Research Misconduct

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Research Misconduct

Content in these slides was adapted from the work of:

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- **Steven Post, PhD**, Professor of Pathology Research, UAMS
- Office of Research Integrity
- National Institutes of Health
- National Science Foundation

Objectives

- Define research misconduct and the various types of misconduct in clinical and basic sciences research
- Discuss procedures for handling allegations
- Review some research misconduct red flags
- Examine real world examples of research misconduct

Research Misconduct: Why does it matter??

- Public safety could be jeopardized
- Public trust in science could be jeopardized
- Current biomedical research is a building block for future research
- Costs related to scientific misconduct can be high

The Anti-Vaccine Movement – A Result of Research Misconduct


robertfkennedyjr
DFW Airport
We have a vaccine to save the world. Its going to cost you $6 trillion dollars
A June 23 post on Mr. Kennedy's Instagram account portrays Microsoft CEO Bill Gates and epidemiologist Dr. Anthony Fauci as Dr. Evil and Mini-Me.
INSTAGRAM (@ROBERTFKENNEDYJR)

Andrew Wakefield M.D.: The anti vaccine movement

- 1998 - Published study in *The Lancet* linking MMR vaccine to autism
- Accused of having “Conflicts of Interest”
- Research considered false
- 2010 - *The Lancet* retracted the paper
- Barred from practicing medicine in UK
- Struck off the medical register by British General Medical Council
- Many parents decided to stop vaccinating their children
- What are the impacts today??

Research Misconduct Defined:

As defined by Office of Research Integrity:

Fabrication, falsification, or plagiarism in proposing, conducting, or reviewing research, or in reporting research results
(42 CFR 93.103)

(Honest error or honest differences in opinion are not research misconduct)

Research Misconduct Defined

A finding of research misconduct requires that:

- There be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, knowingly, or recklessly; and
- The allegation be proven by a preponderance of evidence

What is Fabrication?

- Making up data or results and recording or reporting them.

What is Falsification?

- 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.

What is Plagiarism?

- Appropriation of another person's ideas, processes, results or words without giving appropriate credit.

Note that ORI may consider some plagiarism allegations to be authorship or credit disputes rather than misconduct

What About Self-Plagiarism?

Self-plagiarism – multiple publications of the same content with different titles and/or in different journals

- scientific journals explicitly ask authors not to do this
- may include publishing the same article in a different language

IT'S A SLIPPERY SLOPE TO RESEARCH MISCONDUCT

It doesn't matter if you're an undergraduate researcher, a graduate student, a post-doc, or a principal investigator who is performing federally funded research, writing a research paper, or leading a research program; research integrity matters at every level.

Small lapses in judgment could lead to a slippery slope ending in research misconduct.

Be vigilant against these common lapses:

1. TAKING SHORTCUTS
Lack of care in experimentation that might impact reproducibility

2. CHEATING
Such as puffery, which is inflating your resume, can establish dangerous behavior patterns

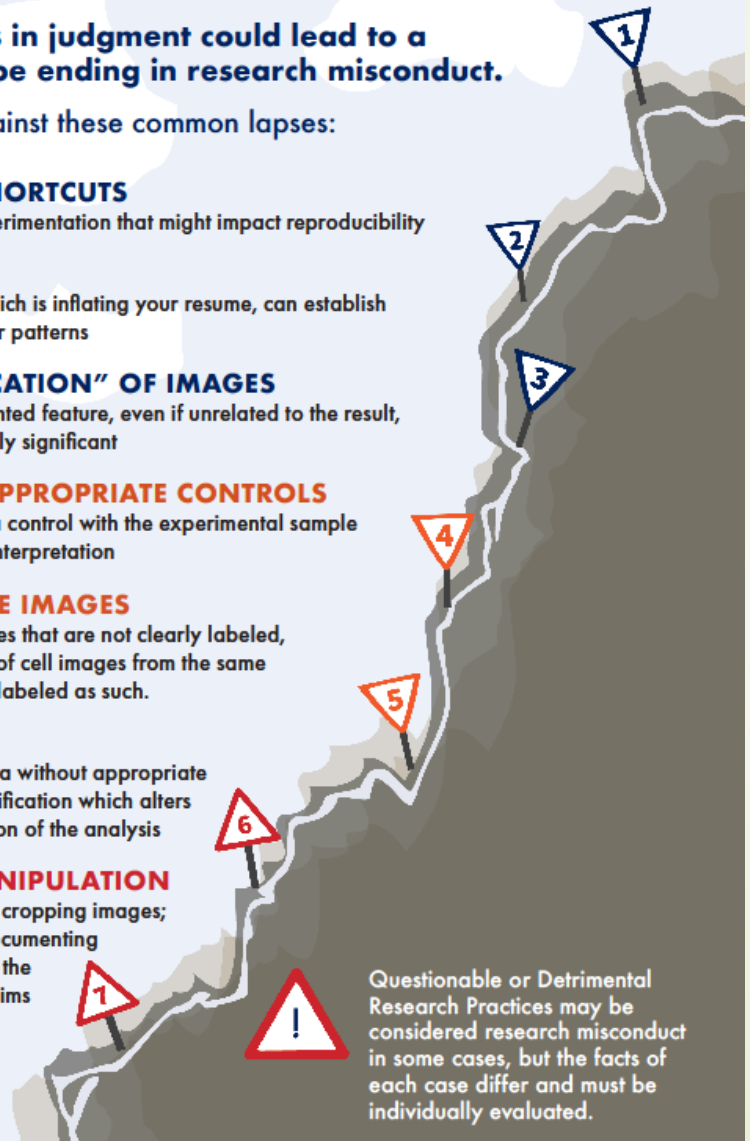
3. "BEAUTIFICATION" OF IMAGES
Removing an unwanted feature, even if unrelated to the result, could be scientifically significant

