

Office of Research Integrity

N E W S L E T T E R

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.



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Observations on ORI Clinical Research Misconduct Cases

Over a 16-year period (1993-2008), there have been on average 3.5 Public Health Service (PHS) findings of research misconduct per year on clinical cases handled by the Office of Research Integrity (ORI). Overall, the 63 clinical cases represent one third of all PHS ORI misconduct findings (63/195).

Clinical research involves studies with people to learn about the disease process and how to treat diseases. In order to determine efficacy of a treatment, these studies are often designed to include people without the disease as control subjects. Clinical research can also be aimed

at disease prevention, studying physiological parameters, or examining specimens from people.

Clinical cases with a finding of research misconduct have an unusual difference from other ORI misconduct cases. The allegations of misconduct in clinical cases are proportionately more likely to be determined to be misconduct by ORI. Specifically, 72% of clinical allegations resulted in a misconduct finding compared with 29% for all other types of research misconduct. What would account for this difference?

(See **Observations**, page 5)

CGS Announces Five RCR Proposal Awards

ORI is pleased to announce progress the Council of Graduate Schools (CGS) has made on its initiative with ORI. CGS is taking a leadership role in promoting the development of model graduate school programs directed to improving research integrity for graduate students. CGS has given awards to seven universities to develop model responsible conduct of research (RCR) programs. These universities will contribute to the final report in which CGS will describe and evaluate best practices that could be adopted by other programs.

Five \$50,000 awards were given to schools that proposed exceptional and innovative plans for fostering scholarly integrity in graduate education:

- **Columbia University**
- **Emory University**
- **U. of Alabama-Birmingham**
- **U. of Arizona**
- **Consortium of:**
 - **Michigan State University**
 - **Pennsylvania State University**
 - **U. of Wisconsin-Madison**

The awards will support strategies to educate students and faculty on (See **CGS Announces Awards**, page 12)

ORI Updates

ORI Welcomes Rhonda Moore and Ginger Lease to DEI Staff

ORI has added two new members to the Division of Education and Integrity (DEI) staff.

Dr. Rhonda Moore, as a Health Science Administrator, will be involved in educational efforts to promote research integrity. Before coming to ORI, Dr. Moore was a Health Science Administrator at the National Cancer Institute (NCI) of the National Institutes of Health. At NCI, she was responsible for the technical review of contract proposals and grant applications for cancer prevention and control.

Dr. Moore received her Ph.D. in Anthropology (Medical) from Stanford University. She completed a Na-

tional Institute of Mental Health (NIMH) Postdoctoral Fellowship in Psycho-oncology at Stanford University Medical School and an NCI Postdoctoral Fellowship in Epidemiology at the University of Texas M. D. Anderson Cancer Center in Houston, Texas. Her research has explored biobehavioral and clinical approaches to the management and treatment of acute and chronic pain in healthy populations and in patients with chronic disease (primary and metastatic breast cancers, as well as cancers of the upper aerodigestive tract). She has published in journals such as *Cancer Nursing*, *Oncology*, and the *European Journal of Cancer Care*. Dr. Moore also has edited two books: *Cancer, Culture and Communication*

(Springer 2004) and *Biobehavioral Approaches to Pain* (Springer 2009).

Ginger Lease will provide administrative program support and specifically will provide editorial assistance for the quarterly newsletter. She has worked in various administrative roles for over 15 years. Some of the roles include Executive Assistant to the Deputy Assistant Secretary for Administration in the Administration for Children and Families; Executive Assistant to the Director of the Division of Security and Emergency Services; Office Administrator for DiFabrizio Trucking; and Secretary for the Credit, Travel, and Accounting Policy Division at the U.S. Department of Agriculture.

Conference on Research Integrity Slated for May 15-17, 2009

The Fifth Biennial ORI Research Conference on Research Integrity will be held in the Conference Center at Niagara Falls, New York, on May 15-17, 2009. Accommodations will be at Crowne Plaza Hotel Niagara Falls, 300 Third Street, Niagara Falls, NY 14303.

The conference has over 50 presentations by researchers discussing their studies, findings, and implications for research integrity. There will be discussions on research misconduct, authorship issues, RCR education, publication issues, questionable research practices, conflict of interest, and international research issues.

The conference hotel is within short walking distance of the Rainbow Bridge to Canada. You can also go behind the falls or observe the falls by standing at their base or by taking an elevator ride and walking through a network of tunnels. The famous "Maid of the Mist" boat ride, which takes you up close to the falls, will be operating until 7:45 p.m. because it is the Victoria Day holiday weekend. So try to plan your itinerary if you want to experience this thrilling ride and remember your passport!

