Kurt A. Engleka (Ingelkay, hard “g”) (he/him)
Adjunct Assistant Professor, Cell & Dev Biol
Assistant Director of Curriculum, BGS
kengleka@pennmedicine.upenn.edu
orcid.org/0000-0001-5539-4076
Mandate that research be ethically sound and of rigorous methodological quality.
GOALS FOR TODAY

Develop an **awareness** of best scientific practices.

Provide you with a basic set of **resources and tools** to promote your use of best scientific practices during your training, research, and career.
YOU AS A SCIENTIST

- Self-Learning
- Other Scientists
- Institutional
- Funding Applications
- Publications
- Research

You as a Scientist
WHAT ARE YOUR PRIMARY GOALS?

• DO GOOD SCIENCE

• KNOW HOW TO IDENTIFY GOOD SCIENCE

• HELP OTHERS IDENTIFY AND DO GOOD SCIENCE

• All, as you CREATE YOUR ‘PROFESSIONAL SELF’!

Other scientists will know you first from quality of your work – that is your ‘professional self’.
RESEARCH INTEGRITY

SHARED VALUES IN SCIENTIFIC RESEARCH

RESEARCH MISCONDUCT

• Fabrication

• Falsification

• Plagiarism
RESEARCH MISCONDUCT

• Serious deviation from accepted practices
RESEARCH MISCONDUCT

- Fabrication
- Falsification
- Plagiarism
- Serious deviation from research practices

Does not include honest error, differences of opinion
UNRELIABLE RESEARCH …

Stifles advances in science and medicine
• Research (including yours) relies on rigor of previous work
• Barrier to effective therapies for patients and increasing life and health spans
Wastes resources (including yours)
Fails current (you) and future generations
Damages credibility of the scientific community and reduces public support
Which reward system leads to misconduct and questionable research practices?

### Survival
- Publish lots of papers
- Get lots of citations
- Acquire funding
- Get promoted

### Good Research Practices
- Rigor/reproducibility
- Scientific collaboration
- Unrestricted access
- Freely sharing data

Value **constancy of results** with the goal of building **reliable knowledge** about the world.
TRAGEDIES

Temptation
Getting my name on this article would look really good on my CV.

Rationalization
It’s only a few data points, and those runs were flawed anyway.

Ambition
The better the story we can tell, the better a journal we can go for.

Group and Authority Pressure
The PI’s instructions don’t exactly match the protocol approved by the ethics review board, but she is the senior researcher.

Entitlement
I’ve worked so hard on this, and I know this works, and I need to get this publication.

Deception
I’m sure it would have turned out this way (if I had done it).

Incrementalism
It’s only a single data point I’m excluding, and just this once.

Embarrassment
I don’t want to look foolish for not knowing how to do this.

Stupid Systems
It counts more if we divide the manuscript into three submissions instead of just one.
AREAS THAT REQUIRE RESPONSIBLE CONDUCT

- Acquisition and Management of Data
- Collaborative Science
- Conflicts of Interest and Time
- Mentoring
- Peer Review
- Research Misconduct
- Responsible Authorship and Publication
- Scientists as Responsible Members of Society
- Use of Animals in Research
- Use of Humans in Research

Provide you with resources and tools to promote best practices
TRAINING IN RCR/SRR

Your training in RCR/SRR is continual.

Why?
See concepts several times; In different contexts

= they are “sticky”!

• On-line instruction (‘Knowledge Link’)

• Workshop-based using ‘Case Studies’

• RCR-focused lab meetings
NIH RCR RESOURCES

Responsible Conduct of Research Training

“...applies to all NIH Institutional Research Training Grants, Individual Fellowship Awards, Career Development Awards (Institutional and Individual), Research Education Grants, Dissertation Research Grants, or other grant programs with a training component ...”
RESEARCH RESOURCE HUB

Hub Home
Initializing Research
Research Team Management
Research Design Tools
Rigor and Credibility
Electronic Notebooks
Data, Analysis, and Management
Dissemination: Presentation and Publication
Commercialization for Societal Impact
Connecting to the Community

Responsible Conduct of Research (RCR) – scientific rigor and reproducibility, research integrity, stewardship

https://research.upenn.edu/resources/hub/
Biomedical Graduate Studies

Responsible Conduct of Research (RCR) and Scientific Rigor and Reproducibility (SRR)

https://www.med.upenn.edu/bgs-rcr-exdes/
Biomedical Graduate Studies

Responsible Conduct of Research (RCR) and Scientific Rigor and Reproducibility (SRR)

Overview

Responsible Conduct of Research (RCR)

BGS requires all of its predoctoral students to be trained in i) Responsible Conduct of Research (RCR), and ii) Scientific Rigor and Reproducibility (SRR).

