

Research Integrity: Why Is This Such a Problem?

Lee M. Ellis, MD, FACS, FASCO

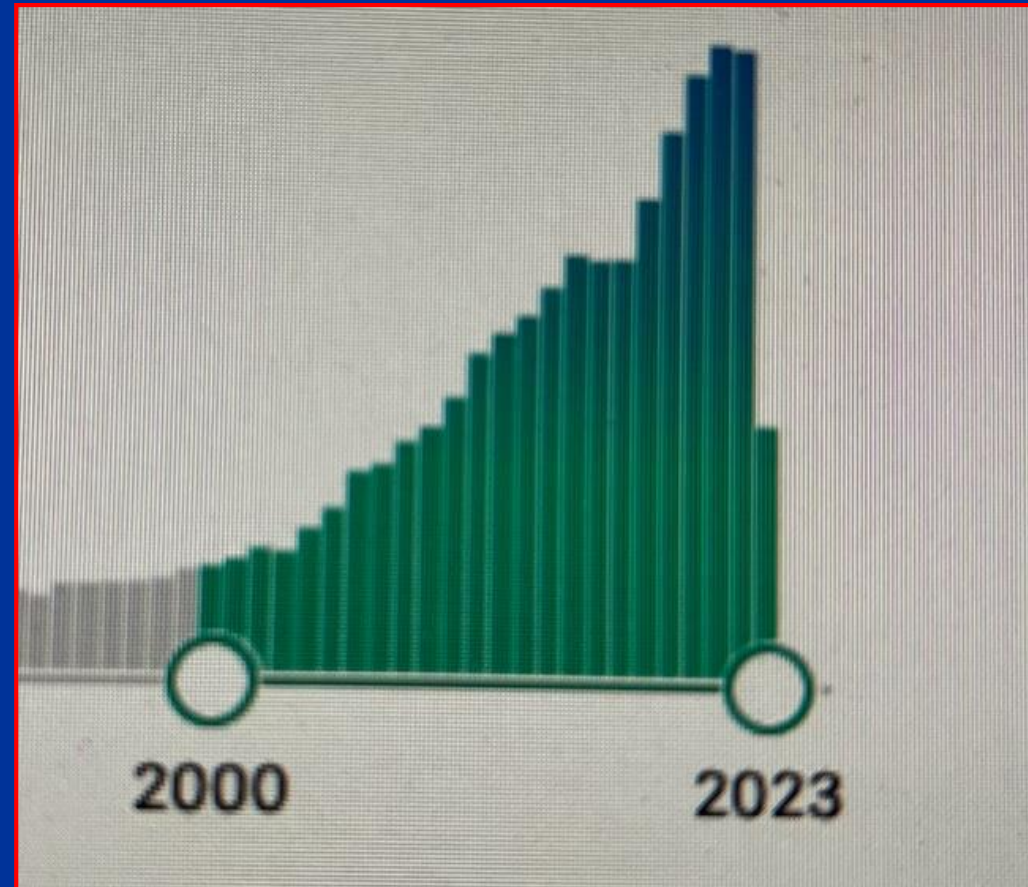
Departments of Surgical Oncology, and
Molecular & Cellular Oncology
UT MD Anderson Cancer Center

Other roles where I am aware of the importance of research integrity

- SWOG (Vice Chair, Translational Medicine)
- JAMA Oncology (Deputy Editor)
- 4 Clinical Trial Data Monitoring Committees
- Daily emails

GCC Workshop: May, 2023

Setting the Tone for Today's Talk/Workshop



In Case You Drift off to Sleep, Remember This Slide

Why Research Misconduct?

- “Publish or perish”
- “Impact factor mania”
- “My H-index is higher than yours”

Sources of Info on Research Misconduct

- RetractionWatch.com
- Pubpeer <https://pubpeer.com/>
- Office of Research Integrity
<https://ori.hhs.gov>
- For Better Science
<https://forbetterscience.com>
- Follow Elizabeth Bik on Twitter
(image manipulation/duplication expert)



Welcome to another edition of The RW Daily.

Know someone who would enjoy The RW Daily? They can subscribe [here](#).

<https://retractionwatch.com/2022/09/03/nobel-prize-winner-gregg-semenza-retracts-four-papers/>



Deepak Kaushal

Leading primate researcher demoted after [admitting he faked data](#).



"Several of the results" [in a homeopathy paper](#) "can only be explained by data manipulation or falsification."



A study of ivermectin, COVID-19, and the microbiome [has been retracted](#). [Earlier](#).

Nobel Prize winner Gregg Semenza retracts four papers

A Johns Hopkins researcher who shared the 2019 Nobel Prize in Medicine or Physiology has retracted four papers from the *Proceedings of the National Academy of Sciences* (PNAS) for concerns about images in the articles.

Gregg Semenza is "one of today's preeminent researchers on the molecular mechanisms of oxygen regulation," the work for which he shared the [2019 Nobel](#), [according to Hopkins](#). But even before that, the pseudonymous Claire Francis began pointing out potential image duplications and other manipulations in Semenza's work [on PubPeer](#), as [described in October 2020 by Leonid Schneider](#).



Gregg Semenza

The four papers retracted yesterday are:

- [Hypoxia-inducible factors mediate coordinated RhoA-ROCK1 expression and signaling in breast cancer cells](#)
- [Mutual antagonism between hypoxia-inducible factors 1 \$\alpha\$ and 2 \$\alpha\$ regulates oxygen sensing and cardio-respiratory homeostasis](#)
- [Anthracycline chemotherapy inhibits HIF-1 transcriptional activity and tumor-induced mobilization of circulating angiogenic cells](#)
- [Hypoxia-inducible factors are required for chemotherapy resistance of breast cancer stem cells](#)

Research Integrity And Its Effects On Drug Development

- Integrity of laboratory research and how this impacts clinical outcomes
 - The issue at hand
 - The spectrum
 - Why does this occur?
 - What can we do to fix this?

Don't Be Surprised if You Feel One or More of the Following Emotions After This Lecture

- Shocked
- Angry
- Embarrassed (Guilty?)
- Entertained
- Discouraged
- Reinvigorated
 - You don't have to publish in CNS to have a successful career and, more importantly, to make significant contributions!
- All of the above

Everything You Need to Know About Research Integrity From One Site

<https://ori.hhs.gov/infographics>

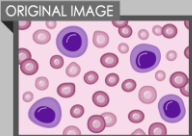
TIPS FOR PRESENTING SCIENTIFIC IMAGES with INTEGRITY

Images should clearly and correctly represent research results. Minor image processing may be acceptable but, as depicted below there's a fine line between enhancing an image and distorting it.

BE AWARE: Undocumented image manipulations can lead to accusations of research misconduct.

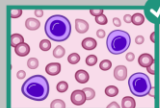
67% of ORI's closed research misconduct cases involved image manipulation.*

*between 2011 and 2015

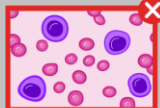


COLOR ENHANCEMENTS

Changing the contrast, color, or brightness



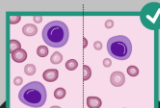
Ensure that the meaning of the image stays the same and fine details are not removed.



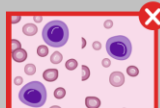
Contrast and saturation were increased causing the background cells to disappear.

SPLICE & PASTE

Combining multiple images into one image



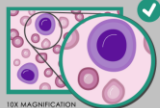
Clearly indicate where two images were joined using a dividing line and labels.



Two images were combined causing them to look like new data.

CROP

Cutting out components and resizing



Use a magnification panel to highlight desired visual data.



Reference information was selectively removed from the image causing loss of data.

WHAT ELSE MUST YOU DO?

- Clearly document all changes made to an image.
- Retain the unprocessed image for your records.
- Follow journal guidelines for permissible processing.

LEARN MORE ABOUT IMAGE PROCESSING:
<http://ori.hhs.gov/ImageProcessing>



WRITE ETHICALLY

FROM START TO FINISH

PREPARE

USE PRIMARY LITERATURE Secondary sources might have misinterpreted the work

HAVE A THOROUGH UNDERSTANDING OF YOUR SOURCES Accurately communicate their ideas and terminology

WRITE

AVOID SELECTIVE REPORTING Present unbiased information by acknowledging conflicting evidence and alternative interpretations

DO NOT PLAGIARIZE

CITE YOUR SOURCES

— USE YOUR OWN WORDS AND SENTENCE STRUCTURE — **MAINTAIN THE INTENDED & MEANING OF THE SOURCE** — **QUOTE VERBATIM TEXT**

PUBLISH

GIFT AUTHORSHIP IS UNETHICAL Only include those who have made substantial contributions to a project

AVOID GHOST AUTHORSHIP Give proper authorship or acknowledgment to those who have contributed to a paper

Learn more about ethical writing: ori.hhs.gov/ethical_writing

Boig, M. In J. L. Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical

RESEARCH TRINEES

WHAT YOU NEED TO KNOW ABOUT RESEARCH MISCONDUCT



Got Questions? Ask ORI.

HOW DO I MAKE AN ALLEGATION OF RESEARCH MISCONDUCT? Is it okay to use ORI's educational materials in my RCR course?

I'm the RIO, and I'm not sure what to do about...?

How do I use ORI's forensic image tools? I think someone plagiarized my work. What do I do?

I reported misconduct but haven't heard anything... what's happening?

I reported misconduct; then my contract wasn't renewed. Is this retaliation?

If we can't answer your question, we can refer you to the people who can.

Email us at AskORI@hhs.gov if you have questions about research integrity.



5 WAYS SUPERVISORS CAN PROMOTE RESEARCH INTEGRITY

Are you a principal investigator, research coordinator, academic advisor, or mentor? Roles such as these place you in a unique position to cultivate exceptional research practices among the next generation of researchers.

- BE AVAILABLE & APPROACHABLE** Your team wants to learn from YOU!
- REVIEW RAW DATA** You are responsible for the integrity of your team's data.
- COMMUNICATE EXPECTATIONS** Prevent misunderstandings by making sure everyone is on the same page.
- PROVIDE TRAINING and GUIDANCE** Avoid making assumptions about anyone's skills or knowledge.
- KNOW YOUR RESEARCH INTEGRITY OFFICER** Be prepared in case you ever suspect research misconduct.



YOU SUSPECT RESEARCH MISCONDUCT NOW WHAT?

- IF YOU ARE SUSPICIOUS**
- AVOID CONFRONTATION** Direct confrontation may lead to retaliation and/or tampering with evidence.
 - KEEP NOTES** Document details and save communications related to the misconduct. This will help you recall important information needed by the institution.
 - EDUCATE YOURSELF** Read your institution's research misconduct policy or contact the U.S. Office of Research Integrity (ORI) with questions.
 - SEEK SUPPORT** You may want to get advice from someone you trust to help you consider all options.
 - CONSULT YOUR RESEARCH INTEGRITY OFFICER (RIO)** RIOs can help you better understand the situation. You can speak in hypotheticals as you consider making an official allegation.

