconduct allegations appear, authors from different countries are being treated differently.

One way to ensure that all co-authors are treated fairly would be to establish a common European policy on scientific dishonesty with uniform procedures for violations. International cooperation within Europe (and between Europe and the United States) might also tackle the problem of scientists who have committed misconduct relocating to countries where employers may be unaware of their behavior.

Any future change will require European countries to adopt current guidance from national or international organizations as a regulation. Thus, countries without either a tradition of reporting misconduct or formal systems for investigating allegations have the opportunity of observing existing models and choosing the best one to adopt. Consensus among the sectors involved, the scientists themselves, research institutions, funding agencies, and governments, should decide the scheme they ultimately choose and its implementation.

The existing legislation also should be analyzed. European countries have different judicial traditions that, in most cases, are not adapted to cases of scientific misconduct. In the absence of appropriate legislation, internal regulations may offer consensual solutions through conciliation or arbitration. Possibly, heterogeneous, influential national and European academic societies and associations may work out principles of good scientific practice for their area of expertise and make them binding on their members. In addition, pan-European research-funding bodies, notably the EC and the European Research Council (ERC), might set up regulatory mechanisms and compel institutions to have research integrity rules and procedures for handling allegations of scientific misconduct.

Ultimately, I believe, the bodies that make grant decisions need to make them contingent upon the willingness of institutions to adhere to scientific integrity guidelines.

ORI would like to thank the following contributors to the *ORI Newsletter*:

Xavier Bosch, Patricia Keith-Spiegel, Gerald P. Koocher, Nancy J. Matchett, Joan Sieber, and Sara Vollmer

Case Summaries

Jennifer N. Arriaga
Universidad Central Del Caribe

Based on the findings of an investigation report by the Universidad Central Del Caribe (UCC) and additional analysis and information obtained by ORI during its oversight review, ORI found that Jennifer N. Arriaga, former Research Assistant in a clinical trial project entitled Brief Strategic Family Therapy for Adolescent Drug Abusers (BSFT) at UCC, engaged in research misconduct in research funded by National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH), cooperative agreement U10 DA13720.

Specifically, ORI found that Ms. Arriaga knowingly and intentionally engaged in research misconduct by fabricating 17 interviews and falsifying 10 subject incentive receipts in the BSFT. The interview record consisted of Timeline Follow Back information, confidentiality self-report forms, and urine drug test results.

The following administrative actions have been implemented for a period of two (2) years, beginning on August 18, 2009:

(1) Ms. Arriaga is debarred from eligibility for any contracting or subcontracting with any agency of the United States Government and from eligibility or involvement in nonprocurement programs of the United States pursuant to HHS' Implementation (2 C.F.R., Part 276 *et seq*.) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 C.F.R., Part 180); and

(2) Ms. Arriaga is prohibited from serving in any advisory capacity to the U.S. Public Health Service (PHS), including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

Norma Couvertier
APT Foundation

Based on the report of an investigation conducted by the APT Foundation and additional analysis conducted by ORI in its oversight review, ORI found that Norma Couvertier, former Research Assistant II, APT Foundation in New Haven, Connecticut, engaged in research misconduct in research supported by National Institute of Drug Abuse (NIDA), National Institutes of Health (NIH), award R37 DA015969.

Specifically, ORI found that Ms. Couvertier engaged in research misconduct by falsifying and fabricating data that were reported on Participant Urine Monitoring and Breathalyzer Result Forms (CRFs) completed by the Respondent for thirty-two (32) of the enrolled study participants in the Computer-Based Training in Cognitive Behavioral Therapy (CBT4CBT) research study.

ORI found that Ms. Couvertier, on 253 occasions, with 32 different study participants, falsified alcohol breathalyzer test results and knowingly and consistently entered a false negative test (indicated by 0.000) rather than identifying the result as a missing data collection (indicated by code 999).

ORI acknowledges Ms. Couvertier's verbal admissions and willingness to cooperate and assist during the APT Foundation's investigation.

Ms. Couvertier has entered into a Voluntary Settlement Agreement in which she has voluntarily agreed, for a period of three (3) years, beginning on September 18, 2009:

(1) to exclude herself from serving in any advisory capacity to the U.S. Public Health Service (PHS), including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant;

(2) that any institution that submits an application for PHS support for a research project on which the Respondent's participation is proposed, or that uses her in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which she is involved must concurrently submit a plan for supervision of her duties to ORI. The supervisory plan must be designed to ensure the integrity of her research contribution. Respondent agreed that she will not participate in any PHS-supported research until such a supervisory plan is approved by ORI.