4. LACK OF APPROPRIATE CONTROLS
Failure to perform a control with the experimental sample could affect result interpretation

5. COMPOSITE IMAGES
Assemblies of images that are not clearly labeled, such as a montage of cell images from the same experiment but not labeled as such.

6. OUTLIERS
Omitting outlier data without appropriate pre-experiment justification which alters the overall conclusion of the analysis

7. IMAGE MANIPULATION
Splicing, cutting, or cropping images; without properly documenting changes, that alters the results or falsely claims a result which was not obtained.



Questionable or Detrimental Research Practices may be considered research misconduct in some cases, but the facts of each case differ and must be individually evaluated.

Assessment of Intent: Reckless, Knowing & Intentional...

- **Reckless:** The person did not exercise the care a reasonable person in the same situation would have exercised, and he/she did so with a conscious awareness of, or indifference to, the risk of adverse consequences and potential resulting harm.

  For example, the person did not secure their data and knew there was a significant risk that it had been manipulated but used the data anyway.

Adapted from the National Science Foundation--2015

Assessment of Intent: Reckless, Knowing & Intentional…

- **Knowing:** The person had an awareness or understanding of his/her actions, or should have known. The person acted consciously or deliberately.

  For example, the person knew that the data was manipulated and should have known that the manipulations would impact the results but used the data anyway.

Assessment of Intent: Reckless, Knowing & Intentional...

- **Intentional:** The person acted with a specific purpose in mind; the person acted with the purpose of committing the misconduct.

  For example, the person specifically manipulated their research data in a way that made their results appear more favorable and their intention was to make the results appear more favorable.

Research Misconduct is NOT:

- Honest error
- Disagreement based on honest differences of opinion
- Authorship disputes
- Sloppy science
- Unethical behavior
- Illegal or improper behavior

Note: These behaviors are unacceptable and will be dealt with by procedures other than Research Misconduct.

Procedures for Handling Allegations of Research Misconduct

- Assessment of Allegations
- Inquiry
- Investigation
- Institutional Decision
- Reporting to Federal Agencies

Note: See UAMS Admin Guide Policy 16.1.04

You suspect research misconduct… now what?

- Know that there are Whistleblower protections
- Contact your mentor or Chair if you can
- Contact the UAMS Research Integrity Officer
- Contact UAMS Office of Research Compliance
- Call the UAMS Compliance Hotline confidentially and anonymously at **1-888-511-3969**

Research Misconduct – Whistleblower Protections

Protections are provided for employees who report suspected misconduct, fraud, or other inappropriate behavior in good faith….

- ***Good Faith*** means having a belief in the truth of one's allegation or testimony based on the information known at the time. An allegation or testimony is not in good faith if made with knowledge or reckless disregard of information that would negate the allegation or testimony.

Research Misconduct – Whistleblower Protections

- UAMS shall take reasonable and practical efforts to protect or restore the position and reputation of any Complainant, witness, or Inquiry or Investigation committee member and **shall take appropriate disciplinary action against any individual who retaliates against someone for making an allegation of Research Misconduct or participating in a Research Misconduct proceeding.**

UAMS Admin Guide Policy 16.1.04

What **not** to do if you suspect research misconduct....

- Ignore your concerns
- Spread rumors
- Once an allegation is reported, do not talk to colleagues -- reputations must be protected until inquiries and investigations (if warranted) are completed

What to do to avoid misconduct

- Ensure that the approved protocol is followed
- Document your work
- Analyze data appropriately
- Retain sufficient data so that the findings of a project can be reconstructed
- Clarify authorship responsibilities:
  - Have authorship discussions early in the research process
  - Understand what authorship means
  - Journals and granting agencies may hold co-authors responsible

Responsible Data Analysis

Responsible data analysis attempts to accurately represent what occurred as part of the study but does not overstate the data's importance.