- THINGS TO CONSIDER**
- REPORTING MISCONDUCT IS DIFFICULT... BUT IT CAN BE WORTH IT.** PEOPLE OFTEN WORRY ABOUT:
 - The reputation and career of the accused
 - How others in the lab will be affected
 - Implications for their own career
 - Possible retaliation
 - REPORTING MISCONDUCT HELPS**
 - Prevent false and misleading information from entering the research record
 - Correct the scientific literature
 - Ensure funding is awarded to responsible research
 - Protect the public's trust in science

- WHEN YOU REPORT**
- BE SPECIFIC** Provide the RIO with specific examples of suspected misconduct and where it occurred (e.g. manuscripts, presentations, posters, grant applications, etc.).
 - BE AVAILABLE** The RIO may require your help identifying and examining evidence, explaining how the research was falsified, fabricated, or plagiarized, and cooperating as a witness.
 - BE PREPARED FOR SILENCE** Institutional policies may limit your access to case details information about research misconduct proceedings.
 - BE PATIENT** Research misconduct proceedings take considerable effort and time to complete.

MAKE AN INFORMED DECISION

If you want to talk anonymously or report misconduct contact ORI at 240-453-8800 or AskORI@hhs.gov.

POSSIBLE RED FLAGS OF RESEARCH MISCONDUCT

- TIME**
 - Usable data are only generated when there is a pressing deadline
 - Experiments are completed faster than usual
- RESULTS**
 - Data are too good to be true
 - Findings can't be replicated by others in the lab
- LACK OF TRANSPARENCY**
 - Raw data can't be produced when requested
 - Research materials and protocols are kept hidden
 - Work is mostly done when no one else is around

If you suspect research misconduct



Journal/Editor Responsibilities

Is the Lancet complicit in research fraud?

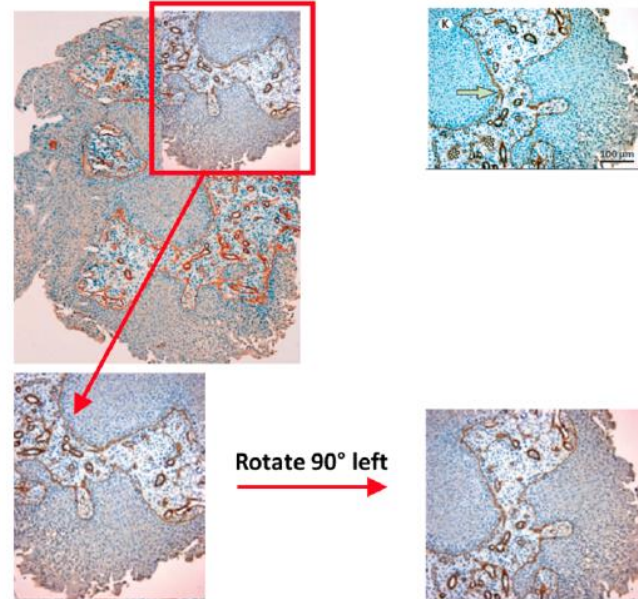
This blog was written jointly by Patricia Murray, Professor of Stem Cell Biology and Regenerative Medicine, University of Liverpool, UK and Peter Wilmshurst.

The editor of a medical journal that charges readers for access to articles whilst knowingly keeping fraudulent articles on its website is as guilty of financial fraud as an art dealer who knowingly sells forged artworks, but there is no moral equivalence. The complicity in fraud by the editor of the medical journal may also cause death and harm to patients.

Identical samples in Fig.4 of Gonfiotti et al (2014) and Fig 3K of Badylak et al (2012)

Fig. 4 in Gonfiotti et al (2014). Immunohistochemical staining at 4 years after transplantation. Immunostaining of implanted airway showing strong immunoreactivity against anti-laminin.

Fig. 3K in Badylak et al (2012). Laminin staining at 1 year after transplantation.



If the inset in Fig. 4 of Gonfiotti et al (2014) (outlined in red) is rotated 90° to the left, it is clear that it is identical to Fig. 3K in Badylak et al (2012). It appears that the colour has been modified in the 2014 paper to increase the levels of red/cyan, but the sample itself is identical.

I am a Deputy Editor of JAMA Oncology

PubPeer

The **PubPeer** Foundation is a California-registered public-benefit corporation with nonprofit status in the US. The overarching goal --- is to improve the quality of scientific research by enabling innovative approaches for community interaction---pubpeer.com is a service run for the benefit of its readers and commenters, who create its content. **Our current focus is maintaining and developing the PubPeer online platform for post-publication peer review.**

Gamma-tocotrienol promotes TRAIL-induced apoptosis through reactive oxygen species/extracellular signal-regulated kinase/p53-mediated upregulation of death receptors

Molecular Cancer Therapeutics (2010) - 12 Comments

pubmed: 20682650 doi: 10.1158/1535-7163.mct-10-0277 issn: 1538-8514 issn: 1535-7163

Ramaswamy Kannappan, Jayaraj Ravindran, Sahdeo Prasad, Bokyung Sung, Vivek R. Yadav, Simone Reuter, Madan M. Chaturvedi, Bharat B. Aggarwal

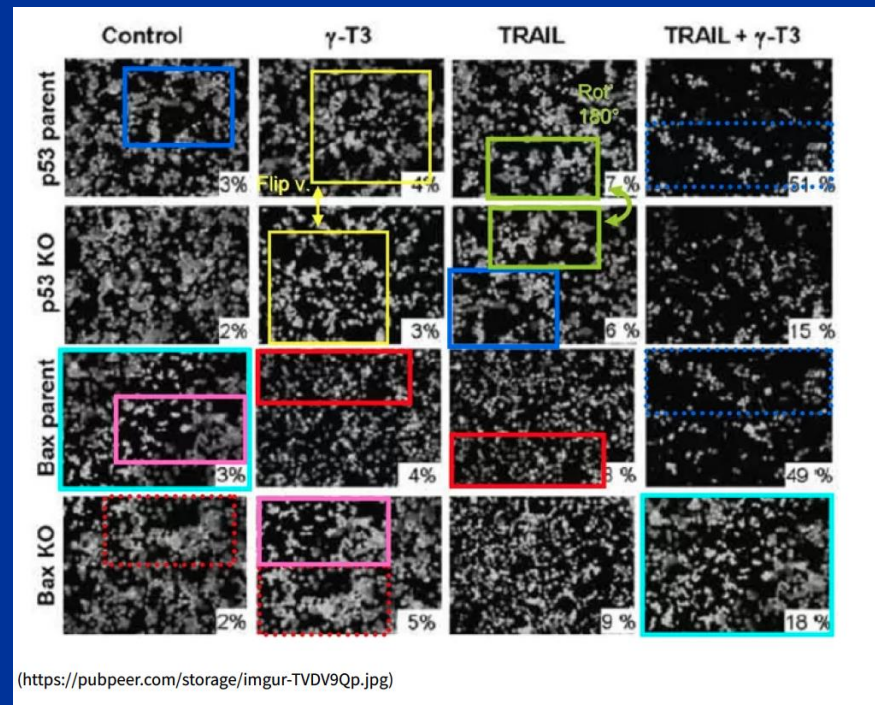
#1 **Paul S Brookes** commented 6 years ago

Seeing this beautiful example of "creative image management" highlighted on Twitter (actually had over 100 re-tweets at last count)....

<https://pubpeer.com/publications/B0EE98F42E52EE4F8B130E20059699>

(<https://pubpeer.com/publications/B0EE98F42E52EE4F8B130E20059699>)

... reminded me of this one that's been sitting in the archives for a few years. It's really one of my favorite examples of the art. Should be in all the textbooks.



Not everything on PubPeer is fraud. Mistakes can be made, and corrected.
Read the comments and decide for yourself.

Not Everyone on PubPeer is Evil

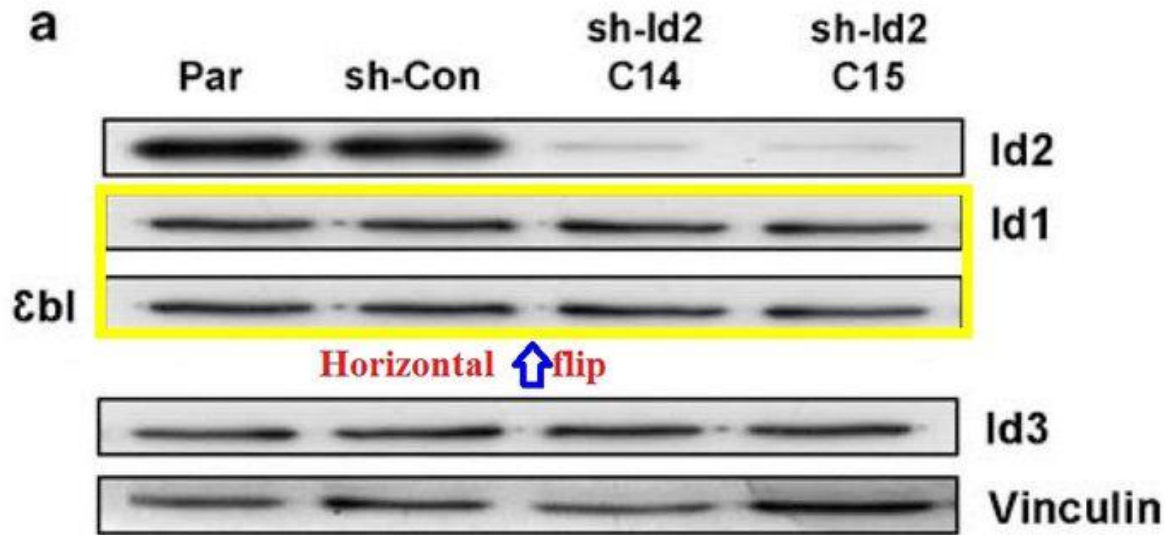



Figure 2a Oncogene. 2008 Dec 4;27(57):7192-200.

“Following the publication of this Article, it was brought to the attention of the Authors that a control for shRNA knock-down of Id2 in Fig. 2 was a duplicated and reversed set of bands from another control in the Figure. The row of bands on the western blot for Id3 is the same blot for Id1 knock-down, but “flipped” horizontally. This does not change the conclusions of the manuscript. The authors have submitted a revised Fig. 2, omitting this band, as they no longer have access to the reagents and cannot repeat this part of the experiment.”