Zhong Bin Deng
Medical College of Georgia

Based on the report of an investigation conducted by the Medical College of Georgia (MCG), the report of the MCG Adjudication Subcommittee, additional analysis conducted

"Imagination is more important than knowledge."

Albert Einstein

Case Summaries

by ORI in its oversight review, and the Respondent's written and oral admissions and expressed remorse, ORI found that Dr. Zhong Bin Deng, former postdoctoral fellow at MCG in Augusta, GA, engaged in scientific misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grant 2 P01 AI42288.

ORI found that Dr. Deng engaged in scientific/research misconduct by falsifying research results reported in a paper published in *Nature Medicine*.[1] Specifically:

Figures 1 and 2 in the *Nature Medicine* paper purportedly show that the autoimmune regulator Aire controls iNKT cell development and maturation. In Figure 1(a), the Respondent falsified the Aire +/+ (thymus and liver) flow cytometry plots by substituting Aire +/- (thymus and liver) flow cytometry plots that were altered to disguise their origins and falsified the Aire -/- (bone marrow) flow cytometry plot by substituting the Aire +/- (bone marrow) flow cytometry plot, also altered to disguise its origin.

- In supplementary Figure 2 of the *Nature Medicine* paper, the Respondent falsified flow cytometry plots as follows: (1) in row 1, the Aire -/- (thymus) flow cytometry plot [plot 2] and the Aire +/+ -/- (thymus) flow cytometry plot [plot 3] are duplicates, thus one of the plots is falsified; (2) in row 2, the Aire -/- (spleen) flow cytometry plot [plot 2] and the Aire -/- +/+ flow cytometry plot [plot 5] are duplicates, thus one of the plots is falsified; (3) in row 3, the Aire -/- (liver) flow cytometry plot [plot 2] and the Aire +/+ -/- (liver) flow cytometry plot [plot 3] are duplicates, thus one of the plots is falsified; and (4) in row 4, the Aire -/- (thymus) flow cytometry plot [plot 2] and the Aire +/+ +/+ flow cytometry plot [plot 4] are duplicates, thus one of the plots is falsified.

Dr. Deng has entered into a Voluntary Settlement Agreement in which he has voluntarily agreed, for a period of two (2) years, beginning on October 2, 2009:

(1) that any institution that submits an application for PHS support for a research project on which the Respondent's participation is proposed, or that uses him in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which he is involved must concurrently submit a plan for supervision of his duties to ORI; the supervisory plan must be designed to ensure the integrity of his research contribution; respondent agreed that he will not participate in any PHS-supported research until such a supervisory plan is approved by ORI;

(2) that any institution employing him submits, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-funded research in which the Respondent is involved, a certification to ORI that the data provided by the Respondent are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported in the application or report; and

(3) to exclude himself from serving in any advisory capacity to the U.S. Public Health Service (PHS), including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

Endnote 1

Mi, Q.-S., Deng, Z.-B., Joshi, S.K., Wang, Z.-Z., Zhou, L., Eckenrode, S., Joshi, R., Ly, D., Yi, B., Delovitch, D.L., & She, J.-X. "The autoimmune regulator (Aire) controls iNKT cell development and maturation." *Nature Medicine* 12:624-626, 2006; hereafter referred to as the "*Nature Medicine* paper."

Disclaimer

The HHS Office of Research Integrity (ORI) publishes the *ORI Newsletter* to enhance public access to its information and resources. Information published in the *ORI Newsletter* does not constitute official HHS policy statements or guidance. Opinions expressed in the *ORI Newsletter* are solely those of the author, and do not reflect the official position of HHS, ORI, or its employees. HHS and ORI do not endorse opinions, commercial products, or services that may appear in the *ORI Newsletter*. Information published in the *ORI Newsletter* is not a substitute for official policy statements, guidance, applicable law, or regulations. The *Federal Register* and the *Code of Federal Regulations* are the official sources for policy statements, guidance, and regulations published by HHS. Information published in the *ORI Newsletter* is not intended to provide specific advice. For specific advice, readers are urged to consult with responsible officials at the institution with which they are affiliated, or seek legal counsel.