Data analysis becomes data manipulation when finding what you want takes precedence over representing what is in the data. "Intentional falsification or fabrication of data or results" includes the following:

- forging: inventing some or all of the reported research data or reporting experiments never performed
- cooking: retaining only those results that fit the hypothesis
- trimming: the unreasonable smoothing of irregularities to make the data look more accurate and precise

(Adapted from the guidelines for integrity in research by Montana Tech at The University of Montana)

Misconduct: Examples from Clinical Research

- Examples of fabrication:
  - Creating records of subject interviews that were never performed
  - Making up progress notes for patient visits that never took place
  - Recording values for lab tests that were never performed

Office of Research Integrity (ori.hhs.gov)

Misconduct: Examples from Clinical Research

- Examples of Falsification:
  - substituting one subject's record for that of another subject
  - altering the dates and results from subjects' eligibility visits
  - altering the results of particular tests on blood samples to show that the test accurately predicted a disease or relapse
  - backdating follow-up interviews to fit the time window determined by the study protocol
  - falsifying the times that blood samples were drawn from human subjects

Office of Research Integrity (ori.hhs.gov)

Red Flags for Misconduct in Clinical Research

- Numerous protocol deviations, such as:
  - Required labs not taken
  - Required tests or visits not performed
- Missing source documents
- Dates of labs do not match subject visit dates
- Inconsistent or clearly inaccurate data
- Questionable or missing signatures on Informed Consent Forms

Why Are These Red Flags?

- Each of the red flags mentioned brings the integrity of the research data into question.
- If you don't follow your protocol, your data may not be generalizable. Attempting to generalize it could require manipulations that result in misconduct.

Misconduct: Examples from Basic Sciences

- Many Research Misconduct findings are related to Manipulations of Microscopic Images and Gels
  - Avoid adding or subtracting details from images
  - Avoid excessive changes to color brightness and contrast

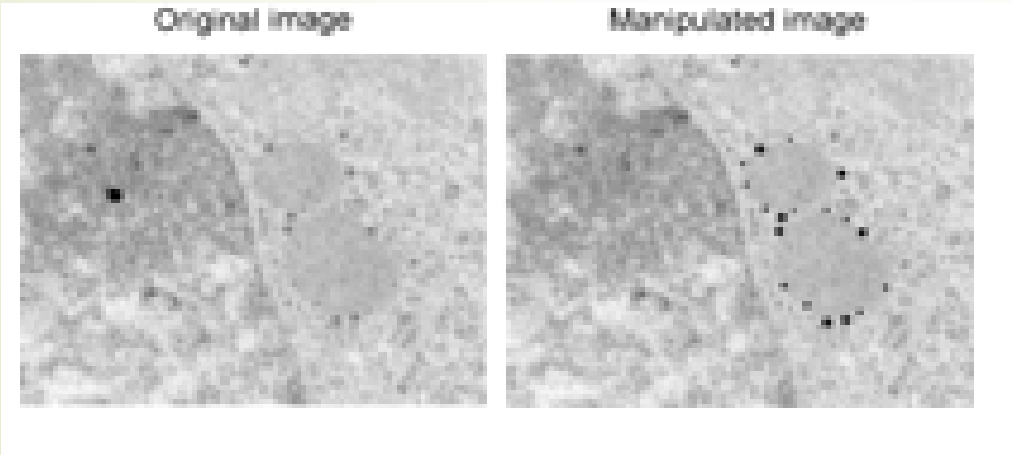
Some Important Principles to Remember:

- Images are frequently "data" in science, and so the question becomes whether their manipulation is a falsification of data in a specific case.
- Whether a matter involves an unfortunate decision about presentation of the data or an intent to deceive depends upon the context of the image, and the effect of the manipulation upon the interpretation of the results.

https://ori.hhs.gov/samples

Questionable Practices Often Seen in Research Misconduct Cases

- Selective Enhancements - removing objects present in the original image or adding something new that was not present in the observation.
  - These manipulations don't simply change the image, they change the context of the remaining objects.
  - This may result in a misstatement to the reader.

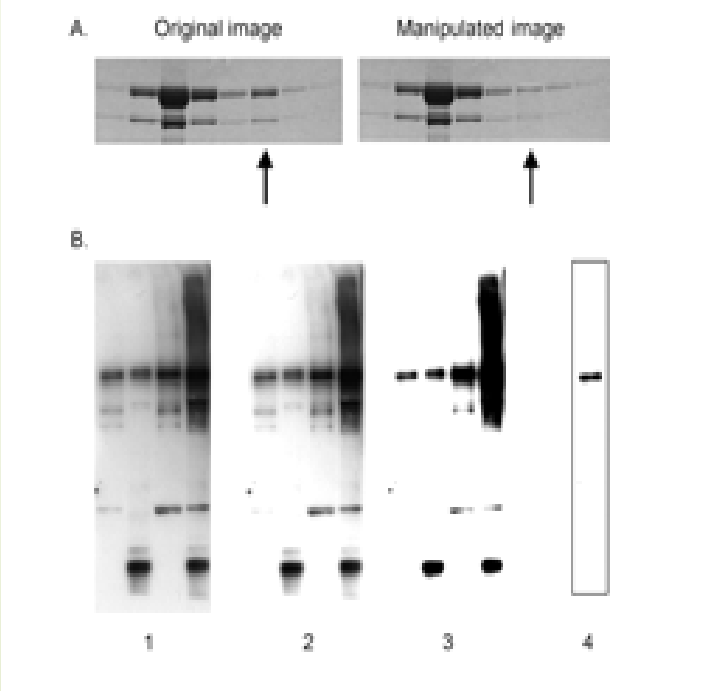


The small grey circles in the original image (left) are prominent as a result of having been stained (with immunological gold). Examination of the altered image (right) reveals that the stained regions were made even more prominent through selective enhancement and additionally the single relatively large dark circle was deleted. These alterations are data falsification.

