Case Scenarios for 2005 Ethics Training

Case 1. Dr. Wode's project has been to characterize the complex of proteins that interact with "protein Z". The material that elutes from an affinity column is fairly pure, and Dr. Wode only detects ~ 7 other bands on his silver stained-protein gel. He carried out mass spectrometric analysis and was able to identify five of the bands. Two of the proteins (X and Y) make sense with respect to the current model in the field. However, the three highest molecular weight proteins correspond to membrane proteins (A, B and C) that do not make sense to Dr. Wode. Dr. Wode has carried out co-immunoprecipitation experiments that showed that the X and Y proteins do in fact interact with critical protein Z in a cell cycle-dependent manner. As a control, Dr. Wode also assayed for the membrane proteins and found that A and B also co-immunoprecipitate with protein Z. The field is very competitive, and Dr. Wode is now writing up these results for publication.

Should Dr. Wode show the entire silver-stained gel, which might lead to questions about proteins A, B and C from the reviewers? Or should Dr. Wode cut off the top of the gel and not mention proteins A, B and C? One of the bands that Dr. Wode is not able to identify is present in material from both the affinity column and a control column. Should Dr. Wode eliminate this extra band using Photoshop?

Unfortunately the protein size marker lane was badly distorted on the gel where the samples electrophoresed nicely, and the marker lane ran nicely on a gel where the samples ran poorly. Can Dr. Wode splice the good sections of the two separate gels together?

By another stroke of bad luck, the autoradiograph showing the controls for the co-immunoprecipitation was ruined when water leaked on Dr. Wode's notebooks during a heavy rainstorm. Can Dr. Wode mention these controls as data not shown? If so, what should Dr. Wode do if reviewers ask for these data? What should Dr. Wode do to avoid this disaster in the future? How should critical data be protected?

Dr. Wode happens to be in a lab where the PI takes a "hands off" approach to manuscript preparation and preparation of figures. What responsibility does the PI have for monitoring these tasks and knowing which piece of primary data was used in each figure?

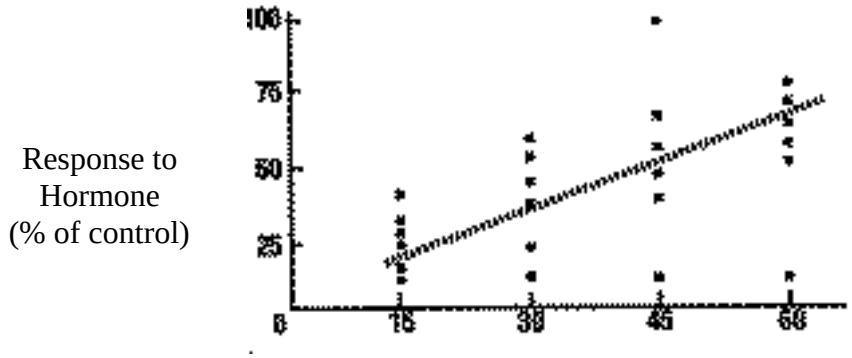
Case 2. Dr. Margaret Clint, a second year postdoctoral fellow in a neuroendocrinology laboratory, has just completed a series of experiments characterizing the receptor for a new class of hormones. During the course of this work, Dr. Clint carried out binding assays for a receptor mutant three times. In two experiments, the data were very consistent and supported the working hypothesis that Dr. Clint and her mentor were evaluating. However, in a third independent experiment, several of the samples showed the opposite effects.

Dr. Clint is supposed to present her data at the weekly meeting of her laboratory group and is now considering how to do so. In this analysis of the binding of hormone to the mutant receptor, should she average all three experiments? Should she average the two sets of data that are the

most consistent? Alternatively, could she present the data of one of the experiments and state that the findings are representative of three independent determinations? What if the experiment had been repeated six times and two of the experiments showed opposite effects?

In a parallel study, Dr. Clint investigated the hormonal response of several clonal cell lines transfected with receptor variants. In analyzing the data, Dr. Clint noted that a number of cell culture plates failed to respond to the hormonal stimulus and that there was considerable variability in the dose response relationship to the hormone. The data from one cell line, with each symbol representing the response of one culture plate, are provided in Figure 1.