Case Summaries

Nagendra S. Ningaraj, Ph.D.
Vanderbilt University School of Medicine

Based on the reports of an investigation conducted by Vanderbilt University School of Medicine (VUSM) and additional analysis by the Division of Investigative Oversight (DIO), ORI, in its oversight review, found that Nagendra S. Ningaraj, Ph.D., former Associate Professor of Neurological Surgery and Cancer Biology, VUSM, engaged in scientific misconduct by falsifying MALDI-MS images and mass spectral tracings and associated text in Figure 21 reported in National Cancer Institute (NCI), National Institutes of Health (NIH), grant application 1 U54 CA119421-01 and by falsifying MALDI-MS images in a presentation during the American Association for Cancer Research (AACR) meeting held on April 16-20, 2005, which cited support from NCI, NIH, grants R25 CA92943 and P50 CA098131.

Specifically, ORI found that:

1. Respondent reversed the images for the control and minoxidil-treated brains in Figure 21 of the 1 U54 CA119421-01 grant application, claiming that minoxidil increased delivery of Gleevec to the tumor. Respondent also reversed the same images in a presentation during the AACR meeting in April 2005.

2. In Figure 21 of the 1 U54 CA119421-01 grant application, Respondent reported mass spectral tracings as having been obtained from brain tumors in Gleevec-treated mice that had been pretreated with minoxidil, while in fact they were pretreated with another potassium channel opener, NS1619, and Respondent falsely stated the minoxidil pretreatment caused an 8-fold increase in Gleevec delivery to brain tumors (compared to non-minoxidil pretreated tumors).

3. Respondent further falsified Figure 21 of the 1 U54 CA119421-01 grant application by juxtaposing the reversed MALDI-MS images (obtained with minoxidil) with the mass spectral tracings (obtained with NS1619) in the same figure and by failing to report that the images and spectra in the figure were actually obtained in totally different experiments, performed on different dates and with different K^+ agonist pretreatments.

Dr. Ningaraj has entered into a Voluntary Settlement Agreement in which he has voluntarily agreed, for a period of three (3) years, beginning on August 31, 2009:

(1) to be prohibited 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;

(2) that any institution that submits an application for PHS support for a research project on which the Respondent's participation is proposed, or which uses him in any capacity on PHS-supported research, or that submits a report of PHS-funded research on which he is involved must submit a plan for supervision of his duties to the funding agency for approval no later than a month before the scheduled funding; the supervisory plan must be designed to ensure the scientific integrity of his research contribution; a copy of the supervisory plan also must be submitted to ORI by the institution; Respondent agrees that he will not participate in any PHS-supported research until such a supervisory plan is submitted to ORI; and

(3) Respondent will ensure that any institution employing him submits, in conjunction with each application for PHS funds or any report, manuscript, or abstract of PHS-funded research in which he is involved, a certification that the data provided by him are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported in the application or report. Respondent must ensure that the institution sends the certification to ORI. The certification shall be submitted no later than one month before funding and concurrently with any report, manuscript, or abstract.

Ryan M. Wolfort, M.D., Ph.D.
Louisiana State University Health Sciences Center-Shreveport

Based on the report of an investigation conducted by Louisiana State University Health Sciences Center-Shreveport (LSUHSC-S) and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Dr. Ryan M. Wolfort, who was a House Officer in the Department of Surgery, and a former graduate student, Department of Molecular and Cellular Physiology, LSUHSC-S, engaged in research misconduct in the reporting of re-

Case Summaries

search supported by National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), grants R01 HL26441 and P01 HL55552.

Respondent's research misconduct related to his dissertation research as a graduate student, which he undertook at the same time that he also was serving as a House Officer at LSUHSC-S. ORI acknowledges Dr. Wolfort's cooperation with the LSUHSC-S misconduct proceedings.

PHS found that Dr. Wolfort engaged in research misconduct by falsifying and fabricating data reported in three publications[1] and one manuscript[2] that had been submitted for publication, reviewed, and returned for revision. Specifically, Dr. Wolfort falsified and fabricated data reported in research examining the contribution of immune mechanisms to early oxidative stress and endothelial dysfunction in mice with induced dietary hypercholesterolemia by:

1. admittedly fabricating tabulations and the associated statistical analyses of RT-PCR data on Nox-2 mRNA expression in the three publications and the manuscript; and

2. falsifying data and the associated statistical claims, specifically by (a) admittedly falsifying the measurements of endothelial function by myographic recordings of aortic ring dilation in reaction to vasoactive substances in the three papers and manuscript, (b) admittedly falsifying the measurement of cytokine by cytometric bead assay in paper 3, and (c) falsifying the measurement of superoxide production by cytochrome c reduction in papers 1 and 2, for which the underlying spreadsheet data the Respondent claims were unintentionally misrepresented, massaged, and improperly collated, but for which Respondent acknowledges that the raw data were missing for all three papers, admittedly because he intentionally erased files and discarded notebooks.