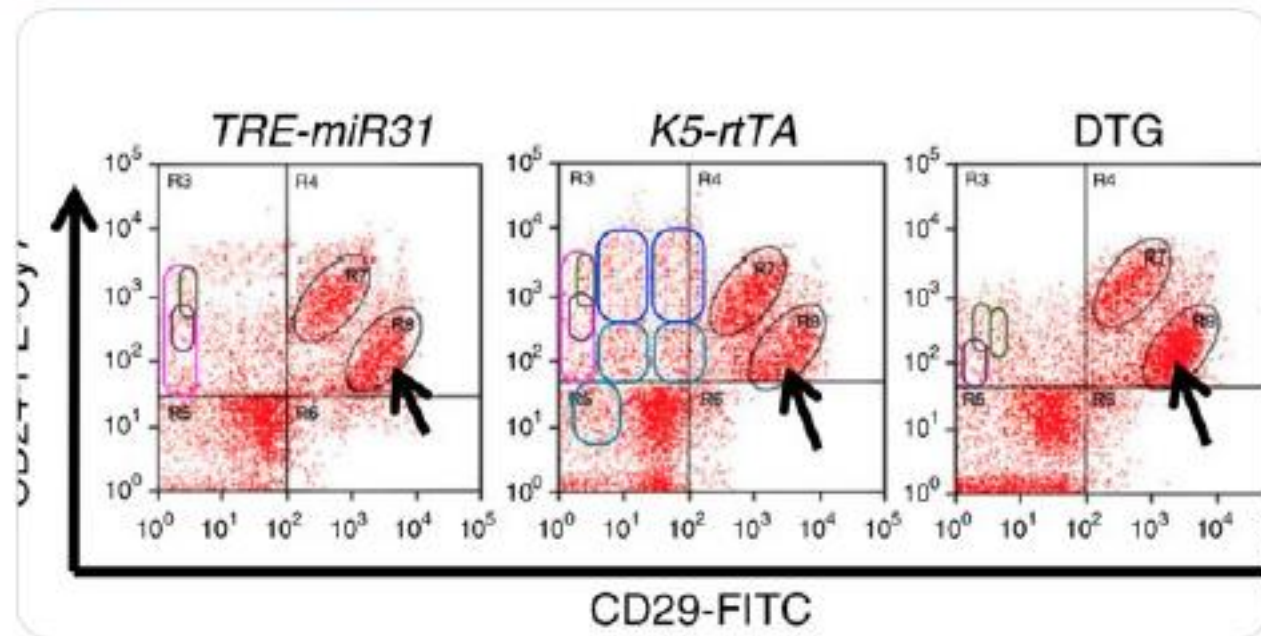
Gray.....Ellis



Elisabeth Bik 
@MicrobiomDigest



Oh dear. @NatureComms making #BadEditorialDecision here by issuing a correction. "The original version of this Article contained an error in Fig. 4. In the original Fig. 4a, different quadrants [...] contained similar unexplained groups of data points."
pubpeer.com/publications/3...



Do individual and institutional predictors of misconduct vary by country? Results of a matched-control analysis of problematic image duplications

Daniele Fanelli^{1*}, Matteo Schleicher¹, Ferric C. Fang², Arturo Casadevall³, Elisabeth M. Bik⁴

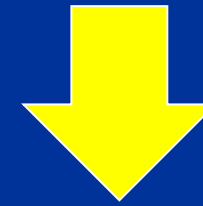
¹ Department of Methodology, London School of Economics and Political Science, London, United Kingdom, ² Department of Laboratory Medicine and Pathology, University of Washington School of Medicine, Seattle, Washington, United States of America, ³ Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States of America, ⁴ Harbers Bik LLC, Sunnyvale, CA, United States of America

* email@danielefanelli.com

PLOS 2022

Abstract

Pressures to publish, perverse incentives, financial interest and gender are amongst the most commonly discussed risk factors for scientific misconduct. However, evidence of their association with actual data fabrication and falsification is inconclusive. A recent case-controlled analysis of articles containing problematic image duplications suggested that country of affiliation of first and last authors is a significant predictor of scientific misconduct. The same analysis found null or negative associations with individual proxies of publication rate, impact and gender. The latter findings, in line with previous evidence, failed to support common hypotheses about the prevalence and causes of misconduct, but country-level effects may have confounded these results. Here we extend and complete previous results by comparing, via matched-controls analysis, articles from authors in the same country. We found that evidence for individual-level risk factors may be significant in some countries, and null or opposite in others. In particular, in countries where publications are rewarded with cash incentives, and especially China, the risk of problematic image duplication was higher for more productive, more frequently cited, earlier-career researchers working in lower-ranking institutions, in accordance with a “misaligned incentives” explanation for scientific misconduct. However, a null or opposite pattern was observed in all other countries, and especially the USA, UK and Canada, countries where concerns for misaligned incentives are commonly expressed. In line with previous results, we failed to observe a statistically significant association with industry funding and with gender. This is the first direct evidence of a link between publication performance and risk of misconduct and between university ranking and risk of misconduct. Commonly hypothesised individual risk factors for scientific misconduct, including career status and productivity, might be relevant in countries where cash-reward policies generate perverse incentives. In most scientifically active countries, however, where other incentives systems are in place, these patterns are not observed, and



Scientific misconduct is more common in countries that reward authors with cash incentives.

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0255334>

In Summary, Your Best, Most Concise, and Timely
Resources on Data Integrity and Interesting Stories are....
Retraction Watch and PubPeer

- Retraction Watch
 - Editors comment on retracted papers
- PubPeer
 - Peers comment on papers (sometimes names disclosed, sometime not)
 - Up to you to determine validity of “concerns”

Note: The US Office of Research Integrity has very focused (*brief summaries*) information limited to those found guilty of misconduct

Drug Development Failure Rates are Too High! (duh)

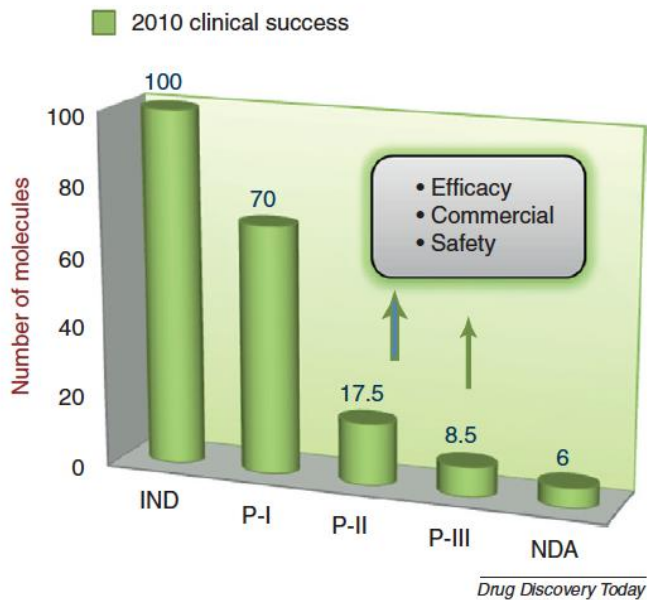
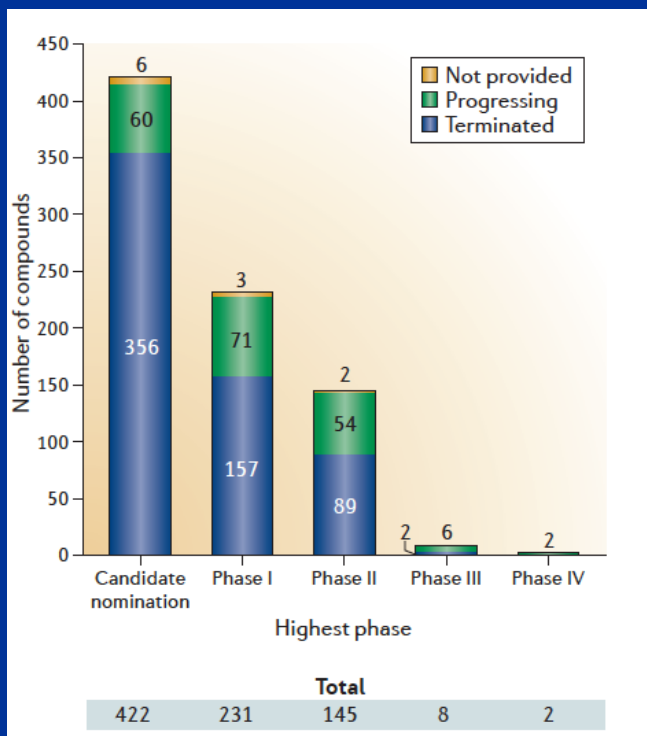


FIGURE 3
Productivity trend during 2009 and 2010. The clinical rate of success is depicted as percentage surviving at each clinical phase based on attrition observed during 2009 and 2010.

Khanna, Drug Disc Today, 2012

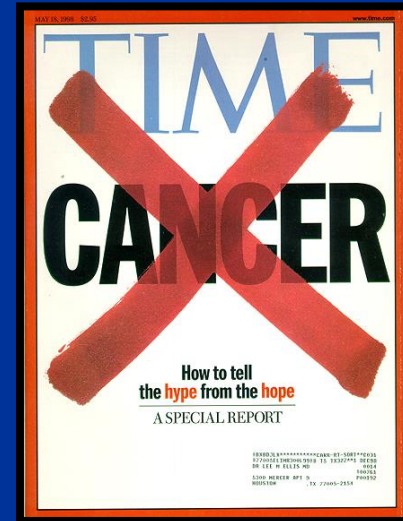
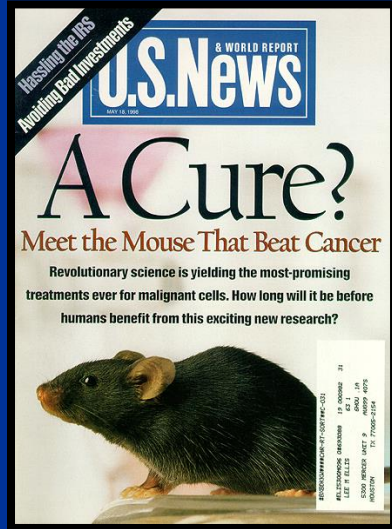


Waring, Nat Rev Drug Disc, 2015

-On average, it costs over a billion dollars to take a drug through Phase III, and the time to do this is 13-15 yrs.
 -To improve upon this dismal ~5% success rate, we must *have more confidence in data* from very early in the drug development process*

* A more recent publication listed this at ~3.5% for cancer

Why Haven't We Made Greater Strides in Treating Patients With Metastatic Disease?



- Perhaps the data leading to clinical trials are not as sound as they should be
 - What is the cause of this?



Bob Radinsky, PhD
MDACC (1989-2000) → Amgen (2000)

“Lee, do you realize that most of what’s published in academia cannot be reproduced?”