For more information, see http://www.roswellpark.org/Education/Continuing_Medical_Education_CME/Upcoming_Conferences/ORI2009

Smithsonian RCR April 30

Dr. Ada Sue Hinshaw, Dean, Graduate School of Nursing, Uniformed Services University, will discuss the impact of nursing research in America, including research integrity issues.

FREE and open to the public

International Updates

Europe and Asia Embrace the Responsible Conduct of Research

Nick Steneck, University of Michigan

Many countries and international organizations are actively pursuing efforts to implement policies for responding to misconduct and for fostering responsible conduct of research (RCR).

Following the publication of its survey of European misconduct policies, "Stewards of Integrity" (<http://www.esf.org/publications/corporate-publications.html>), the European Science Foundation (ESF) convened a Member Organization Forum on Research Integrity (<http://www.esf.org/activities/mo-fora/research-integrity.html>) in Madrid, Spain, in November 2008, to (1) exchange ideas and good practices, (2) encourage countries not yet involved to take up the issue of responsible conduct policies, and (3) "channel European input to the Second World Conference on Research Integrity."

At the end of the forum, it was agreed that Member Organization working groups should be established to (1) raise awareness and share information, (2) develop a code of conduct for research, (3) establish basic guidance for national research integrity organizations, and (4) foster research on research integrity.

ESF has since set up four working groups to address these topics, and they convened a meeting of the chairs of these groups to develop and plan for future activities. Updates and progress reports can be found on the ESF web site (<http://www.esf.org>).

In January 2009, the European Forum for Good Clinical Practice

(EFGCP) held its annual meeting in Prague and focused on "Research Integrity: A European Perspective." Nearly 40 presenters and well over 100 participants spent two days discussing what is known about integrity in clinical research. Many sessions, which were planned by a committee chaired by Frank Wells, United Kingdom, discussed ways to detect or prevent misconduct. Specific ideas and proposals were developed in a series of workshops on (1) the role of monitoring in the detection of misconduct, (2) the role of audit in the detection of fraud, (3) the role of research ethics committees in preventing misconduct, (4) the role of statistical analysis in revealing research misconduct, (5) ways to conduct an inquiry into alleged misconduct, and (6) the role of nationally competent authorities.

The mix of academic, government, and industry participants and substantial input from those involved in the approval process for drugs and devices gave the Prague meeting a unique flavor. The delegation of regulatory authorities for different aspects of research in the United States to ORI, the Office of Human Research Protection (OHRP), and FDA tends to divide discussions of research integrity along these regulatory lines: ORI promotes discussions of research misconduct and ways to foster integrity. OHRP focuses its regulatory and educational efforts on protecting human subjects engaged in research. FDA monitors and promotes responsible practices in research related to drug and device approval.

At the EFGCP meeting, the three perspectives came together to discuss what is a common problem for all research: responding to misconduct and promoting integrity. The mix produced a number of creative suggestions for action, which EFGCP and some of its members will pursue. Reports on this and other projects are posted at <http://www.efgcp.be/>

Moving around the globe to Asia, the Second World Conference on Research Integrity is being planned and will be held in Singapore in mid-2010 (tentatively, July 2010). As with the First World Conference, held in Lisbon, Portugal, in September 2007, the main aim of this conference will be to provide a forum for research leaders to come together to address challenges and harmonization efforts to promote integrity in research. Preliminary plans call for special emphasis on integrity in international collaborations, research publication, and training in RCR. Program details and dates will be posted on the ORI web site by mid-to late-April.

In preparation for the Second World Conference, the conference organizers, Nick Steneck representing ORI and Tony Mayer representing Nanyang Technological University, Singapore, will gather information about national and international efforts to respond to and promote integrity in research. If you are involved in or know of efforts that should be included, send a message to nsteneck@umich.edu.

Expanding RCR Resources

New Web Resource Addresses Whistleblowing Issues

Sara Vollmer, University of Alabama, Birmingham

Like Agamemnon when he had only two choices, sacrifice his daughter or fail his troops, we are often held responsible for the outcome of our choices, even when a very difficult situation into which we are put is no fault of our own. Deciding on what constitutes research misconduct and how to report it are probably among the most difficult decisions a researcher may have to make. With the increase in the incidence of research misconduct that is observed but appears to go unreported, it is clear that the dilemma of what to do will be faced by most researchers at some time during their careers.

Thus, we invited a team of administrators, scientists, philosophers, film makers, and an entertainer to work together to develop a video,

“Whistle Blower.” This team had worked together on a prior video, “In the Lab: Mentors and Students Behind the Scenes,” which is a docudrama on issues of mentoring, cooperation, and research misconduct.

