

The Aftermath of Scientific Fraud

Scientists who have come face to face with scientific misconduct consider its consequences years later.

Scientific fraud became front-page news at the end of last year, when South Korean stem cell researcher, Woo Suk Hwang, admitted to fabricating data about cloned human embryonic stem cell lines that he claimed were created from patients. Much of the press coverage focused on the fallout of Hwang's actions on the public's trust in science and the already fragile image of stem cell research. But looking beyond the headlines, the repercussions of scientific misconduct also resonate on a more personal level.

"It was my darkest professional hour when I found out that a talented student who I had great hopes for systematically manipulated data. It changed me forever," says Francis Collins, director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH). Collins retracted five papers published in 1995 and 1996 about a possible genetic cause of leukemia when Amitav Hajra, a graduate student working in his laboratory, first at the University of Michigan and then at the NIH, admitted to having fabricated the results.

The incident derailed Hajra's plans of becoming a physician-scientist; he was barred from applying for federal grants for four years and was denied both a doctoral and medical degree from the University of Michigan. But the incident also harmed others. "In the short run it had a profoundly negative impact on other people in the lab, especially the post-doc working most closely with Hajra. He wondered for some time whether his career had just gone south," says Collins. "Eventually he did recover but it was an enormous challenge. It took several years of doing experiments over." The former postdoctoral fellow, Paul Liu, is now a senior investigator at NHGRI.

Collins was praised for the forthright way he handled the case of misconduct, which had been discovered by a reviewer of a paper that Hajra had submitted to the journal *Oncogene*. But the incident changed the way that Collins oversees his research group. "It caused me to become more skeptical, which is something I am not entirely happy about," he says. "I always had a skeptical eye in terms of looking at the technical aspects of data, but until this awful experience that did not include a concern about whether the data were real or fabricated. Now it does."

Dealing with Misconduct

Cases of possible scientific misconduct involving research funded by the NIH and other agencies within the US Department of Health and Human Services (HHS) are brought to the attention of the Office of Research Integrity (ORI) in Rockville, Maryland by the institute where the incident occurred. ORI, established in 1992 as part of the HHS, steps in to review the findings of the institutional investigation and to determine a punitive action for those responsible. The most common action taken by ORI consists of barring the guilty individual from receiving federal funds for 3 to 4 years, but the extent of the punishment depends on several criteria, such as the nature of the misconduct and who was responsible.

Although the integrity of Collins and Liu was never questioned by the University of Michigan or by the NIH, Steven Burden was less fortunate. In 1989, Burden became the innocent target of an investigation by the Massachusetts Institute of Technology (MIT) in Boston, where he was an associate professor. Burden discovered he could not replicate data

in a study his group had published in the journal *Nature* (the first author of the paper having recently left the lab). "As we were following-up on experiments reported in the *Nature* study we found disparities between the contents of tubes containing reagents used in the earlier experiments and the labeling of these tubes," recalls Burden. "Initially, these errors appeared innocent and possibly innocuous, but they took on a more ominous note when I asked [the former postdoc] to return to MIT to clear up the confusion." Two days after returning to MIT, the postdoc admitted himself to a psychiatric hospital and was not available while the experiments were being repeated. It took Burden and others in the laboratory three months to determine that the published data were wrong, to send letters to colleagues whose work might be directly affected, and to submit a correction to *Nature*.

Burden points out that although NIH's Office of Scientific Integrity—the predecessor of ORI—completely cleared him of any wrongdoing, the investigation forced him to leave MIT. "It was a difficult struggle to look for a position under the veil of the investigation," emphasizes Burden, who is now a tenured professor at the Skirball Institute at New York University Medical School in New York City. "The one redeeming experience from this exceedingly distressful period was the heartening support I received from colleagues at MIT and elsewhere, which was critical to continue with my career."

The case was never fully resolved, but in Burden's opinion "there is little question it was fraud. After comparing the data reported by [the former postdoc] and the data we subsequently collected, I had little doubt that the data were fabricated." Bur-

den's former postdoc spent several years in laboratories at the University of California, San Francisco and at Guy's Medical School in London, until problems arose, in one case involving experiments being sabotaged.

Blowing the Whistle

In the cases of both Burden and Collins, the problematic data were generated by a postdoctoral fellow and a graduate student, respectively. But what happens when the person heading the laboratory is the one suspected of fraud? "In cases where the PI is responsible for misconduct, the lab may be shut down putting students and postdocs in jeopardy. This causes serious morale problems during the investigation. It is very harmful for innocent people," says Chris Pascal, director of ORI.

In one of the biggest cases of misconduct in German history, Friedhelm Herrmann and Marion Brach, two investigators at the Max Delbrück Centre for Molecular Medicine in Berlin, retracted 11 papers published between 1991 and 1999 containing data they admitted had been fabricated. Eberhard Hildt, currently an investigator at the Robert Koch-Institut in Berlin, was a postdoctoral fellow in the lab when allegations of misconduct were raised against Herrmann and Brach in 1997. "The consequence for me was that I had to leave the lab," he says. Others were in a more difficult position. "The students had the problem of how to finish their thesis with no funding. In the end, the university provided for them," says Hildt. Today the case is far behind him, but he is aware of the dangers involved. "I try to avoid any kind of structure that would promote fabrication. I tell students not to have any result in mind that they have to demonstrate. We just do an experiment and see what happens," he says.