“Glenn Begley has been prospectively collecting this data from studies done at Amgen”

Glenn’s results: Only 6 of 53 (11%) studies could be reproduced



Reports on Issues With Data Reproducibility



Re-tested 70+ drugs from 221 independent studies¹

→ 0 reproduced

→ **Minocycline**: effective in four separate ALS mouse studies **worsened** symptoms in a clinical trial of more than 400 patients²



Sponsored replication of 12 spinal cord injury studies

→ 2/12 successfully reproduced³



Conducted in-house target validation studies

→ 14/67 reproduced⁴



Attempted to reproduce 53 "landmark" oncology publications

→ 6/53 reproduced⁵

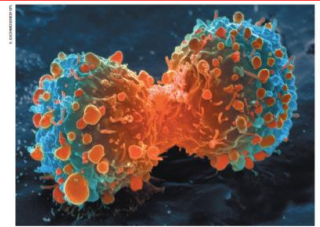
1. Scott et al. Amyotroph Lateral Scler. 9, 4-15 (2008).

2. Gordon et al. Lancet Neurol. 6, 1045-1053 (2007).

3. Stuart et al. Experimental Neurology 233, 597-605 (2012).

4. Prinz et al. Nat Rev Drug Discov. 10, 712 (2011).

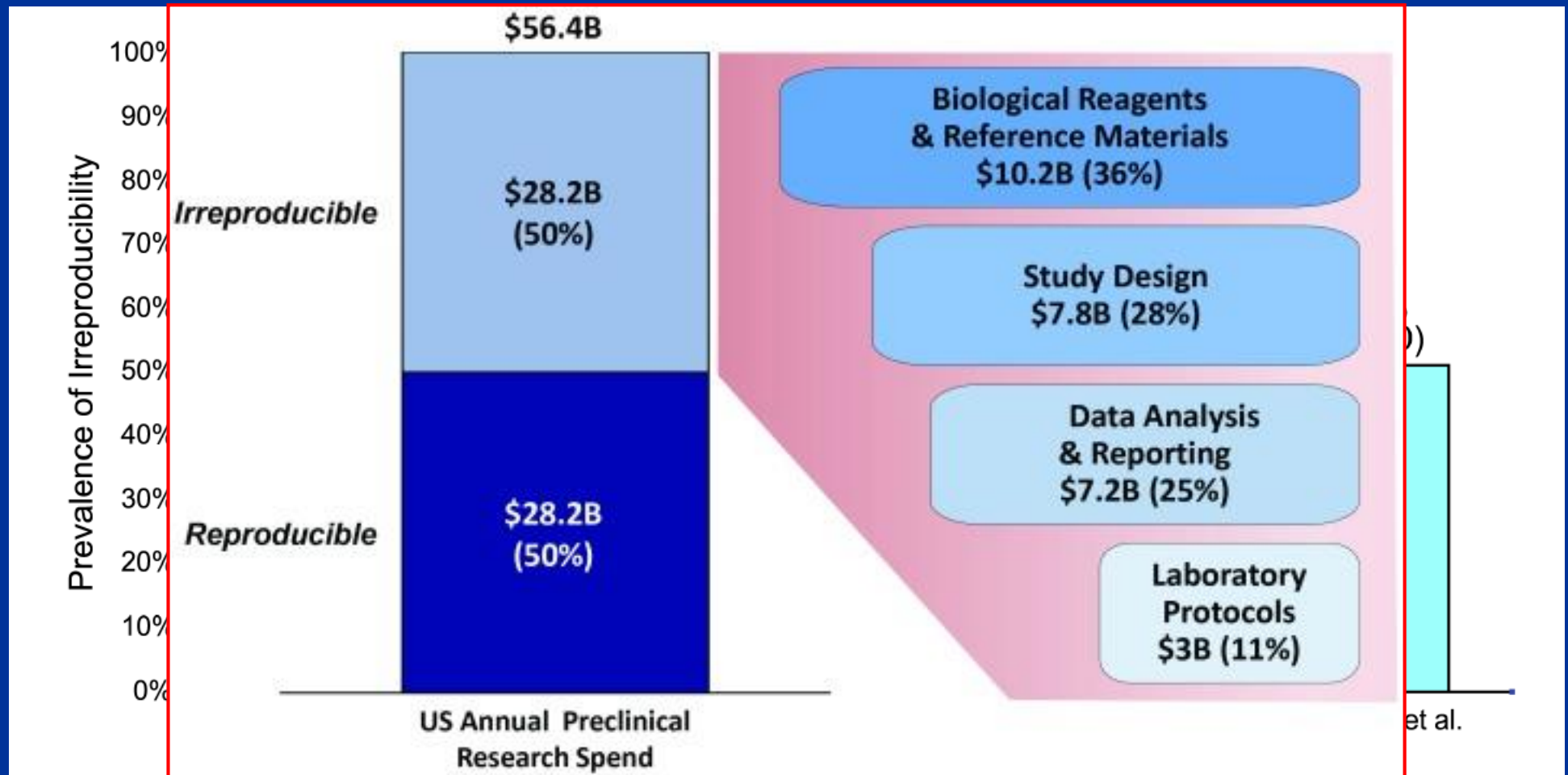
5. Begley and Ellis. Nature. 483, 531-3 (2012).



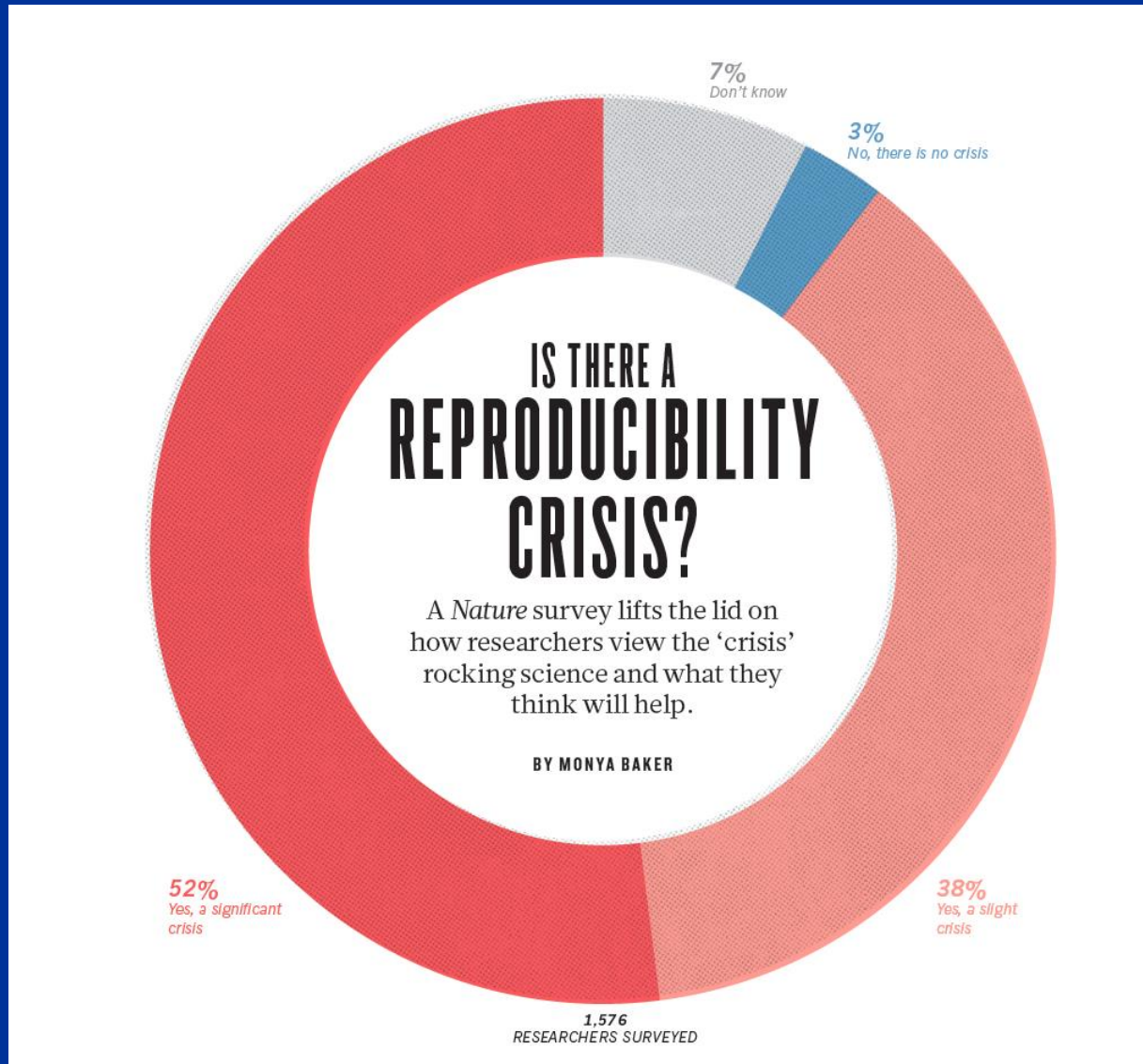
Raise standards for
preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

The Prevalence of the Lack of Reproducibility in *Recently* Published Studies



Nature Survey, May 2016



Is Amgen's Data on Data Reproducibility, Reproducible?

Errington et al. eLife 2021;

REPRODUCIBILITY IN CANCER BIOLOGY

Challenges for assessing replicability in preclinical cancer biology

50/193 = 26%
reproducibility rate

Abstract We conducted the [Reproducibility Project: Cancer Biology](#) to investigate the replicability of preclinical research in cancer biology. The initial aim of the project was to repeat 193 experiments from 53 high-impact papers, using an approach in which the experimental protocols and plans for data analysis had to be peer reviewed and accepted for publication before experimental work could begin. However, the various barriers and challenges we encountered while designing and conducting the experiments meant that we were only able to repeat 50 experiments from 23 papers. Here we report these barriers and challenges. First, many original papers failed to report key descriptive and inferential statistics: the data needed to compute effect sizes and conduct power analyses was publicly accessible for just 4 of 193 experiments. Moreover, despite contacting the authors of the original papers, we were unable to obtain these data for 68% of the experiments. Second, none of the 193 experiments were described in sufficient detail in the original paper to enable us to design protocols to repeat the experiments, so we had to seek clarifications from the original authors. While authors were *extremely or very helpful* for 41% of experiments, they were *minimally helpful* for 9% of experiments, and *not at all helpful* (or did not respond to us) for 32% of experiments. Third, once experimental work started, 67% of the peer-reviewed protocols required modifications to complete the research and just 41% of those modifications could be implemented. Cumulatively, these three factors limited the number of experiments that could be repeated. This experience draws attention to a basic and fundamental concern about replication – it is hard to assess whether reported findings are credible.

TIMOTHY M ERRINGTON*, **ALEXANDRIA DENIS[†]**, **NICOLE PERFITO[‡]**,
ELIZABETH IORNS AND **BRIAN A NOSEK**

The Spectrum of Reporting Preclinical and Clinical Data

Not all non-reproducible events are due to evil people

Honest Sloppy Selective Reporting Falsification Fabrication



What are the consequences?

