



Research Integrity and Scientific Misconduct

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Office of Research Integrity
Office of Accountability and Compliance

SON Research Seminar
9.21.23

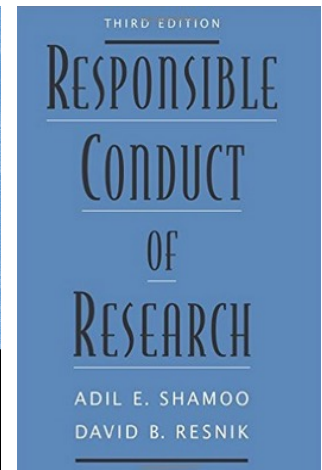
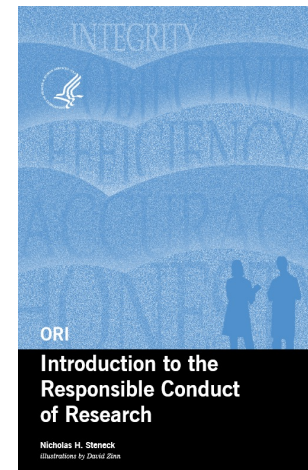


Defining Research Integrity

- the use of honest and verifiable methods in proposing, performing, and evaluating research
- reporting research results with particular attention to adherence to rules, regulations, guidelines
- following commonly accepted professional codes or norms

R³ → Rigor, Reproducibility, and Responsibility

RCR → Responsible Conduct of Research





Standard RCR Topics



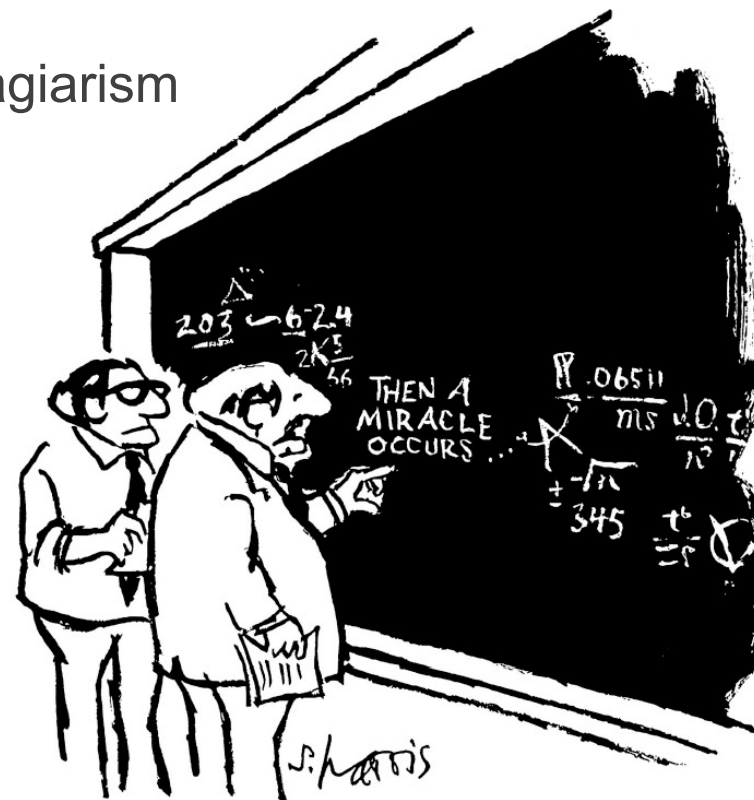
- Research Misconduct
- Conflict of Interest
- Human Subject Protections
- Laboratory Animal Welfare
- Mentor/Mentee Relationship
- Collaborative Science
- Peer Review
- Authorship and Publication
- Data Acquisition and Analysis
- Secure and Ethical Data Use
- Safe Research Environments



Defining Research Misconduct

FFP → Fabrication, Falsification, or Plagiarism

- in proposing, performing, or reviewing research, or in reporting research results
- Defined in 42 CFR § 93.103 Code of Federal Regulations



"I think you should be more explicit here in step two."



Cases that triggered federal changes

- Several cases of misconduct disclosed to the public 1974-1981

“Patchwork Mouse”

> [Transplant Proc.](#) 1973 Mar;5(1):707-10.

