U.S. Department of Health and Human Services • Office of the Secretary • Office of the Assistant Secretary for Health

VOLUME 21, NO. 3 HTTP://ORI.HHS.GOV JUNE 2013

Office of Research Integrity

NEWSLETTER

The *ORI Newsletter* is published quarterly by the Office of Research Integrity, Office of the Assistant Secretary for Health, Department 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 at http://ori.hhs.gov.

IN THIS ISSUE

Divergent Views on Instruction in Responsible Conduct of Research

Diana Arsenieva, Ph.D., Oak Ridge Institute for Science and Education (ORISE) Fellow, ORI

At the "ORI at 20: Reassessing Research Integrity" conference on April 3, 2013, the Director of ORI, Dr. David E. Wright; Dr. Alan K. Price, former director of the Division of Investigative Oversight at ORI; and Dr. Nicholas H. Steneck (University of Michigan), a recognized leader in the field of Research Integrity, set the tone of the Responsible Conduct of Research (RCR) panel. They provided historical perspectives on the development of a federal response to misconduct in science and on the development of, and shortfalls in, RCR instruction. The term "RCR" was coined by the Institute of Medicine report of 1989, and the proposed requirement for RCR training was endorsed and expanded by both the Ryan Commission of 1995 and the Raub Implementation Group of 1996. The RCR training concept was created with an implicit goal of reducing research misconduct, as a pre-emptive measure, and with an assumption that problems stem from ignorance of standards. Since the National Institutes of Health first required RCR instruction in 1990 for all trainees who were paid from research awards, institutions

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Perspectives of Journal Editors and Publishers on Scientific Integrity Issues

Raju Tamot, Ph.D., Oak Ridge Institute for Science and Education (ORISE) Fellow, ORI

The surge in allegations and findings of research misconduct and retraction notices in the past decade has dispelled the myths that scientific research is always done in good faith and that scientific fraud is the product of rare psychopathology. This surge also has raised doubts about the idea that science is self-correcting and that the peer review process and replication of the original findings are adequate measures to detect fraudulent practices. The current academic and scientific system has created intense competition and pressure on scientists. It rewards scientists for securing funding and publishing their findings in prestigious journals. Journal editors are aware of these pressures. They also know that such pressures will cause some proportion of submissions to have errors or have fabricated data and/or manipulated images.

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A Whistleblower's Views: Before, During, and After

Sandra L. Titus, Ph.D., ORI

Dr. Mary Ann Allen provided her recollections and thoughts about reporting research misconduct when she was a graduate student. Her presentation at the "ORI at 20: Reassessing Research Integrity" conference was divided into three organizing sections: (1) how she decided to make an allegation, (2) what happened once she filed the allegation, and (3) whether reporting had any long-term impact.

Before the Allegation

Dr. Allen described the dilemma she and five other fellow students experienced when they discovered multiple instances when their advisor, a principal investigator (PI), had fabricated data in grant proposals. She gave an account of how the group members dealt with whether they had observed research misconduct; at first, they were unsure about what to do or who might be able to help them. They weighed and discussed the pros and cons of reporting. The six students debated for over a month, collected more evidence, investigated it further, and finally decided to report their findings to the institution. Dr. Allen suggested that it would be valuable to have a federal hotline number to call so that one could be anonymous, seek advice about whether the observation was research misconduct, and then decide whether and how to report it.

During the Process

Dr. Allen further described how she felt intimidated by her institution's review process. She also was concerned about the impact reporting the allegation would have on the ability of the six students in the laboratory to complete their graduate studies. Once the students reported their findings of research misconduct, some faculty members were greatly supportive, whereas others were quite angry. She reported, "At times, I felt shunned and surrounded by gossip and rumors." Comments were directed at them stating that the six students had done a terrible thing by turning in, or possibly even framing, their PI. They felt as if they were being kept in the dark during the long institutional review process and were not provided much information or emotional support. She conveyed how hard it was to wait during the lengthy process and also deal with the paucity of information.

The laboratory was eventually closed, and several doctoral students chose to leave with master's degrees. As a result, she urged institutions to create stronger rules against retaliation and be more supportive to all parties during the process. She also suggested having two mentors, though it may not always be practical (yet not unheard of). Two mentors would help both in uncovering a problem with the fraudulent PI and in dealing with the fallout from the misconduct allegation.

After the Finding

Although Dr. Allen has successfully completed her Ph.D. at another university (four years devoted to her second graduate-degree project), she described recent residual fallout from being a whistleblower. When she was looking for a postdoctoral position, she learned something troubling. Someone commented to her future advisor that she may not be a good hire, because she had been a whistleblower (and was therefore perceived to be a troublemaker). Fortunately, her advisor did not view her reporting research misconduct as a negative quality, and she is now a Research Associate at the University of Colorado, Boulder.

Recent Study on Mentors' Involvement in RCR

Sandra L. Titus, Ph.D., ORI and Janice M. Ballou, M.A., Mathematica Policy Research, Inc.

