Rigor and Reproducibility:
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
and
SWOG

www.thelancet.com/oncology Vol 16 July 2015

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?

if we used an audience response system

Potential Audience Responses After This Session

At the end of my talk, you will feel:

A. Entertained
B. Angry
C. Discouraged (how can I trust anything I read?)
D. Reinvigorated (it is OK to publish in something other than *CNS*)
E. All of the above

Drug Development Failure Rates are Too High! *(duh)*

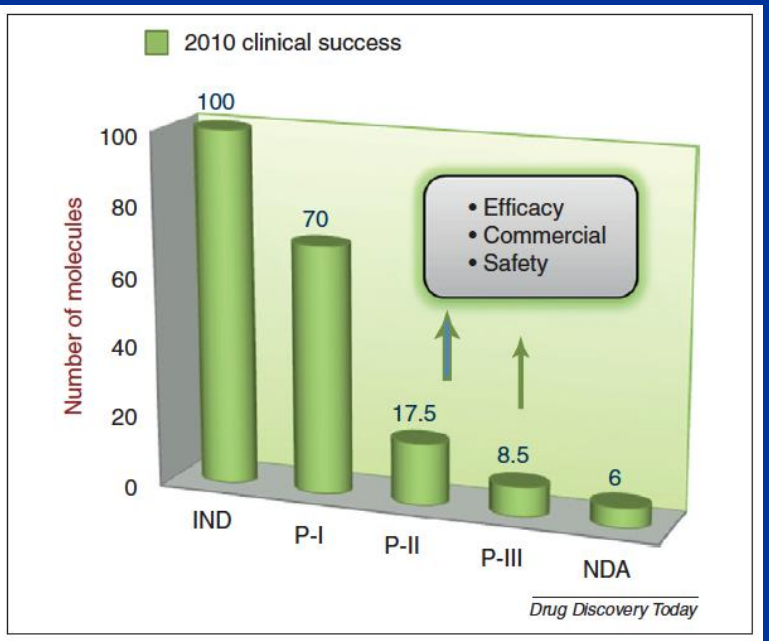
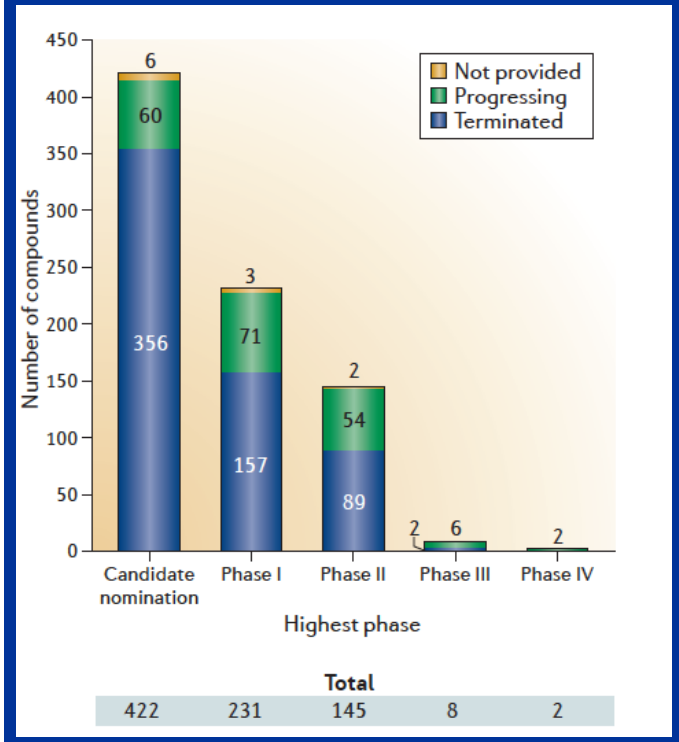


FIGURE 3

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

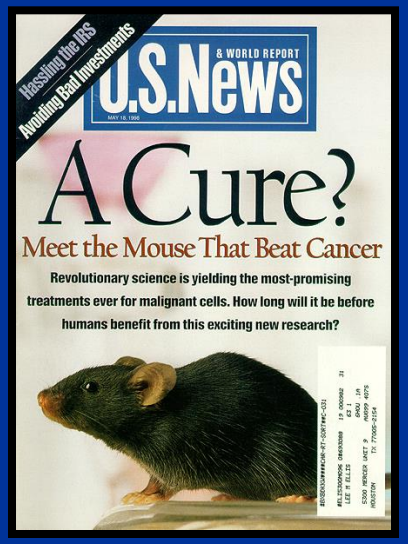
Bob Radinsky, PhD

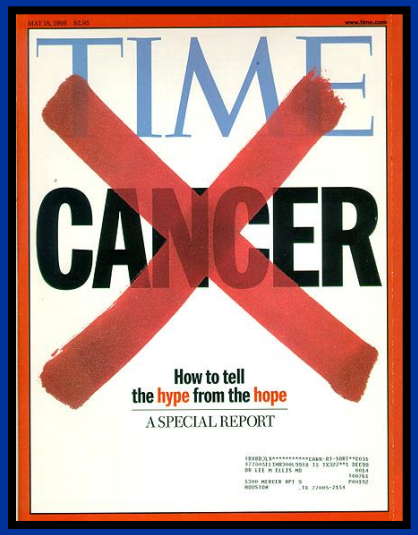
MDACC (1989-2000) ➔ Amgen (2000)

"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"

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?

Reports on Issues With Data Reproducibility

ALS Therapy Development

ndent studies[1]

arate ALS mouse
cal trial of more

National Institute of Neurological Disorders and Stroke
National Institutes of Health

rd injury studies

BAYER

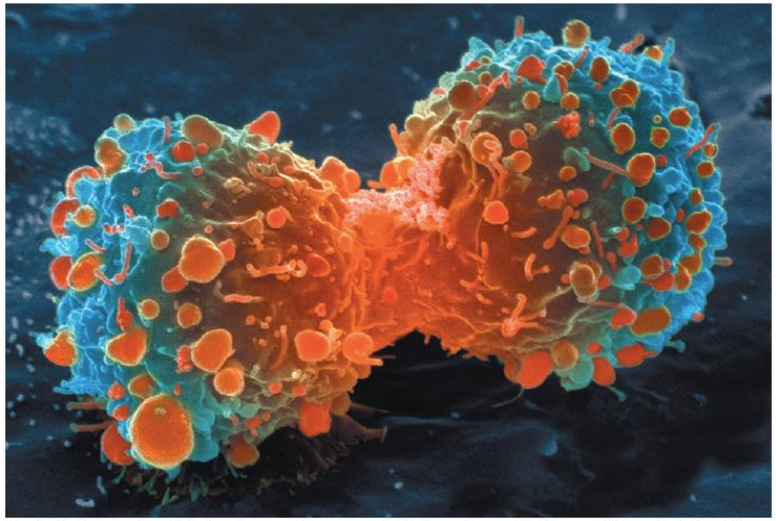
studies

AMGEN®

Attempted to reproduce 53 "landmark" oncology publications

→ 6/53 reproduced[5]