Acceptance of phenotypically differing cultured skin in man and mice

W T Summerlin, C Broutbar, R B Foanes, R Payne, O Stutman, L Hayflick, R A Good

PMID: 4633094



Fact, fiction and fraud

Michael Stoker

The Patchwork Mouse: Politics and Intrigue in the Campaign to Conquer Cancer. By Joseph Hixson. Pp. x+228. (Anchor/Doubleday: Garden City, New York, 1976). \$7.95.

In this book Joseph Hixson tells the story of Dr William Summerlin, and much more besides. Summerlin, a dermatologist turned immunologist, claimed that tissue which had been kept in culture could be grafted across transplantation, even species, barriers. But, in 1974, when working at the Sloan-Kettering Institute in New York, he



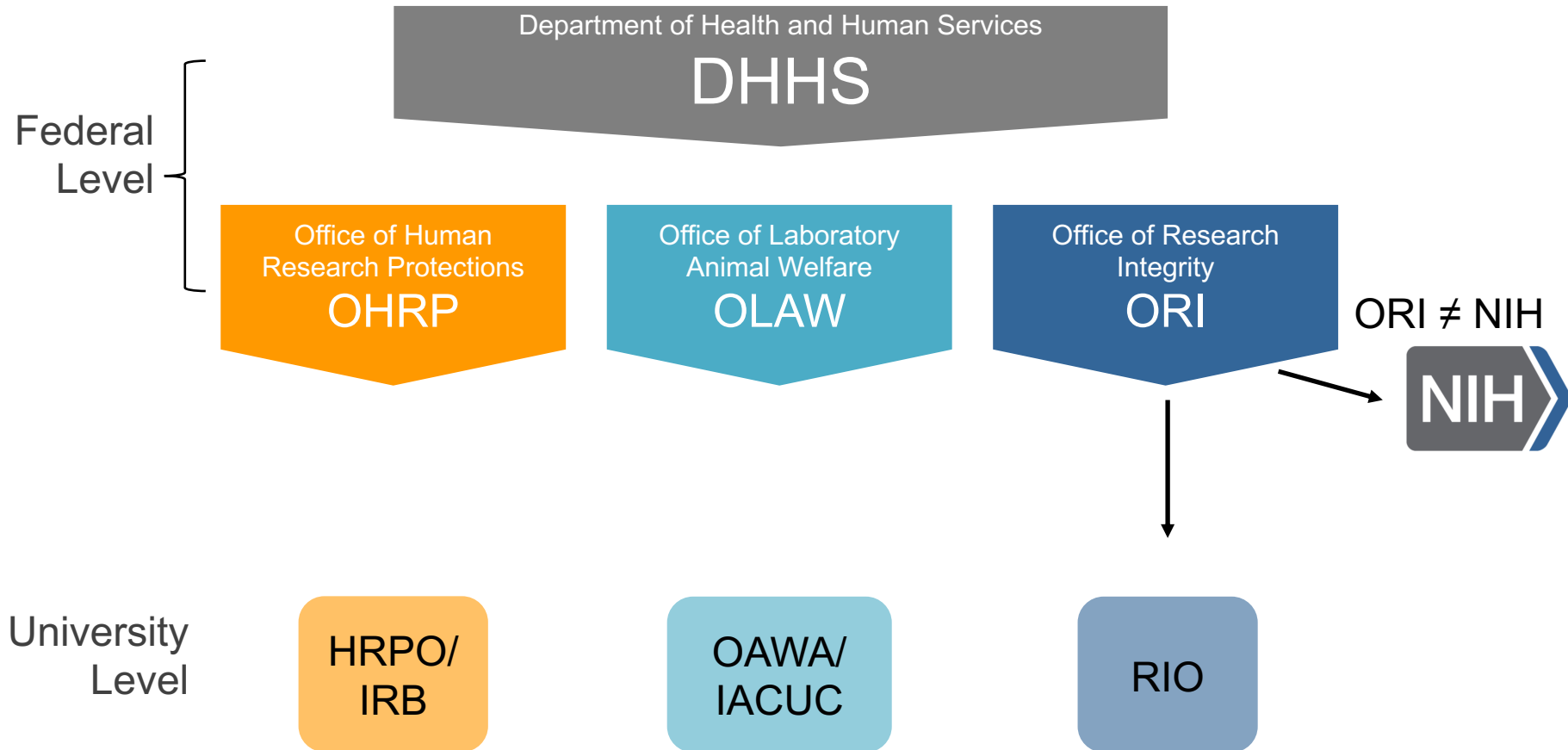
was caught red (or rather black) handed after using a felt pen to touch up some supposedly successful pigmented skin grafts in white mice. The subsequent enquiry revealed other evidence or de-

