**Plan for Instruction in Methods for Enhancing Reproducibility**

Instruction in Methods for Enhancing Rigor and Reproducibility is an integral part of the PSTP curriculum. Instruction starts in the first year of graduate school, as part of the First-Year Group curriculum, and is part of the Responsible Conduct of Research Instruction. This 1.5-hr session introduces students to the importance of enhancing rigor and reproducibility in their own research.

**Rigor & Reproducibility Discussion Guide (FYG)**

1. What is the problem? *(there is a slide with these two statistics on it, can also talk about retractions and other issues)*
   1. Bayer R&D scientists able to reproduce only 20-25% of published reports
   2. At Amgen, only 6/53 (11%) of recent clinical oncology reports could be reproduced
      1. authors shared reagents and Amgen agreed not to name their paper
2. Discuss in small groups and report out or discuss as a whole class: what’s going on? Is science broken? What could explain these results? What are your experiences with trying to reproduce published results? Some ideas students may come up with include:
3. Inability for others to replicate exact conditions (such as methods, raw data, cell lines, reagents)
4. Experimental design was flawed
5. Conclusions were overstated
6. Go back to basics: shouldn’t things work if we just Keep Calm and Stick to the Scientific Method? Ask class to name the steps.
7. Show full model of scientific method, discuss if needed
   1. Ask: Where can this process break down? Alternatively, where can errors be introduced?
8. Show scientific method with problem areas listed and discuss/compare to ideas brought up by students
9. Generate Hypothesis
   1. Operating with a desire to “prove” your hypothesis
10. Design study to test hypothesis
    1. Low statistical power
    2. Failing to account for animal or strain backgrounds
    3. Poor controls
11. Collect Data
    1. Using invalid reagents (antibodies, cell lines, etc): current move to require proof of validation of reagents as a requirement for publication
    2. Poor record keeping
12. Analyze Data
    1. Cherry picking
    2. Failing to consider correct controls
13. Interpret Data
    1. P-hacking
    2. Model bias
14. Publish
    1. Inadequate description of methods: page limits restrict methods sections. Journals are now requiring more extensive methods sections, supplemental methods sections
    2. Failing to share data
15. Failing to share reagents
16. Break class into four groups and have students consider the readings (recommended to bring one or two extra copies of each to class). Students should discuss the question, and then report back to class what they conclude or what issues came up.
    1. Who should be responsible for validating reagents and datasets? (the researcher, the lab, the community, the journal?) Reference article: The Great Big Clean-up [http://www.the-scientist.com//?articles.view/articleNo/43821/title/The-Great-Big-Clean-Up/](http://www.the-scientist.com/?articles.view/articleNo/43821/title/The-Great-Big-Clean-Up/)
    2. Are all statistically significant results scientifically significant? Reference article: Statistical Errors<http://www.nature.com/news/scientific-method-statistical-errors-1.14700>
    3. Should researchers always make their code available? Reference article: <http://www.nature.com/news/2010/101013/full/467775a.html>
    4. Does the sex of your biological sample always matter? Reference article: <http://www.nature.com/news/policy-nih-to-balance-sex-in-cell-and-animal-studies-1.15195>
17. End with discussion of best practices for researchers and for the community as a whole. Provide additional reading if there are relevant or recent articles of interest, or based on specific questions and discussions points raised in class.

**BBSP 705-Best Practices for Ensuring Rigor and Reproducibility in Research**

The major effort for instruction in rigor and reproducibility comes in BBSP 705, “Best Practices for Ensuring Rigor and Reproducibility in Research”, which is comprised of five 1.5-hr sessions taught over two weeks immediately after final exams are over at the conclusion of the first year of graduate school. The target audience is therefore rising 2nd year graduate students. For the PSTP, all students who enter the program are required to attend at least 4 of the 5 sessions to pass the course.

The course was organized around what we term the “hypothesis wheel”, which aptly describes the scientific method of hypothesis generation and testing (Fig. 1), and where the process can go wrong (colored text). Therefore, we organized the course to address these common areas that lead to problems in rigor and reproducibility. The syllabus for the course is below.



**Figure 1. Schematic representation of the “hypothesis wheel” of the scientific method.**

***BBSP 705, “Best Practices for Ensuring Rigor and Reproducibility in Research”- Course Syllabus***

Course Description:The goal of this class is to introduce topics concerning rigor and reproducibility in research early in students’ careers (i.e. 2nd year in graduate school) in a campus-wide and consistent format to ensure that each trainee contributes to the integrity of UNC research culture. The importance of reproducibility and rigor in academic science has been highlighted in multiple publications in a myriad of journals, all describing the problems arising from irreproducible research and suggesting ways to increase rigor and reproducibility. This subject matter is both timely and important. The NIH now requires that all R, F, and T grants include a section addressing Rigor and Reproducibility, both for proposed research (R and F grants) and for training (F and T grants). We have based this class on addressing rigor and reproducibility at all stages of the classic scientific method of hypothesis testing (i.e. generating a hypothesis 🡪 designing an experiment 🡪 collecting, analyzing, and interpreting data 🡪 publishing), and identifying the areas in which one’s research can lead to incorrect conclusions and erroneous publications. Our goal is to make the class both informative and engaging, as well as interactive, by stimulating and fostering class discussion based on real-world scenarios.

Course objectives (learning outcomes): The objectives of this course are to introduce 2nd year graduate students in biomedical research programs to best practices in research to ensure rigor and reproducibility. These best practices include those for hypothesis generation, reagent validation, experimental design, appropriate use of experimental models, data analysis, data management and record keeping, and publishing. While no course can truly “teach” rigor and reproducibility, the goal is to make students aware of the most common mistakes, bad practices, and poor habits that can lead to errors in research, and also how to correct these errors.

Course Assignments: There will be no official assignments for the class, although individual instructors may request students to read articles before class. Students will be expected to attend at least 4 of the 5 sessions and to actively participate in class discussions. Grading will be based on attendance and participation in the class discussions.

**Course Schedule**

**Session 1:** Experimental Design

* Importance of Proper Controls
* Power Calculations
* Biological vs Technical Replicates
* Quantification of Western blots

**Session 2:** Experimental Rigor

* Hypothesis Generation
* How to Avoid Hypothesis Bias
* Importance of Blinding and Randomization
* Defining Outliers and Exclusion Criteria

**Session 3:** Experimental Models

* Recognizing the Limitations of Your Experimental Model
* Assuring the Validity of Cultured Cell Lines
* Validating Antibodies
* Balancing Sex Differences in Animal Models and Cell Lines

**Session 4:** Data Management and Record Keeping

* Importance of Recording Metadata
* Scientific Coding
* How to Manage Large Data Sets (Storage and Computation)
* Electronic Lab Notebooks/How to Keep Track of Electronic Data

**Session 5:** Publishing and Peer Review

* Understanding Peer Review
* Dos and Don’ts of Image Manipulation
* Plagiarism
* Honesty in Reporting
* Journal Requirements to Ensure Rigor and Reproducibility

Lastly, we incorporate Rigor and Reproducibility into PHCO 732, “Grant Writing”. Students are constantly challenged by faculty to assess whether their experiments are rigorous, and whether the experimental design is sufficient to ensure reproducibility.