S. GSCHMEISSNER/SPL



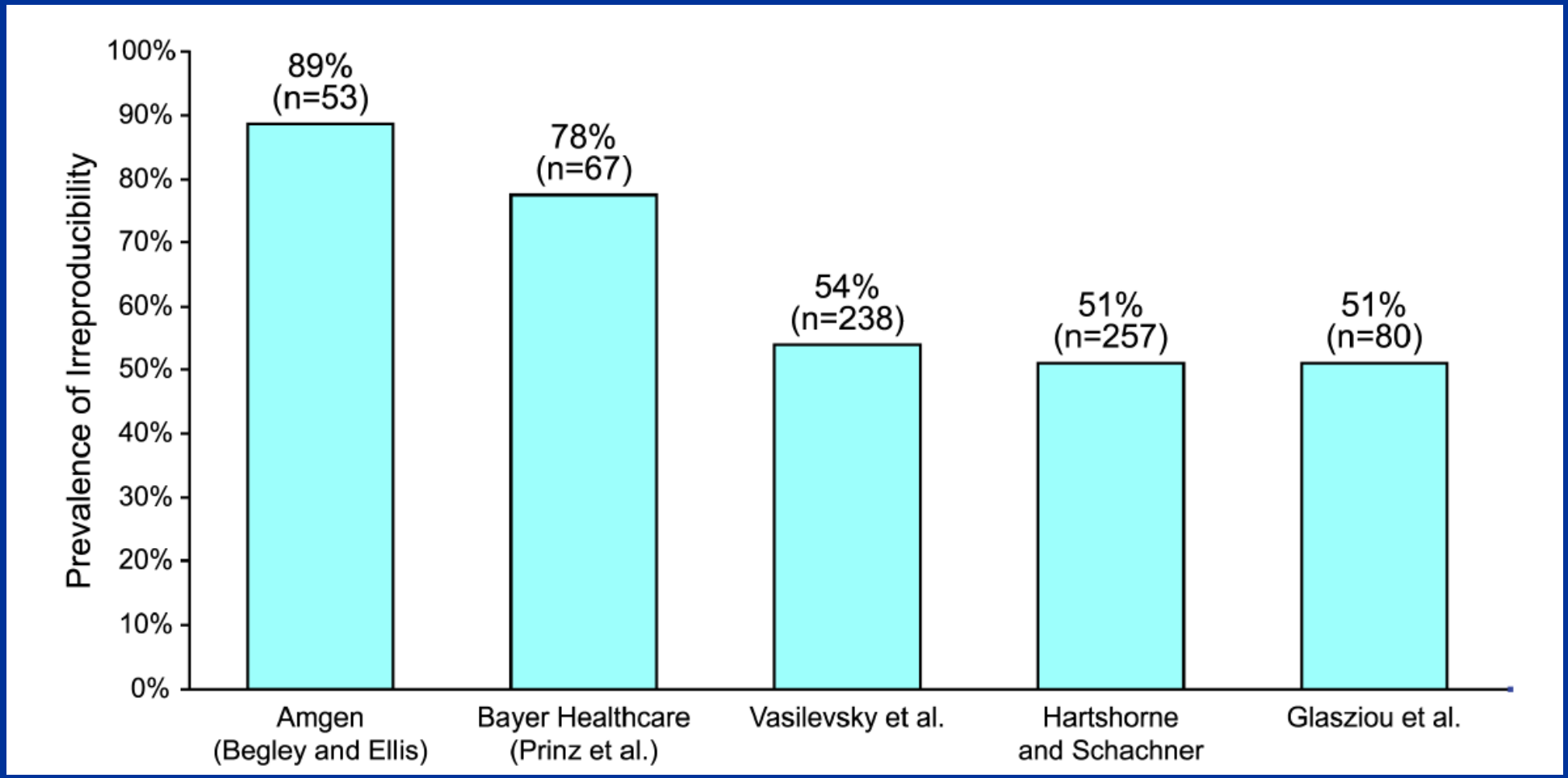
Many landmark findings in preclinical oncology research are not reproducible, in part because of inadequate cell lines and animal models.

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.

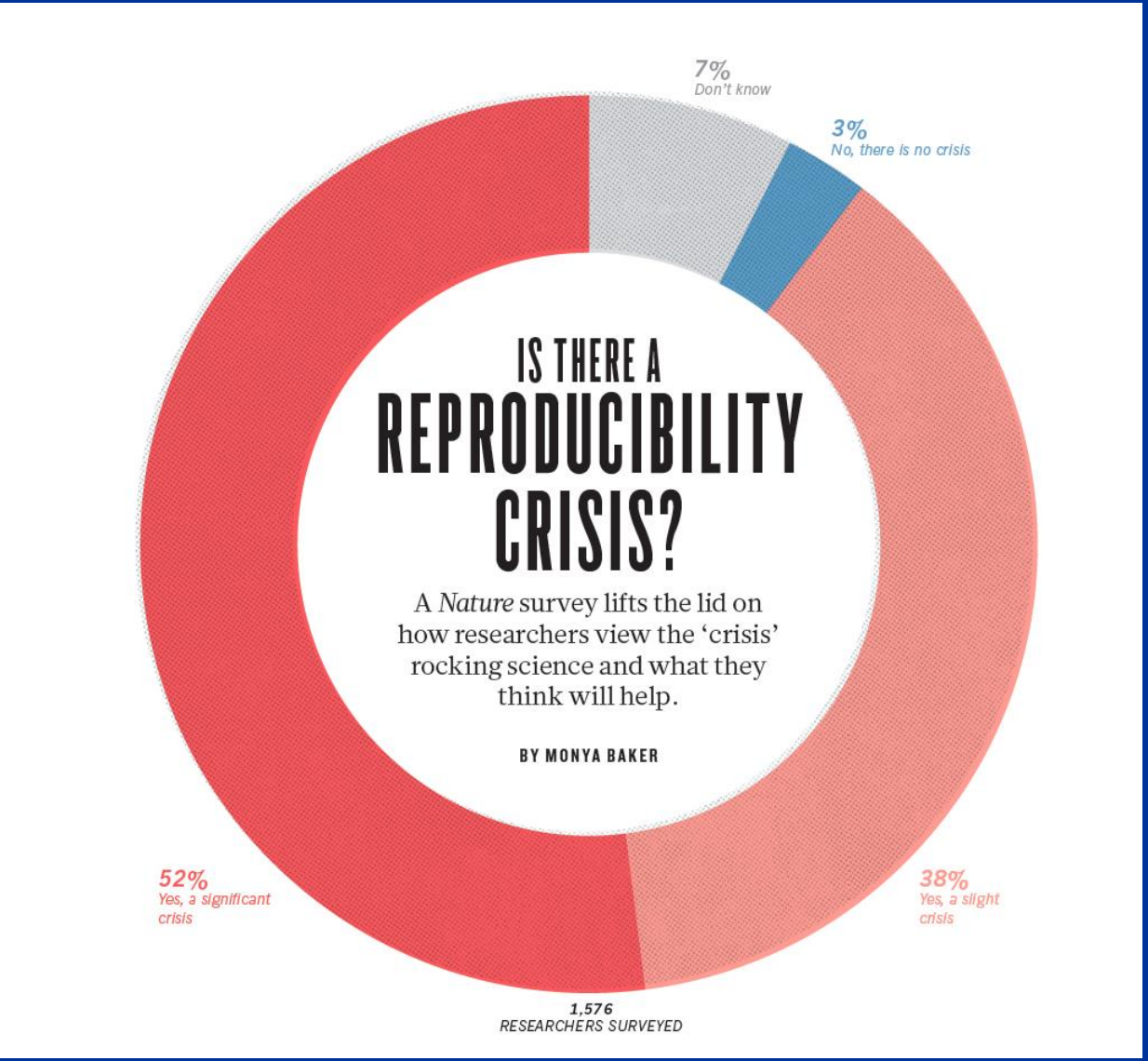
1. Scott et al. Amyotroph Lateral Scler. 9, 4-15 (2008).
2. Gordon et al. Lancet Neurol. 6, 1045–1053 (2007).
3. Stuart et al. Experimental Neurology 233, 597–605 (2012).
4. Prinz et al. Nat Rev Drug Discov. 10, 712 (2011).
5. Begley and Ellis. Nature. 483, 531-3 (2012).