This new product is a video-driven illustration with lessons showing students how to anticipate the issues that would arise in a case of possible misconduct and to think ahead about what to do. It has recently been made available on the web for all universities and research centers to use free of charge. See <http://www.uab.edu/graduate/rcr/index.html>

We developed this video from an actual misconduct case that oc-

curred at a major university last year. The fictional adaptation was first written by a focus group of faculty members; scriptwriters and an entertainer rewrote the case many times based on feedback from the scientists and administrators. The format of the video includes probing questions along with our responses. The answers were developed in cooperation with Nancy Matchett, Institute of Professional Ethics at the University of Northern Colorado.

The authors of the site are Jeffrey Engler, Sara Vollmer, Harold Kincaid, Douglas Cromey, and Dean Bryan Noe from the University of Alabama, Birmingham; we thank the Council of Graduate Schools for funding.

AAAS Develops RCR Resource Site

Mark Frankel, Ph.D.

Trust and accountability are integral to the research enterprise. To demonstrate its commitment to protecting the integrity of science, the American Association of Advancement of Science (AAAS), in collaboration with the National Academies, has established a web site for students, researchers, administrators, and policymakers to help facilitate access to materials on scientific misconduct and research integrity.

Research in science has many components, including authorship, use

of research animals, peer review, data sharing, protection of human subjects, conflict of interest, and responsible conduct in research education. This web site brings together a diverse array of resources from many scientific disciplines. It makes timely information available, such as upcoming events, lists of recent literature, web and media resources, policies, codes and guidelines, past conferences, and international resources. Visit <http://www.aaas.org/spp/sfrr/integrity>

DISCLAIMER

All authors who generously shared their thoughts have indicated that they are speaking for themselves and not for their specific organizations.

We thank the following authors:

Douglas Adams, Mark Frankel, Nick Steneck, and Sara Vollmer

Research Misconduct

Observations *(from page 1)*

Clinical trials, a type of clinical case, generally involve more people who can see the research records and underlying source documents. Since there are requirements on how to keep proper records, such as the Food and Drug Administration's good clinical practice (GCP) or the trials' protocol specifications, team members are more likely to know the established rules for records. Dr. Peter Abbrecht, Medical Expert, Division of Investigative Oversight (DIO), points out that although staff have different roles to perform on a clinical trial, they have opportunities to observe others actually breaking the protocol rules. In one case, a technician was unable to draw a blood sample in the presence of another team member, yet a sample was submitted for analysis and later determined to be the technician's own blood. The team member who observed this act was alerted to the falsification and reported it. In another case, the research assistant who had been asked to generate a report on subjects in the study noted that new patients had suddenly been entered into the study by the investigator. The research assistant examined source data and determined that the cases had been fabricated.

Audits also are more commonly done in clinical research; there are internal and external auditors who have defined roles to examine the source data for omissions, irregularities, deviations, non-compliance with protocol, etc. Audits are such a powerful determinant that ORI advises institutions that an audit

report in a clinical study may obviate the need for an inquiry, when the audit has uncovered evidence of possible research misconduct.

Dr. Linda Youngman, DIO Scientist-Investigator, believes that: "The high proportion of allegations that are determined to be misconduct is a testament to the fact that emphasis on regular audits in clinical trials, which help to detect problems early, is a key ingredient to preventing research misconduct."

Prosecuting clinical cases also differs from other types of misconduct. Clinical trials are easier to show "intent" to fabricate or falsify because there are numerous and obvious ways that the data can be manipulated to lead to desired goals. Dr. Nancy Davidian, DIO, Deputy Director, reports that: "While research misconduct occurs at all stages of clinical trials (eligibility, treatment, post-treatment, and follow-up), the most commonplace misconduct is at the time of enrollment." DIO speculates that falsification and fabrication of eligibility occur because there is often enormous pressure to enroll subjects and there may be per capita rewards attached to each study subject's enrollment. This in part explains further why clinical trial cases are different from bench science cases.

John Dahlberg, Director of DIO, points out that: "We know that audits in clinical trials make a difference and that if institutions required audits, they would be more likely to find cor-

rectable problems, as well as research misconduct. When they require more monitoring and auditing of research records, then ORI will have more confidence that research misconduct is appropriately being detected."

It is unfortunate that bench research does not have markers comparable to clinical research which can be more easily audited. This may evolve as institutions or groups routinely learn to use electronic lab notebook systems that will allow more people to have the opportunity to review and evaluate the records of others in the group. In the meantime, we must rely on the lab director to create an atmosphere that limits opportunities to cheat and that requires ongoing participation with an advisor, particularly concerning the examination of source data and establishing and enforcing standards.

Seeking Contributions for *ORI Newsletter*

The ORI Newsletter is interested in providing a forum for occasional commentary by outside experts. We also want to promote collaboration between organizations and will consider posting relative information. Ideas for future newsletters can be submitted to ASKORI.