Scientific Rigor and Reproducibility (SRR)

Training in RCR is achieved through lecture, web-based programs, small group workshops, and RCR-focused lab meetings. Training places an emphasis on the involvement of faculty and satisfies requirements set by the NIH for individual fellowships and training grants.

PhD Student Requirements

Training in SRR is achieved through lecture and SRR-focused lab meetings. Training similarly places an emphasis on the involvement of faculty and satisfies requirements set by the NIH for individual fellowships and training grants.

Faculty Requirements

Students and faculty share responsibility in complying with required training. It is imperative to understand that failure to comply with training puts funding for training, and consequently research in general, at serious risk at Penn. BGS requires and actively monitors compliance.
CASE STUDIES

• You will read ‘Case Studies’ often

• These are a source for discussion

• In small groups to promote comfortable discussion

• Each group has a ‘facilitator’
  • One who guides, not lectures
  • (for some topics) there will be no perfect answer
CASE STUDY

The researcher rationalizes that 2 of the runs were flawed, and only reports the single “best” run during a lab meeting.

The result excites the PI so much they include it as a figure in a submitted grant proposal.
How do you rate this researcher in terms of:

**SHARED VALUES IN SCIENTIFIC RESEARCH**

**HONESTY**
convey information truthfully and honoring commitments

**ACCURACY**
report findings precisely and take care to avoid errors

**EFFICIENCY**
use resources wisely and avoid waste

**OBJECTIVITY**
let the facts speak for themselves and avoid improper bias

*STENECK, N. H. 2007. ORI - Introduction to the Responsible Conduct of Research.*

What about the PI? What is/was their role?
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Stupid Systems
It counts more if we divide the manuscript into three submissions instead of just one.
You seek out your mentor who encourages you to quantify the outcomes. You find a result that, although statistically insignificant, appears highly reproducible.

You are unsure how to proceed as the result really does not answer your original question and is not significant anyways.
CASE STUDY

What would you do in this case?

It is significant that a result is repeatable especially with working controls and a quantified outcome!

It is often worth re-thinking both the design and premise of your experiment in these cases.

Perhaps there is some critical uncontrolled variable or there are multiple underlying causative factors.

There may be an exciting discovery that is distinct from the original question!
RCR TAKEAWAYS

- Identify and perform good science marked by rigor/reproducibility
- Transparency
- Scientific collaboration

Know and understand your institution's policies, standards and expectations on research

Adhere to good scientific practices

Know and uphold shared values in scientific research
If you observe misconduct or feel you are being pressured to perform misconduct, seek out a colleague who you trust and can assist you.

- PI, senior lab member, faculty advisor, program administrator
- Go up the chain step-by-step

Science self-corrects so give involved scientists chances to remedy any disagreement.
RCR TAKEAWAYS

• DO GOOD SCIENCE

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• HELP OTHERS IDENTIFY AND DO GOOD SCIENCE

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READY, SET, EXPERIMENT!

NEW STUDENT WELCOME AND ORIENTATION
2023

Kurt A. Engleka (Ingelkay, hard “g”) (he/him)
Assistant Director of Curriculum, BGS
Mandate that research be ethically sound and of rigorous methodological quality.
REPRODUCIBILITY IS FOUNDATIONAL BUT DIFFICULT TO ACHIEVE

*Investigating the replicability of preclinical cancer biology*

Timothy M Errington, Maya Mathur, Courtney K Soderberg, Alexandria Denis, Nicole Perfito, Elizabeth Iorns, Brian A Nosek

**REPRODUCIBILITY IN CANCER BIOLOGY**

Challenges for assessing replicability in preclinical cancer biology

Timothy M Errington, Alexandria Denis, Nicole Perfito, Elizabeth Iorns and Brian A Nosek

46% replication rate
FACTORS THAT AFFECT REPRODUCIBILITY

Technical
- Unvalidated reagents
  - antibodies, cell lines
  - RNAi
- Contaminated cell lines
- Batch effects
- Sophisticated techniques
- Natural variability

Human
- Inadequate method reporting
- Poor archiving
  - Reagents, data, code
  - Mistakes/fraud (minor)

Experimental Design
- Study design flaws
  - small sample size
  - non-validated system
- Inappropriate statistics
- HARKing
- P-hacking/multiple testing
- Confirmation bias

Culture
- Publication bias
- Novelty over replication
- Lack of incentives
- Hyper competitiveness
What short-circuits self-correction?