The Prevalence of the Lack of Reproducibility in Recently Published Studies



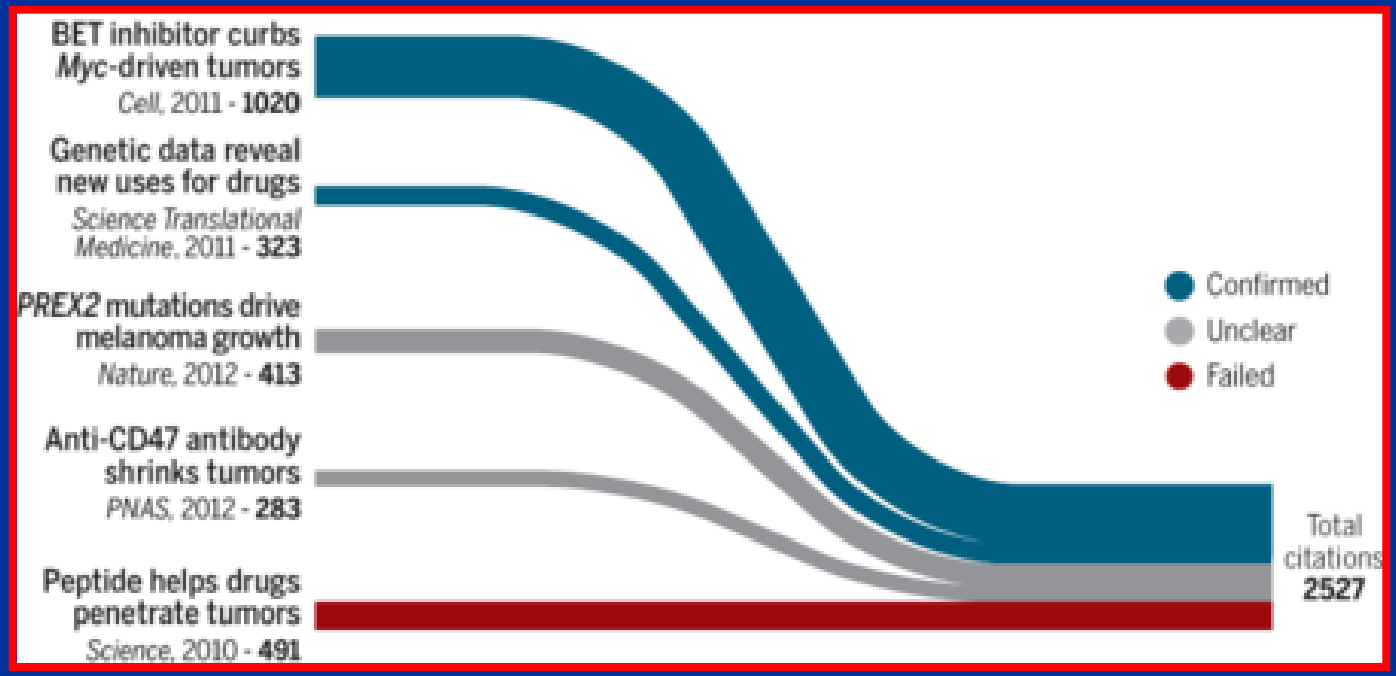
Freedman et al. PLoS Biol, 2015

Nature Survey, May 2016



Reproducibility Project: Cancer Biology

eLIFE



CANCER BIOLOGY

19 JANUARY 2017 | VOL 541 | NATURE

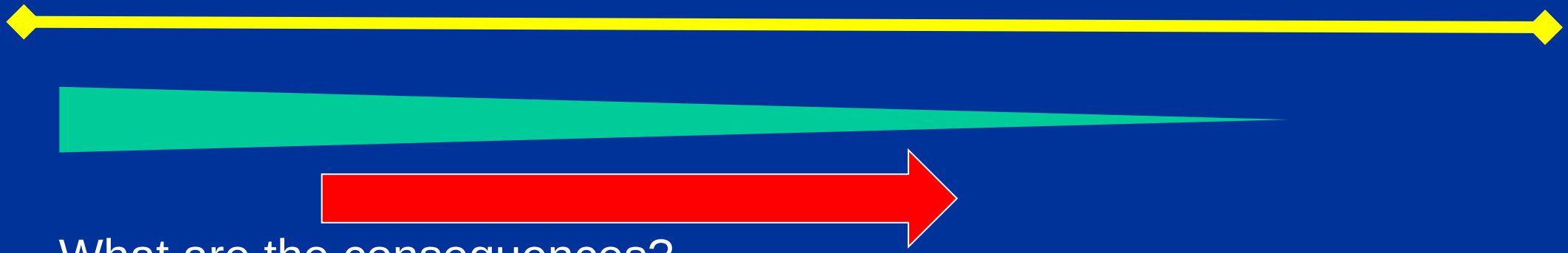
Reproducibility project yields muddy results

An ambitious effort to replicate cancer studies is provoking controversy.

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 Economics of Reproducibility in Preclinical Research

Leonard P. Freedman[1]*, Iain M. Cockburn[2], Timothy S. Simcoe[2,3]

1 Global Biological Standards Institute, Washington, D.C., United States of America, 2 Boston University School of Management, Boston, Massachusetts, United States of America, 3 Council of Economic Advisers, Washington, D.C., United States of America

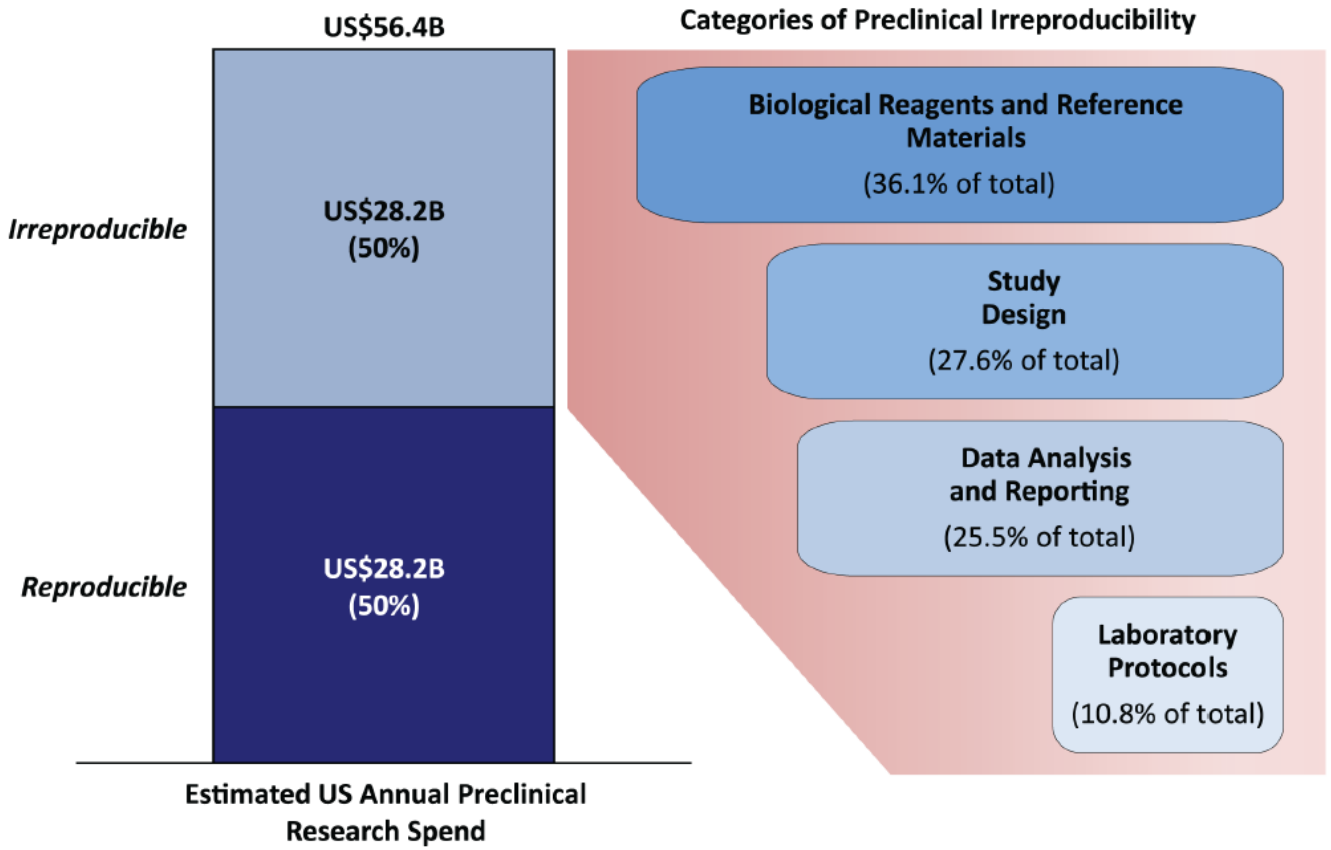


Fig 2. Estimated US preclinical research spend and categories of errors that contribute to irreproducibility. Note that the percentage value of error for each category is the midpoint of the high and low prevalence estimates for that category divided (weighted) by the sum of all midpoint error rates (see S1 Dataset). Source: Chakma et al. [18] and the American Association for the Advancement of Science (AAAS) [19].