https://ori.hhs.gov/education/products/RIandImages/practices/default.html

Another questionable practice often seen in Research Misconduct Cases

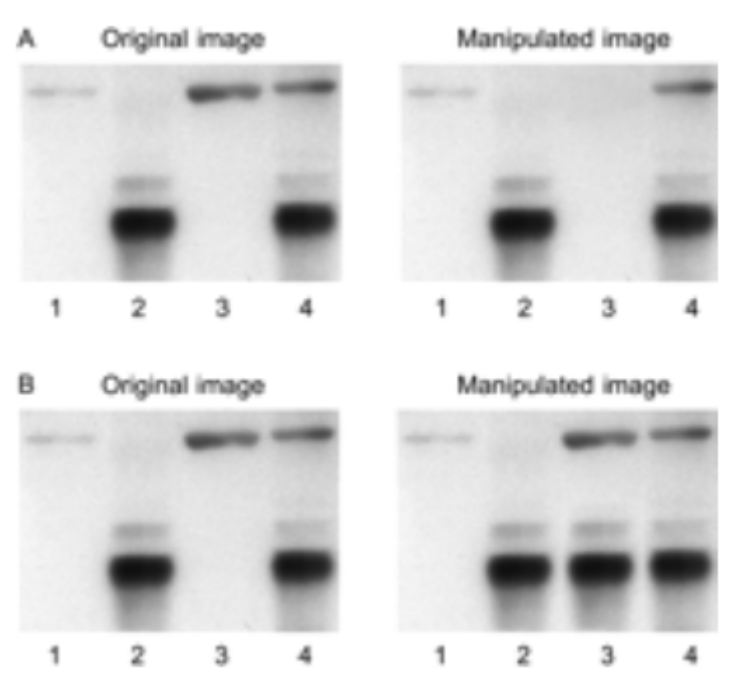
- Contrast/brightness adjustments - this can lead to fading or disappearing of significant features of the image or adding features (artifacts) that could be interpreted as being part of the image.



Panel A: A single band in the original (left) was selectively enhanced to create the altered image (right). This is an instance of data falsification.
Panel B: Image 1 is the original. Images 2 and 3 result from incremental increases in contrast over the entire original. Image 2 is acceptable; however image 3, from which a significant number of bands have disappeared, is not. Image 4, just one lane (leftmost) of image 3, is likewise unacceptable.

https://ori.hhs.gov/education/products/RIandImages/practices/default.html

Another questionable practice often seen in Research Misconduct Cases



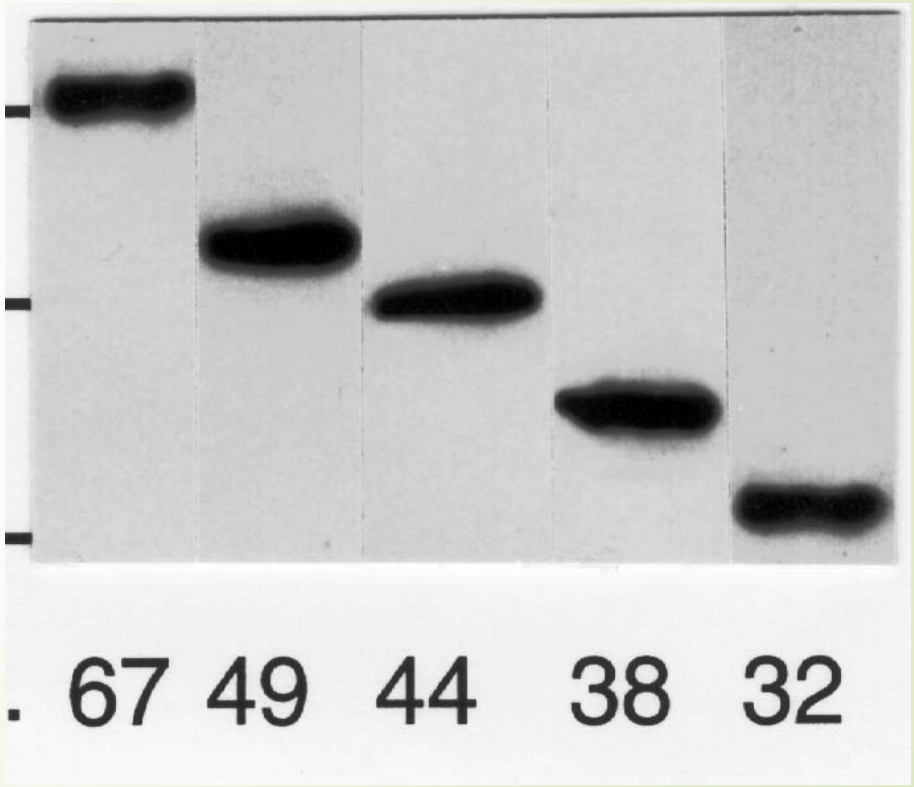
These images show the removal of data in panel A (top), and addition of data, or the cloning and placement of a band where it did not originally exist, in panel B (bottom). Both these manipulations are improper and both are misconduct.

