

Responsible Conduct of Research - Module Three

Case Studies - AY20-21

A. Authorship

Bob Powell, a postdoctoral fellow in biochemistry, has just completed a manuscript detailing the results from the first project in which he had taken a leading role. The focus of his project has been to discern the ways in which humans metabolize sulfites, a class of chemicals commonly used to preserve wines and dried fruits. Although he had developed the rough outlines of the project on his own, he owes much to individuals both inside and outside his lab. As he is writing up the paper, he deliberates on whether the following people should be identified as coauthors to recognize their contribution to the work. Who should be coauthors and who should simply be acknowledged?

A1. Author or not? A colleague at another university, a toxicologist specializing in food additives, shared with Bob his unpublished work on the *in vivo* activity of sulfites, information that allowed Bob to choose the ideal animal model for the experiment--the *Abyssinian* field mouse.

A2. Author or not? A friend of his, who happened to be a wildlife specialist, provided Bob with much advice on rearing and maintaining a colony of *Abyssinian* field mice such that he would have a stable pool of animal subjects.

A3. Author or not? A highly experienced technician in the lab who gave Bob advice on modifying an assay he had been using, which finally allowed him to measure successfully sulfite metabolites in mouse urine. This technician also assisted in writing up the methods section of the paper.

A4. Author or not? The number of assays that Bob had to conduct was quite sizable and more than he could manage on his own, given other demands of the project. Thus, an undergraduate college student collected most of the urine samples and conducted all of the assays yielding the data.

A5. Author or not? A senior researcher in a neighboring lab who took an interest in Bob's career offered to review the initial drafts of Bob's paper. By the end of the writing process, this researcher had helped Bob outline the paper, suggested a few additional experiments that strengthened the paper's conclusions, and made a number of editing changes in the penultimate draft that enhanced the paper's clarity.

B. Conflict of Interest

Jim Gibbons is a respected investigator in the area of HIV infection. His laboratory is currently trying to develop new peptide-based reagents for inhibiting the initial interaction of the virus with T-cells. The work is progressing well, and he and his postdoc, Helen Andrews, are finishing off the final experiments showing that bacitracin, a small peptide antibiotic, is a potent inhibitor of this interaction. Dr. Gibbons received a manuscript in the mail from the editor of a prestigious journal asking him to review a manuscript that had just been submitted to the journal. The first page of the manuscript bears the title, "Bacitracin is a potent inhibitor of HIV infection of T-cells." The authors were unknown to Dr. Gibbons and were located at a different institution.

B1. Should Dr. Gibbons simply hold the manuscript as long as possible to give Helen time to complete her experiments and draft a quick manuscript?

B2. Should Dr. Gibbons read the manuscript before he decides?

B3. Should Dr. Gibbons share the information with his postdocs?

B4. Should Dr. Gibbons agree to review the manuscript?

C. Collaboration (based on an article in Science (2011) 332:163)

In 1989, Mark Holodniy was sent by his PI, Tom Merigan at Stanford, to learn about a new procedure developed by Cetus, the polymerase chain reaction (PCR). Merigan and Holodniy wanted to use this new PCR technique to develop an assay to follow HIV infection. As a way to encourage the development of new technology, the federal Bayh-Dole act requires university scientists working on federal grants to assign their patent rights to the university. Holodniy and Merigan, when hired by the university, signed an agreement with Stanford that said “I agree to assign” intellectual property rights to the University. When Holodniy, as an employee of Stanford and paid from federal research grants, visited Cetus, he was asked to sign a visitor’s agreement that contained a non-disclosure clause promising to not divulge any company secrets and to honor Cetus’s intellectual property policies. The agreement also indicated that Holodniy “will assign and do hereby assign” rights to any resulting patents to Cetus.

In 1999, Stanford was awarded the first of three patents to use Cetus’s patented PCR process to measure HIV viral RNA in serum to quantify viral load and to help inform treatment strategies. Both groups, Cetus and Stanford, contributed to the work of developing PCR and correlating the results with viral load and clinical data. Meanwhile, Roche, who bought Cetus in 1991, began to manufacture HIV monitoring kits based on the work between Cetus and the Stanford scientists. They have subsequently developed a market for the kits worth millions of dollars a year. In 2000, Stanford demanded that Roche pay the university royalties based on the Stanford patent. When Roche refused, Stanford sued.

In 2007, a lower California district court ruled in favor of Stanford indicating that the agreement between Holodniy and Cetus violated the Bayh-Dole act (and was, therefore, not valid) by entering into an independent third-party agreement with Cetus that did not include Stanford. However, this court also declared Stanford’s patents invalid because they were “obvious.” In 2009, the U.S. Court of Appeals ruled in favor of Roche citing that Holodniy had given away his rights to Cetus by signing the visitor form. Additionally, the language in the agreement between Holodniy and Stanford only indicated that he “would agree to assign”, not that he “had assigned” his rights as he did in the Cetus agreement.

In an appeal to the Supreme Court, Stanford argued that the Court of Appeals ruling undermines the Bayh-Dole act and that it would “create serious uncertainty about who owns patents from government sponsored research in universities.” Major research universities and the American Association for the Advancement of Science supported the Stanford position while the Pharmaceutical Research and Manufacturers of America supported Roche’s position, arguing that it was a simple contractual agreement and that the Holodniy-Cetus agreement had precedence. The Supreme Court ruled in favor of Roche.

C1. Why do companies require non-disclosure agreements from visiting academic scientists and consultants?

C2. What is the reason for including an agreement that any intellectual property developed as a result of the information exchange between a visitor/consultant and the company belongs to the company?

C3. How do you think it happened that Stanford and Cetus scientists worked together on the project but the only patent filed was just from Stanford and the only production/sales was from Roche/Cetus?

C4. What's the overall message to scientists in academics collaborating with those in industry?

C5. What if you were a graduate student or postdoc working with the people developing this assay and doing the clinical correlation of the data. How do you think it might affect your ability to publish your work?