Freedman et al. PLoS Biol, 2015

The Spectrum of Reporting Preclinical and Clinical Data

- Inappropriate Stats
- Cell line contamination
- Journals don’t like negative data
  - Therefore, PIs don’t like negative data

Selective Reporting of Laboratory Studies

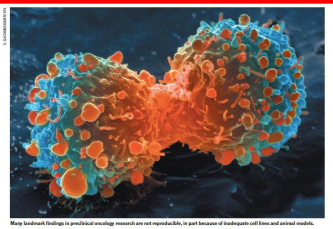
- Journals prioritize “positive” results
  - If a drug works in 2 cell lines, and does not in 8, we only see the results on the 2 cell lines
- Students, post-docs, ***and*** faculty need publications for advancement
  - *“Publish or perish”*
  - In many labs, 2 trainees work on the same project competing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

The Spectrum of Reporting Preclinical and Clinical Data

The more difficult issue to address

Let's Talk About "Misconduct"

Do Investigators Intentionally Falsify or Fabricate Data?



Many landmark findings in preclinical oncology research are not reproducible, in part because of inadequate cell lines and animal models.

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.

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

Stimulus-triggered fate conversion of somatic cells into pluripotency

Haruko Obokata[1,2,3], Teruhiko Wakayama[3]†, Yoshiki Sasai[4], Koji Kojima[1], Martin P. Vacanti[1,5], Hitoshi Niwa[6], Masayuki Yamato[7] & Charles A. Vacanti[1]

30 JANUARY 2014 | VOL 505 | NATURE

Does Misconduct Occur in the Clinic?

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

Keith will give a *great* talk on this case if I ever finish my talk!

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)

Ivan Oransky
RetractionWatch.com

Key Breast Cancer Study Was a Fraud

Los Angeles Times

April 27, 2001 | THOMAS H. MAUGH II and ROSIE MESTEL | TIMES MEDICAL WRITERS

A key study pointing to the effectiveness of high-dose chemotherapy and bone marrow transplants in treating metastatic breast cancer was based on faked data, cancer experts said Thursday.

The American Society of Clinical Oncology announced that an unscrupulous South African researcher, Dr. Werner Bezwoda, has led thousands of women with breast cancer to undergo expensive, debilitating and often fatal bone marrow transplants. His data were fraudulent, suggesting the controversial procedure was more effective than it actually is, the society concluded.

"Bezwoda . . . duped us all," Dr. Larry Norton, the organization's president-elect, said at a news conference.

The new revelations do not mean that bone marrow transplants are worthless, the oncology society said, only that they have not yet been proven effective. Several large clinical trials are underway to determine precisely how beneficial they are, and the society reiterated its position that women should undergo the procedure only if they are enrolled in a clinical trial.

The oncology society also urged insurance companies to help pay for ongoing clinical trials, but concluded that the companies had no responsibility to pay for bone marrow transplants performed outside those trials.

FALSE HOPE: BONE MARROW TRANSPLANTATION FOR BREAST CANCER

NEJM, 2007

By Richard A. Rettig, Peter D. Jacobson, Cynthia M. Farquhar, and Wade M. Aubry. 355 pp. New York, Oxford University Press, 2007. $49.95. ISBN 978-0-19-518776-2.

China's drug industry clinical trial data falsified

Companies were thought to be cutting corners because of the lack of profitability in China's pharmaceutical market.

By Jen Offord

October 2, 2016 17:46 BST

A government investigation in China has found that the result of 80% of the country's clinical trials are fabricated, according to a report.

The investigation, which took place over a year, examined data from 1,622 clinical trials of pharmaceutical drugs which were awaiting approval by the country's regulator for mass production, and found that there was no basis for the results recorded.

No Institute Is Immune!

Two Expressions of Concern in Blood for MD Anderson's Aggarwal, who has threatened to sue Retraction Watch

with 36 comments

Another withdrawal by MD Anderson's Aggarwal, again for unclear reasons

IRB mishap costs MD Anderson team a paper on prostate cancer

Third retraction for GWU biologist as university seeks to dismiss his $8 million lawsuit

The retracted paper, published in *Development* in 2004, "Metastasis-associated protein 1 deregulation causes inappropriate mammary gland development and tumorigenesis," analyzed the role of a protein, MTA1, in mammary gland development and cancer. It was published while Kumar was at M.D. Anderson in Houston, and has been cited 81 times, according to Thomson Scientific's Web of Knowledge.

We All Need to Be Aware of This Issue

Two more retractions appear for prominent MIT cancer researcher Robert Weinberg

with 8 comments

Possibly … als may have bee…

So in pl… like they ca… euphem…

As PIs, we have to keep track of data in real time, not just when ready for submission to *CNS*.

I don't know the lead researcher but noticed he won the Wolf Prize in Medicine in 2004 and is a member of the U.S. National Academy of Sciences. Though unclear at this point, if postdocs were responsible, it serves as a cautionary tale – be vigilant! The most innocent seeming postdoc, staff scientist, or graduate student may be manipulating data or doing other bad things behind your back! Double check everything! The lab director is ultimately responsible!

An IRB Approved Survey Conducted at The MD Anderson Cancer Center

OPEN ACCESS Freely available online

PLOS ONE

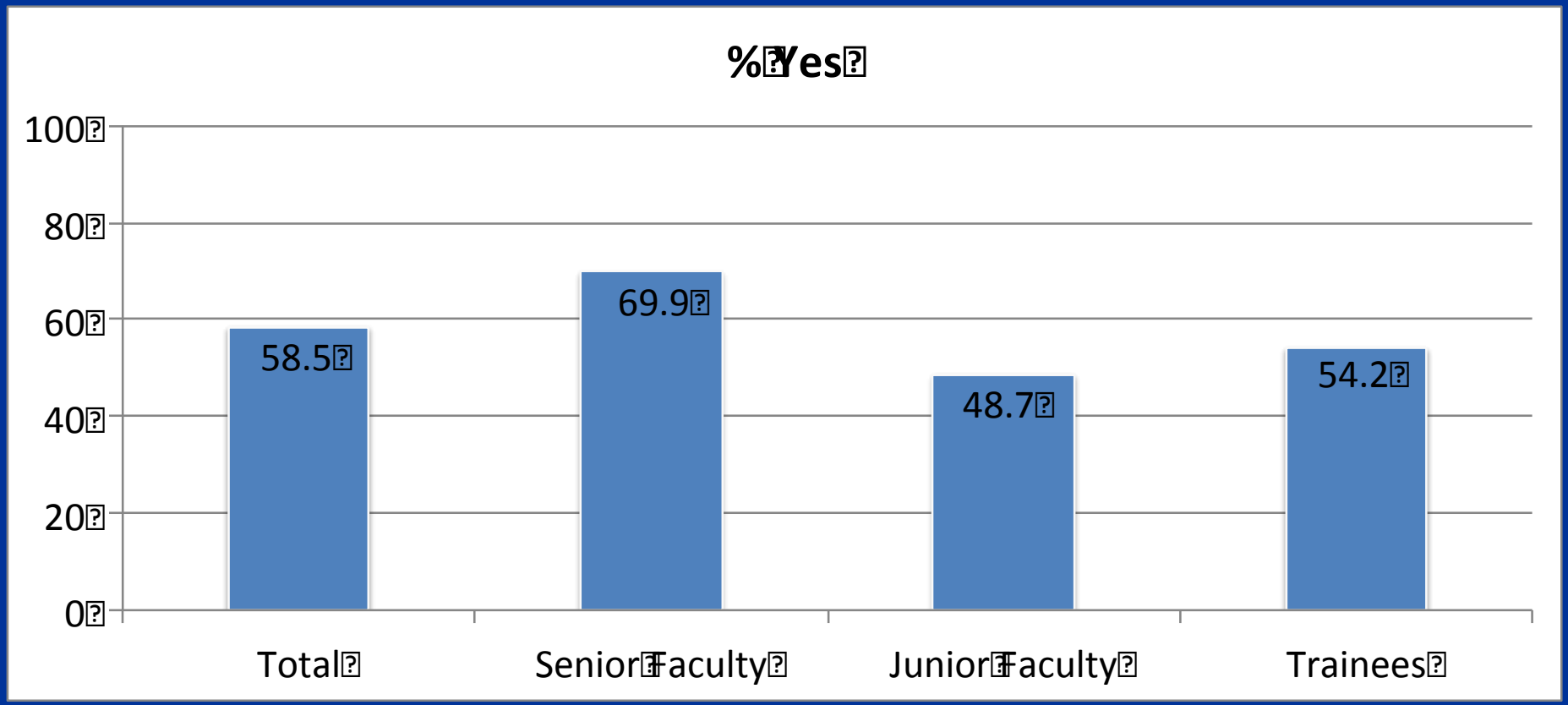
A Survey on Data Reproducibility in Cancer Research Provides Insights into Our Limited Ability to Translate Findings from the Laboratory to the Clinic

Aaron Mobley[1], Suzanne K. Linder[2], Russell Braeuer[1], 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?