- Clinical trials that are bound to fail
- Wasted time and effort of investigators and trainees
- A waste of money to try build on studies that are not sound
- Loss of confidence from our community

The Spectrum of Reporting Preclinical and Clinical Data

Honest Sloppy Selective Reporting Falsification Fabrication



- Inappropriate Stats
- Cell line contamination/drift
- Journals don't like negative data
 - Therefore, PIs don't like negative data

Selective Reporting of Laboratory Studies

- Journals prioritize “positive” results
 - If a drug works in 2 cell lines, and does not in 8, we only see the results on the 2 cell lines
- Students, post-docs, and faculty need publications for advancement
 - “*Publish or perish*”
 - In many labs, 2 trainees work on the same project competing with each other...*guess who wins?*
- Therefore, we tend to report only the “positive” data and ignore the negative data

Highlight negative results to improve science

Publishers, reviewers and other members of the scientific community must fight science's preference for positive results – for the benefit of all, says Devang Mehta.

The pressure to publish a positive story can also lead scientists to spin their results in a better light, and, in extreme instances, to commit fraud and manipulate data. In fields such as biotechnology and genomics, social scientists have already pointed out that hyping up the science could foster unrealistic expectations in an already sceptical public, counter-intuitively leading to greater distrust when real-world advances come at a slower pace.

We need reviewers and publishers to commit to publishing negative results in their journals. We need academic conferences to embrace honest discussions of failed experiments. We need funding agencies to support scientists who produce/report *negative results*. And, as scientists, we must acknowledge that all reliable studies should be reported (and accessible), irrespective of its outcome.

The Spectrum of Reporting Preclinical and Clinical Data

The more difficult issue to address

Honest Sloppy Selective Reporting Falsification Fabrication



Let's Talk About
"Misconduct"

*Do Investigators Intentionally Falsify
or Fabricate Data?*

To: Ellis, Lee M

Dear Sir,

I read your article titled "Raise standards for preclinical cancer research" published in Nature. I felt so happy to learn that the scientific community has been realizing a fact that people in cancer research field have been publishing fraud/non-reproducible data.

I lost my father, 2 of my uncles, aunt and two sister-in-laws because of cancer. Above bitter experiences made me to dedicate my life in finding solution to cancer. With a well-defined career goal of finding treatment to cancer, I entered into cancer research. After completion of Ph.D. from a Nobel Laureate group in Germany, I went to US to work on cancer. As a postdoc in the US, I had to change 7 research labs in 7 years due to the following reason:

PI's wanted me to produce falsified data and I refused to do so. Many PIs fired me as soon as they realized that I don't do wrong things. To cover them up, they sabotaged my professional life as well personal character.

Situation in cancer research field is so bad that nearly 90% of scientists in cancer research field, especially in the US, have been publishing fraud data. [REDACTED]

- 1) Publish fraud data
- 2) Meet all legal requirements to get grants from funding agencies
- 3) Lobby with the members of funding agency study sections by offering donations, effortless favor and get grants
- 4) Bargain high salaries with institutions where they are working using funding as bait

Does Misconduct Occur in the Clinic?

Dr. Baggerly will “wow” you with his talk on this!!

The Anil Potti retraction record so far

Tracking retractions as

with 16 comments

A [60 Minutes segment Sunday on Anil Potti](#) has drawn national attention to the case, so we thought this would be a good time to compile all of the retractions and corrections in one place.

Duke has [said](#) that about a third of Potti's 40-some-odd papers would be retracted, and another third would have “a portion retracted with other components remaining intact,” so this list will continue to grow. We'll update it as we hear about new changes.

Retractions:

1. [“Gene-expression patterns predict phenotypes of immune-mediated thrombosis,”](#) in *Blood*
2. [“Upregulated Oncogenic Pathways in Patients Exposed to Tobacco Smoke May Provide a Novel Approach to Lung Cancer Chemoprevention,”](#) in *CHEST*
3. [“Characterizing the Clinical Relevance of an Embryonic Stem Cell Phenotype in Lung Adenocarcinoma,”](#) in *Clinical Cancer Research*
4. [“An Integrated Genomic-Based Approach to Individualized Treatment of Patients With Advanced-Stage Ovarian Cancer”](#) in the *Journal of Clinical Oncology (JCO)*
5. [“Pharmacogenomic Strategies Provide a Rational Approach to the Treatment of Cisplatin-Resistant Patients With Advanced Cancer”](#) also in the JCO
6. [“Gene Expression Signatures, Clinicopathological Features, and Individualized Therapy in Breast Cancer”](#) in the *Journal of the American Medical Association (JAMA)*
7. [“Validation of gene signatures that predict the response of breast cancer to neoadjuvant chemotherapy: a substudy of the EORTC 10994/BIG 00-01 clinical trial,”](#) in *The Lancet Oncology*
8. [“Genomic signatures to guide the use of chemotherapeutics,”](#) in *Nature Medicine*
9. [“A Genomic Strategy to Refine Prognosis in Early-Stage Non-Small-Cell Lung Cancer,”](#) in the *New England Journal of Medicine (NEJM)*
10. [“An Integrated Approach to the Prediction of Chemotherapeutic Response in Patients with Breast Cancer”](#) in *PLoS ONE*
11. [“A genomic approach to colon cancer risk stratification yields biologic insights into therapeutic opportunities”](#) in the *Proceedings of the National Academy of Sciences (PNAS)*



Dr. Anil Potti is an oncologist in Grand Forks, North Dakota. He is a Board Certified Medical Oncologist and Clinician and takes special interest in serving patients with blood and cancer problems. An alumnus of the University of North Dakota, he has received numerous awards like the Alpha Omega Alpha (AOA) Award, Resident of the Year Award and several Outstanding Teacher of the Year Awards. Presently, Dr. Potti looks forward to dedicating his efforts to helping cancer patients and their families in this region. As he says, “sure, the weather may be cold, but the people sure are warm.”

Ivan Oransky
RetractionWatch.com

Famous Fraudulent Papers The Impacted Patient's Lives!

- Breast cancer and bone marrow transplants
 - Bezwoda et al. 1999 ASCO Annual Meeting
- Autism and vaccines
 - Wakefield et al. 1998 The Lancet
- Stem cells and tracheal transplants
 - Macchiarini et al. Karolinska, The Lancet

Wikipedia provides great summaries

Vaccines and Autism

Wakefield, et al. Lancet 1998

- Wakefield did not conduct the study according to ethical standards for research.
- Wakefield lied in the *Lancet* paper when he wrote that the participating children were referred independently after being diagnosed with IBD or other major GI issues. In fact, many of the children were chosen specifically by Wakefield, and others were recruited with the help of the same lawyer who was paying him to conduct the study.
- Wakefield subjected vulnerable autistic and other developmentally challenged children to a variety of difficult GI tests, including colonoscopy and lumbar puncture (i.e., spinal tap), without any medical indication to benefit the children.
- Even before publication of the study, Wakefield was working on patenting his own version of a measles vaccine, which he would sell at a great profit as a supposedly “safe” alternative to the MMR vaccine. The father of one of the children in Wakefield’s study was a cofounder of the planned business that would market this product.
- Unrelated to the particular paper in question, the GMC panel also found that Wakefield had paid children at his own son’s birthday party £5 each so he could draw their blood for use in his research. He later joked about this during a lecture.
- And more including financial conflict of interest

The Retraction Watch Leaderboard

Who has the most retractions? Here's our unofficial list (see notes on methodology), which we'll update as more information comes to light:

1. [Yoshitaka Fujii](#) (total retractions: 183) See also: [Final report of investigating committee](#), [our reporting](#), [additional coverage](#)
2. [Jochim Boldt](#) (175) See also: [Editors-in-chief statement](#), [our coverage](#)
3. [Hironobu Ueshima](#) (123) See also: [our coverage](#)
4. [Yoshihiro Sato](#) (113) See also: [our coverage](#)
5. [Ali Nazari](#) (96) See also: [our coverage](#)
6. [Jun Iwamoto](#) (88) See also: [our coverage](#)
7. [Diederik Stapel](#) (58) See also: [our coverage](#)
8. [Yuhji Saitoh](#) (56) See also: [our coverage](#)
9. [Adrian Maxim](#) (48) See also: [our coverage](#)
10. [Chen-Yuan \(Peter\) Chen](#) (43) See also: [SAGE](#), [our coverage](#)
11. [Shahaboddin Shamshirband](#) (42) See also: [our coverage](#)
12. [Fazlul Sarkar](#) (41) See also: [our coverage](#)
13. [Hua Zhong](#) (41) See also: [journal notice](#)
14. [Shigeaki Kato](#) (40) See also: [our coverage](#)
15. [James Hunton](#) (37) See also: [our coverage](#)
16. [Hyung-In Moon](#) (35) See also: [our coverage](#)
17. [Dong Mei Wu](#) (35) See also: [National Natural Science Foundation of China finding](#)
18. [Antonio Orlandi](#) (34) See also: [our coverage](#)
19. [Dimitris Liakopoulos](#) (33) (NB: We're counting a book he co-authored as a single retraction. The book has 13 retracted chapters with DOIs that are not included in this figure.) See also: [our coverage](#)
20. [Amelec Vilorio aka Jesus Silva](#) (33) See also: [our coverage](#)
21. [Jose L Calvo-Guirado](#) (32) See also: [our coverage](#)
22. [Jan Hendrik Schön](#) (32) See also: [our coverage](#)
23. [Naoki Mori](#) (31) See also: [our coverage](#)
24. [Bharat Aggarwal](#) (30) See also: [our coverage](#)
25. [Soon-Gi Shin](#) (30) See also: [our coverage](#)
26. [Victor Grech](#) (29) See also: [our coverage](#)
27. [Tao Liu](#) (29) See also: [our coverage](#)
28. [Jun Ren](#) (29) See also: [our coverage](#)
29. [Cheng-Wu Chen](#) (28) See also: [our coverage](#)
30. [A Salar Elahi](#) (27) See also: [our coverage](#)
31. [Prashant K Sharma](#) (27) See also: [our coverage](#)

We note that all of the top 31 are men, which agrees with the general findings of a [2013 paper suggesting that men are more likely to have papers retracted for fraud](#).

