Research Data and Integrity

IT’S A MATTER OF PUBLIC TRUST

Gretchen Brodnicki, JD
Dean for Faculty and Research Integrity
Harvard Medical School
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Faculty Disclosure

• Pfizer (through my husband)* helps pay Gretchen’s mortgage

  *P.S. Thanks honey!
Academic Scientist Have Many Responsibilities

- Data Integrity & Reproducibility
- Grant Application and Management
- Subject Protection
- Personnel management
- Material Management
- Publication & Promotion
Agenda

• Research Misconduct
  ◦ History/Trends
  ◦ Risk Factors and What You Can Do
Recent History

- **U.S. v. Poehlman**
  - Longitudinal Menopause Study
  - 17 grant applications over 8 years
  - Repaid hundreds of thousands of dollars
  - Sentenced to 1 year and 1 day in prison

- **Andrew Wakefield**
  - Published findings in the *The Lancet* in 1998 suggesting a link between MMR vaccine and autism
  - General Medicine College revoked his license
  - *The British Medical Journal* also found findings to be “fraudulent” (timelines misrepresented to suggest direct impact of the vaccine)
What is Research Misconduct?

- Principles and Procedures for Dealing with Faculty Misconduct
  - [http://hms.harvard.edu/content/principles-and-procedures-dealing-allegations-faculty-misconduct](http://hms.harvard.edu/content/principles-and-procedures-dealing-allegations-faculty-misconduct)
  - "Research Misconduct" means fabrication, falsification, or plagiarism in
    - proposing,
    - performing, or
    - reviewing research, or
    - in reporting research results.
      - 42 CFR 93
Research Misconduct Definition

- **Fabrication** is making up data or results and recording or reporting them.
- **Falsification** is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- **Plagiarism** is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Research misconduct does **not** include honest error or differences of opinion. 42 CFR 92.
Research Misconduct, Definition cont.

- Following the investigation, a finding of research misconduct requires: (42 CFR Sec. 93.104):
  - (a) There be a significant departure from accepted practices of the relevant research community; and
  - (b) The misconduct be committed intentionally, knowingly, or recklessly; and
  - (c) The allegation be proven by a preponderance of the evidence.
The Rest of the Iceberg

The File Drawer problem

Researcher degrees of freedom

- p-hacking
- HARKing
- Arbitrary stopping
- Acting on confirmation bias
- Selective reporting of subsets

Some examples

- A collaborator tries to undercut your position as first author on a manuscript.
- You discover that a colleague in the lab has been eliminating data points from a database without statistical analysis.
- You can regularly hear the PI in the next lab screaming at the members of that lab and understand from them that he is pushing for results to support a publication, and the competing renewal of his program project grant.
Common hurdles and pitfalls

- Overwhelmed, uninterested, and even poorly intended mentors
- Uncertainty of grant funding
- Competition
- Increased regulatory requirements
- Complexity of collaborations/multidisciplinary and global research
- Data reproducibility
- Authorship disputes
- Public trust vs. skepticism
You receive an email from *Science*

- As part of its review process, *Science* used iThenticate to assess whether any part of your submission had been previously published. They’ve identified some issues.

- How do you respond? Consider the following factors:
  - 1 sentence or many?
  - Which section?
    - Introduction, methods, results?
  - Anything other than text copied?
Lipoic acid injection reduces

sensitivity to noxious thermal and mechanical stimuli in

mice (130). Collectively, these observations agree

with the results that no low-threshold Ca\(_{\text{2+}}\) current remains in small DRG

neurons of CaV3.2\(^{-}\) mice (31)—cells known to be peripheral nociceptors

(218). Thus, these results provide explicit evidence for the role of

CaV3.2 T-type channels in pain perception and propose that CaV3.2 may be

a good candidate to target for treatment of pain at the

peripheral level. Inflammatory and visceral pain CaV3.2\(^{-}\) mice also show a decreased pain response to visceral

pain, an observation that agrees with a previous report that no low-threshold

Ca\(_{\text{2+}}\) currents remained in small dorsal root ganglion (DRG) neurons in

these

mice (31). This result proposes that small DRG neurons conduct substantial role in carrying visceral pain

signals. Recently, it was reported that

T-type Ca\(_{\text{2+}}\) channels in primary sensory neurons in colonic and

DRG cells are involved in mediating colonic pain transmission (136, 137). In this context, it is notable that

CaV3.2

174
TC neurons were often shifted from tonic to low-threshold burst firing (A), whereas wild-type TC neurons never showed such a transition in firing mode (I). The bottom panel displays the applied current steps. Injection of prepulse, which slightly hyperpolarized the membrane potentials, elicited low-threshold burst firing in PLCβ4/ TC neurons (I), but not in wild-type TC neurons (K). (M) Spike numbers in a burst induced by various prepulses that hyperpolarized the membrane potentials to between -73 and -63 mV in wild-type (closed circle) and PLCβ4/ (open circle) TC neurons.

Modified from References (36, 37). Figure 6.