Mobley at al. PlosOne 2013

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%

Mobley at al. PlosOne 2013

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 condenmed. 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 is ….from 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. Boulbes, Tracy Costello, Keith Baggerly, Fan Fan, Rui Wang, Rajat Bhattacharya, Xiangcang Ye, and Lee M. Ellis

Under first review at Clinical Cancer Research

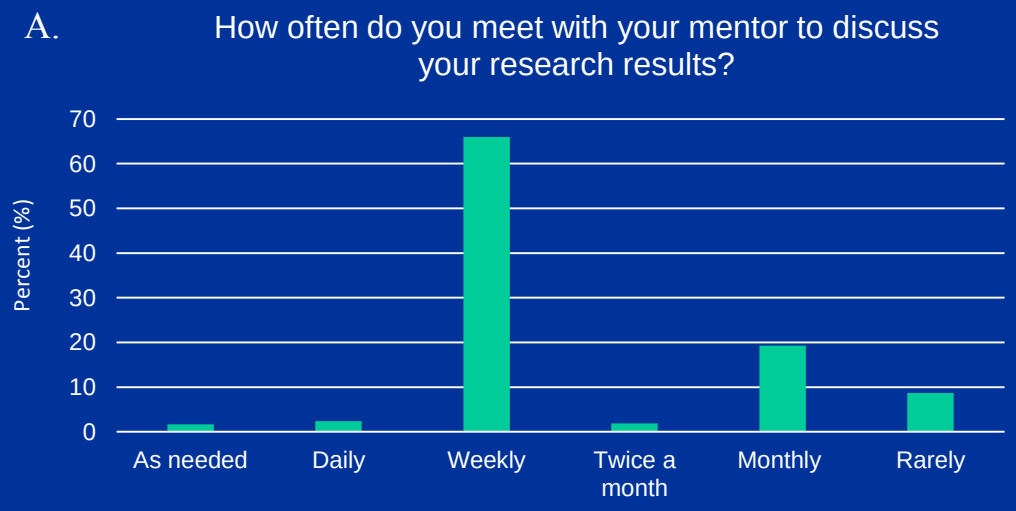
Population Characteristics (n=467)

Characteristics	N (%)
Population	Students 10.7%
	Postdocs 89.3%
Field of expertise	Cancer Biology 60.6%
	Biology (Other) 10.5%
	Neuroscience 6.9%
	Microbiology/Virology 6.2%
	Biotechnology 4.5%
	Immunology 2.6%
	Chemistry 2.5%
	Physics 2.6%
	Molecular Biology/Biochemistry 1.9%
	Plant Biology 1.7%
Career goals	PI in Academia 39.4%
	Undecided 40.9%
	Industry/Private sector 11.8%
	Academia/Government (Other) 2.6%
	Writing/Editing/Publishing 1.4%
	Science Policy/Regulatory Affairs 1.3%
	Other 2.6%

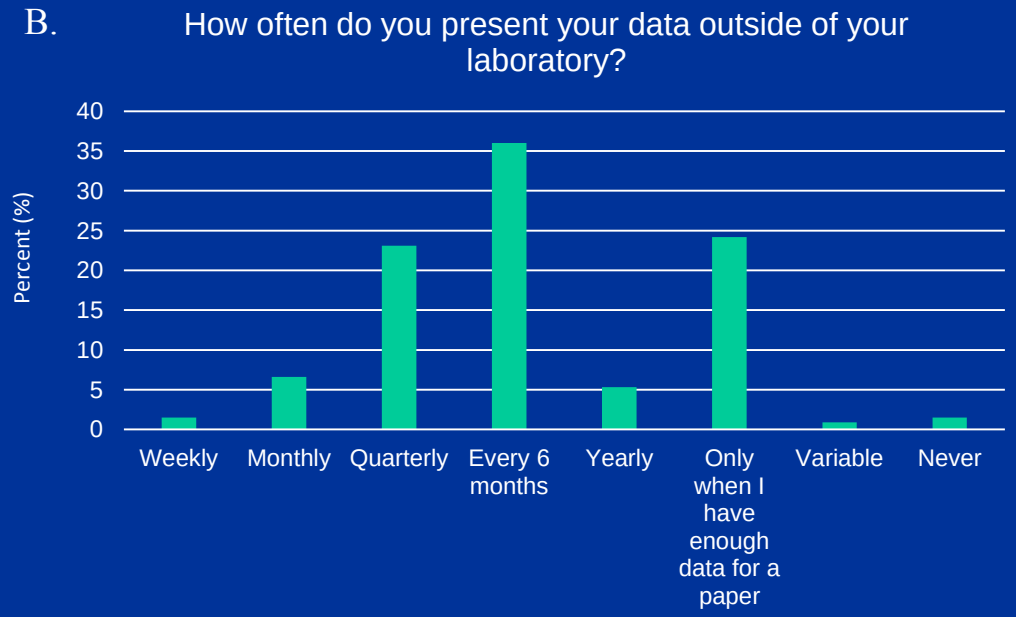
eligibility criteria of 1) being a graduate student or postdoctoral fellow and 2) performing bench science, 467 of our total 576 respondents were deemed eligible.

Mentors supervision

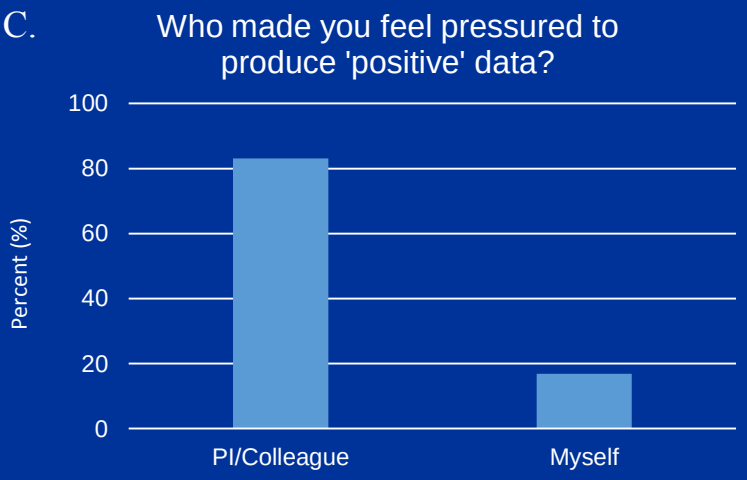
A.



B.



C.