The importance of public confidence in scientific findings and trust in scientists cannot be overstated. Thus, it becomes critical for the scientific community to focus on enhancing the strategies used to educate future scientists on ethical research behaviors. What we are lacking is knowledge on how faculty members shape and develop ethical research standards with their students. We are presenting the results of a survey with 3,500 research faculty members. We believe this is the first report on how faculty work with and educate their Ph.D. students on basic research standards. Specifically, we wanted to determine whether individual faculty members, who are

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John Krueger, Ph.D., Scientist Investigator Retires from ORI after 20 Years

Dr. John Krueger was an investigator at ORI for over 20 years and was involved in the various transitions of the Investigative Division at ORI. He is known within ORI for first applying image processing to evaluate evidence in ORI cases, and then for developing the procedures to detect and to interpret manipulated images in science. John pioneered these efforts as falsified images moved from "paper" to "bytes" and to the Internet, and as their analysis moved from NIH Image to Photoshop. Dr. Krueger's work resulted in his creating and publicizing several tools that are known as ORI's "forensic droplets" (*http://ori.hhs.gov/droplets*), used within ORI and others, notably institutional faculty conducting investigations, RIOs, RCR instructors, and even the occasional journalist. The common challenge of dealing with problem images enabled him to advance ORI's communications with journals. John's efforts also restarted and formalized one route for correcting the literature in misconduct cases, that is, by the linking of the PubMed search results to research misconduct findings. We hope that John continues to pursue these interests and develop other teaching tools in retirement…. But fully expect that he will first head off to see the photo manipulation exhibit at the National Gallery of Art, entitled "**Faking It: Manipulated Photography before Photoshop**."

We asked Dr. Krueger to recall some of his fondest memories of working at ORI. Much to our surprise, he chose instead to share the following handwritten note. It had been sent to him by the respondent in one of his cases that resulted in a PHS finding of scientific misconduct.

> *"Most people say that it is the intellect which makes a great scientist. They are wrong: it is character."*
>
> **Albert Einstein**
> (1879-1955)

February 2, 2004

Dear Dr. Krueger:

I just wanted to drop you a note to thank you for your kind voice mail message you left me several weeks ago. I can't tell you how much that meant to me. The past few years have been very difficult for me, but I have learned a lot from this experience. Everyone at ORI has been very kind and professional through this process. It's great to know that my efforts to do the right thing have been noticed. Thank you again for your going above and beyond what is expected.

Warm regards,
(Respondent)

John said that this gracious note remains extraordinarily unusual. He said, "It demonstrated perspective and humility and reveals what is lost in the current 'blogospherics' that tend to depersonalize the individual dimensions in many ORI cases."

Recent Study *(from page 2)*

advisors or mentors, differ in how they implemented components of responsible conduct of research (RCR) with their Ph.D. students. Mentors were more likely than advisors or supervisors to report working with all of their Ph.D.'s, who graduated in the past 5 years, on the 17 recognized critical components of RCR training and research skill development. We also found about half of the faculty members believe RCR is an institutional responsibility versus a faculty responsibility. Less than a quarter have had opportunities to participate in faculty training to be a better mentor, advisor, or research teacher, and about one third of faculty did not or could not remember whether they had guidelines related to their responsibilities to Ph.D. students. We discuss the implications of our findings and focus on ways that Ph.D. research mentoring can be enhanced.

Reference

S.L. Titus and J.M. Ballou, "Ensuring Ph.D. Development of Responsible Conduct of Research Behaviors: Who's Responsible?" *Science and Engineering Ethics*, May 18, 2013, doi: 10.1007/s11948-013-9347-4.

Clarification on the Issues Involving the Philippe Bois Research Misconduct Case

On April 18, 2013, the Office of Research Integrity (ORI) published a notice of two findings of research misconduct by Dr. Philippe Bois in the *Federal Register* at 78 Fed. Reg. 23255.

The *Federal Register* described the terms of the settlement agreement and set forth ORI's research misconduct findings in full. Nonetheless, in an item headed "Lawsuit settlement" under "Seven days: 19-25 April 2013: *Nature* News & Comment" published online, the terms of the settlement are not accurately characterized. ORI is concerned that the scientific community has been misinformed about the outcome and significance of this case and wishes to correct the view stated in the news item that Philippe Bois, Ph.D., "successfully appealed the ORI findings" and that he "inadvertently fabricated" data.

In brief, Dr. Bois filed a request for an administrative hearing before a Department of Health and Human Services (HHS) Departmental Appeals Board Administrative Law Judge (ALJ) under 42 C.F.R. Part 93, Subpart E, to contest ORI's misconduct findings for falsifications in two figures, Figure 4B in *Mol. Cell. Biol.* 25:6112, 2005 (*MCB*), and Figure 1A in *J. Cell Biol.* 170:903, 2005 (*JCB*), and the administrative actions imposed.

The request for hearing was denied by the ALJ.

In a subsequent lawsuit filed by Dr. Bois, U.S. District Judge Amy Berman Jackson affirmed the ALJ's decision to deny the hearing request regarding one finding, Figure 1A, *JCB*, because the ALJ's ruling that Dr. Bois had failed to raise a genuine dispute over facts material to that finding was not arbitrary and capricious.