5/15/23

An IRB Approved Survey Conducted at The MD Anderson Cancer Center

OPEN ACCESS Freely available online



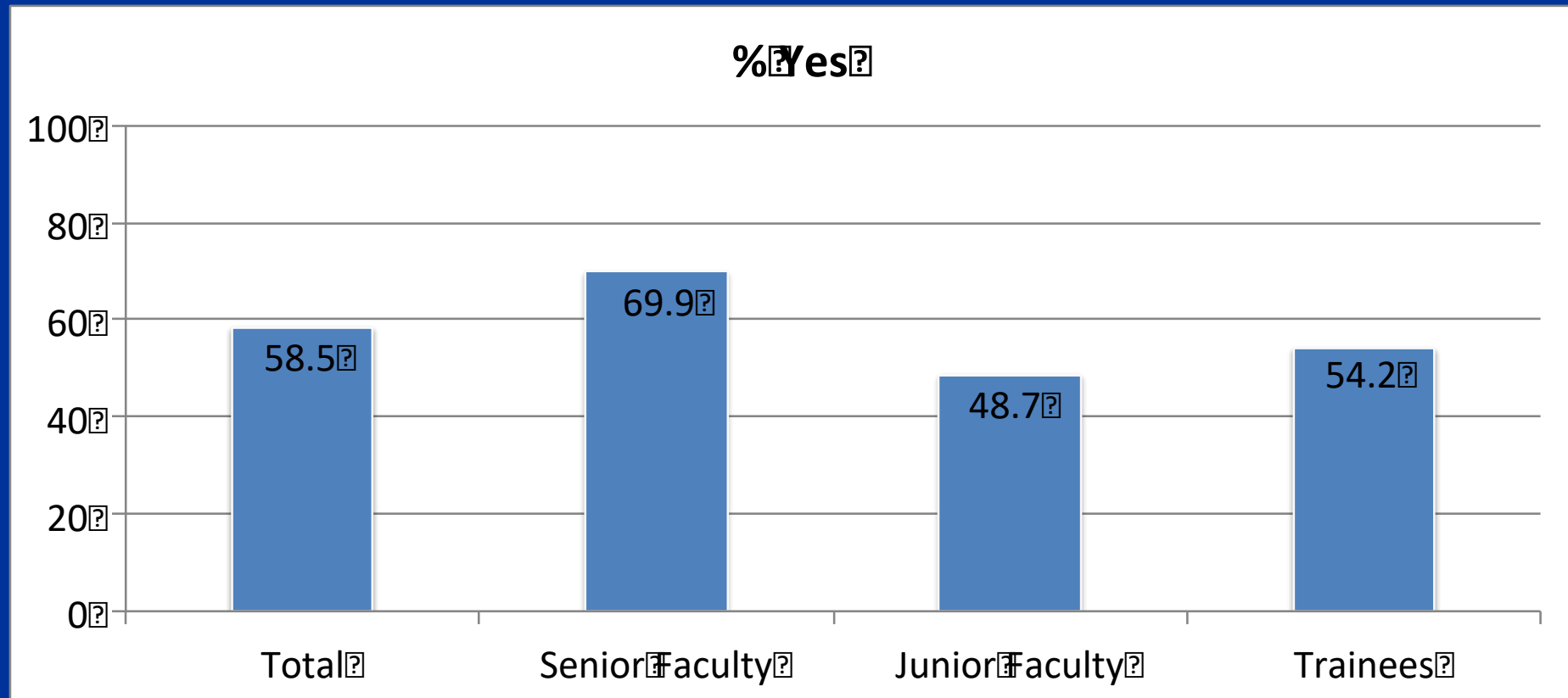
A Survey on Data Reproducibility in Cancer Research Provides Insights into Our Limited Ability to Translate Findings from the Laboratory to the Clinic

Aaron Mobley¹, Suzanne K. Linder², Russell Braeuer¹, Lee M. Ellis^{1,3*}, Leonard Zwelling^{4*}

240 responses in 6 hrs
311 responses after 3 days

IRB Approved Protocol
PI: Len Zwelling, MD
Co-PI: Lee Ellis

Have You Ever Tried To Reproduce A Finding From A Published Paper And Not Been Able To Do So?



Driving Forces for Irreproducible Data

(>90 respondents-Trainees Only)

- Were you ever **pressured to publish findings** of which you had doubt?
 - 22%
- Have you noted **pressure from a mentor** to prove that his/her hypothesis was correct, even though the data you generated may not support the hypothesis?
 - 31%
- Are you aware of mentors who require a **high impact publication** before a trainee can leave the lab?
 - 49%

Selected Comments From the Survey

- crumbling of integrity and value - bean counters judging science by journal names - institutional failure on dealing with alleged fraud.
- Everything here in US is screwed up. There is nothing to do other than move out. Who publishes more deserve respect, while others who are honest and cast doubt about their own results (or third party results) as condemned. There is no way out. It is either join the "bright team" or be labeled as incompetent.
- ... my previous mentor and also our current neighbor lab PI push too much to produce best data all the time. .. sometimes it make trainee consider manipulates data only to escape from stress. Especially, many international trainees (postdoc) also have VISA issue. Thus, PI starts push them with visa issue trainees feel a lot of stress and eventually it make them can do whatever PI WANT.
- From my experience, no one will help you if you stand up for what is right.The system is unfortunately broken
- Pressure isfrom the job market and funding dynamics. The impact factor insanity is destroying science. A small group of powerful editors and friends control everything.

A Survey on Data Reproducibility and the Effect of Publication Process on the Ethical Reporting of Laboratory Research

Delphine R. Boulbes¹, Tracy Costello², Keith Baggerly³, Fan Fan¹, Rui Wang¹,
Rajat Bhattacharya¹, Xiangcang Ye¹, and Lee M. Ellis^{1,4} Clin Cancer Res; 2018

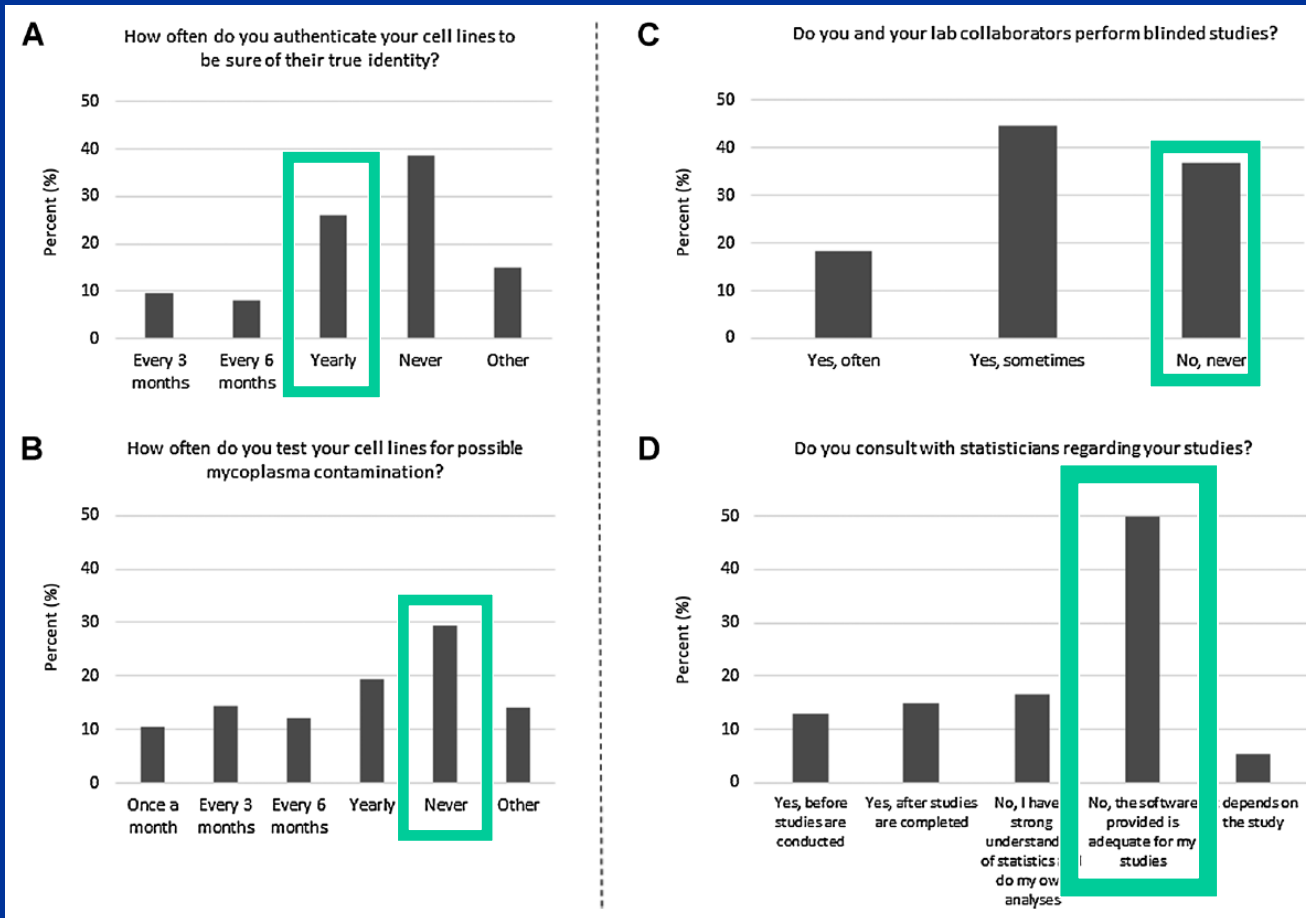
Population Characteristics (n=467)

Students 10.7%

Postdocs 89.3%

Cancer Biology 60.6%

Best Research Practices



Take home points

- < 50% of investigators verify cell lines at least every year
- Just over half test for mycoplasma yearly
- < 20% of investigators perform blinded studies as a routine
- < 50% consult with a statistician