EEG power density at delta waves was decreased in Cav3.1−/− mice compared with wild-type mice during NREM sleep. Sample traces show EEG and EMG signals recorded from REM (A) and NREM (B) sleep states in wild-type (Cav3.1+/+) mice (upper) and Cav3.1−/− mice (lower).
Is this Plagiarism?

• An investigator copies a paragraph from another researcher’s published manuscript, cites the article in the bibliography, but does not indicate that the material is a direct quotation.

• An investigator publishes a book that includes articles written by others. Although she credits the authors with a general acknowledgement, she does not indicate who wrote which article.

• At a national meeting, an investigator projects a slide that includes material from a published paper, but does not attribute the slide to the author.

• An investigator reuses the text she included in both the methods and analysis sections of an article she previously published in her new manuscript.
Is this Plagiarism?

- After a collaboration, Dr. A publishes work based on ideas developed jointly with Dr. B without giving credit to Dr. B.
- HMS White Paper on Plagiarism and Research Misconduct:
  - [http://hms.harvard.edu/sites/default/files/assets/About_Us/COI/files/plagiarism_statement_121510.pdf](http://hms.harvard.edu/sites/default/files/assets/About_Us/COI/files/plagiarism_statement_121510.pdf)
Questions of Research Integrity

- Data falsification and fabrication
  - **Julie** is a well-liked, trusted and senior postdoctoral fellow in John’s lab
  - She is actively interviewing for faculty appointments, with a couple options to consider.
  - **Mary** is a new postdoctoral fellow in John’s lab, and is working to become expert in the technique Julie mastered so that her work can be continued after she leaves.
  - Mary is having trouble repeating the experiments. They require stimulating the cells, leaving them for 24 hours, then staining the cells, and capturing the image of the experiments using a fluorescent microscope.
Questions of Research Integrity

• No. 2 – Data falsification and fabrication
  ◦ She asks Julie to assist her, and they run experiments side-by-side so that Mary can follow Julie’s technique.
  ◦ After 24 hours, as expected Julie culture showed cell surface expression to Receptor X, but Mary’s culture showed the opposite.
  ◦ Mary asked Julie to review Julie’s notebooks, sure that she was missing a step. Julie promised to pull her data together when she returned from her latest job talk. In Julie absence, Mary asked John for access to the lab data, but Julie’s notes were not stored on the lab server, and so John did not have the materials to share. John expressed concern about Mary’s ineptitude in repeating Julie’s work.
Questions of Research Integrity

- No. 2 – Data falsification and fabrication, cont.

  - At a loss, Mary turned to the primary paper that Julie had published in Science on this topic, and Mary noted that the image depicted appears to have unusual artifacts. Mary downloaded the image from the journal’s website, and, using ImageJ, was able to determine that Julie had substantially altered the image submitted for publication, potentially to misrepresent the results of the research.

  - What should Mary do?

  - If she tells John, what should John do?

  - What if Mary learns that John is aware Julie falsified data and promoted her work for publication, and included it in grant applications nonetheless?
Incidence of Misconduct: A Look at Retractions

Fang et al., PNAS, 2012
What can we do?

- Develop recordkeeping and review system for your group
- Develop defined onboarding process/orientation for new members of the group/lab focused on data integrity, standards for publishing, expectations
- Periodically review lab notebooks/CRFs
- Review raw data for figures in a journal article and grant
- Welcome comments/criticisms/ideas and challenges to data at group and lab meetings
What can we do?

• Don’t always allow presentation in PowerPoint
  • Use Tools – eTBlast, Google to periodically scan for copied text
• Submit images in .tiff/.jpeg. Don’t flatten images.
• Nature’s Image Integrity Policy: http://www.nature.com/authors/editorial_policies/image.html
  • “All digitized images submitted with the final revision of the manuscript must be of high quality and have resolutions of at least 300 d.p.i. for colour, 600 d.p.i. for greyscale and 1,200 d.p.i. for line art.”
What can we do?

- Maintain a complete set of verifiable data and never destroy any primary data
  - Be careful about shared files
  - Ensure versioning/audit trail of primary data
- Drafting hint: Don’t keep your own previous work open when writing a new manuscript/grant
- Don’t rely solely on the peer review process to catch errors and identify issues
- Raise awareness
- What else?
Faculty Policies on Integrity in Science

• Guidelines for Investigators in Scientific Research
• Guidelines for Editors and Authors of Medical Textbooks
• Guidelines for Investigators in Clinical Research
• Principles and Procedures for Dealing with Allegations of Faculty Misconduct
• Faculty of Medicine Statement on Research Sponsored by Industry
Faculty Policies on Integrity in Science, cont.

- Policy on Conflicts of Interest and Commitment
- Authorship Guidelines
- Letters of Reference
- Guidelines for Attribution of Credit and Disposition of Research Products

http://hms.harvard.edu/content/faculty-policies-integrity-science
Questions/Concerns/Reports

• Gretchen Brodnicki, J.D., Dean for Faculty and Research Integrity
  Gretchen_Brodnicki@hms.harvard.edu
  617-432-2496

• Office for Academic & Research Integrity – Anonymous Reporting
  https://hms.az1.qualtrics.com/jfe/form/SV_9o5D05etE0EJh2d
  617 432 5555