However, the Court also found that the ALJ's dismissal of Dr. Bois's hearing request for the second finding, Figure 4B, *MCB*, was arbitrary and capricious and the judge vacated the debarment of Dr. Bois. Judge Berman Jackson wrote:

This ruling should not read as any sort of exoneration, and does not purport to address the merits of Dr. Bois's case; rather it is simply a determination that Dr. Bois must have the opportunity to present his highly factual defense, which may or may not withstand cross-examination and any rebuttal evidence ORI elects to present.

While HHS's Motion for Reconsideration was pending in U.S. District Court, Dr. Bois and HHS reached a settlement whereby Dr. Bois denied that he committed research misconduct but agreed not to further appeal ORI's findings of research misconduct for the falsification of the two figures in *MCB* and *JCB*. He further agreed to have his research supervised for a period of three years. **There is no other factual statement by ORI, no agreed-to statement by Dr. Bois, and no ruling by a judge that the conduct described in the finding set forth above was "inadvertent."** Honest error is not included in the definition of research misconduct.

ORI is Seeking Articles to Publish in the ORI Newsletter

ORI invites you to consider submitting an article for possible inclusion in a future *ORI Newsletter*. Preferably, articles should be on mentoring, authorship, RCR education, responsibilities with international research, developing collaborations, research misconduct, etc. Articles are typically 750-2,000 words and can have a scholarly focus or be a commentary. If you are interested in submitting an article, please contact Sandra Titus prior to submitting your article at (240) 453-8400 or by email at sandra.titus@hhs.gov.

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have had the responsibility for developing the format and content appropriate for their particular trainee populations. In 2010, NIH added a requirement of eight hours of face-to-face training and a strong recommendation to include nine core areas of instruction. Thus, the field of RCR has gone through 20 years of uncoordinated growth that have resulted in multiple theories and approaches to RCR instruction; yet, after 20 years, there are doubts about its efficacy.

Misconduct in research and questionable research practices are typically viewed as stemming from unethical choices or breaking rules. Several well-established disciplines contributed to development of the RCR field: ethics, psychology, philosophy, and criminology. Ethicists Dr. Eric T. Juengst (Director of the Center for Bioethics, University of North Carolina, Chapel Hill), Dr. Kenneth D. Pimple (Director of Teaching Research Ethics Program, Indiana University), and criminologist Dr. Douglas J. Adams (Department of Sociology and Criminal Justice, University of Arkansas), delivered thought-provoking presentations. They shared their perspectives on alternative ways to think about the anatomy of research misconduct and approaches to its prevention.

Dr. Juengst suggested we consider that there are two types of scientists. He described the first type as a humble, upstanding citizen who plays by the rules aimed at sustaining the research community. This type of scientist follows ethical standards (e.g., do not lie, cheat, or steal); Dr. Juengst illustrated how these ethical standards can be translated into RCR rules, such as do not fabricate, falsify, or plagiarize. This upstanding individual is likely to be meticulous, somewhat boring, and slow in producing ground-breaking research. The other type of scientist is a hero, person with exceptional abilities, talented innovator, motivated, opportunistic, and aggressively competitive individual who has a track record of success. These two types of scientists have different ethical values and possess different value to science. Creativity and invention can sometimes be in tension with following rules and maintaining standards. Is it possible that the talented innovator might also be a rule breaker, thus more susceptible to committing research misconduct? Will competitiveness drive this innovator to cut corners to secure victory?

Of course, real-life scientists are somewhere in between those two extremes. Dr. Juengst's analogy brings us to the realization that the ever-increasing competition for funding and permanent positions in biomedical sciences, as well as the high preference for publishing only new and ground-breaking research, encourages and selects for the hero type of scientist. Hence, the virtuous team player finds himself disadvantaged. Personal traits that the modern research community fosters in a successful scientist may also lend themselves to the apparent increase in research misconduct.

Dr. Adams explained how concepts from criminology (the control of misconduct) and sociology (the social control of all behavior) are important to understand in order to deter research misconduct and to improve RCR training. He also suggested that controlled access and increased guardianship may reduce opportunities to commit research misconduct in research studies. Thus, he made a strong case that principal investigators (PIs) can be proactive in preventing research misconduct in their laboratories. PIs can encourage group interaction through discussing common goals, projects, and challenges at laboratory meetings (informal control by group members), through sharing laboratory space and scientific expertise, and by keeping logs of research activities within the laboratory (increased guardianship). His emphasis on informal group dynamics provides RCR instructors with additional tools to use in discussing the importance of collaboration and mentoring. He also insinuated that a scientist who is isolated and not connected to a research group has a greater risk of succumbing to pressure and has increased opportunity to commit research misconduct.

Dr. Pimple also emphasized that instruction, combined with socialization, can be a powerful tool to use in shaping human behavior, which is well known to occur in military and seminary training. The intense training forces individuals to adapt to the requirements and norms of

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the group, or else the group will not support, accept, and protect them. In addition, he pointed out that it is widely believed that research misconduct is caused by pressure to publish and other stressors. Thus, if this is so, he pointed out that times of transition, like graduation and job searches, as well as high-stakes deadlines, such as submission of grant proposals, may merit heightened scrutiny and increased oversight (as well as moral support) to minimize the risk of corner-cutting.