https://ori.hhs.gov/education/products/RIandImages/practices/default.html

Some Real World Examples of Research Misconduct

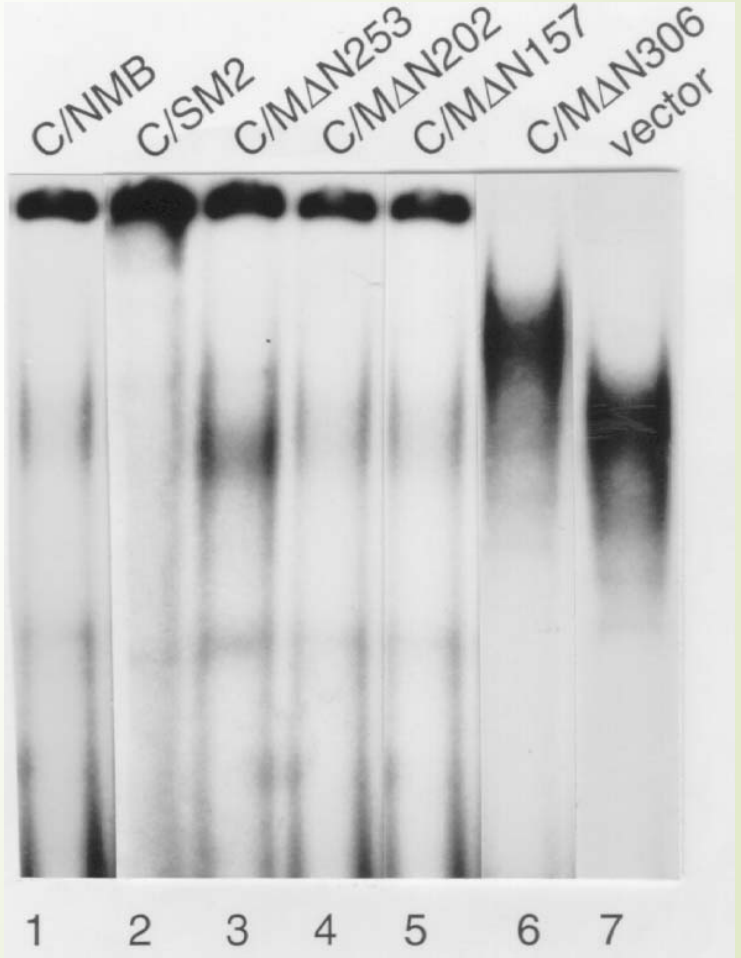
Images from Closed ORI Misconduct Cases

- Forensic analysis revealed that the 67 kDa band is the same data as the 32 kDa band – the same data was reused and presented as if different.