©1976 Nature Publishing Group

- Office of Research Integrity (ORI) formed in 1992



Research oversight





HRPO/
IRB

Institutional Review Board

- Risks to subjects are minimized
- Selection of subjects is equitable
- Obtain and document informed consent
- Prior approval for any protocol deviation
- Protection of privacy of subject and confidentiality of data



"These medicines all taste pretty good—let's approve them."



OAWA/
IACUC

Institutional Animal Care and Use Committee

- Review and approve all animal use research proposals
- Review the institution's animal care program
- Inspect (at least twice a year) the institution animal facility
- Receive and review concerns raised about the care and use of animals





RIO

Research Integrity Office

- Promote Research Integrity
- Investigate Research Misconduct

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UMB Policy and Procedures Concerning Research Misconduct Section III-1.10(A)

- Integrity in research is the responsibility of the entire academic community.
- All members of the university community (students, staff, faculty, and administrators) share responsibility for developing and maintaining standards to assure honesty, accuracy and objectivity in science.
- Misconduct in carrying out academic activities undermines the integrity of the educational system and the scientific enterprise, and erodes the public trust in the university community



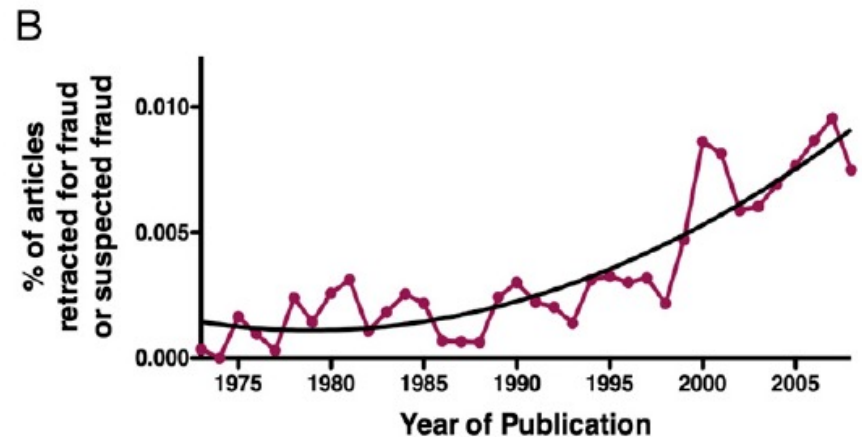
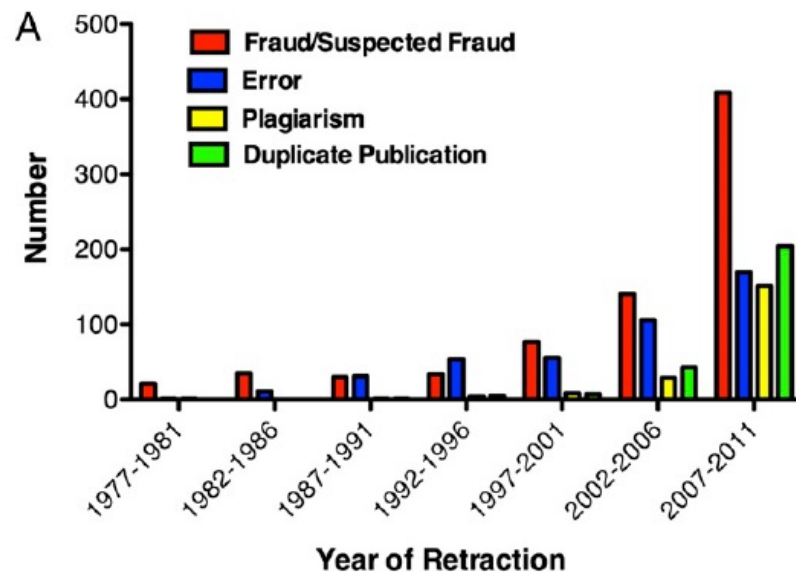
“FFP” of Research Misconduct