Another approach to preventing misconduct was recommended by Dr. Adil Shamoo (Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine). Dr. Shamoo argued that random data audits (akin to tax audits) were a powerful and unused tool which would prevent research misconduct as well as identify it. He suggested that random audits of only 1 percent of projects would reduce misconduct and be economically beneficial. He also argued that because institutions receive large overhead funding for each grant, they should invest some of that money in auditing to ensure the integrity of the research being done by their researchers. Random data audits were initially proposed by Dr. Shamoo in an article in *Nature* published in 1987 and recommended in general in the 1989 report by the Office of Inspector General. However, that proposition has faced serious and continuing opposition from the scientific community. Dr. Shamoo also noted that institutions have been very reluctant to conduct audits except for human subject protection audits which were developed after highly publicized scandals in which human subjects were endangered.

Conference participants agreed that there are RCR training programs demonstrating some efficacy. Such programs include face-to-face format, online training, group discussions, and team-based learning and combined approaches. Philosopher Dr. Gary Comstock (North Carolina State University) spoke of advantages of teaching critical thinking skills rather than focusing on rule-based compliance in RCR training courses. As Dr. Mike Mumford (Department of Industrial Organizational Psychology, University of Oklahoma) noted, a successful program cannot be merely a "single shot" training, and effects cannot be expected to be immediate. Dr. Mumford said, "Most of the RCR training programs, as implemented by institutions, have had a zero effect on occurrence of research misconduct." According to Dr. Lynn E. Olson (Ohio State University), RCR training is necessary, but not sufficient. Indeed, being able to learn RCR training materials and get an excellent post-training test score is obviously a far cry from making an ethical choice needed when one is faced with an emotionally charged situation that may have adverse consequences. With that in mind, teaching practical stress management techniques, as mentioned by Dr. James DuBois (Saint Louis University), might be tremendously useful for researchers to use to avoid actions leading to research misconduct or to handle stress in other situations, such as being accused of research misconduct.

Experts also agreed that systematic evaluations of effectiveness are needed to continuously improve RCR instruction programs. Evaluation leads to accountability and helps in planning future efforts. Dr. Mumford advised that multiple evaluation instruments are needed, as well as clear goals and outcomes to be measured. The long-term institutional goal should be to build a thriving climate of research integrity. PIs must be trained to become good mentors and leaders, responsible for developing and maintaining ethical standards in their laboratories. Dr. Mumford suggested that to attract the interest of researchers rather than cause disdain for the wasted time, RCR training needs to be positioned and taught as professional training. Dr. Larry Gruppen (Department of Medical Education, University of Michigan Medical School) presented the "competencies" model as a training approach. This model contains a "built-in" evaluation system and is based not on methods or hours devoted, but on outcomes—the competencies of trainees to act correctly and professionally in relevant situations.

The presentations demonstrated that there is no simple way or agreed-upon approach to effective RCR training and deterrence of research misconduct. Yet there is a plethora of good practical ideas

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and goodwill to tackle the problem. Many of these authors plan to submit papers for consideration in the "ORI at 20: Reassessing Research Integrity Conference Proceedings" to be published in a special edition by *Accountability in Research*.

> *"The only ethical principle which has made science possible is that the truth shall be told all the time. If we do not penalise false statements made in error, we open up the way, don't you see, for false statements by intention. And of course a false statement of fact, made deliberately, is the most serious crime a scientist can commit."*
>
> **C.P. Snow**
> (1905-1980)

Perspectives *(from page 1)*

In the past, clinical journal editors had innovatively worked with the National Institutes of Health to create a standard data repository for clinical research. Using this data repository, editors, reviewers, and other scientists could see the design, data collection, proposed end points, analysis, and findings and would be able to verify the data analysis. Editors had played a pivotal role in the creation of the Clinical Trials Registry (CTR). Many clinical journals now refuse to review a manuscript that has not provided total transparency of their data in the CTR or similar registries (see article on clinical trials and FDA's new role in *ORI Newsletter*, Vol. 20, No. 4, September 2012). However, the non-clinical journals do not have such a data integrity structure in place.

Journals are the most pivotal conduits through which scientists communicate their findings. However, journal editors are increasingly finding that they need to examine source data and detect manipulation of images, in addition to having to deal with allegations of research misconduct and retractions. Three editors provided "ORI at 20: Reassessing Research Integrity" conference attendees with their approaches and concerns. Dr. Véronique Kiermer represented the Nature Publishing Group; Dr. Martin Frank represented the American Physiological Society (APS); and Dr. Ushma S. Neill represented the *Journal of Clinical Investigation* (*JCI*).

