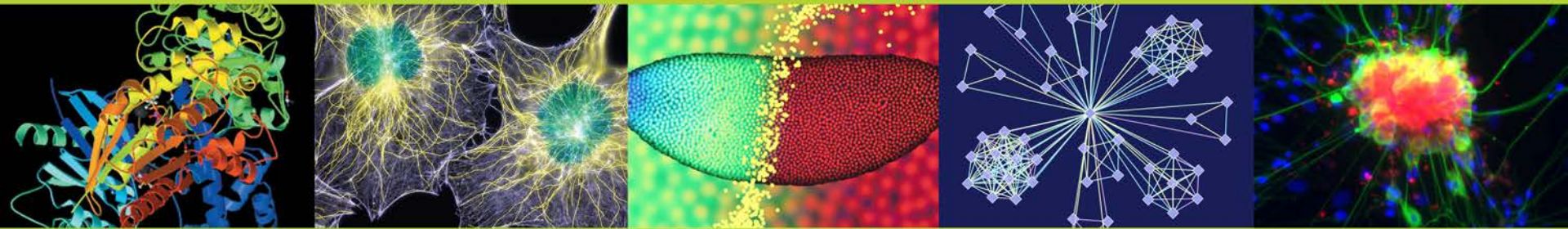# Why We Care About Rigor and Reproducibility and What We Are Doing

Richard Okita, PhD, Program Director

National Institute of General Medical Sciences (NIGMS)

National Institutes of Health (NIH)

Publications Questioning Findings

- 2005 Publication from John Ioannidis "Why Most Published Research Findings are False" PLOS Medicine

- 2011 Publication from Prinz et al. "Believe it or Not: How Much Can We Rely on Published Data on Potential Drug Targets?" Nature Reviews Drug Discovery

- 2012 Publication from Begley and Ellis "Drug Development: Raise Standards for Preclinical Cancer Research" Nature

NIH National Institute of General Medical Sciences

Senator Shelby to Dr. Collins

- This is a great concern. Dr. Collins, I don't want to ever discourage scientific inquiry, and I know you don't, or basic biomedical research. **But I think we on this subcommittee, we need to know why so many published results in peer-reviewed publications are unable to be successfully reproduced. When the NIH requests $30 billion or more in taxpayer dollars for biomedical research – which I think is not enough – should reproducibility, replication of these studies, be part of the foundation by which the research is judged. And how can NIH address this problem? Is that a concern to you?**

NIH National Institute of General Medical Sciences

NIH Response

- 2012 Landis et al., "A Call for Transparent Reporting to Optimize the Predictive Value of Preclinical Research" Nature

- 2014 Collins and Tabak "Policy: NIH Plans to Enhance Reproducibility" Nature

- October 9, 2015 NIH Issued Notice 16-011 "Implementing Rigor and Transparency in NIH & AHRQ Research Grant Applications"

NIH National Institute of General Medical Sciences

NOT-OD-16-011 – Grant Review

- For most research grant applications submitted for due dates on or after 1/25/2016.

- Focus on four areas deemed important for enhancing rigor and transparency:

  1) the scientific premise of the proposed research,
  2) rigorous experimental design,
  3) consideration of relevant biological variables, and
  4) authentication of key biological and/or chemical resources.

NIH National Institute of General Medical Sciences

Collins and Tabak "NIH Plans to Enhance Reproducibility" Nature 2014

- As a funding agency, the NIH is deeply concerned about this problem.

- Factors include poor training of researchers in experimental design.

Courses in Experimental Studies

- CellBio 302QC – Advanced Experimental Design for Biologists (Credits 2 - Credit Level Graduate) at Harvard

- Faculty Instructors: Randall King and David Glass

- Course Description: This course will focus on both the theory and practice of experimental design. The emphasis is on project planning and vetting, individual experimental design, and trouble shooting. Special focus will be placed on methods to avoid experimental bias, and potential sources of inappropriate interpretation. Also the importance of system validation is especially emphasized.

NIH National Institute of General Medical Sciences

Experimental Design for Biologists

- Experimental Design for Biologists, 2nd Ed. August 2014

- Author: David Glass

- Summary: Experimental Design for Biologists is a unique and successful handbook on the theory and practice of effective design of scientific experiments, based on a well-conceived course by the author. Experimental Design for Biologists, Second Edition, is an essential resource for designing a sound research plan, critical to the success of graduate students.