Research Integrity and Reporting Transparency

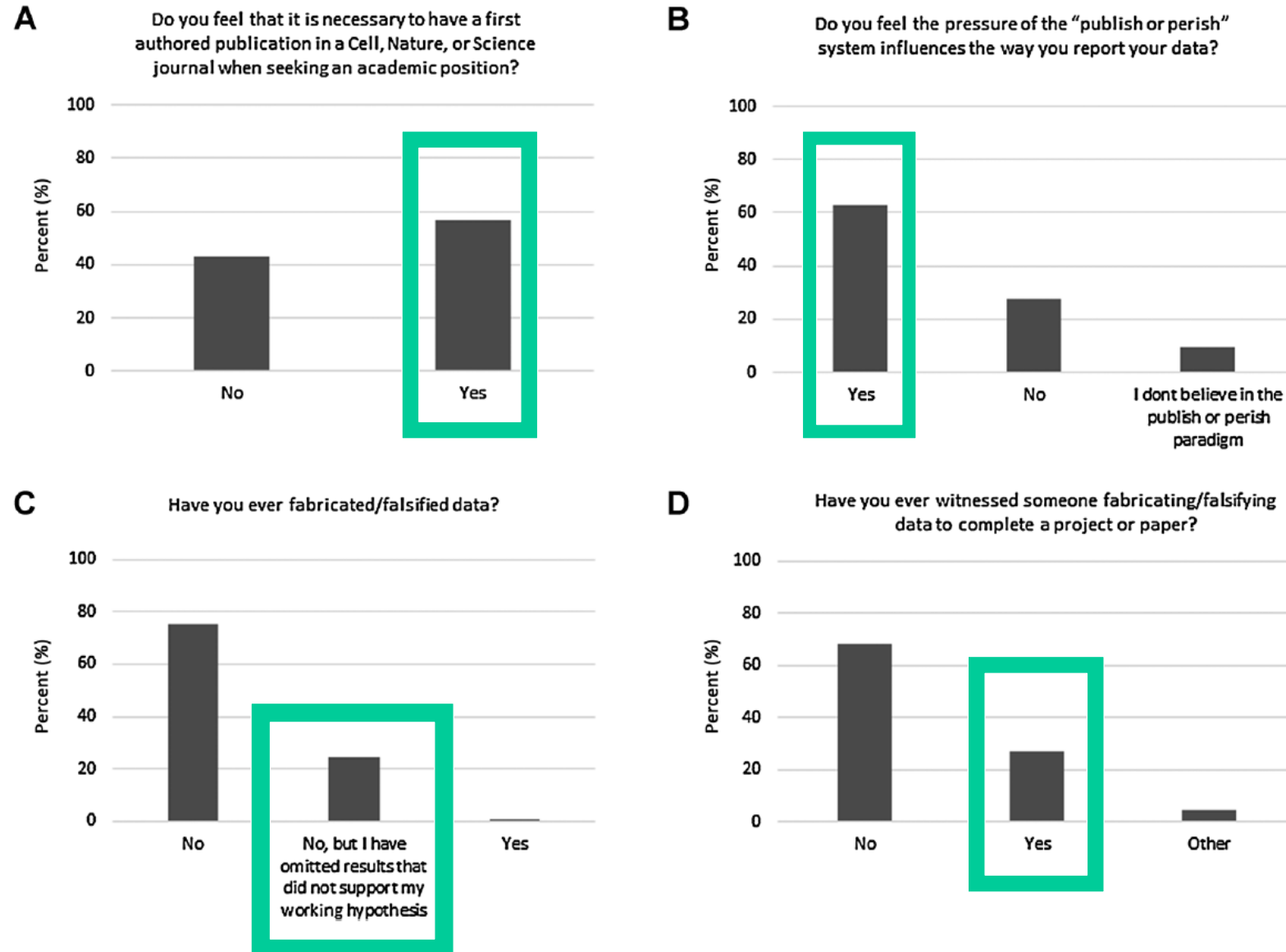


Figure 3.

Responses to questions about research integrity and transparency. Responses were provided by all 467 respondents to questions 5 (A), 27 (B), 10 (C), and 11 (D).

The Publication Process

- For 35% of participants, the revision process was >12 months for a high impact journal
- The cost of revision was >25K (40%) and >100K in 10%
- In 25% of those surveyed, the manuscript did *not improve significantly after revision*
(in their opinion)

Comment in Pubpeer

The findings of this paper are not particularly surprising. But I thought the conclusions and discussion was solidly grounded in the evidence they found. Your supervisor can tell you all they like that your career advancement doesn't depend on your results as long as you do good work, but then you see the big weightings on publication record in your fellowship application and you know what the real deal is. Unfortunately as sensible as the conclusions are, I see the likelihood of their implementation any time soon as likely as my negative results getting into Nature.

The Erosion of Research Integrity: *The Need For a Culture Change*

- Integrity of laboratory research and how this impacts clinical outcomes
 - The issue at hand
 - The spectrum
 - Why does this occur?
 - What can we do to fix this?

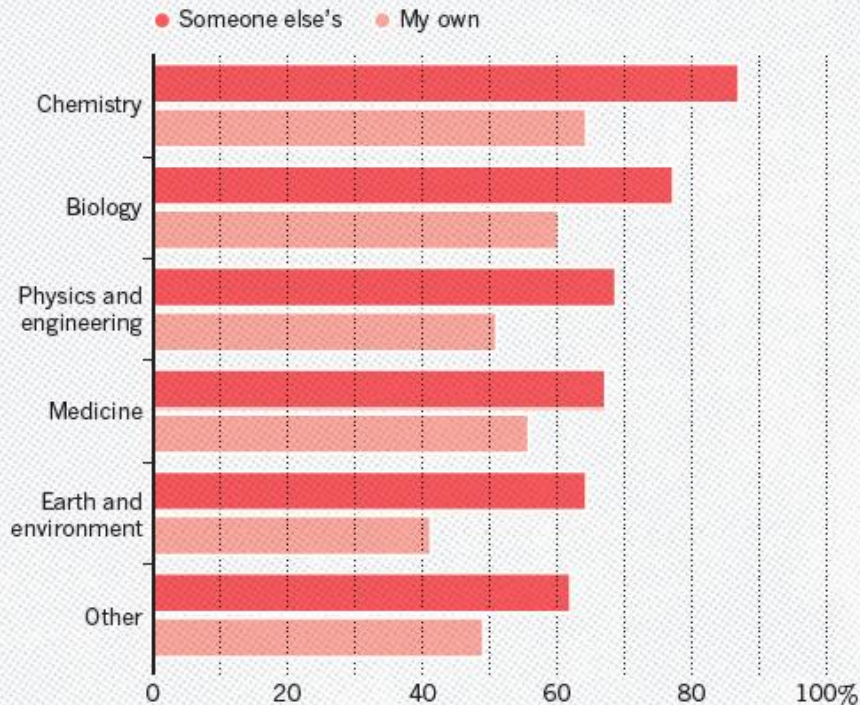
Causes of “Massaging” of Data

Trainees	Faculty
<p>Occurs when trainees have a strong mentor - trainees do not want to challenge the hypothesis of the mentor - sometimes this is cultural - it is hard to challenge a mentor in the US when English is a 2nd language</p>	<p>“Publish or Perish” has morphed into only getting recognition for pubs in CNS (Cell, Nature, Science) – -Promotion and tenure for young faculty -Endowed Chairs for established investigators</p>
<p>Need high impact publications to obtain a job (or many pubs)</p>	<p>Grants: Preliminary data (Biosketch) for subsequent grants – some institutes require faculty to bring in 90-100% of salary off of grants</p>
<p>Cannot leave that lab as a post-doc, or cannot complete thesis as a student, unless you have a high impact publication</p>	<p>Stature and gratification (human nature)</p>
	<p>Financial gain: Patents and sublicensing</p>

Nature Survey, May 2016

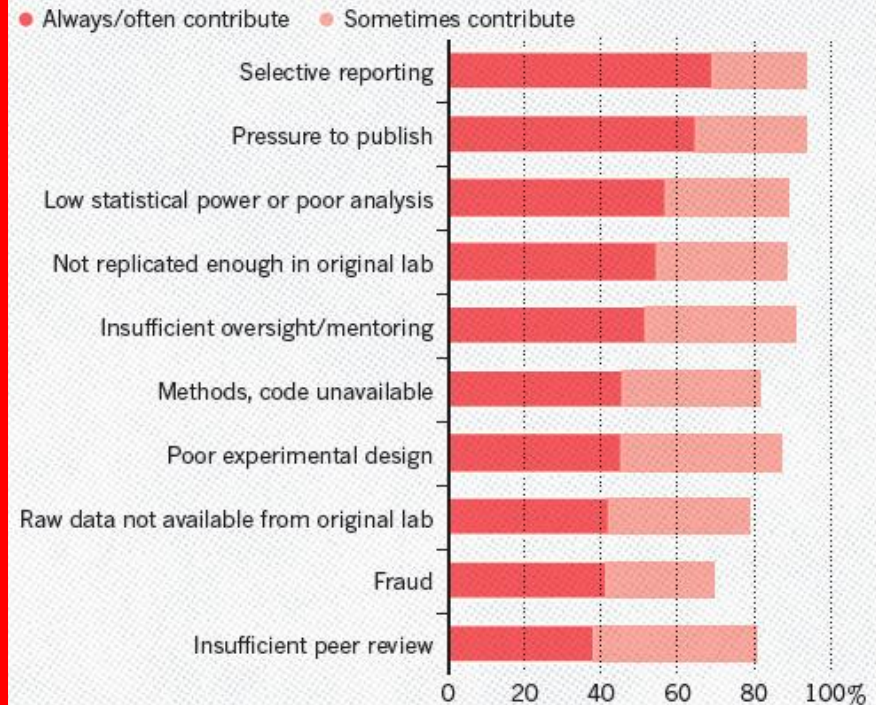
HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?

Most scientists have experienced failure to reproduce results.



WHAT FACTORS CONTRIBUTE TO IRREPRODUCIBLE RESEARCH?

Many top-rated factors relate to intense competition and time pressure.



Let's Talk About
High Impact Publications
and *"Impact Factor Mania"*

And what this does to our culture!

Quote to a Post-Doc From a Successful Physician Scientist

*“You are nothing unless you
publish in CNS!”*

Causes for the Persistence of Impact Factor Mania

mBio 2014

Arturo Casadevall,^a Ferric C. Fang^b

Departments of Microbiology & Immunology and Medicine, Albert Einstein College of Medicine, Bronx, New York, USA^a; Departments of Laboratory Medicine and Microbiology, University of Washington School of Medicine, Seattle, Washington, USA^b

“...associating the value of research with the journal where the work was published rather than the content of the work itself. The mania is causing profound distortions in the way science is done that are deleterious to the overall scientific enterprise.”

distortions in the way science is done that are deleterious to the overall scientific enterprise. In this essay, we consider the forces responsible for the persistence of the mania and conclude that it is maintained because it disproportionately benefits elements of the scientific enterprise, including certain well-established scientists, journals, and administrative interests. Our essay suggests steps that can be taken to deal with this debilitating and destructive epidemic.

Should we eliminate the Impact Factor?