Dr. Véronique Kiermer's Perspective

Dr. Véronique Kiermer discussed *Nature* (Nature Publishing Group) journals' processes and instruments for handling allegations of research misconduct. She informed the audience that whenever a problem with submitted or published articles is detected, her publishing group focuses on examining the data at hand rather than on conducting an investigation to determine intent. Upon confirming the validity of a problem, her group first seeks an explanation from the author(s). Sometimes, more examination of the data, in light of the author's explanation, fails to resolve the issue or determines that further assessment is needed. Then, the journal editor escalates the case to the Executive Editor-level person who will make the decision on whether to refer the matter to the institution as an allegation of misconduct.

Since journal editors have neither the authority nor the capacity to investigate or adjudicate cases of research misconduct, Dr. Kiermer described her experiences in working with institutions that conduct investigations. She described her concerns and observations about the limitations of some institutional investigations. She believes that the processes of the institutional investigations are not universally reliable, because they investigate one of their own, and it inherently constitutes a conflict of interest. Further, the quality of the investigations is highly variable. Last, she pointed out that the issue of confidentiality makes the process opaque to journals; therefore, journals are not always informed about the details of the investigation, even after its conclusion.

Regardless of findings of research misconduct, Dr. Kiermer stressed how important it is for her journals to correct the scientific record. She discussed the instruments that

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journals have at their disposal for this purpose. Her publishing group typically uses *corrigendum*, if there was a serious error, but raw data could be provided to support the original conclusion, and no conclusive evidence of misconduct was found.

In contrast, retractions are used if (1) the extent of errors (honest or not) means that the data no longer support the main conclusion of the paper; or (2) there is uncertainty but the authors no longer stand by the data; or (3) institutional investigation has made a finding of misconduct affecting the results and requests retraction. Although journals have various ways to indicate the reason for the retraction, Dr. Kiermer drew attention to the overall stigma associated with the word "retraction." She cited Van Noorden (2011), who reported that there has been a tenfold increase in the number of retraction notices in the past decade and half of these were due to researcher misconduct. And she noted that Fang and colleagues had reported that half of the retractions were related to research misconduct (see *http://www.pnas.org/content/early/2012/09/27/1212247109.abstract*).

Since retractions are generally assumed to be associated with misconduct, Dr. Kiermer stated that she believes the mere use of the word creates a dilemma for authors who then become more reluctant to report honest errors. She suggested that it would be pragmatic to decouple retractions from the word "misconduct." She also called for new initiatives to promote transparency and rigor in reporting research results and to check questionable research practices. She concluded her presentation by saying that journals, funding agencies, and institutions need to work in tandem and focus on education, mentoring, and a supportive environment to promote responsible research behaviour in scientists.

Dr. Martin Frank's Perspective

After giving a brief overview of the APS, which publishes 14 peer-reviewed journals, its Executive Director, Dr. Martin Frank, reported that APS ethics issues and questions had doubled in three years (2009-2011). Addressing the various flagged issues was very time consuming and overwhelming for APS staff. Although the issues covered the gamut of ethical inquiry, a majority of the APS ethical cases involved figure manipulation, most of them detected by the art department. Dr. Frank noted that the Society began to seriously review its ethics policies and to develop a consistent plan after several names of APS authors appeared in the news, on the ORI web site, and on "Retraction Watch."

The APS first revisited its ethics policies and developed plans to restructure its ethics query processes to guarantee the quality of the content of their journals. They held an ethics retreat with their Editors in Chief, revised author guidelines, and established digital art review processes. The Society also drafted template letters for ethical concerns and produced better stated proactive plans to enforce the new ethics policies. These efforts led to enhanced guidelines and more consistency in enforcing ethics policies.

Dr. Frank believes that these efforts promoted the education of the editors and authors. In addition, the APS hired a full-time in house Publications Ethics Manager, whose primary responsibilities are to: address publication ethics concerns, facilitate the query process, update and revise policies and develop author guidelines, and promote best practices in publication ethics. The Manager also acts as a *liaison* between the APS, authors, complainants, respondents, and institutions. The hiring of the Publications Ethics Manager has helped the Society maintain consistency in process between journals, clarity of journal policies, resolution time (of allegations of research misconduct), and communication between journals and institutions. The Society's educational efforts and retention of the Publications Ethics Manager contributed to a reduction in ethical questions from 251 in 2011 to 158 in 2012.

Dr. Frank also described how the Committee on Publication Ethics (COPE) is working to create standards. They hold a forum for editors and publishers of peer-reviewed journals so that they can

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discuss all aspects of publication ethics. COPE guidelines state that publishers have an obligation not just to publish quality work, but to correct errors and maintain the integrity of the academic record as well. He noted the need for publishers to work with journal editors to: communicate journal policies; review journal policies periodically; maintain the policies to protect the integrity of the academic record; assist the parties responsible for the investigation of suspected research and publication misconduct and, where possible, facilitate resolution of these cases; and publish corrections, clarifications, and retractions.

Dr. Ushma S. Neill's Perspective

Dr. Ushma S. Neill, the former Executive Editor of JCI and currently the Editor at Large, shared her experiences working on research misconduct issues with ORI. She praised ORI's helpfulness, responsiveness, recommendations, friendliness, and willingness to make assessments hypothetically.