Dr. Wolfort has entered into a Voluntary Exclusion Agreement in which he has voluntarily agreed, for a period of two (2) years, beginning on July 13, 2009:

(1) to exclude himself 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 pursuant to HHS' Implementation (2 C.F.R., Part 276 *et seq.*) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 C.F.R., Part 180); and

(2) 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.

Endnote 1

Wolfort, R.M., Stokes, K.Y., & Granger, D.N. "CN4+ T lymphocytes mediate hypercholesterolemia-induced endothelial dysfunction via a NAD(P)H oxidase-dependent mechanism." *Am J Physiol Heart Circ Physiol* 294:H2619-H2626, 2008; hereafter referred to as "paper 1." (Identified for retraction.)

Wolfort, R.M., Manriquez, R., Stokes, K.Y., & Granger, D.N. "Platelet-derived RANTES mediates hypercholesterolemia-induced superoxide production and endothelial dysfunction." *Arterioscler Thromb Vasc Biol,* Vol. 28 (pages unavailable), as Epub 2008, July 17; hereafter referred to as "paper 2." (Identified for retraction.)

Wolfort, R.M., Stokes, K.Y., & Granger, D.N. "Immune cell-mediated endothelial cell dysfunction during hypercholesterolemia involves interferon-[gamma] dependent signaling." *Am J Physiol Heart Circ Physiol*, as Epub 2008, September 5; hereafter referred to as "paper 3." (Retracted in *Am J Physiol Heart Circ Physiol* 295(5):H2219, 2008 November.)

Endnote 2

Manuscript submitted to the journal *Free Radicals in Biology and Medicine (FRBM)*, by Ryan M. Wolfort, Katherine C. Wood, Robert P. Hebbel, and Neil Granger, "Mechanisms underlying the vasomotor dysfunction in sickle transgenic mice," Ms Number FRBM-D-08-00454.

"Science is an international endeavor. Wherever it is done, it connects us to the scientists, scholars, and philosophers of the past and the future. Our work as a scientific community can make human lives better, healthier, and longer, and can improve the economies of nations, regions, and the world. To be a scientist is both a privilege and a passion."

Excellence Everywhere, Burroughs Wellcome Fund, 2009

Save the Date

THE SECOND WORLD CONFERENCE ON RESEARCH INTEGRITY
Singapore, July 21-24, 2010
http://www.wcri2010.org/

This conference will explore ways to promote high ethical standards in conducting research. With the increasing numbers of international collaborations, there is likely a greater need for consensus and commitment to high standards in designing, conducting, analyzing, and reporting research. Developing global networks and understanding may help to ensure responsible research and to maintain the public's confidence in researchers and their results.

The conference is aimed at leaders and key decision makers in research funding organizations (grant agencies and research councils).

Those interested in attending should register on the conference web site. To obtain further information or to propose ideas and topics for discussion, contact the conference co-chairs: Nick Steneck (nsteneck@umich.edu) and Tony Mayer (tonymayer@ntu.edu.sg).

Office of Research Integrity
1101 Wootton Parkway, Suite 750
Rockville, Maryland 20852

Office of the Director .... (240) 453-8200
Fax ..... (301) 443-5351

Division of Education
and Integrity ..... (240) 453-8400
Fax ..... (301) 443-5351

Assurances Program ..... (240) 453-8400
Fax ..... (301) 594-0042

Division of Investigative
Oversight ..... (240) 453-8800
Fax ..... (301) 594-0043

Research Integrity
Branch/OGC ..... (301) 443-3466
Fax ..... (301) 594-0041

http://ori.hhs.gov

DEPARTMENT OF
HEALTH AND HUMAN SERVICES

Office of the Secretary
Office of Research Integrity
1101 Wootton Pkwy, Suite 750
Rockville MD 20852

Official Business
Penalty for Private Use $300

DATED MATERIAL