Commentary

A View on Promoting Research Integrity: Attention to Deterrence

Douglas Adams, Department of Sociology and Criminal Justice, University of Arkansas

In the 1960s and 1970s, a “research revolution” in the study of policing occurred. One outcome was the realization that cops and citizens are actually “co-producers” of crime deterrence, that the police cannot do it alone. Another realization was the importance of citizen involvement in crime deterrence.

After all, Agents of Formal Control, like the police, depend on citizens to comply with the law and to report law breakers. Since interaction with Agents of Informal Control—family, friends, and co-workers—occurs everywhere, all the time, informal social control is very difficult to evade.

If deterring “crime,” that is, “misconduct,” and deterring research misconduct can be considered functionally similar, then those interested in the responsible conduct of research (RCR) have much to learn from the science of policing.

The Compliance Office, including the Research Integrity Officer (RIO) and the Institutional Review Board (IRB), of any organization serves as the “law enforcement” component of the research community. In order to assist

with the coproduction of compliance, RIOs might reach out to their research community in a proactive, positive, and helpful manner. For example, if they make themselves available, people may come to discuss their concerns about possible research misconduct; if the IRB staff are approachable, they may assist with submissions of IRB protocols. In addition, the Compliance Office should provide assistance to special student populations, such as honors or graduate students or foreign-trained postdocs. If successful, the Compliance Office would be regarded as a “member in good standing” of the overall research community, rather than being marginalized.

Faculty, students, and staff serve as the “citizens” or “informal agents” of the research community. In order to enhance the coproduction of compliance, the informal network of a research group’s social relations should be encouraged to be as dense and as multiplex as possible. Group-based, especially college-based, RCR training would be one way to achieve this. Another would be “paired research” or “collaborative research” carried out by work-pairs of students, especially

those working on honors or master’s degrees. In addition, research groups should be organized into supervisory units of 4 to 8 students, and the Principal Investigator should organize weekly meetings to collaboratively discuss the group’s project.

The research community will continue to grow larger, more diverse, and possibly more transient. Research groups are increasingly geographically decentralized. All of these trends threaten to further weaken formal and informal social controls; thus, the potential opportunity for research misconduct will grow.

An increase in the use of formal mechanisms of control to deter scientific misconduct is limited to what a researcher can tolerate without feeling under siege. However, one might feel more empowered and participate, and be in compliance without being aware of it, when more informal social controls are used. For instance, such controls might require members of an organization to spend more time together on a research project or on a group exercise during an interdisciplinary training session. After all, modeling best practices of RCR is everyone’s responsibility.

Article Explores International Cultural Barriers

In a February 21, 2009, commentary for *The Lancet* entitled “Cultural Challenges and Their Effect on International Research Integrity,” Drs. Bosch and Titus explore some of the main issues that researchers need to consider when they decide to do international research. They provide us with an overview of the serious ways that research

can go awry at the planning, designing, conducting, interpreting, and publishing stage of research. Xavier Bosch, who conducts research in Portugal, became interested in this topic because he is concerned about the confusion that he sees even with researchers who collaborate between European nations. In conducting the

review of the literature, Sandra Titus added that they were surprised at the paucity of information that was available which would help researchers know what to think about in preparing to pursue international collaborations. This article can be found at <http://ori.hhs.gov/publications/studies.shtml>

Case Summaries

Luk Van Parijs, Ph.D., Harvard Medical School, Brigham and Women's Hospital, California Institute of Technology, and Massachusetts Institute of Technology

Based on the reports of separate investigations conducted by Harvard Medical School (HMS)/Brigham and Women's Hospital (BWH), California Institute of Technology (CalTech), Massachusetts Institute of Technology (MIT), and additional analysis conducted by the Office of Research Integrity (ORI) in its oversight review, the U.S. Public Health Service (PHS) found that Dr. Luk Van Parijs, former Graduate Student, Department of Pathology, HMS, former Research Fellow and Instructor of Pathology, BWH, former Postdoctoral Fellow, Department of Biology, CalTech, and former Associate Professor, Department of Biology, Center for Cancer Research, MIT, engaged in scientific misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grants U19 AI56900, R21 AI49897, R01 AI42100, P01 AI35297, R37 AI25022, R01 AI32531, National Cancer Institute, NIH, grant R01 CA51462, and National Institute of Environmental Health Sciences (NIEHS), NIH, grant P30 ES02109, and National Institute of General Medical Sciences (NIGMS), NIH, grant R01 GM57931.

PHS found that Respondent engaged in scientific misconduct by including false data in NIAID, NIH, grant applications R01 AI54519-01A1, R01 AI54973-01, and R01 AI54973-01A1, NCI, NIH grant application 2P30CA14051-34, and National In-

stitute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH grant application R21 DK69277-01.