- Poor Training in Experimental Design/Statistics
- Lack of Openness/Transparency
- Publication Practices – Blind to negative data
- Culture – “Survival” reward system
YOU AS EXPERIMENTALIST

- Self-Learning
- Other Scientists
- Institutional
- Funding Applications
- Publications
- Research

You as experimentalist
A GOOD EXPERIMENTALIST…

Designs non-biased, effective experiments using a well-conceived plan

Produces results with

- high reproducibility
- high predictive value

Key concepts:
• AWARENESS of different frameworks
  • hypothesis, model, question
• Parameters defined PRIOR to experimentation
• AVOID biases and inappropriate data filters
EXPERIMENTS ARE WELL-CONCEIVED PLANS

- **Experiment is:** the whole

- **Experimental design**
  - Clearly-defined hypothesis including statistical procedures
  - System validation

- **Data collection**
- **Analysis**
- **Interpretation**
GOOD EXPERIMENTALISTS ARE AWARE OF TRAPS

Publication

Observe/Next Experiment

Design Experiment

Generate Hypothesis

Evaluate Results

Analyze Data/Test Hypothesis

Perform Experiment

HARKing

Failure to control for bias

Poor statistics/Low statistical power

Poor quality control

P-hacking

Publication bias

Poor Reporting
Non-transparent/Poor data visualization

GOOD EXPERIMENTALISTS ARE AWARE OF TRAPS

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GOOD EXPERIMENTALISTS AVOID TRAPS

Follow through

Stick to the plan

Evaluate Results

Observe/Next Experiment

Generate Hypothesis

Design Experiment

Perform Experiment

Analyze Data/Test Hypothesis

Good quality control

Correct statistics/High statistical power

Controlled for bias

Reward reproducibility
Balance with novelty/impact

Transparent/Informational data figures

Publication

Good experimentalists avoid traps.
Be aware: Opportunities for deception are plentiful.

Your expectations can influence what you see.

It is easy to be fooled!

Good experimentalists are aware of these traps.
WHAT’S IN IT FOR YOU?

Promotes experimental quality: learn something new every experiment

Facilitates reproducibility

Avoids bias

Saves time, resources, and avoids frustration
EXPERIMENTAL DESIGN WITHIN BGS

- Self-Learning
- Thesis Research
- Other Scientists
- You as experimentalist
- Thesis Defense
- Preliminary Exams
- Lab Rotations
- Classes
- RCR and SRR Training
You will be asked about the experimental basis of knowledge!

Example Exam Question

Given an observation
- describe/interpret data
- formulate a hypothesis
- describe experiments to test the hypothesis
- describe controls
- make predictions
- summarize the results and analysis
- make own conclusions
LABS PERFORM SCIENCE DIFFERENTLY

- Alternative hypotheses/interpretations considered or hypothesis myopia?
- Raw data with all controls shown to the PI? Other senior lab member(s)?
- Equipment/protocols/workflows validated to answer a scientific question? Are there checks embedded to maintain rigor/reproducibility?
- Statisticians/data analysts consulted before experiments?
- Data/code organized, archived and open to all?
CANDIDACY EXAMS

Two years from now you will face your preliminary exam where you will submit and defend a detailed plan about research.

What will you do?
Why will you do it?
Where will you do it?
Who will help you?
How will you do it?
How well do you have to do it?
When will you do it?
How many times will you do it?
How will you interpret the data?
What will happen if you see only a slight difference?
EXPERIMENTAL DESIGN…

requires a detailed plan and sticking to it!

How EXACTLY is the experiment performed?
What EXACTLY is measured?
What EXACTLY will you learn?

Details are critical and we want to hear them!
TAKEAWAYS

• The main goal of a good experimentalist: perform non-biased, effective experiments using a well-conceived plan.

• Design experiments so that you learn something each time.
SCIENCE DELIVERS!
PERFORM EXPERIMENTS!

Set up your experimental system
Think Bayesian
Beware of multiple testing
Check your reagents
Experimental Quality
Test and replicate
Blind and randomize
Learn statistics (and consult a statistician)
Use standards
Make a plan and stick to it (and report it)

Give the data the final word!
CASE STUDIES

- Controls and variables
- Replication
- Feasibility and risk
- Idea Creation
SMALL GROUPS

Groups 1 - 4  251 BRB
Groups 5 – 9  252 BRB
Groups 10-16 BRB Lob
Group 17  253 BRB
Group 18 BRB Lob
Group 19 BRB Aud

Spillover BRB Lobby
RESOURCES

**LET'S EXPERIMENT:**
A GUIDE FOR SCIENTISTS WORKING AT THE BENCH

- Free online course available self-paced, anytime
- Tailored for students BEFORE stepping into the lab

[https://courses.ibiology.org/courses](https://courses.ibiology.org/courses)
• Based on Experimental Design for Biologists by David J. Glass

BGS RCR/SRR WEBSITE

Responsible Conduct of Research (RCR) and Scientific Rigor and Reproducibility (SRR)

Overview

Responsible Conduct of Research (RCR)

Description

Modalities

Resources

Case Study Modules

Scientific Rigor and Reproducibility (SRR)

PhD Student Requirements

MD/PhD Student Requirements

Research Misconduct

PREFACE

BACKGROUND

POLICIES AND GUIDELINES

CASE STUDIES

COMMENTS/RESOURCES