- Fabrication
 - making up data or results and recording or reporting them
- Falsification
 - manipulating research materials, equipment, or processes, or changing or omitting data/results such that the research is not accurately represented in the record
- Plagiarism
 - appropriation of another person’s ideas, processes, results, or words without giving appropriate credit

Does NOT include honest errors or differences in opinion

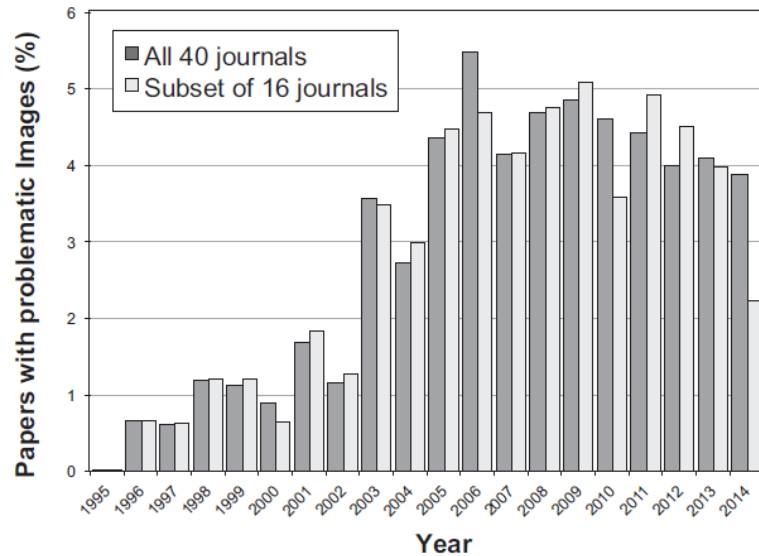
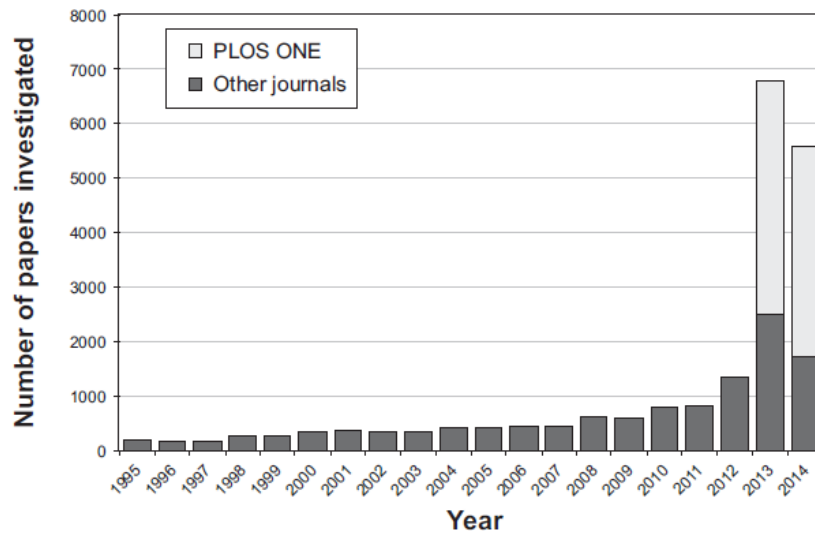


Misconduct accounts for the majority of retractions





Prevalence of inappropriate image duplication (subset)