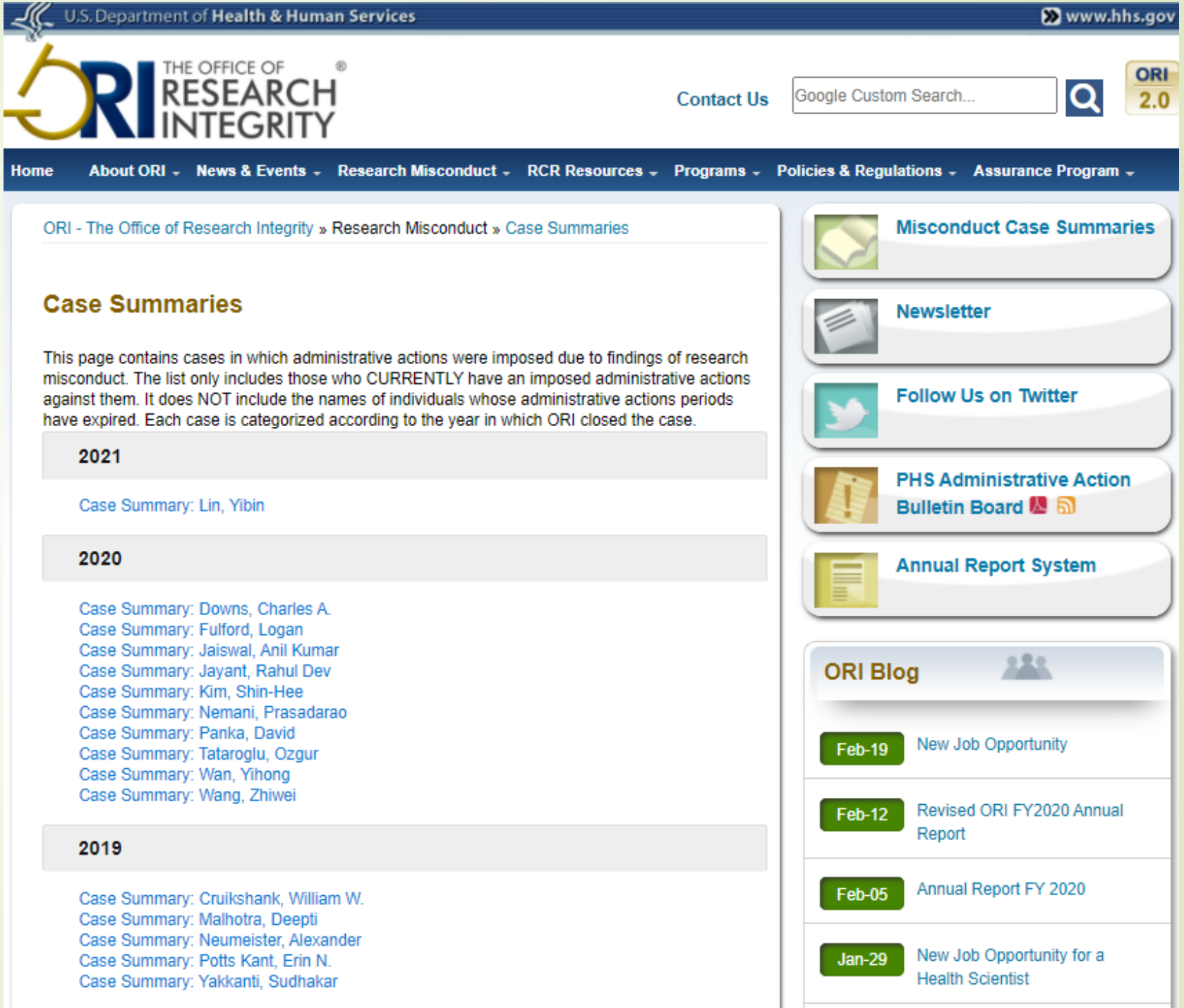


Images from Closed ORI Misconduct Cases

- Forensic analysis revealed that 3 lanes were the same data – lanes were duplicated and presented as if different data.



https://ori.hhs.gov/case_summary



U.S. Department of Health & Human Services www.hhs.gov

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ORI - The Office of Research Integrity » Research Misconduct » Case Summaries

Case Summaries

This page contains cases in which administrative actions were imposed due to findings of research misconduct. The list only includes those who CURRENTLY have an imposed administrative actions against them. It does NOT include the names of individuals whose administrative actions periods have expired. Each case is categorized according to the year in which ORI closed the case.

2021

Case Summary: Lin, Yibin

2020

Case Summary: Downs, Charles A.
Case Summary: Fulford, Logan
Case Summary: Jaiswal, Anil Kumar
Case Summary: Jayant, Rahul Dev
Case Summary: Kim, Shin-Hee
Case Summary: Nemani, Prasadarao
Case Summary: Panka, David
Case Summary: Tataroglu, Ozgur
Case Summary: Wan, Yihong
Case Summary: Wang, Zhiwei

2019

Case Summary: Cruikshank, William W.
Case Summary: Malhotra, Deepti
Case Summary: Neumeister, Alexander
Case Summary: Potts Kant, Erin N.
Case Summary: Yakkanti, Sudhakar

Misconduct Case Summaries

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ORI Blog

Feb-19 New Job Opportunity

Feb-12 Revised ORI FY2020 Annual Report

Feb-05 Annual Report FY 2020

Jan-29 New Job Opportunity for a Health Scientist

Psychiatry researcher faked clinical data for research with federally funded grants worth millions of dollars

- A former New York University School of Medicine, Langone Medical Center psychiatry researcher Alexander Neumeister, MD, falsified and/or fabricated clinical data for research supported by six federally funded grants, according to a finding from the Office of Research Integrity (ORI) published in January 7, 2020.
- According to ORI, Dr. Neumeister engaged in research misconduct by “intentionally, knowingly, and/or recklessly falsifying and/or fabricating data in the clinical records of research” funded by six National Institute of Mental Health grants.
- The misconduct resulted in “inclusion of falsified and/or fabricated research methods and results” in four publications appearing in 2013 and 2014.

The $3 Million Research Breakdown

How a star psychiatrist at the University of Illinois at Chicago violated protocols and put children at risk.

- Dr. Mani Pavuluri, the University of Illinois at Chicago – renowned child psychiatrist, violated human subjects protection requirements and committed research misconduct.
- UIC IRB also violated regulations and did not provide appropriate oversight.
- UIC required to repay $3.1 million in NIH grant funds!

https://www.propublica.org/article/university-of-illinois-chicago-uic-research-misconduct-letters-documents

NIH Suspended Some Grants to Duke Amid Concern for Patient Safety

Ivan Oransky, MD

May 21, 2019

The move came after a December 15, 2017, letter from Duke to NIH referring to "allegations of research misconduct against several investigators in the Duke Department of Psychiatry and...potential issues concerning clinical research irregularities such as not adhering to the research plan, inadequate reporting of adverse events to the [institutional review board] IRB and regulatory agency, and signing data forms without conducting assessments," according to a March 12, 2018, letter from the NIH to Duke that was recently obtained by *Medscape Medical News*.

