NIH Rigor and Reproducibility Training Module 2: Blinding and Randomization

Potential Discussion Points and Questions:

Starting Points:

- Blinding: keeps the investigators unaware of assigned sample designations (e.g., wild-type vs. mutant, untreated vs. treated) until after completion of the experiment and, if possible, analysis of the results[1,2]
- Randomization: experimental method to reduce bias and minimize the likelihood of chance altering the results of an experiment[3]
- Sample blinding and randomization are key elements to reduce selection and other biases, permit reliable statistical testing, and are critical particularly to the interpretation of preclinical proof-of-concept studies[4]

Lead-in Questions:

- Can you think of a particular instance in which blinding and randomization could have a dramatic impact on the results?
- Have you ever blinded and/or randomized samples in your own experiments?

Follow-up Questions:

- Here, the reviews state that the paper will be accepted for publication if the authors can demonstrate a particular result, which will increase the paper's significance. Have you ever felt pressure, either from your PI or reviews of a submitted paper, to obtain a specific result?
- Are you aware of the distinction between two types of experimental approaches – hypothesis-driven or discovery-driven? Is one better than the other? What are the advantages and pitfalls of each?
- Was there a general problem here with concepts of randomization and appropriate sample size?
- What specific problems in experimental design and execution can you identify?
- Do you think the PI suggested the best approach to blind and randomize the experiment? Is there an additional element that should have been included? Do you think most PIs would suggest blinding an experiment, unless they had an experience in the past that warranted it?
- In your own lab/department, how willing do you think someone would be to blind samples for you? Should this be a priority for you? How would you randomize samples?

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[1] Modified from Schulz, KF and DA Grimes. Blinding in randomized trials: who go what. *Lancet.* 2002 Feb 23; 359(9307): 696-700. http://apps.who.int/rhl/LANCET_696-700.pdf

[2] Modified from Festing, MFW et al. Guidelines for the design and statistical analysis of experiments using laboratory animals. *ILAR J*. 2002; 43(4): 244-258. http://ilarjournal.oxfordjournals.org/content/43/4/244.full

[3] Modified from Suresh, KP. An overview of randomization techniques: An unbiased assessment of outcome in clinical research. *J Hum Reprod Sci.* 2011 Jan-Apr; 4(1): 8-11. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3136079/

[4] Unger, EF. All is not well in the world of translational research. *J Am Coll Cardiol.* 2007; 50(8): 738-740. http://content.onlinejacc.org/article.aspx?articleid=1138418

- How realistic is the feasibility of blinding (expertise in the lab, contact with potential blinders)?
- The electrophysiological experiment discussed here was unable to be performed on the two channels simultaneously by the same individual. Do you think there was a better way to test the drug?
- The drug used in this example apparently degrades dramatically over the course of a few hours. This is a property that ideally should have been obvious to the graduate student, Miles, but do you think it's easy to overlook a detail like this?
- If you were in Miles' situation, do you think you or your PI would have discovered that the drug was degrading?
- Would you have confirmed that the drug degraded over time? If so, how? Run a positive control? Let the drug degrade for a period of time (all day) and then do the experiment?
- If the results were what they hoped/expected – in this case, if the mutant showed a greater effect because they recorded from those cells first, do you think they would have thought about drug degradation and explored this further? Would you have done so? (Confirmation bias)