Pointing the finger at an established scientist is potentially damaging to the person who takes the initiative. "The whistleblower is usually on the losing side," says Walter F. DeNino. In 2000, he was a research assistant in the laboratory of Eric

Poehlman, an expert on menopause at the University of Vermont College of Medicine (UVM), when he alerted university officials to discrepancies in one of the patient data sets Poehlman was using. "Other people had noticed something was wrong but no one wanted to speak out," he says. "To be honest, legal protection for the whistleblower is limited. I was forced to find legal counsel to deal with the after effects. Poehlman was very aggressive during the investigation." DeNino left UVM to take courses at Columbia University in New York City and has applied to medical school there. "[The incident] did not deter me from my plans, but it did make me more interested in ethics," he explains.

Poehlman was barred for life from obtaining federal research grants, in addition to facing hefty fines and possible jail time. The researcher pleaded guilty in March 2005 to having falsified research in 17 grant applications (amounting to about \$2.9 million in funding from the NIH and the US Department of Agriculture) and in 10 research articles published from 1992 to 2002, all of which were retracted or corrected. In September 2001, while the investigation was under way, Poehlman resigned from UVM and moved to the University of Montreal. He subsequently left this position in January 2002 and has been living in Canada since. He faces a plea hearing and sentencing "in the next several months," says ORI's Pascal. Russell Tracy, associate dean for research and academic affairs at UVM, says the case "caused a great deal of sorrow and pain to a relatively large number of people who knew Eric Poehlman and liked him. A smaller number of people had close professional ties. Their concern was that it would affect their ability to be scientists."

Colleagues and Collaborators

Being the coauthor of a paper that is retracted can be damaging, especially in the early stages of a person's career. In cases where collaborators are not aware that data in a study were falsified, ORI

does not hold them accountable of wrongdoing. "Our view is a legal issue. We will not blame them and will not hold them responsible," says Pascal. But the UK-based Committee on Publication Ethics (COPE) has a somewhat stricter view. "At COPE we would say any author has a responsibility of taking publishing ownership. There may be a situation where one author falsified data or has a conflict of interest and others are not aware of it. Perhaps the coauthors did not know the full picture. They should then withdraw their names from the publication," says Sabine Kleinert, a member of COPE and an executive editor of the medical journal *The Lancet*.

The question of authorship was recently highlighted in the case of Gerald P. Schatten, a biologist at the University of Pittsburgh. His name appeared last in the list of authors of the now retracted 2005 *Science* paper on cloned human embryonic stem cells by Hwang and his team from Seoul National University in South Korea. Schatten was recently found guilty, by a panel at the University of Pittsburgh, of "research misbehavior" for allowing himself be listed as a senior coauthor when he had performed none of the experiments and had not verified the data. *Science* is now conducting its own investigation to examine how the Korean stem cell papers were handled and the journal's policies in general; these findings are expected to be reported in April.

Setting the Record Straight

Most countries outside the United States do not have an independent institute like ORI dedicated to handling scientific misconduct but instead use an ad hoc system for investigating possible misconduct cases. Ulf Rapp of the University of Würzburg, Germany headed a task force commissioned by the DFG, Germany's main funding agency, to investigate the Herrmann-Brach case. He says the commission found that at least 94 papers, including reports of clinical trials, had been manipulated and several people were probably involved.

The Herrmann-Brach case and the commission's findings prompted the DFG to establish new guidelines for dealing with scientific misconduct. Every publicly funded German research institute is now required to sign a copy of the guidelines and to agree to uphold them.

Rapp was disappointed with the ultimate outcome of the case. According to him, only 11 papers (out of the 94 thought to contain falsified data) were retracted or corrected, and the scientists involved in the research, apart from Herrmann and Brach, continue to work. "From the start all I wanted to do was set the scientific record straight. It was just about the papers," Rapp says.

But setting the record straight may be more challenging than anticipated. When a retraction is published it appears in PubMed (the online database of biomedical and life sciences journal literature) linked to the original paper, thereby alerting scientists to the problem. John Budd, professor of information science at the University of Missouri-Columbia has, however, found that retracted papers continue to be cited in the scientific literature at rates comparable to those for nonretracted papers.

"There is essentially no difference," says Budd. "My guess is that people become aware of the published works through mechanisms other than databases."

Lies, Big and Small

It may be a scientist's worst nightmare, but by most accounts, outright fraud is rare. Since 1992, more than 2700 allegations of possible misconduct were brought to ORI's attention, resulting in over 160 findings of actual misconduct. In a recent study, Brian Martinson, an investigator with the HealthPartners Research Foundation in Minneapolis, gathered responses from 3,247 NIH-funded researchers to a mailed survey about different ethical behaviors. Based on the results published in *Nature* last year, 0.3 percent of scientists admitted to fabricating research data and 1.4 percent to plagiarism. "These behaviors are not the lion's share," says Martinson. However, 33 percent of those surveyed admitted to "lesser" offenses, such as inappropriately including their names as authors on papers where they had made little or no contribution, changing a study's design to satisfy a sponsor, overstating results, with-

holding findings, and so on. Discussions in focus groups of 51 scientists revealed that most of them "are uncomfortable with these behaviors but say they must do them to survive in their work," says Martinson.

So, is it possible to prevent misconduct in scientific research? "If someone is intent on fabricating data there is not much you can do," says Burden. But Burden is now even more cautious about the people he recruits to work in his lab. "If I am uneasy about a person, I do not offer them a position," he says. "It is a shame because I think there should be a diversity of personalities in science, but I am consciously risk averse." He also believes that having a focused research program helps him to avoid mistakes and to identify them rapidly when they do occur. "There is continuity in terms of the projects we work on, so there is a good chance we will pick up errors ourselves." Talking to students and postdoctoral fellows about safeguarding the integrity of data may also help. "Anyone who comes to my lab is aware of the incident," says Collins. "That is a small silver lining of the case. As awful as it was, I use every opportunity to tell people about it."

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