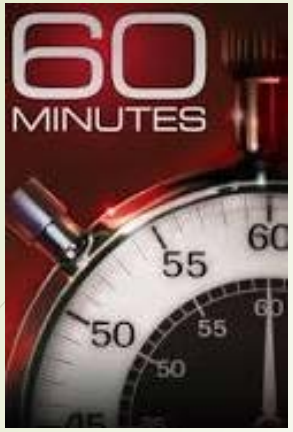
Duke University settles research misconduct lawsuit for $112.5 million

By Science News Staff Mar. 25, 2019 , 1:50 PM

- Dr. Erin Potts-Kant, Duke University, included fraudulent data in funding applications and reports for federal grants worth $200 million.
- She was fired for also embezzling money from Duke.
- Duke must now pay $112.5 million to the federal government to settle a lawsuit brought by the whistleblower who reported the misconduct!

Anil Potti, MD, found guilty of research misconduct....

- 60 Minutes refers to it as “One of the biggest medical research frauds ever.”
- According to ORI Case Summary, Potti:
  - Submitted incorrect or false data in a grant application,
  - Altered data (discarded samples that did not fit his model),
  - Disregarded accepted scientific methodology which resulted in false data being reported.



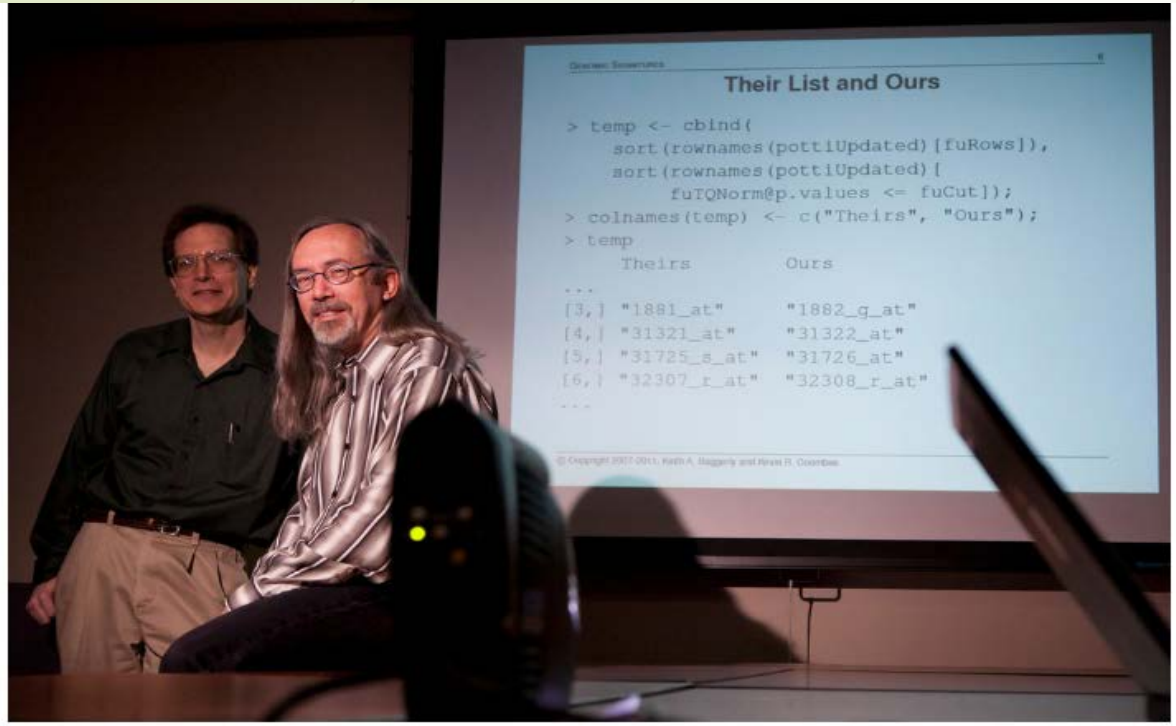
Deception at Duke: Fraud in cancer care?

Were some cancer patients at Duke University given experimental treatments based on fabricated data? Scott Pelley reports.

On **MAR 5, 2012 4:40 PM EST** / **60 MINUTES**

https://www.youtube.com/watch?v=eV9dcAGaVU8

Research Misconduct Can Be Discovered By Anyone....



Keith Baggerly, left, and Kevin Coombes, statisticians at M. D. Anderson Cancer Center, found flaws in research on tumors. Michael Stravato for The New York Times

"In raising these concerns, I have nothing to gain and much to lose."
— Bradford Perez

Research Concerns

This document was written by Bradford Perez, then a third-year medical student, in late March or early April 2008. Working in the laboratory of Anil Potti, Perez presented what biostatisticians describe as an excellent critique of the flawed methodology employed Duke genomics researchers.

I want to address my concerns about how my research year has been in the lab of Dr. Anil Potti. As a student working in this laboratory, I have raised my serious issues with Dr. Potti and also with Dr. Nevins in order to clarify how I might be mistaken. So far, no sincere effort to address these concerns has been made and my concerns have been labeled a "difference of opinion." I respectfully disagree. In raising these concerns, I have nothing to gain and much to lose.

In fact, in raising these concerns, I have given up the opportunity to be included as an author on at least 4 manuscripts. I have also given up a Merit Award for a poster presentation at this year's annual ASCO meeting. I have also sacrificed 7 months of my own hard work and relationships that would likely have helped to further my career. Making this decision will make it more difficult for me to gain a residency position in radiation oncology. As a third year medical student, these are all very important things that I have given up. As a result of these circumstances, I am spending another year of my life pursuing a more meaningful research project. The reason that I have made the decision to leave the lab and make these concerns known is because it is important that the work be done right for the sake of our patients and for field of genomic medicine.