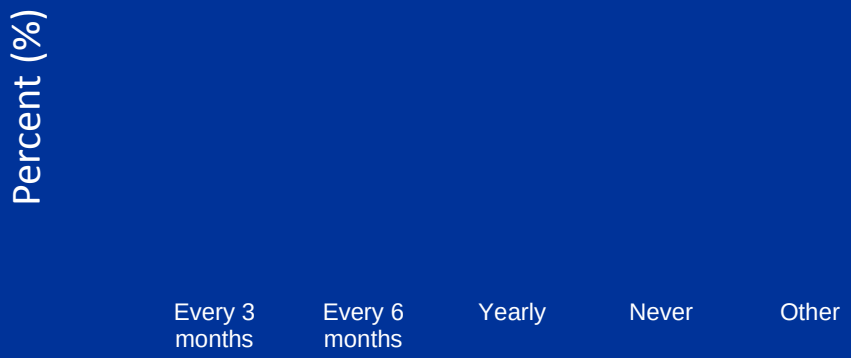


We Will Now Use The Audience Response System

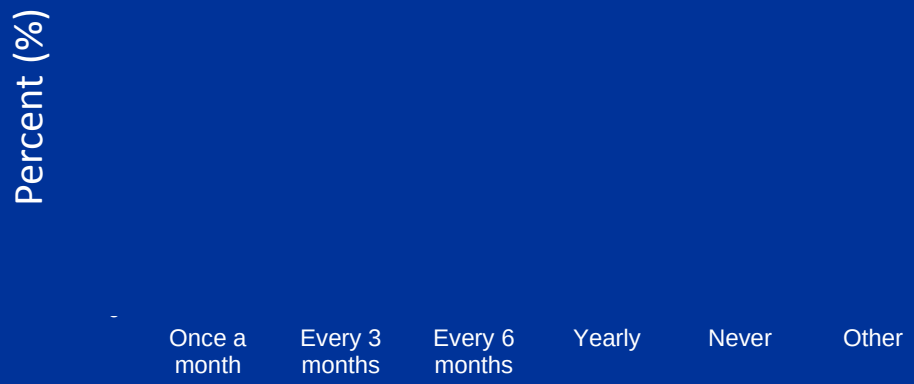
Raise your hand

Best Research Practices

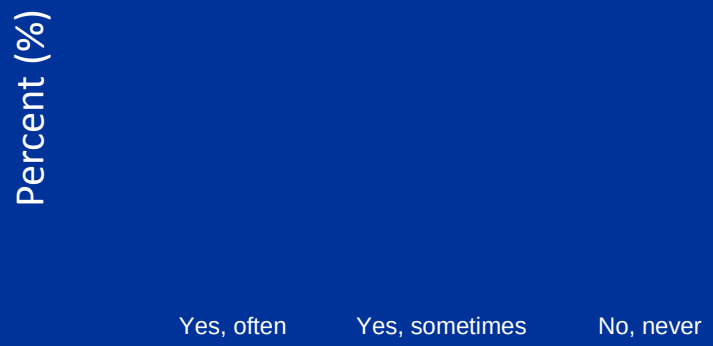
How often do you authenticate your cell lines to be sure of their true identity?



How often do you test your cell lines for possible mycoplasma contamination?



Do you and your lab collaborators perform blinded studies?

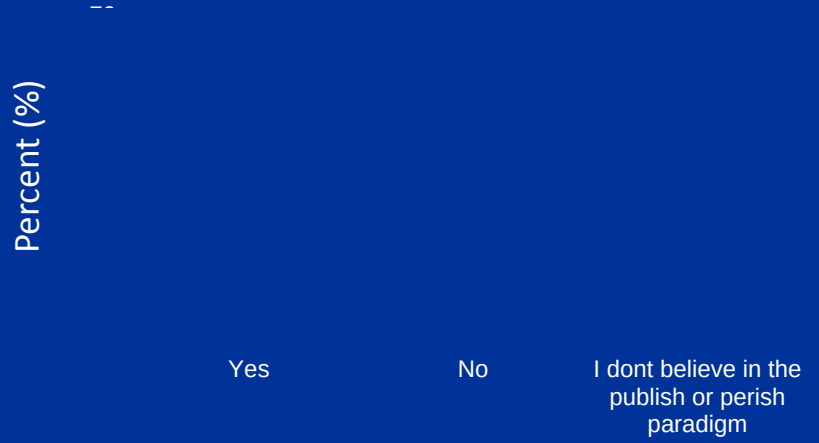


Do you consult with statisticians regarding your studies?

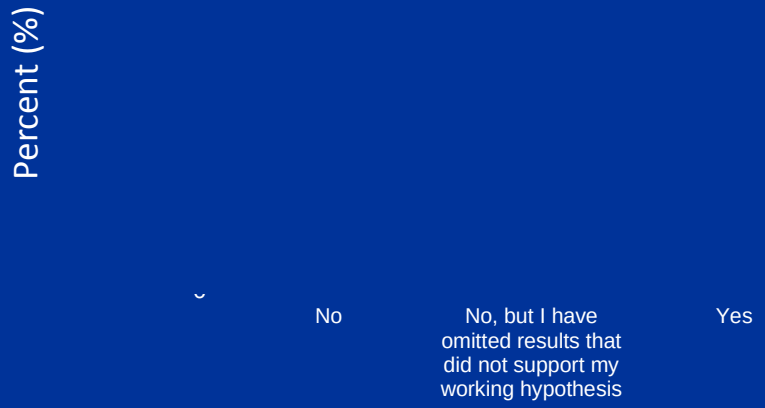
Research Integrity and Reporting Transparency

Do you feel that it is necessary to have a first authored publication in a Cell, Nature, or Science journal when seeking an academic position?

Do you feel the pressure of the 'publish or perish' system influences the way you report your data?



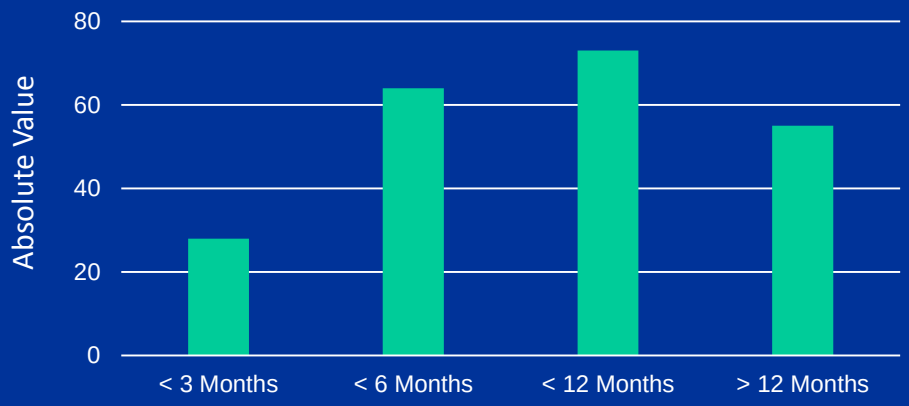
Have you ever fabricated/falsified data?



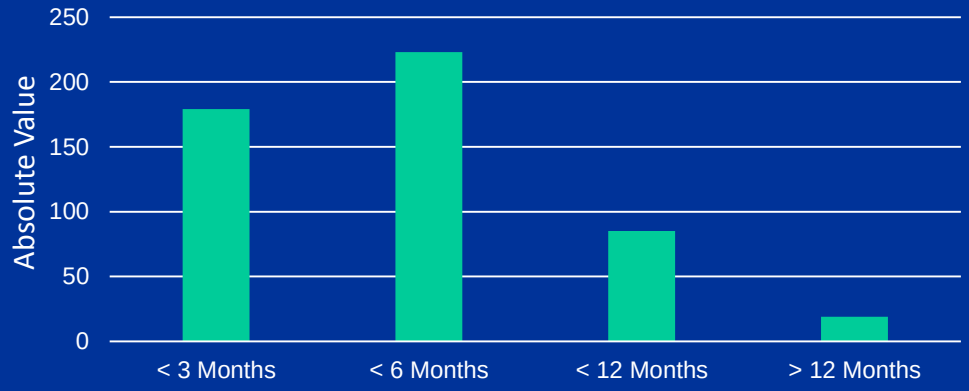
Have you ever witnessed someone fabricating/falsifying data to complete a project

Publications Process

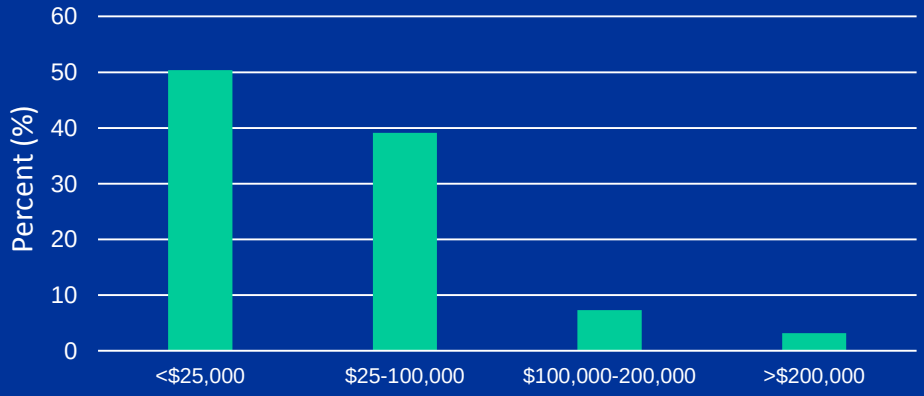
When your manuscript is submitted and accepted by a high impact journal, how long is the average revision process?