Dr. Neill said that 60 percent of the misconduct cases involving her journal were identified by production editors; 20 percent by referees and editors, and the remaining 20 percent by post-publication readers. The journal has to routinely deal with plagiarism, blot doctoring, photo reuse and creative cropping, and tabular data doctoring. She showed several examples of blot doctoring, image manipulation and reuse, and tabular data doctoring that had the obvious intent to obfuscate and misrepresent data. According to her, the more serious allegations involved issues like reagent theft, lack of Institutional Review Board approval, and infringement of proprietary rights of coauthors.

JCI evaluates instances of potential research misconduct in a manner similar to that of the Nature Publishing Group. When an allegation is made, JCI editors evaluate it internally and attempt to adjudicate it at the author level by examining source data and asking for clarification of images. If their assessment at this level fails to satisfy them, they screen it hypothetically with ORI's help, and if necessary, they also prepare materials to be sent to the appropriate institutional Research Integrity Officers.

Editors Protect the Scientific Record

The deliberations of this panel reaffirmed the conviction that journals, institutions, and ORI have a synergistic role in maintaining the integrity of the research record. The presentations also demonstrated that editors have an important and complex role to detect, evaluate, seek guidance, refer, and maintain an accurate scientific record. They have a direct front-line role and have created clear structures, though with variations between journals. All the editors conveyed an increased awareness of the need to examine source data and ask questions when they are concerned about data integrity.

Last, journals are beginning to hire "ethics" consultants to help in their evaluations, so they are becoming very proactive. Journals clearly do not want to adjudicate about whether something is research misconduct or not, but rather they focus on whether they trust the data sufficiently to allow them to be published.

Journals hold a primary role in sustaining integrity in research. Their role is exemplified by a focus on the scientific record and their ongoing educational efforts to write stories about integrity and promote better standards and practices. Like ORI, they too want to prevent fraudulent papers from being published as well as inform readers if the published papers are proven to be fraudulent.

References

1. F.C. Fang, R.G. Steen, and A. Casadevall, "Misconduct accounts for the majority of retracted scientific publications," October 1, 2012, *http://www.pnas.org/content/early/2012/09/27/1212247109*, doi:10.1073/pnas.1212247109.

2. R. Van Noorden, "Science Publishing: The trouble with retractions," 2011. *Nature* 478: 26-28.

"Honesty is the first chapter in the book of wisdom."

Thomas Jefferson
(1743-1826)

Case Summaries

Andrew Aprikyan, Ph.D.
University of Washington

Based on the report of an investigation conducted by the University of Washington (UW), the UW School of Medicine Dean's Decision, the Decision of the Hearing Panel at UW, and additional analysis conducted by ORI, ORI found by a preponderance of the evidence that Dr. Andrew Aprikyan, former Research Assistant Professor, Division of Hematology, UW, engaged in research misconduct in research supported by National Cancer Institute (NCI), National Institutes of Health (NIH), grant CA89135 and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH, grant DK18951, and applies to the following publications and grant applcations:

- *Blood* pre-published online on January 16, 2003 ("NEM")
- *Experimental Hematology* 31:372-381, 2003 ("CMA")
- *Blood* 97:147-153, 2001 ("ISB")
- R01 CA89135-01A1
- R01 HL73063-01
- R01 HL79615-01

Blood pre-published online on January 16, 2003, has been retracted and *Experimental Hematology* 31:372-381, 2003, has been corrected.

Specifically, ORI finds that by a preponderance of the evidence, Respondent falsified and/or fabricated results relating to the above publications and grants. Specifically, Respondent:

1. falsely reported sequencing data in the NEM manuscript to strengthen the hypothesis that NE mutations contributed to the phenotype observed in severe congenital neutropenia (SCN) patients. Specifically:

   a. Respondent falsely reported in Figures 2A and 3 that patient 3 had the R191Q neutrophil elastase (NE) mutation, when the majority of the sequencing experiments showed that the mutation was not present.

   b. Respondent fabricated text (p. 12) reporting that sequencing of RT-PCR products confirmed the expression of the NE mutants in the SCN patients and that no mutations were present in the granulocyte colony stimulating factor receptor (G-CSFR) gene and the Wiskott-Aldrich Syndrome (WAS) gene in SCN patients, when based on the lack of original records the experiments were not performed. The false claim for G-CSFR sequencing was also reported in CA89135-03.

2. falsely reported a two-fold increase in apoptosis of human promyelocytic (HL-60) cells transfected with NE mutants compared to wild type NE in Figure 4A, NEM, Figure 6A, CMA, Figure 8, HL73063-01, and Figure 7, HL79615-01. Respondent used arbitrary flow cytometry data files to generate histograms with the desired result. The false results supported the hypothesis that the NE mutations were sufficient for impaired survival of human myeloid cells.

