Research Integrity | Case Study 1: Truth or Consequences

Julio Cruz and Samantha Bergen are both graduate students working with Dr. Mark Chan, an eminent environmental chemist. Although both are in their fourth year of study, neither has published a manuscript. Both are beginning to worry that if they do not publish soon they will not be able to obtain good postdoctoral positions.

Finally, Julio's project starts to look promising. After many months of effort, he believes he has been able to synthesize RG198, a compound that is to serve as an intermediary in the formation of his thesis molecule, WX5, which he believes will degrade plastic in an environmentally sound way. Julio now has to repeat his experiment to make more RG198 and perform a series of analyses on the compound to verify some of its properties.

Dr. Chan is very excited about Julio's progress, and tells him to repeat his experiment and to begin to write up the results, because even the synthesis and some properties of the intermediate molecule are unique enough to be published in an important journal, such as Nature.

Although only small amounts of RG198 are available, Julio and Dr. Chan agree that they must push ahead and work quickly. In order to help Julio as he works on manufacturing more RG198 for the next set of experiments, Dr. Chan recruits Samantha to assist Julio in some analyses. Samantha has not been very successful with her project, which involves transforming asbestos into a non-toxic compound, and Dr. Chan feels that performing the analyses will teach her some skills that she could apply to her own project. Dr. Chan promises her a second authorship on the paper if the results of her analytic studies pan out. Although Julio does not think highly of Samantha, believing her to be sloppy, he wants to move ahead with his research. He gives her the RG198 in two batches for the analytic studies.

Samantha completes the first set of analyses on the first batch and is excited by the results, which verify three of the four chemical groups that RG198 is supposed to have. On the next batch, Samantha performs another set of experiments, using another analytical tool that will identify the fourth chemical group. On the day she is doing the first experiment on the second batch of RG198, she phones Julio from the analytical facility across the street from the lab and asks him if a contaminant might have gotten mixed up in the compound, since the spectral pattern is not what is expected for the molecule.

Julio asks Samantha to save the remaining material from the second batch, telling her that he will perform the second round of analyses. But when Samantha comes back to the lab a few hours later, she does not give him the leftover RG198. She tells Julio that she obtained positive results and that her mistake in the original interpretation was due to tiredness, and to the fact that she had focused inadvertently on a reference sample, not on RG198. There is no way for Julio to validate her findings, since there is not enough RG198 left to do another run. Samantha tried to reassure Julio by
showing him the graphical readout from the instruments from the experiments on the second batch, pointing to the results for the fourth chemical group.

Dr. Chan is ecstatic about the findings, and tells Julio to quickly write up a manuscript. Julio doesn't want to accuse Samantha of manipulating research results, but later in the day he looks through her research notebook and sees a written procedure and data for the first batch of experiments. For the second batch, he sees that she has put only the readout in the notebook, which looks too clean to him. It also has no accompanying text. He wonders what might have happened. Perhaps she used a reference sample and some mechanical manipulation to make the fourth chemical group peak appear so pure.

Julio is unsure about whether he can trust Samantha's findings, but he proceeds to write up the manuscript about his synthesis of RG198 and its analysis by Samantha. The article is published in Nature, but in the next several months other scientists who repeat his synthesis are finding different spectra than what he reported in his second batch of experiments. During that time, Julio has been able to synthesize more of the compound, and even succeeds in making WX5. When he repeats the analysis on the fourth chemical group in RG198, he finds a different spectral pattern from what Samantha found and what was published. He believes that she must have done something to the data.

*http://cuny1.columbia.edu/projects/rer/rer_misconduct/case/#1*
Dr. Berg has spent the majority of his research career investigating liver diseases. About 5 years ago, Dr. Berg has published a paper in a prestigious journal, describing the effects of nuresin on hepatocyte function. Since then, Dr. Berg has been pursuing the mechanisms of nuresin action in depth. He has successfully published several other papers, and last year he has obtained NIH funding supporting the continuation of these studies.

Mike is a graduate student who has recently joined Dr. Berg’s laboratory. A senior student, Debbie, is teaching Mike how to perform the assay measuring a specific hepatocyte function in the presence of nuresin and various receptor antagonists. They are using the protocol that was designed when Dr. Berg’s assistant first attempted measurement of the hepatocyte function and first tested nuresin, 5 years ago.