Figure 1



Dr. Clint was also perplexed as to how to present the hormone response data shown in Figure 1. She consulted Dr. Joseph Atwood, a senior research fellow in the laboratory. Dr. Atwood responded, "Why don't you clean up the data? Seriously, you may never get the paper published unless you do." He then suggested that the four culture points failing to show a response (along the X-axis at approximately 10% response) be dropped because the cells were probably dead. He also pointed out that she might eliminate the top data point at the 45 minute interval as an outlier. She said, "Perhaps I should repeat a few of the experiments or try to improve the culture conditions?" "No," said Dr. Atwood, "If you're convinced of your results, why go through the time and expense of more repetitions?" Somewhat dismayed, Dr. Clint thanked him and turned back to her work.

What do you think about Dr. Atwood's comments on publication practices and his suggestions for "cleaning up" the data? How should Dr. Clint go about determining which points to include and which to exclude in Figure 1? What other course(s) of action would you recommend to her?

Dr. Atwood's perception about improving the chances of publication by "cleaning up" the data is not uncommon. How might journal editors and reviewers work toward correcting this perception?

One day, Dr. Clint's mentor asked her to prepare an abstract for an upcoming meeting, as

well as a preliminary report of her findings for publication. Unfortunately, the abstract was due in one week.

Is Dr. Clint ready to write an abstract? How should she present the data discussed above? What should Dr. Clint discuss with her mentor?

Case 3. Dr. Fong, a postdoctoral fellow in your laboratory, has been characterizing the offspring of smart-gene knockout mice. The construct was made by inserting a neo gene into the third exon. This knock out strain has just been generated and therefore is still in a mixed genetic background. Furthermore the protein blots of brain tissue show an unexpected smaller band that is faint but may specifically be reacting with the anti-smart gene anti-peptide antibodies (possibly a truncated derivative of the smart protein?). Dr. Fong presents her results in a group meeting and concludes that 70% of the offspring are slower in two of the behavioral assays the lab routinely carries out. Dr. Bhat examines another set of offspring in the same assays but concludes that only two or three out of the ten offspring are abnormal. You have heard that another laboratory has recently generated a similar mutant mouse and are worried about the competition. How should you proceed in light of these results? How should these behavioral data be documented? How much effort should be put into characterizing the immunoreactive protein band?

Case 4. Dr. Cott has been studying the subcellular localization of the "Key" protein. The favored model in the lab is that the "Key" protein moves between endosomes and the plasma membrane. In examining the Key protein labeled with GFP in living cells, Dr. Cott sees predominantly peri-nuclear staining consistent with endosomes, but no clear plasma membrane staining. However, by changing the filters used for visualization and exposing for very long periods, Dr. Cott can also observe some signal at the plasma membrane even though the rest of the cell is then badly over-exposed. How should Dr. Cott present these data? Can he show the plasma membrane localization by itself as a separate figure?

Dr. Cott also has been imaging the subcellular localization of the "Lock" protein, and has cells that are transiently transfected with a construct expressing GFP-labeled Lock. Before treatment with his favorite inhibitor, the Lock protein is in the Golgi in 55% of the cells (though most of the other cells show low signal or a diffuse distribution of Lock-GFP). After treatment with the inhibitor, the Lock protein is in the endoplasmic reticulum in 65% of the cells (again many cells show low signal or a diffuse distribution, and a few also show Golgi localization). Dr. Cott thinks that the redistribution of the Lock protein to the endoplasmic reticulum makes sense with respect to what is known about his favorite inhibitor. How can Dr. Cott present his data? Can he present a field of cells that show Golgi localization for his "without inhibitor" figure and a field of cells that show localization in the endoplasmic reticulum for his "with inhibitor" figure? What is the definition of a "representative example"?

Case 5. Dr. Williams is a Prinicipal Investigator who has a large laboratory at one of NIH's institutes. The laboratory includes about 15 junior researchers, post-doctoral fellows, and

graduate students. Twelve members of his group have been working on a project related to the relationship between hormones and obesity. They have isolated a key hormone in mice that is necessary to maintain normal weight. They publish a paper on this new finding, with Dr. Williams as the senior author. Two months after the paper has been published, Dr. Williams receives an inquiry from a researcher at a large university who has had difficulty replicating some of the group's work. The researcher requests to see the orginal data used to support a figure presented in the paper. Dr. Williams asks members of his team for the original data related to the figure and they report that the experiments that generated that data were conducted by Dr. VF, a post-doctoral fellow who recently left the laboratory to return to his native country. When Dr. VF left the institute, he was told to leave the original data at the institute and to take copies. A search of the laboratory for the original data has been less than satisfactory. The group discovers that there are several problems with the data, including the lack of a bound notebook and the availability of some “post-it” sticky notes written in Dr. VF's native language. They also have trouble retrieving data that were stored on his computer, which has been infected by a virus.

How should Dr. Williams deal with this issue?