Training Modules to Enhance Data Reproducibility (R25) RFA-GM-15-006

- Develop training modules with the potential to enhance data reproducibility.

  - Experimental design:

  - Laboratory practices:

  - Analysis and reporting:

  - Culture of science:

Training Modules to Enhance Data Reproducibility (R25) RFA-GM-15-006

Grant	PI Name	Institution	Title
1 R25 GM116149-01	SCHLOSS, PATRICK DAVID	UNIVERSITY OF MICHIGAN	Development of reproducible informatics skills among microbiome researchers
1 R25 GM116146-01	CARROLL, AARON E	INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS	Utilizing Established YouTube Infrastructure for Training Module Development
1 R25 GM116167-01	ALLISON, DAVID B	UNIVERSITY OF ALABAMA AT BIRMINGHAM	Beyond textbook, yet simple, statistical tools for reproducible animal research
1 R25 GM116155-01	FREEDMAN, LEONARD PAUL	GLOBAL BIOLOGICAL STANDARDS INSTITUTE, L	Enhancing Data Reproducibility through Cell Authentication Training
1 R25 GM116166-01	BENNETT, CHRISTINA NOEL	AMERICAN PHYSIOLOGICAL SOCIETY	Controls in Animal Studies Professional Skills Course
1 R25 DA041326-01	DICICCO-BLOOM, EMANUEL MURRAY	SOCIETY FOR NEUROSCIENCE	Promoting Awareness and Knowledge to Enhance Scientific Rigor in Neuroscience

NIH National Institute of General Medical Sciences

Administrative Supplements to NIGMS T32 awards in 2015 and 2016 (PA-16-142, PA-16-060, PA-15-136)

Develop courses and other training tools to provide graduate students with a strong foundation in research design and methods in areas related to conducting reproducible and rigorous research

NIH National Institute of General Medical Sciences

[Jointly Sponsored Neuroscience T32](#) ([PAR-17-076](#))

- **Experimental design and statistical methodology.**

  Programs are expected to provide formal instruction in the strict application of the scientific method to ensure that trainees understand the practices that underlie robust and unbiased experimental approaches, methods, analyses, data interpretation and transparent reporting of results.

NIH National Institute of General Medical Sciences

Jointly Sponsored Neuroscience T32 (PAR-17-076)

- **Elements may include:**

  - **Education in the design of well-controlled experiments;**

  - **Determination of appropriate sample size;**

  - **Appropriate use of statistics in data analysis;**

  - **Proper data storage; data labelling; data organization and archiving;**

  - **Standards for image collection and manipulation;**

  - **Figure preparation;**

  - **Criteria for inclusion and exclusion of data for analysis.**

NIH National Institute of General Medical Sciences

Jointly Sponsored Neuroscience T32 (PAR-17-076)

- A detailed description of the plan for training in statistical methodology as it applies to neuroscience research that emphasizes the importance of considering statistical principles in research design; the appropriate use of statistics in data analysis, interpretation of results and forming conclusions; and the practical application of statistics to data in different experimental paradigms.

- An introductory statistics course is not sufficient to achieve these goals.
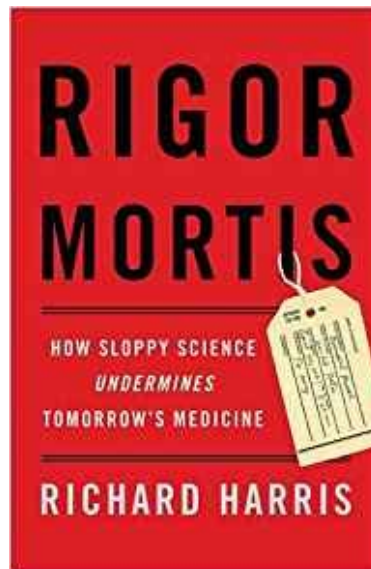
Graduate Training – What to Expect

- The PARENT T32 Program Announcement will include a requirement for Rigor and Reproducibility/Transparency training.

- NIGMS is developing its own independent T32 Predoctoral and MSTP T32 Program Announcements that will include a requirement for Rigor and Reproducibility training.

The Challenge Isn't Going Away

Rigor Mortis: How Sloppy Science Creates

Worthless Cures, Crushes Hope, and Wastes Billions

by Richard Harris, April 4, 2017

Questions and Comments