Excerpt from *The Cancer Letter*, https://cancerletter.com/articles/20150109_9/

Fallout from Potti Case

- Study subjects did not receive appropriate treatment; some died
- Lawsuits were filed
- Papers were retracted
- Duke's reputation called into question
- Professional reputations destroyed

Consequences of Misconduct

- Recognition on federal websites and in the media
- Retraction of publications
- Suspension or termination of grants
- Repayment of grant funds
- Debarment
- Prohibition from service on PHS advisory committees, peer review committee, or as consultants
- Criminal charges, fines, penalties and/or imprisonment

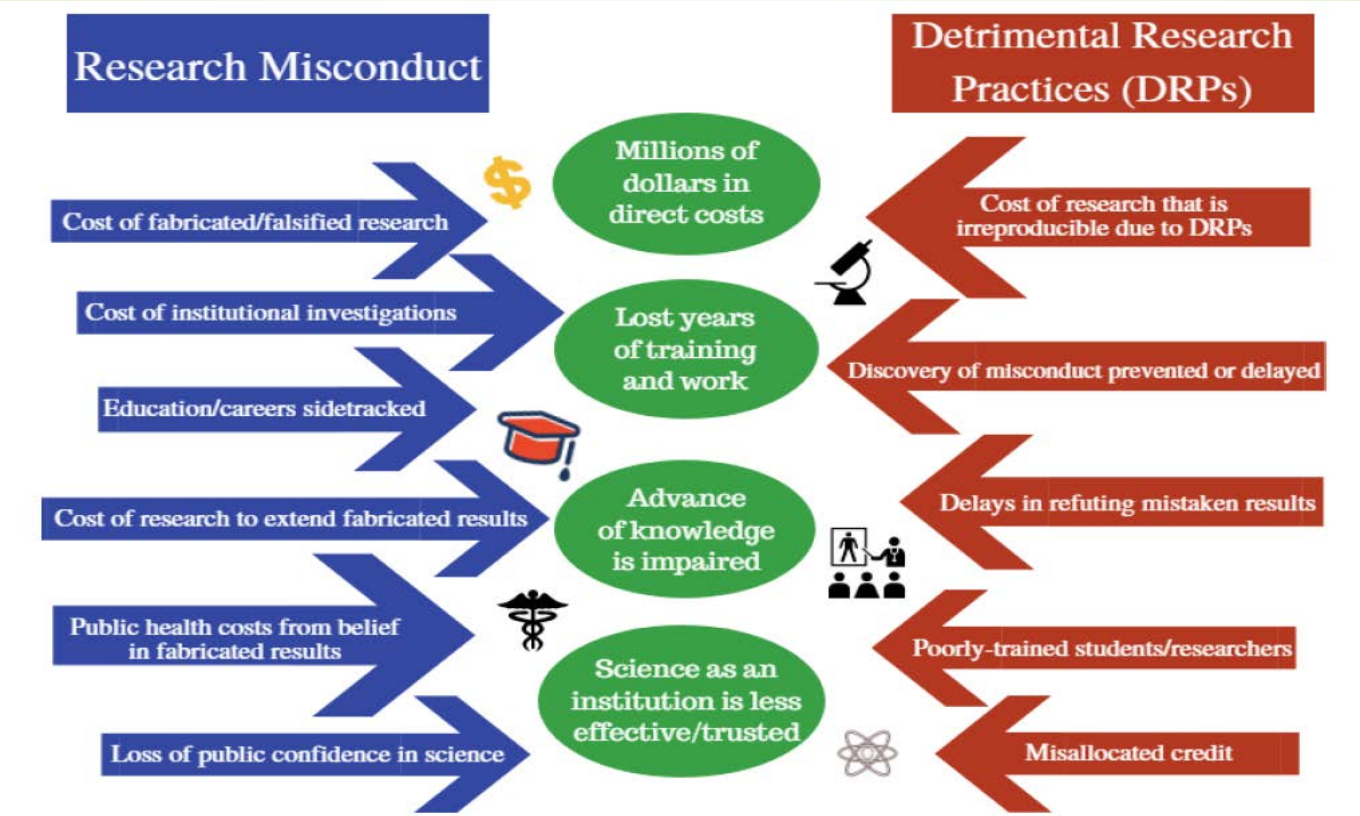


FIGURE 5-1 Costs and consequences of research misconduct and detrimental research practices (DRPs).

“Values first. Logic and data second.”

-Bruce A. McPheron, PhD, Executive Vice President and Provost, The Ohio State University

For Research Misconduct and/or Data Integrity Concerns:

- **Dr. Shuk-Mei Ho**, UAMS Research Integrity Officer….501-686-5347
- **Darri Scalzo**, UAMS Research Compliance Officer…501-686-8062
- **Nancy Rhea**, UAMS Research Compliance Analyst..501-686-5186

- *Confidentially and anonymously report research misconduct or concerns at **1-888-511-3969***