Specifically, PHS found that the Respondent engaged in scientific misconduct by including false data in seven published papers, three submitted papers (with two earlier versions submitted for one of these), one submitted book chapter, and multiple presentations as follows:

1. While at HMS/BWH, Dr. Luk Van Parijs falsified the expression of IFN-gamma and K.-126 in flow cytometry dot plots for the immunized, naive, tolerized, and tolerized + IL-12 experimental groups in Figure 4, *JEM* 186:1119-1128, 1997, by using the same non-stained cell population in the lower left quadrant to falsely represent CD4+ T cells negative for IFN-gamma and K.-126 in each experimental group.

2. That Dr. Luk Van Parijs falsified the expression of different proteins in flow cytometry dot plots in Figure 1, *Immunity* 8:265-274, 1998, in Figure 1C, *Immunity* 11:281-288, September 1999, and in Figure 5, *Immunity* 11:763-770, December 1999, by using portions of the same dot plot to represent different cell populations expressing different proteins. Specifically:
 - a. While at HMS/BWH, Dr. Van Parijs used portions of the same dot plot to represent T-cell populations expressing the 3A9 T cell receptor and CD4+ (top panel) or CD8+ (bottom panel) in 3A9+ (wild type), in 3A9/lpr (Fas-), or in 3A9/gld (FasL-) transgenic mice in Figure 1, *Immunity*, 1998, where:
 - i. The CD4/3A9 dot plots for the 3A9+ and 3A9/gld transgenic mice were the same, and the 3A9+ dot plot was a subset of the 3A9/lpr dot plot;
 - ii. The CD8/3A9 dot plots for the 3A9+ and 3A9/lpr transgenic mice were the same in the lower left and lower right quadrants, and the 3A9/gld dot plot was a subset of the wild type dot plot.
 - b. While at CalTech, Dr. Van Parijs used portions of the same dot plot to represent the expression of hIL-2R beta and GFP in T cells infected with WT or Delta 355+8F IL-2R mutant in Figure 1C, *Immunity*, September 1999, where the Delta 355+8F dot plot was a subset of the WT dot plot.
 - c. While at CalTech, Dr. Van Parijs used portions of the same dot plot to represent the expression of B220 and IgM in infected (GFP+) and not infected (GFP-) spleen cells isolated from reconstituted mice in Figure 5, *Immunity*, December 1999, where the Infected (GFP+) dot plot for control mice was a subset of the not infected (GFP-) dot plot for FLIP mice.

3. While at MIT, Dr. Luk Van Parijs falsely claimed in the text of RNA Interference Technology (Cambridge University Press, July 2004) and in Figure 2 of *Nature Genetics* 33:401-406 (2003) that experiments depicting the functional silencing of genes in hematopoietic stem cells (HSCs) and in non-cycling dendritic cells by lentiviral-mediated RNAi were performed, when they were not.

Specifically, in *Nature Genetics*:

- a. Figure 2b falsely showed the transduction of bone marrow-derived

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dendritic cells infected with pLL3.7 Bim by flow cytometry, and knock-down of Bim expression by Western blot.

b. Figure 2d falsely showed the efficiency of pLL3.7 CD8 lentiviral infection in HSCs by flow cytometry for GFP expression (left panel), and falsely showed stable gene expression in progeny by flow cytometry for GFP expression in spleen cells from chimeras derived from infected HSCs (right panel). Figure 2e falsely showed the reduction of CD8+ T cells in spleen cells from chimeras derived from pLL3.7 CD8 infected HSCs (right panel) and controls (left panel).

4. While at MIT, Dr. Luk Van Parijs falsified figures in grant applications submitted to the National Institutes of Health (NIH), a presentation in 2003, and Figure 6A, *Immunity* 19:243-255 (2003), by falsely claiming that the image in the figure represented an immunoprecipitation assay for Ras-GTP and a Western blot for total Ras protein, when it actually represented a Western blot for Bcl-2 and beta-actin in T cells, previously published as Figure 5C, *J. Immunol.* 168:597-603 (2002). Dr. Van Parijs also admitted to falsification or fabrication of data in multiple submitted manuscripts, grant applications submitted to NIH, and presentations as follows.

5. While at MIT, Dr. Luk Van Parijs admitted that in multiple presentations and submitted manuscripts in 2004, he falsely claimed that the bifunctional lentiviral vectors, U6-shRNA-rat insulin promoter (RIP)-Myc had been made, when they had not, and that transgenic mice carrying these lentiviral vectors with shRNA silencing Bim or Pten pro-

teins in pancreatic cells showed accelerated tumorigenesis and death.

6. While at MIT, Dr. Luk Van Parijs admitted that in multiple presentations in 2003 and 2004 and in grant application R21 DK69277-01 submitted to NIH in 2003, he falsely claimed that the number of CD8+ T cells and the incidence of diabetes was reduced by silencing CD8 expression with the pLL3.7 CD8 lentivirus in non-obese diabetic (NOD) transgenic mice, when the NOD transgenic mice data did not exist.