Mike is trying to understand the measurement and he asks Debbie about the composition of the “solution B” used at the critical measuring point of the assay. Debbie shows him the recipe used for solution B. Mike notices that this solution is not controlled for pH. He asks Debbie whether she or anyone else has ever checked the pH and Debbie says that it is probably fine and that he shouldn’t worry about it.

Months later, while doing literature searches on liver function for his PhD dissertation proposal, Mike reads an older research paper describing the pH sensitivity of hepatocyte function measurements and he remembers his dilemma concerning solution B. At this point, Mike has already been assigned a portion of the grant project and is performing the experiments by himself. He decides to measure the pH of solution B and he discovers that it is below normal. He then does an experiment testing the effects of nuresin on hepatocyte function and he discovers that if solution B is at normal pH, no effect of nuresin can be observed.

Mike informs Debbie about his finding. Debbie points out to Mike that all her papers and PhD research, as well as Dr. Berg’s NIH grant, are based on the results obtained from that assay and are thus in jeopardy. Nevertheless Mike decides to inform Dr. Berg. Dr. Berg appears very upset and tells Mike that they will discuss this later. However, several weeks have passed and Dr. Berg has not mentioned this incident in the lab meetings. Debbie and Dr. Berg’s assistant continue their experiments using the old protocol. Mike asks Debbie again about this and she advises him to forget about the control experiment he had conducted, and instead focus on his PhD dissertation proposal.

Dr. Conway is a tenured associate professor of biochemistry at a large research institution. His research group consists primarily of graduate students. Since Conway likes to see work in progress, he requires all of his students to participate in individual meetings as well as group meetings with him every week. He insists on seeing each piece of data and working through the projects with his students.

Elizabeth is a second year graduate student in the biochemistry department, and Conway is her thesis research adviser. Elizabeth has recently completed the majority of the coursework that is required by her program and is becoming more involved in her thesis project. Her research focuses on purifying a novel protein complex from mammalian cells and testing its effect on the regulation of a specific cell cycle gene. Although she has completed only a few experiments, some of her initial data look promising.

Conway has not published a manuscript in more than a year. Sensing that many of his peers are making progress in areas related to his own, he is feeling pressure to extend his publication record, in order to remain competitive in their field of research. In order to remedy his current situation, he decides to begin writing a manuscript that includes some of Elizabeth's data. He is aware that many of the experiments have not yet been reproduced or are still in the process of being repeated. He meets frequently with Elizabeth about her progress, and they go over all of her data regularly. Based on this involvement, there is little chance that he could have been misled about the preliminary status of the work.

On a recent occasion, he asked Elizabeth if he could look through her notebook, because he would like to evaluate and think about her data. Elizabeth willingly gave him her notebook. Conway finished writing and putting together the figures, and he submitted a manuscript for publication without telling Elizabeth. Conway listed Elizabeth as first author on the paper and himself as the second and final author. He submitted to the journal Molecular and Cellular Biology and recommended an editor who has been a personal and professional friend of his for many years.

When Elizabeth realizes that her adviser has submitted a paper with her name on it without her consent, she is very upset with him. If any of the data turn out to be erroneous, her scientific career could be damaged. She has just begun her involvement in a research environment, and she is unsure about how to react or if she should do anything at all. She tries to convince herself that maybe this is the way things are done. She has been working in Conway's lab for only a short time, and she is not very comfortable with him yet. She wonders if she should talk with some of the other graduate students about what has happened, hoping that they can help her deal with the situation.
Olga is a prolific young researcher working in a highly specialized area at the small university where she is junior faculty. Olga knows she has to publish a lot to get tenure, but she dislikes the “slice and dice” approach to publishing. Instead of submitting each little publishable part of her work, she is waiting until she has a significant set of studies which test a theoretical position and can then be published as a whole.

Similarly, the complex grant application she recently submitted is rich in sophisticated detail and designed to test an original theoretical position accompanied by a significant body of work.

When Olga hears from the federal funding agency, she is disappointed to see that not all the peer reviewers regarded her proposal favorably. One argued that it was trivial and of no importance to the field. The grant was not funded.

Olga quickly regroups. Since she has many well-trained students and some start-up funds, she decides to conduct the research without the grant funding. She feels impelled to conduct the research and publish the outcome because she is quite certain she knows who shafted her proposal—Philippe, a powerhouse in the world of grants and faculty clout who has a reputation for “bad-mouthing” the work of competitors at less prestigious institutions than his.