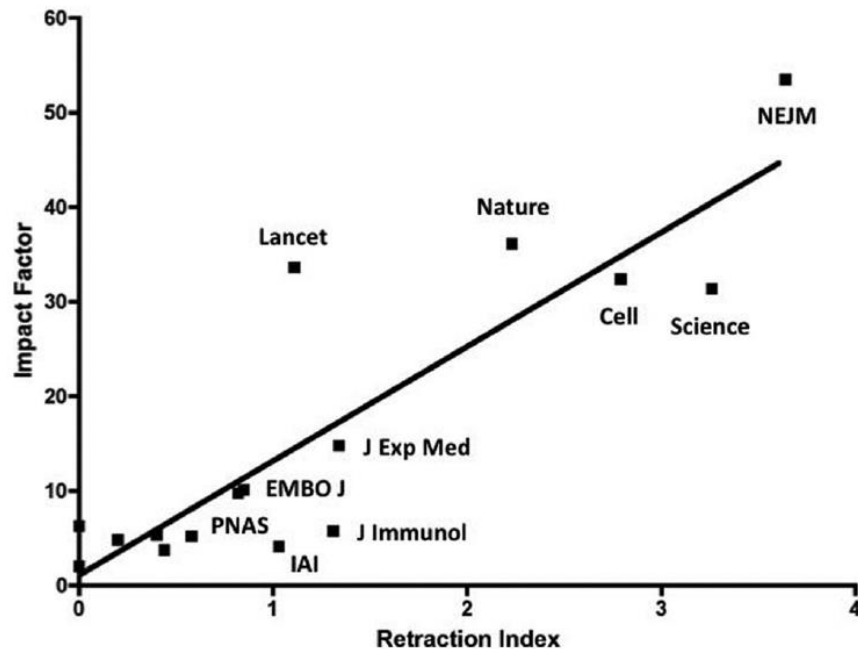
Nathan S. Blow, Ph.D., Editor-in-Chief, *BioTechniques*

EDITORIAL

Fang and Casadevall
Infection and Immunity, 2011

Retracted Science and the Retraction Index[▽]

Articles may be retracted when their findings are no longer considered trustworthy due to scientific misconduct or error, they plagiarize previously published work, or they are found to violate ethical guidelines. Using a novel measure that we call the “retraction index,” we found that the frequency of retraction varies among journals and shows a strong correlation with the journal impact factor. Although retractions are relatively rare, the retraction process is essential for correcting the literature and maintaining trust in the scientific process.



The higher the impact factor, the higher the retraction index (also in the New York Times)

“A man who has committed a mistake, and doesn’t correct it, is committing another mistake.”
—attributed to Confucius

Misconduct accounts for the majority of retracted scientific publications

PNAS, 2012

Ferric C. Fang^{a,b,1}, R. Grant Steen^{c,1}, and Arturo Casadevall^{d,1,2}

Departments of ^aLaboratory Medicine and ^bMicrobiology, University of Washington School of Medicine, Seattle, WA 98195; ^cMediCC! Medical Communications Consultants, Chapel Hill, NC 27517; and ^dDepartment of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461

Edited by Thomas Shenk, Princeton University, Princeton, NJ, and approved September 6, 2012 (received for review July 18, 2012)

Nobel winner declares boycott of top science journals

Randy Schekman says his lab will no longer send papers to Nature, Cell and Science as they distort scientific process

How journals like Nature, Cell and Science are damaging science

Monday 9 December 2013 14.42 EST

Leading academic journals are distorting the scientific process and represent a "tyranny" that must be broken, according to a Nobel prize winner who has declared a boycott on the publications.

Schekman criticises Nature, Cell and Science for artificially restricting the number of papers they accept, a policy he says stokes demand "like fashion designers who create limited-edition handbags." He also attacks a widespread metric called an "impact factor", used by many top-tier journals in their marketing.

*Final, Final Comment on Impact
Factor Mania*

Strive for Nature

But Don't Lie or Die for Nature

(or compromise your ethics)

The Erosion of Research Integrity: *The Need For a Culture Change*

- Integrity of laboratory research and how this impacts clinical outcomes
 - The issue at hand
 - The spectrum
 - Why does this occur?
 - What can we do to fix this?

Overall, We Need to Be Kinder as Reviewers, Mentors, and Editors

- Research can be challenging when we are seeking significant gains in knowledge!
 - And sometimes, the unexpected findings may be the most interesting findings!
- We should not torture our trainees to the point where they “*massage*” data in order to satisfy the PI, have a paper published in a high impact journal, or both!
- PIs need to implement *best research practices* and not just expect a *CNS* paper to land on your desk
 - PIs should have updates and input from start to finish.

2014

- Case Summary: Ahvazi, Bijan
- Case Summary: Chen, Li
- Case Summary: Cokonis, Melanie
- Case Summary: Deb, Kaushik
- Case Summary: Dzhura, Igor
- Case Summary: Freeman, Helen C.
- Case Summary: Fu, Jun
- Case Summary: Patel, Parag
- Case Summary: Suzuki, Makoto
- Case Summary: Takahashi, Takao
- Case Summary: Warne, James P.
- Case Summary: Xing, H. Rosie
- Case Summary: Zou, Zhihua



May, 2023

<https://ori.hhs.gov/frequently-asked-questions>

2016

- Case Summary: Cullinane, Andrew R.

2018

- Case Summary: Baughman, Brandi M.
- Case Summary: Eloutub, Maria Cristina Miron

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

2015

- Case Summary: Anderson, David
- Case Summary: Asherin, Ryan
- Case Summary: Bitzegeio, Julia
- Case Summary: Blaylock, Brandi Lyn
- Case Summary: Briones, Teresita L.
- Case Summary: Dasmahapatra, Girija
- Case Summary: Fujita, Ryousuke
- Case Summary: Geraedts, Maria C.P.
- Case Summary: Kang, Bin
- Case Summary: Littlefield, Peter
- Case Summary: Massè, Julie
- Case Summary: Potti, Anil
- Case Summary: Reddy, Venkata J.
- Case Summary: Xiao, Dong

And, in 2021, there was a case of misconduct in the TMC!

2017

- Case Summary: Baughman, Brandi
- Case Summary: Chegini, Nasser
- Case Summary: Chetram, Mahandranauth
- Case Summary: El-Remessy, Azza
- Case Summary: Endo, Matthew
- Case Summary: Mirchandani, Alec
- Case Summary: Sauer, Frank

- Case Summary: Sen, Shiladitya
- Case Summary: Skau, Colleen T.
- Case Summary: Srivastava, Rakesh
- Case Summary: Wang, Li

2019

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

2021

-3 cases

2022

-11 cases

2023

-2 cases as of 5/15/23

Are We Doing Enough to Punish Those Who Violate Our Trust?
What are the consequences of being found guilty of misconduct?

Most Common ORI Actions

- Retract paper(s)
- Have research supervised for 3 yrs
- No service on committees for 2-3 yrs
- Most can still receive NIH funding

- For those found guilty of fraud, we must have a punishment that fits the crime.
- What is the deterrent for such behavior?
- Indeed, the entire system needs an overhaul, but let's start with making outright fraud something that can be deterred by tough punishment and prohibits this person from ever having the chance to do this again.
 - This is, of course, even more important for clinical fraud

The Primary Inquiry Rests With Your NIH Funded Institution

What the Office of Research Integrity Does

- Implements PHS regulations requiring institutions to respond to allegations of research misconduct
- Assures institutions requesting PHS funding have mechanisms in place to deal with allegations of research misconduct
- Provides assistance and guidance to institutions
- Can perform own investigation
- Leaves primary responsibility with the individual institutions
- Institutional Research Integrity Officer

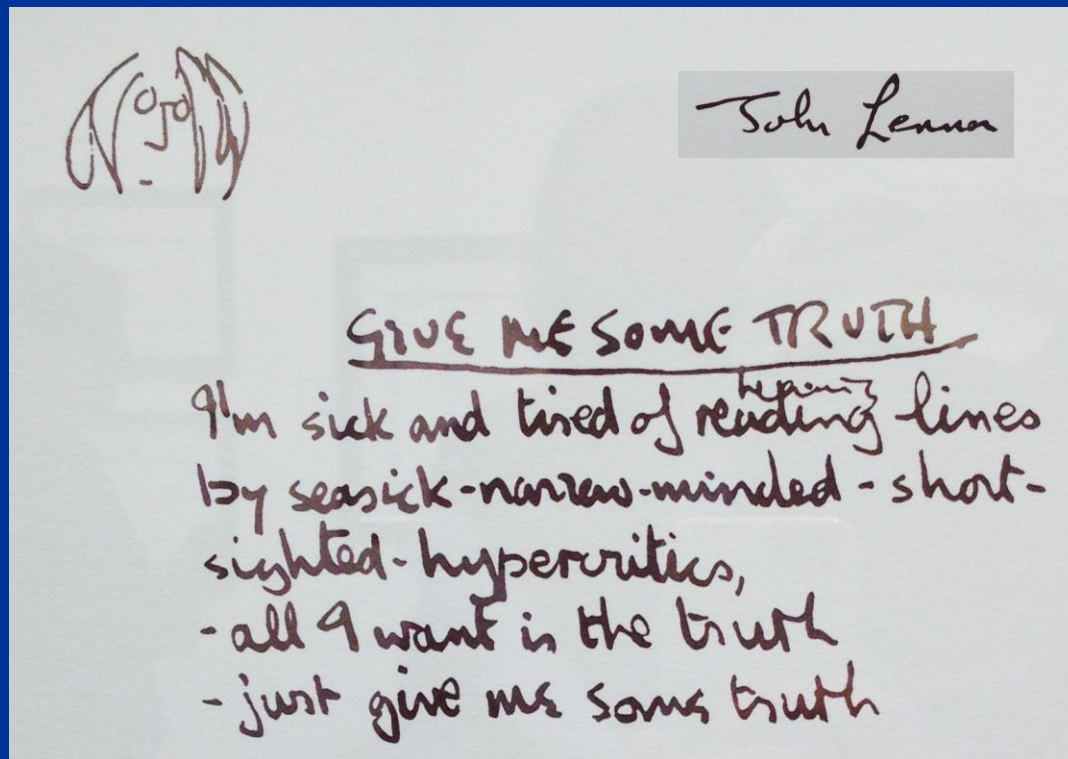
INHERENT CONFLICT OF INTEREST

Mechanism for Addressing Misconduct Is Institutional Dependent

- Allegations may be brought to Department Head, Division Head, or to the Provost and Executive Vice President (EVP)
- Provost & EVP and Res Integrity Officer (RIO) will assess the allegations
- Information-gathering and initial fact finding.
 - Conduct an Inquiry Panel of at least 3 faculty chosen by Provost & EVP and the Res Integrity Officer.

INHERENT CONFLICT OF INTEREST

“....you’ve uncovered a thorny problem in academia—selfishness. In moments of weakness or at the extremes, this creates an undertow away from integrity in science and public health. This is the single biggest limitation in our field,.....”



A handwritten note on a piece of paper. At the top left is a scribble that looks like "N-J". To the right, the name "John Lennon" is written in cursive. Below that, the phrase "GIVE ME SOME TRUTH" is underlined. The main body of the note is written in cursive and reads: "I'm sick and tired of reading ^{hyper} lines by seasick-narrow-minded-short-sighted-hypercritics, - all I want is the truth - just give me some truth".

N-J

John Lennon

GIVE ME SOME TRUTH

I'm sick and tired of reading ^{hyper} lines
by seasick-narrow-minded-short-
sighted-hypercritics,
- all I want is the truth
- just give me some truth

THE RIGHT TO
SEARCH
FOR TRUTH
IMPLIES ALSO
A DUTY;
ONE MUST NOT
CONCEAL ANY
PART OF WHAT
ONE HAS
RECOGNIZED
TO BE TRUE.

ALBERT EINSTEIN
1879 - 1955