7. While at MIT, Dr. Luk Van Parijs admitted that in multiple presentations, submitted manuscripts, and grant applications submitted to NIH in 2004, he falsely claimed that transgenic mice had been generated with the mono-functional lentiviral vectors with c-Myc, Ras or Akt under the control of the CD4 promoter, when they had not, and that transgenic mice had been generated with the bi-functional lentiviral vectors with CD4-c-Myc, Ras or Akt- and U6-shRNAs targeting luciferase, Bcl-2, or Bim proteins, when they had not. The effect of these misrepresentations was the reported false conclusion that a cytokine-stimulated proto-oncogene network regulated CD4+ T-cell survival and responses to foreign and self antigens.

8. While at MIT, Dr. Luk Van Parijs admitted that in presentations and submitted manuscripts in 2004, he falsely claimed that mice injected with plasmids carrying shRNAs for Bcl-2, Akt1 and Akt2, complexed to polyethylene imine (PEI), showed a significant reduction in c-myc-induced tumor growth, when the experiments had not been done.

9. While at MIT, Dr. Luk Van Parijs admitted that in presentations in 2004, he falsely claimed that shRNAs designed using algorithms developed in 2004 were more effective to silence target genes than the shRNAs designed with algorithms in 2002.

10. While at MIT, Dr. Luk Van Parijs admitted that in multiple presentations, submitted manuscripts, a grant application submitted to NIH, and in the text of *Current Opinion in Molecular Therapeutics* 6:136, 2004, he falsely claimed that an in vivo RNAi screen was developed to identify genes in cytokine and apoptosis pathways that accelerated or suppressed Myc-induced tumorigenesis in lethally irradiated mice, by using bi-functional lentiviral vectors that expressed c-Myc under control of the CMV enhancer-beta-actin promoter (CAG) and U6-driven shRNAs designed to silence 168 selected genes, when the experiments had not been done.

11. While at MIT, Dr. Luk Van Parijs admitted that in a submitted manuscript in 2004 and a grant application submitted to NIH in 2003, he falsely claimed that with the use of retroviral vectors with Bim and activated Ras, Akt or Myc, he showed that the IL-2-stimulated activation of proto-oncogene pathways functioned to promote the survival of T cells following antigen encounter by regulating Bim and Bcl-2 pathways, when the experiments that were performed were inconclusive.

Dr. Van Parijs has entered into a Voluntary Exclusion Agreement in which he has voluntarily agreed, for a period of five (5) years, beginning on

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December 22, 2008: (1) to exclude himself from any contracting or sub-contracting with any agency of the United States Government and from eligibility or involvement in non-procurement programs of the United States Government referred to as “covered transactions” pursuant to HHS’ Implementation (2 CFR, Part 376 et seq.) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 CFR, 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.

M. Nguyen, M.D., University of California, Los Angeles

Based on a University of California, Los Angeles (UCLA), report and Respondent’s own admission, the U.S. Public Health Service (PHS) found that Dr. M. Nguyen, former Associate Professor at UCLA, engaged in scientific misconduct in research supported by National Cancer Institute (NCI), National Institutes of Health (NIH), grant 1 R01 CA69433, National Center for Complementary and Alternative Medicine (NCCAM), NIH, grant 1 P50 AT00151-01, and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH, grant T32 DK03688. Specifically, PHS found that Respondent engaged in scientific misconduct:

1. Dr. Nguyen’s laboratory conducted a single experiment on the effect of *Livistona* extract on the growth of 10^6 mouse fibrosarcoma (FSA) cells injected into C3H mice. The drug was

administered in the drinking water of the treated mice, and tumor sizes were measured twice weekly with calipers. Dr. Nguyen falsified and fabricated the results of this experiment in Figure 3 of *Oncology Reports* 8:1355-1357, 2001:

a. The data reported for the control group were from an experiment in nude mice implanted with human breast tumor implants, rather than with mouse fibrosarcoma cell implants, as Dr. Nguyen reported in the paper. The control data for FSA implanted C3H mice could not be located in the laboratory records.

2. Dr. Nguyen’s laboratory conducted a single experiment on the effect of *Livistona* extract on the growth of 10^8 MDA-MD-231 cells injected into nude mice. The drug was administered in the drinking water of the treated mice and tumor sizes measured twice weekly with calipers. Dr. Nguyen falsified and fabricated the results of this experiment in Figure 9 of NIH grant application P50 AT00151-01, dated May 19, 1999, by:

a. Falsely stating in the associated text that there were ten mice per group and that the experiments were repeated once, while in fact, there were only five mice per group with no repetition of this experiment;

b. Omitting data on the control curve for two of the measurement times (at 2 and 3.5 weeks) and falsely reporting the times at which three other measurements were taken.