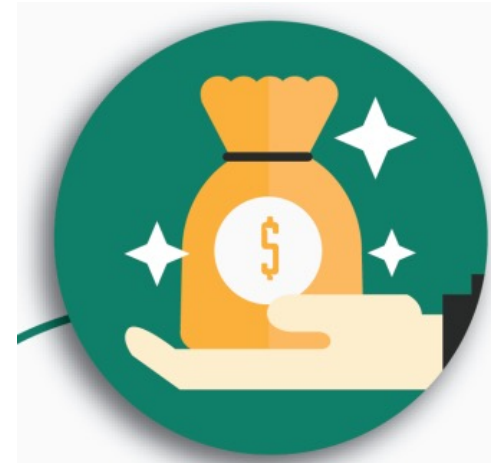




Impacts of Research Misconduct: Funding

- 291 articles retracted from 1992-2012

~\$2,324,906,182 in
NIH grant funding



- Just the tip of the iceberg → not all misconduct results in retractions



Impacts of Research Misconduct: Public Health

- Example of vaccination status

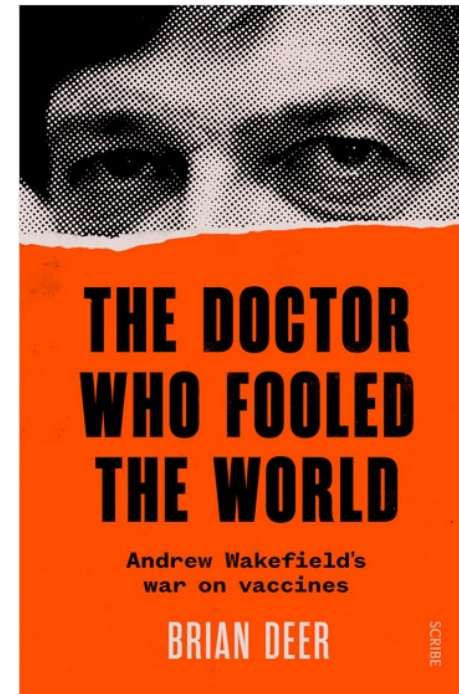
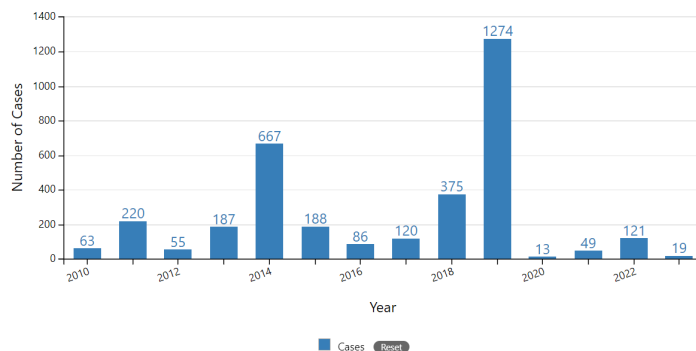
Table 3. Most Cited Retracted Articles

First author	Journal	Year published	Year retracted	Times cited*	Reason for retraction
Wakefield	<i>Lancet</i>	1998	2004; 2010	758	Fraud
Reyes	<i>Blood</i>	2001	2009	740	Error
Fukuhara	<i>Science</i>	2005	2007	686	Error
Nakao	<i>Lancet</i>	2003	2009	626	Fraud
Chang	<i>Science</i>	2001	2006	512	Error
Kugler	<i>Nature Medicine</i>	2000	2003	494	Fraud
Rubio	<i>Cancer Research</i>	2005	2010	457	Error
Gowen	<i>Science</i>	1998	2003	395	Fraud
Makarova	<i>Nature</i>	2001	2006	375	Error
Hwang	<i>Science</i>	2004	2006	368	Fraud
Potti	<i>The New England Journal of Medicine</i>	2006	2011	361	Fraud
Brugger	<i>The New England Journal of Medicine</i>	1995	2001	336	Fraud
Van Parijs	<i>Immunity</i>	1999	2009	330	Fraud
Potti	<i>Nature Medicine</i>	2006	2011	328	Fraud
Schön	<i>Science</i>	2000	2002	297	Fraud
Chiu	<i>Nature</i>	2005	2010	281	Error
Cooper	<i>Science</i>	1997	2005	264	Fraud
Le Page	<i>Cell</i>	2000	2005	262	Error
Kawasaki	<i>Nature</i>	2004	2006	243	Fraud
Hwang	<i>Science</i>	2005	2006	234	Fraud

*As of June 22, 2012

Number of measles cases reported by year

2010-2023* (as of June 8, 2023)





Impacts of Research Misconduct: Institution Reputation

Duke University to Pay \$112.5 Million to Settle Claims of Research Misconduct

The New York Times

 Share full article  



Duke University's medical school. A dozen papers by a former researcher in the pulmonary, allergy and critical care department have been retracted since reports of falsified data surfaced. Madeline Gray for The New York Times

In a statement announcing the settlement, Vincent E. Price, president of Duke University, said that the payment would include reimbursement of the grants obtained as a result of the falsified data, as well as additional penalties.