3. falsified NE and ß-actin Western blots in Figure 4B *Blood*, pre-published online January 16, 2003, Figure 5B of the manuscript initially submitted to *Blood* April 2002, and Figure 6B *Experimental Hematology* 31:372-381, 2003, by falsely labeling lanes to support the hypothesis that accelerated apoptosis in mutant NE transfect HL-60 cells was due to the mutation and not the level of protein present. Specifically:

   a. Respondent used portions of a single NE Western blot to represent: Figure 4B as HL-60 cells transfected with L92H, R191Q, and wtNE, when the cells were transfected with R191Q, P110L, and D145-152; Figure 5B as HL-60 transfected with wtNE, mutNE, and EGFP when they were cells transfected with NE mutants, P110L, D145-152, and 194.

   b. Respondent used portions of a single ß-actin Western blot to represent: Figure 4B as HL-60 cells transfected with L92H, R191Q, and wtNE, when they were cells transfected with I31T, P110L, and G185R mutants; Figure 5B as HL-60 cells transfected with wtNE, mutNE, and EGFP, when they were cells transfected with P110L, I31T, and INE; Figure 6B as HL-60 cells transfected with G185R, mock, D145-152, and P110L NE mutants, when they were cells transfected with

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I31T, P110L, G185R, and 32. The false ß-actin Western blot in Figure 6B was also included in HL73063-01, Figure 8 (where the I31Tlane was labeled correctly), and HL79615-01, Figure 7.

4. falsified the reported methodology for flow cytometry experiments in Figure 4A, NEM, Figure 1 and 2, and Tables 2 and 3, CMA, and Figures 4, 5, and 6, ISB, to validate the key hypothesis showing accelerated apoptosis in SCN and CN patients. The methodology claimed that flow cytometry experiments were gated for GFP+ populations, or that cell purity was greater than 96%, when based on the available original records, the experiments were not performed as stated.

5. falsified Figure 2, CMA, Figure 2, HL73063-01, Figure 3, HL79615-01, and Figure 5, CA89135-01A1, demonstrating that the overnight cultures of CD34+ and CD33+ bone marrow cells from SCN/AML patients showed normal cell survival, and only the CD15+ overnight cultures showed accelerated apoptosis, when the actual record available contradicted this result. Respondent used flow cytometry data files to generate histograms with the desired result to support the hypothesis that the progression from SCN to leukemia (AML) involves acquired G-CSFR mutations that override the pro-apoptotic effect of the NE mutations in primitive progenitor cells.

Dr. Aprikyan has entered into a Settlement Agreement in which he denied ORI's findings of research misconduct based on the UW Faculty Adjudication Hearing Panel decision. The settlement is not an admission of liability on the part of the Respondent. Respondent entered into the Agreement solely because contesting the findings would cause him undue financial hardship and stress, lead to lengthy and costly appellate proceedings, and he wished to seek finality. Respondent agreed not to appeal the ORI findings of research misconduct set forth above. He has agreed, beginning on March 12, 2013:

(1) if within two (2) years from the effective date of the Agreement, Respondent receives or applies for U.S. Public Health Service (PHS) support, Respondent agreed to have his research supervised for a period of two (2) years; Respondent agreed that prior to the submission of an application for PHS support for a research project on which his participation is proposed and prior to his participation in any capacity on PHS-supported research, Respondent shall ensure that a plan for supervision of his duties is submitted to ORI for approval; the supervision plan must be designed to ensure the scientific integrity of his research contribution; Respondent agreed that he shall 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 supervision plan;

(2) if within two (2) years from the effective date of the Agreement, Respondent receives PHS support, Respondent agreed that for two (2) years, 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) Respondent agreed not to serve 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 two (2) years beginning with the effective date of the Agreement.

Matthew Poore
Advanced Liquid Logic, Inc.

Based on the report of an inquiry conducted by Advanced Liquid Logic, Inc. (Liquid Logic), the Respondent's admission, and additional analysis conducted by ORI, ORI found that Mr. Matthew Poore, former Technician, Liquid Logic, engaged in research misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), contract HHSN272200900030C.

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ORI found that the Respondent engaged in research misconduct by falsifying data that were included in one (1) presentation and one (1) report to NIAID and in laboratory records at Liquid Logic.

ORI finds that Respondent knowingly and intentionally falsified reverse transcription-polymerase chain reaction (RT-PCR) results by reporting the results from previous experiments as the actual results, when the experiments had not been performed. Specifically:

- in Liquid Logic laboratory documents, the Respondent falsified the RT-PCR results of human immunodeficiency virus (HIV) viral loads in whole blood patient samples by falsely changing previous results for two (2) samples from negative to positive and one (1) sample from positive to negative. The latter falsified sample result, changed from HIV positive to negative, was included in an April 1-June 30, 2012, quarterly report and a July 12, 2012, presentation to NIAID.
- in Liquid Logic laboratory documents, the Respondent falsified the RT-PCR whole blood lysis results of testing samples as 100 and 200 HIV viral copies per milliliter, when the experiments were not performed by the Respondent. These falsified results were included in an April 1-June 30, 2012, quarterly report to NIAID.
- in Liquid Logic laboratory documents, the Respondent falsified the graphs of RT-PCR results of the *Escherichia coli* bacteriophage MS2, an internal control, viral loads for three (3) clinical samples, when the results were actually from prior experiments of two (2) controls and one (1) unrelated clinical sample. The Respondent falsified the MS2 graphs in an effort to conceal that RT-PCR experiments of the clinical samples had not been performed.