3. Dr. Nguyen’s laboratory conducted a single experiment (1998-99) testing

the anti-angiogenic effects of *Livistona chinensis* extract on human umbilical vein endothelial cells (HUVEC). HUVEC cells were counted from duplicate wells when exposed to extract, and controls were counted from single wells:

a. Figure 8 of NIH grant application P50 AT00151-01, dated 5/19/99, plots the data as a bar graph. However, the same data were reported in Figure 1 of *Oncology Reports* 8:1355-1357, 2001, by falsely expressing them as the rate of growth obtained by measuring the uptake of radioactive thymidine into cellular DNA and plotting the data as normalized to control values. UCLA concluded that Figure 1 was falsified by claiming the data were obtained by a state-of-the-art technique not actually employed by the Respondent to obtain the data for that figure. This falsification did not bear upon the findings of the paper.

4. Dr. Nguyen’s laboratory tested whether the levels of bFGF (basic fibroblast growth factor) and VEGF (vascular endothelial growth factor) in nipple fluid aspirates were significantly elevated in breast cancer patients in comparison to values from normal lactating and non-lactating breasts. Dr. Nguyen falsified the number of subjects who were lactating in *The Lancet* 356:567-569, 2000, by claiming that bFGF data were obtained from four separate subjects, while in fact, the data were from both breasts of two subjects.

Dr. Nguyen has entered into a Voluntary Settlement Agreement with ORI. As part of that Agreement, Dr. Nguyen admits to UCLA’s findings of fact but denies ORI’s findings that

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the actions rise to the level of scientific misconduct. The settlement is not an admission of liability on the part of the Respondent. Dr. Nguyen voluntarily agreed, for a period of three (3) years, beginning on December 29, 2008:

(1) 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; and

(2) That although Respondent is not currently engaged in PHS-supported research, any institution that submits an application for PHS support for a research project on which the Respondent's participation is proposed or that uses the Respondent in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which the Respondent is involved, must concurrently submit a plan for supervision of the Respondent's duties to the funding agency for approval. The supervisory plan must be designed to ensure the scientific integrity of the Respondent's research contribution. Respondent agreed to ensure that a copy of the supervisory plan also is submitted to ORI by the institution for ORI approval. Respondent agreed to not participate in any PHS-supported research until such a supervisory plan is submitted to ORI.

Nima Afshar, Ph.D., University of California, San Francisco

Notice is hereby given that the Office of Research Integrity (ORI) and the Assistant Secretary for Health have taken final action in the following case: Nima Afshar, Ph.D., Uni-

versity of California, San Francisco: Based on a University of California, San Francisco (UCSF) report and Respondent's own admission, the U.S. Public Health Service (PHS) found that Dr. Nima Afshar, former postdoctoral fellow at UCSF, engaged in research misconduct in research supported by National Cancer Institute (NCI), National Institutes of Health (NIH), grant T32 CA108462 and National Institute of General Medical Sciences (NIGMS), NIH, grant R01 GM59704.

PHS found that Respondent engaged in research misconduct in the performance of research on yeast to test whether disruption of the tight controls, to prevent re-replication, on the initiation of DNA replication could produce gene amplifications with a copy number greater than two (2).

Specifically, Respondent falsified files containing raw scanned micro array images from another researcher's experiments to demonstrate that in experiments that she claimed to have conducted, she successfully observed gene amplifications with a copy number greater than two (2); there were 36 such instances of falsifying data files.

Dr. Afshar has entered into a Voluntary Settlement Agreement in which she has voluntarily agreed, for a period of three (3) years, beginning on December 22, 2008:

(1) To exclude herself 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; and

(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 the Respondent in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which the Respondent is involved, must concurrently submit a plan for supervision of the Respondent's duties to the funding agency for approval. The supervisory plan must be designed to ensure the scientific integrity of the Respondent's research contribution. Respondent agrees to ensure that a copy of the supervisory plan also is submitted to ORI by the institution for ORI approval. Respondent agrees that she will not participate in any PHS-supported research until such a supervisory plan is submitted to ORI.

Kazuhiro Tanaka, M.D., Ph.D., National Institute of Dental and Craniofacial Research, NIH

Based on the report of an investigation conducted by the National Institutes of Health (NIH) and additional analysis conducted by the Office of Research Integrity (ORI) in its oversight review, the U.S. Public Health Service (PHS) found that Dr. Kazuhiro Tanaka, former Visiting Postdoctoral Fellow, Molecular Biology Section, Craniofacial Developmental and Biology and Regeneration Branch (CDBRB), National Institute of Dental and Craniofacial Research (NIDCR), NIH, engaged in scientific misconduct in research supported by PHS funds from the NIDCR, NIH Intramural Program.