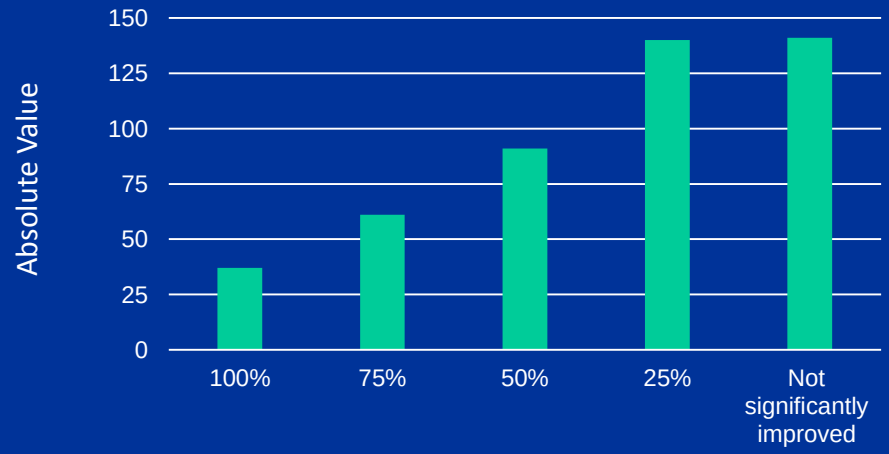
When your manuscript is submitted and accepted by a low impact journal, how long is the average revision process?



After revision, can you estimate the cost of the revision including salaries and cost of supplies and services?



After revisions, how much more convincing is the major finding reported in the manuscript?



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

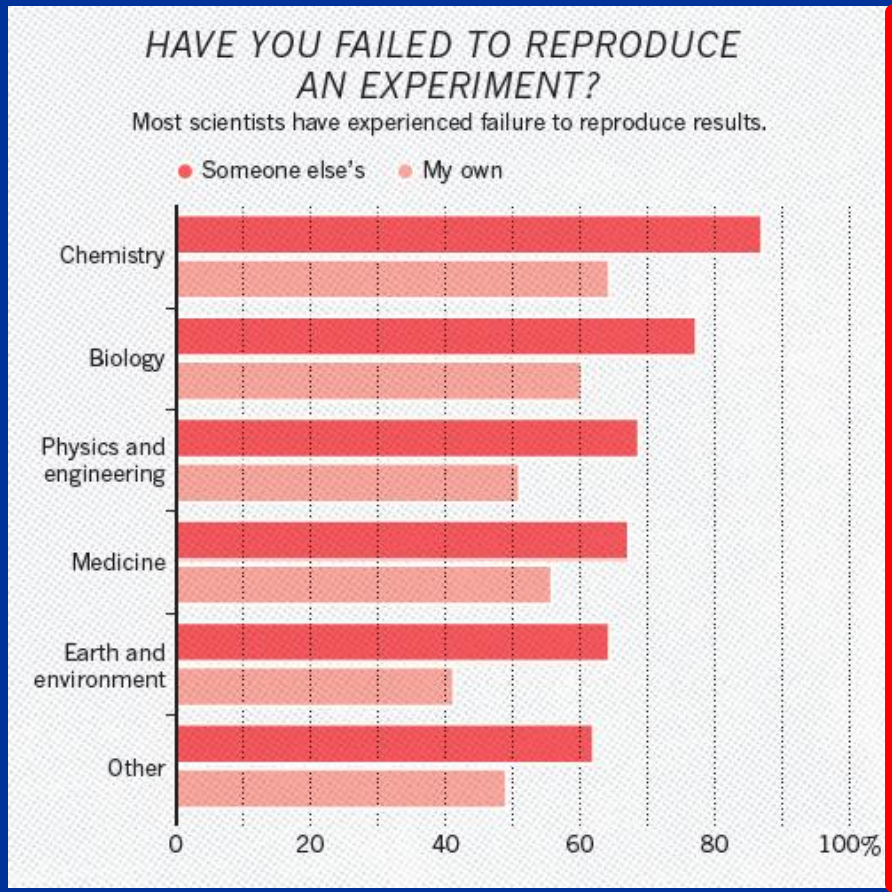
- Integrity of laboratory research and how this impacts clinical outcomes
  - The issue at hand
    - The spectrum
  - Why does this occur?
  - What can we do to fix this?

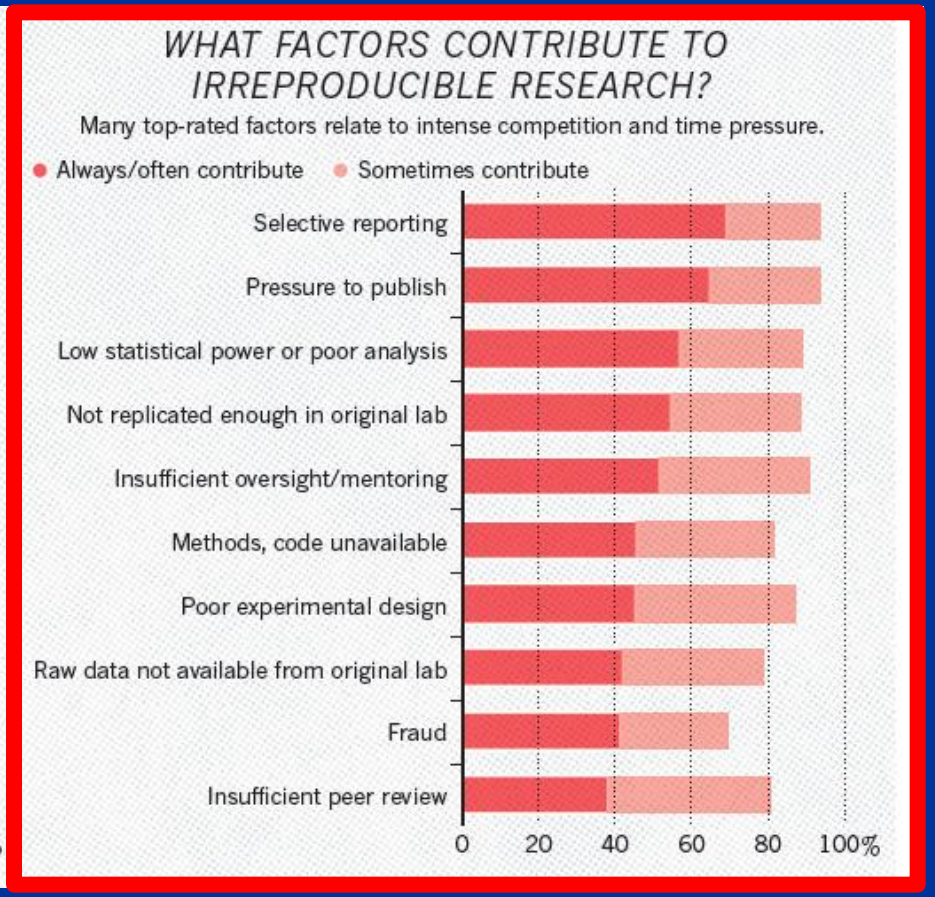
Audience participation: Find the Fraud

Causes of “Massaging” of Data

Trainees	Faculty
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	
Need high impact publications to obtain a job (or many pubs)	
Cannot leave that lab as a post-doc, or cannot complete thesis as a student, unless you have a high impact publication	

Nature Survey, May 2016





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?