Mr. Poore has entered into a Voluntary Settlement Agreement and has voluntarily agreed for a period of three (3) years, beginning on April 1, 2013:

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

(2) 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.

Philippe Bois, Ph.D.
St. Jude Children's Research Hospital

Notice is hereby given that effective on March 14, 2013, a Settlement Agreement was made and entered into by and between Dr. Philippe Bois and the United States Department of Health and Human Services (HHS), Kathleen Sebelius, Howard K. Koh, Nancy Gunderson, and Donald Wright (collectively HHS) by and through the United States Attorney for the District of Columbia in *Bois v. HHS, et al*., Civil Action no. 11-cv-1563, which was pending before the U.S. District Court for the District of Columbia.

In the Settlement Agreement, HHS and Dr. Bois agreed to settle the proceedings before the District Court of the District of Columbia as well as to resolve all administrative matters pending at HHS.

ORI found that Philippe Bois, Ph.D., former postdoctoral fellow, Department of Biochemistry, St. Jude Children's Research Hospital, engaged in research misconduct in research funded by National Institute of General Medical Sciences (NIGMS), National Institutes of Health (NIH), grant R01 GM071596, and National Cancer Institute (NCI), NIH, grants P30 CA021765, P01 CA071907, R01 CA072996, and R01 CA100603.

In the Settlement Agreement, the parties agreed that ORI found by a preponderance of the evidence that the Respondent committed
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misconduct in science and research misconduct by:

1. knowingly and intentionally falsely reporting that FOXO1a was not expressed in cell lysates from alveolar rhabdomyosarcoma (ARMS) tumor biopsies, by selecting a specific FOXO1a immunoblot to show the desired result, in Figure 1A of the following paper: Bois, P.R., Izeradjene, K., Houghton, P.J., Cleveland, J.L., Houghton, J.A., & Grosveld, C.G. "FOXO1a acts as a selective tumor suppressor in alveolar rhabdomyosarcoma." *J. Cell. Biol*. 170:903-912, September 2005 ("*JCB* 2005")
2. falsifying data showing SDS-PAGE for papain digestion of VBS3 and αVBS, by falsely labeling lane 1 to represent papain only digestion, by falsely labeling lane 5 to represent papain digestion of the αVBS peptide, and by falsely inserting a band in lane 3 to represent the αVBS peptide, in Figure 4B of the following paper: Bois, P.R., Borgon, R.A., Vornhein, C., & Izard, T. "Structural dynamics of α-actinin-vinculin interactions." *Mol. Cell. Biol*. 25:6112-6122, July 2005 ("*MCB* 2005").

The parties further agreed that Dr. Bois denied committing research misconduct and, pursuant to 42 CFR Part 93, filed a timely request for a hearing at which to contest ORI's findings. An HHS Administrative Law Judge (ALJ) denied Dr. Bois' request for a hearing. HHS subsequently entered a debarment order against Dr. Bois. Dr. Bois filed the above referenced lawsuit in the United States District Court for the District of Columbia asking the Court to vacate the debarment order and remand the matter for further proceedings before HHS, including but not limited to granting Dr. Bois' request for a hearing.

On March 2, 2012, Judge Berman Jackson of the United States District Court for the District of Columbia issued an order vacating HHS' debarment order, affirming Finding 1, and remanding the matter to HHS for further proceedings regarding Finding 2. On March 30, 2012, HHS filed a Motion for Reconsideration before Judge Berman Jackson.

On March 14, 2013, Dr. Bois and HHS entered into a Settlement Agreement (Agreement) to settle and dismiss the pending civil action. The terms of the Settlement Agreement include that Dr. Bois denied that he committed research misconduct but he agreed not to further appeal ORI's findings of research misconduct set forth above. Dr. Bois and HHS further agreed to the following administrative actions beginning on March 14, 2013:

(1) to have his research supervised for a period of three (3) years beginning on the effective date of the Agreement; he agreed that prior to the submission of an application for U.S. Public Health Service (PHS) support for a research project on which his participation is proposed and prior to his participation in any capacity on PHS-supported research, he shall ensure that a plan for supervision of his duties is submitted to ORI for approval; the supervision plan must be designed to ensure the scientific integrity of his research contribution; he agreed that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and approved by ORI, with such review and approval to be conducted promptly by ORI and not unreasonably withheld; he agreed to maintain responsibility for compliance with the agreed upon supervision plan;

(2) that for three (3) years beginning with the effective date of the Agreement, 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 Dr. Bois is involved, a certification to ORI that the data

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"If humanity does not opt for integrity we are through completely. It is absolutely touch and go. Each one of us could make the difference."

R. Buckminster Fuller
(1895-1983)

Case Summaries *(continued)*

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, 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 a period of three years (3) beginning with the effective date of the Agreement.

Dr. Bois further agreed to dismiss his lawsuit with prejudice and to withdraw further proceedings before HHS. Dr. Bois and HHS both agreed to waive or abandon all other claims.

This notice supercedes the notice regarding this matter that was previously published in: *Federal Register* 76:111, June 9, 2011.

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