PHS found that Respondent engaged in scientific misconduct by falsifying

Case Summaries

data that were included in three published papers:

Kazuhiro Tanaka, Yoshihiro Matsumoto, Fumihiko Nakatani, Yukihide Iwamoto, and Yoshihiko Yamada, "A zinc finger transcription alpha A-crystallin binding protein 1, is a negative regulator of the chondrocyte-specific enhancer of the alpha1(II) collagen gene," *Molecular and Cellular Biology (MCB)* 20:4428-4435, 2000;

Kazuhiro Tanaka, Noriyuki Tsumaki, Christine A. Kozak, Yoshihiro Matsumoto, Fumihiko Nakatani, Yukihide Iwamoto, and Yoshihiko Yamada, "A Kruppel-associated box-zinc finger protein, NT2, represses cell-type-specific promoter activity of the alpha2(XI) collagen gene," *MCB* 22:4256-4267, 2002; and

Ying Liu, Haochuan Li, Kazuhiro Tanaka, Noriyuki Tsumaki, and Yoshihiko Yamada, "Identification of an enhancer sequence with the first intron required for cartilage-specific transcription of the alpha2(XI) collagen gene," *Journal of Biological Chemistry (JBC)* 275:12712-12718, 2000. Specifically, PHS found that the Respondent:

1. Falsified the results for CRYBP1 or Sox9 binding to the Col2a1 DNA sequence in electrophoretic mobility shift assays in Figure 1D and Figure 7 in *MCB* 20:4428-4435, 2000. He used duplicate copies of bands or duplicate copies of parts of lanes to falsely represent results from reportedly different experimental conditions;

2. Falsified the results for NT2 binding to the Col11a2 DNA sequence in

electrophoretic mobility shift assays in Figures 2D and 6B, and falsified the Western blot for NT2 mutant proteins in Figure 8B in *MCB* 22:4256-4267, 2002. He used duplicate copies of bands, parts of bands, or duplicate copies of parts of lanes to falsely represent results from reportedly different experimental conditions in Figures 2D and 6B; and falsely represented results for the Figure 8B Western blot by using duplicate copies of bands to represent NT2 Delta1 (lane 2) and NT2 Delta4 (lane 5) mutant proteins;

3. Falsified the Western blot for Sox9 protein expression in Figure 4B, *JBC* 275:12712-12718, 2000, by using duplicate copies of lanes 1 and 2 to represent the Sox9 expression in cell extracts from both Balb 3T3 and undifferentiated ATDC5 cells; and

4. Falsified the Northern blots in multiple panels of Figure 3, *MCB* 20:4428-4435, 2000. He used duplicate copies of bands for CRYBP1, for Type II collagen, for Type X collagen, and for GAPDH and 18S EtBr stained control bands to falsely represent results of RNA expression from these different genes in ATDC5 cells. He also used duplicate copies of bands to falsely represent the RNA expression in ATDC5 cells grown under different conditions for either collagen Type II in Figure 3, *MCB*, 2000, or collagen alpha1(X) in Figure 5 in *MCB* 22:4256-4267, 2002. Similarly, duplicate copies of 18S EtBr stained control bands were used in both figures with reportedly different experimental conditions.

Both Respondent and PHS are desirous of concluding this matter with-

out further expense of time and other resources, and the parties have entered into a Voluntary Exclusion Agreement. The settlement is not an admission of liability on the part of the Respondent. Respondent neither admits nor denies ORI's finding of scientific misconduct. Respondent acknowledges that original data relating to the above-referenced falsified figures are missing. Dr. Tanaka has voluntarily agreed, for a period of three (3) years, beginning on January 14, 2009:

- (1) To exclude himself from any contracting or subcontracting with any agency of the United States Government and from eligibility or involvement in non-procurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 CFR, Part 376 et seq.) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 CFR, 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.

"The scientific endeavor is based on vigilance, not trust."

Jonathan King, Professor of Molecular Biology, MIT, *Science and Engineering Ethics*, 1999, 5:215-217.

Office of Research Integrity

NEWSLETTER

CGS Announces Awards *(from page 1)*

topics such as conflicts of interest, plagiarism, human subjects research, and laboratory management.

An additional 13 universities will join the project as affiliate partners:

- **Duke University**
- **Georgia Institute of Technology**
- **Howard University**
- **Marquette University**
- **Northern Arizona University**
- **Princeton University**
- **Purdue University**
- **Simmons College**

- **U. of California-San Diego**
- **U. of New Mexico**
- **U. of North Carolina-Chapel Hill**
- **U. of West Florida**
- **Wake Forest University**

In partnership with CGS, all universities participating in the project will promote the adoption and adaptation of their models and best practices nationwide. In conjunction with the awards, CGS announces that it has launched a dedicated web site for the Project for Scholarly Integrity, at <http://www.scholarlyintegrity.org>

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

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