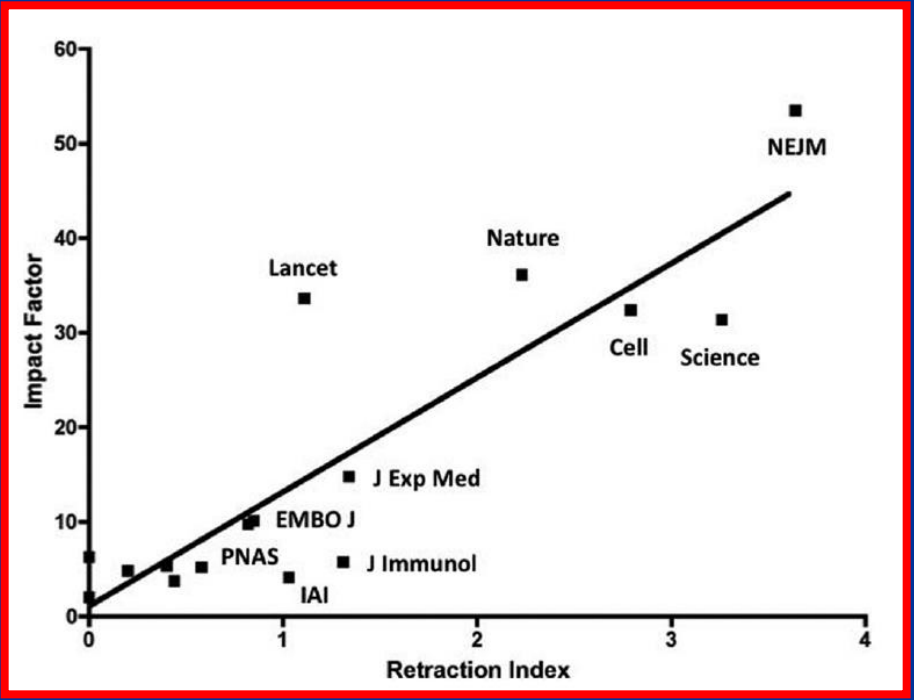
Nathan S. Blow, Ph.D., Editor-in-Chief, *BioTechniques*

Fang and Casadevall
Infection and Immunity, 2011

EDITORIAL

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 [a]Laboratory Medicine and [b]Microbiology, University of Washington School of Medicine, Seattle, WA 98195; [c]MediCC! Medical Communications Consultants, Chapel Hill, NC 27517; and [d]Department 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.

One final comment on impact factor mania!

I Wonder if This Paper Would Be Accepted Today?

April 25, 1953 NATURE

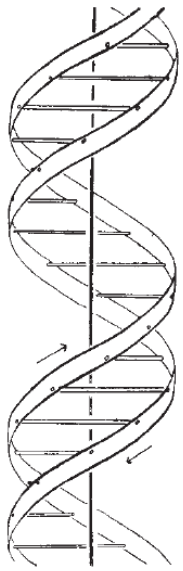
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There

J. D. Watson
F. H. C. Crick
Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

Hypothetical reviewer comments

- *Only 2 authors?*
- *No data, simply building on of the work of others*
- *Unlikely be cited often*
- *Better off suited for a specialty journal*

Impact Factor at Time of Publication vs *Actual Impact*

Highest *Impact Factor* Publications (IF)

- Cancer Cell (24)
- JNCI x 2 (13)
- JCI (17)

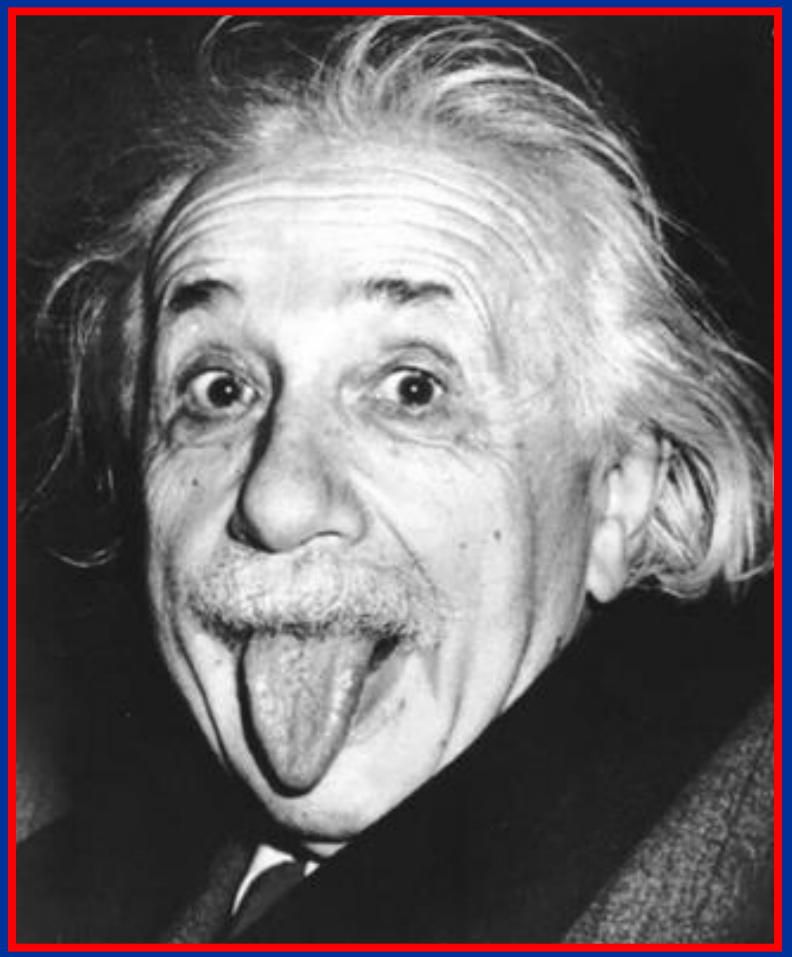
Publications with *Actual Impact* – clinical (IF)

- Cancer Research (8)
- Clinical Cancer Research (6)
- JCO (11)

Our Current Research Metrics Are Crazy!!!!

The ***h*-index** is an author-level metric that attempts to measure both the productivity and citation impact of the publications of a scientist or scholar.

>



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?

The erosion of research integrity: the need for culture change

Panel: **Suggested approaches to improve data reproducibility in preclinical studies***

Publication requirements:

- Appropriate statistical analysis determined a priori
- Use of REMARK biomarker criteria
- Expanded methods sections
- Expedited data deposition to public databases
- Cell line identification confirmation
- Validation of reagents including antibody specificity
- Blinded assessments by at least two independent observers
- Pre-established inclusion and exclusion criteria
- Sign off by all coauthors that all relevant data, both positive and negative, have been submitted either in the manuscript or online
- Expanded materials and methods sections online
- Change the emphasis of the NIH biosketch (abbreviated CV) to highlight actual contributions to science and medicine
- Assessment of faculty candidates should include more than the number of publications in high-impact journals
- Sharing of unique resources (eg, cell lines and mouse models) with a standard single page material transfer agreement
- Journals should allow and encourage publication of negative results
- Journals should allow so-called imperfect data—biology is not all or none
- Mechanisms for online feedback on studies (eg, PubPeer, PubMed Commons) and allow commentary without the need for a subscription
- Reviewers of manuscripts should focus on the most relevant issues, and limit requests for additional studies that are not necessary for the underlying theme of the study
- Appropriately severe punishment for investigators found guilty of research misconduct (eg, ban such scientists from obtaining government funding for research)
- Provide academic security for people who report unethical behavior (so-called whistle blowers)
- The principal investigator should be responsible for keeping track of data in real time, so that deviations from the so-called perfect story are noted early; the principal investigator should be held responsible for the integrity of all data, and for inclusion of all relevant studies, whether they are negative or positive
- Journals should welcome publications validating or refuting previous publications
- Published articles should not be convoluted and should have a clear message; dense articles are difficult to review, probably leading to suboptimal reviews and requests for irrelevant experiments
- Allow submission of negative data in response to primary reviews of manuscripts; the temptation to selectively report positive data is probably highest when a paper is under revision

*Some have already been implemented.

Feb, 2018

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

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

2016

Case Summary: Cullinane, Andrew R.
Case Summary: D'Souza, Karen M.
Case Summary: Forbes, Meredyth M.
Case Summary: Li, Zhiyu
Case Summary: Malhotra, Ricky
Case Summary: Pastorino, John G.
Case Summary: Walker, Kenneth

2017

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

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 funds 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

-MLA/CC: W. Plunkett

INHERENT CONFLICT OF INTEREST

Mechanism for Addressing Misconduct Is Institutional Dependent

- Allegations may be brought to Departme…, Division Head, or to the Provost and …ive Vice President (EVP)
- Provost & EVP and Rese… …egrity Officer (RIO) will assess the allegations
- Information-g… …g and initial fact finding.
  - Co… …y an Inquiry Panel of at least 3 faculty chosen by …& EVP and the Res Integrity Officer.

INHERENT CONFLICT OF INTEREST

Bill Plunkett, PhD

If you trust no one at your own institute….

- Most Universities *(or University systems)* have a website for abuse, fraud, and/or unethical behavior

"….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,….."