Within 18 months, Olga has completed the set of studies and is writing them up. In reviewing the most recent literature, however, she finds that her exact design and theory testing have just been published by someone else. Namely, Philippe, the very person she suspected of panning her grant proposal! If that isn’t painful enough, she also realizes that any work she now publishes will be regarded as derivative or unoriginal—and she might even be accused of stealing his work.
Gail is an Associate Professor who has published extensively and rightly considers herself one of the leading experts in her field. She knows the drill for developing and submitting a proposal for funding. Her most recent proposal is based on considerable prior research that she and colleagues have conducted, and it employs methodology that she knows will produce valid findings.

Gail is anxious about her proposal being reviewed and funded. Prior to submitting, she ran it by a network of capable colleagues with whom she works collaboratively to develop and critique ideas. They all share the same dedication to medical research with important long-term implications for public health, as well as short-term implications for federal policies and funding.

When Gail finally receives the funder’s evaluation, she is happy to see that she received a high score on her proposal. However, the score is below the cut-off point at which it can be funded. Gail turns to see what objections and concerns the reviewers had with her proposal. She plans to revise and resubmit for the next funding cycle.

Gail is flabbergasted to read what the reviewers said. In their feedback, they find that her methods are “flawed”. And they suggest changes to the study design that Gail is certain would significantly compromise the quality of the science as well as its impact on the development of her field. They clearly did not understand her approach, which is highly novel.

Gail is considering re-submitting the proposal employing the reviewers’ suggested methodology, then actually doing the study as she proposed it in the first place, explaining that “pilot testing” indicated that her methodology would work best.

However, Gail worries that this is deceptive. And who knows if the same reviewers would be evaluating her resubmission? Perhaps she is better off proposing her original “flawed” methodology—with a direct response to reviewers—in hopes that she will receive new reviewers or that her reviewers will be unusually open minded. Gail has two months before the revised proposal is due. She feels caught between a rock and a hard place.
Dr. John Leonard is one of very few molecular biologists working in a particular field. Dr. Leonard receives a paper to review, about a protein called survivin, which he and a graduate student in his laboratory are researching. The article was submitted by Dr. Mark Morris to Protein Interactions, a medium-impact journal, and the editor asked Dr. Leonard and two other experts in the field to review the paper. The article suggests a new interaction between survivin and the protein GFX and provides evidence for the fact that both proteins are necessary for the full survival-promoting function of survivin in a cell. The article also describes, though, that if there is too much survivin inside cells they die.

But the paper is fraught with problems: poor controls, inconsistent data in figures, and alternative explanations are not considered and claims are overstated. Dr. Leonard gives the paper to his graduate student Melissa Zane, who gives it a detailed critique and recommends significant revisions. Ms. Zane has never reviewed an article before, and Dr. Leonard thinks that doing so would be a good educational experience for her. Ms. Zane notes the finding about too much survivin being toxic to cells, a problem she has had working with the protein, and discusses it with Dr. Leonard. Both agree that they should lower the dosage of survivin in her experiments; the cells actually survive for a week, longer than her experience before, and then they die.

Dr. Leonard submits Ms. Zane's and his own comments about the research to the editor, suggesting that the paper be accepted only after a few more experiments are performed to validate some of the conclusions. One of the other reviewers has comments similar to Dr. Leonard's, and the editor asks Dr. Morris, the author, to make the revisions before he will accept the paper.

But in the next few weeks the interaction between GFX and survivin that is discussed in the paper remains in Dr. Leonard's mind. GFX was not a line of inquiry that Dr. Leonard and Ms. Zane were following in their research. They were focusing on other stimulatory proteins, but unsuccessfully. Dr. Leonard suggests to Ms. Zane that she add a compound to the cell culture system that stimulates the cell to produce its own GFX, a method that is somewhat different from what was in the paper by Dr. Morris that is under review. The enhancement method works. The cells live for a month.

Ms. Zane and Dr. Leonard draft a paper based on the results, which includes appropriate controls. Science, a prestigious journal, accepts the paper. Several months later, Protein Interactions publishes a revised paper from the laboratory of Dr. Morris. But after Dr. Morris sees the article in Science he suspects that Dr. Leonard, who was an anonymous peer reviewer on the paper, might have taken some of the ideas for the Science article from his paper under review. Dr. Morris knows that Dr. Leonard hadn't been working on GFX because it was hard to purify, and deduces that he used material in the unpublished manuscript to stimulate GFX activity.