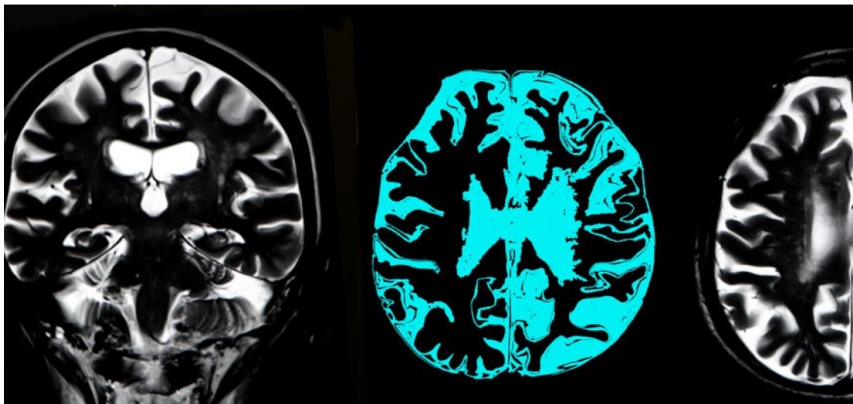
“This is a difficult moment for Duke,” Dr. Price said. “This case demonstrates the devastating impact of research fraud and reinforces the need for all of us to have a focused commitment on promoting research integrity and accountability.”



Research Misconduct in the news

Explosive Report Claims a Leading Alzheimer's Theory May Use Fabricated Results

HEALTH 25 July 2022 By MARIANNE GUENOT, BUSINESS INSIDER



Haruko Obokata, a researcher at the Riken Center for Developmental Biology, at a news conference in Osaka, Japan, in April. After having two articles published in the journal Nature, she was accused of fabricating data and of plagiarism. Kimimasa Mayama/European Pre-Agency

ty to clinical trial



Stanford president's research under investigation for scientific misconduct, University admits 'mistakes'



The New York Times

Stanford President Will Resign After Report Found Flaws in His Research

Marc Tessier-Lavigne was cleared of accusations of scientific fraud and misconduct. But the review said his work had "multiple problems" and "fell below customary standards of scientific rigor."

(Graphic: MICHELLE FU/The Stanford Daily)



Scientists behaving badly

Table 1 Percentage of scientists who say that they engaged in the behaviour listed within the previous three years (n = 3,247)			
Top ten behaviours	All	Mid-career	Early-career
1. Falsifying or 'cooking' research data	0.3	0.2	0.5
2. Ignoring major aspects of human-subject requirements	0.3	0.3	0.4
3. Not properly disclosing involvement in firms whose products are based on one's own research	0.3	0.4	0.3
4. Relationships with students, research subjects or clients that may be interpreted as questionable	1.4	1.3	1.4
5. Using another's ideas without obtaining permission or giving due credit	1.4	1.7	1.0
6. Unauthorized use of confidential information in connection with one's own research	1.7	2.4	0.8 ***
7. Failing to present data that contradict one's own previous research	6.0	6.5	5.3
8. Circumventing certain minor aspects of human-subject requirements	7.6	9.0	6.0 **
9. Overlooking others' use of flawed data or questionable interpretation of data	12.5	12.2	12.8
10. Changing the design, methodology or results of a study in response to pressure from a funding source	15.5	20.6	9.5 ***
Other behaviours			
11. Publishing the same data or results in two or more publications	4.7	5.9	3.4 **
12. Inappropriately assigning authorship credit	10.0	12.3	7.4 ***
13. Withholding details of methodology or results in papers or proposals	10.8	12.4	8.9 **
14. Using inadequate or inappropriate research designs	13.5	14.6	12.2
15. Dropping observations or data points from analyses based on a gut feeling that they were inaccurate	15.3	14.3	16.5
16. Inadequate record keeping related to research projects	27.5	27.7	27.3

Note: significance of χ^2 tests of differences between mid- and early-career scientists are noted by ** ($P < 0.01$) and *** ($P < 0.001$).



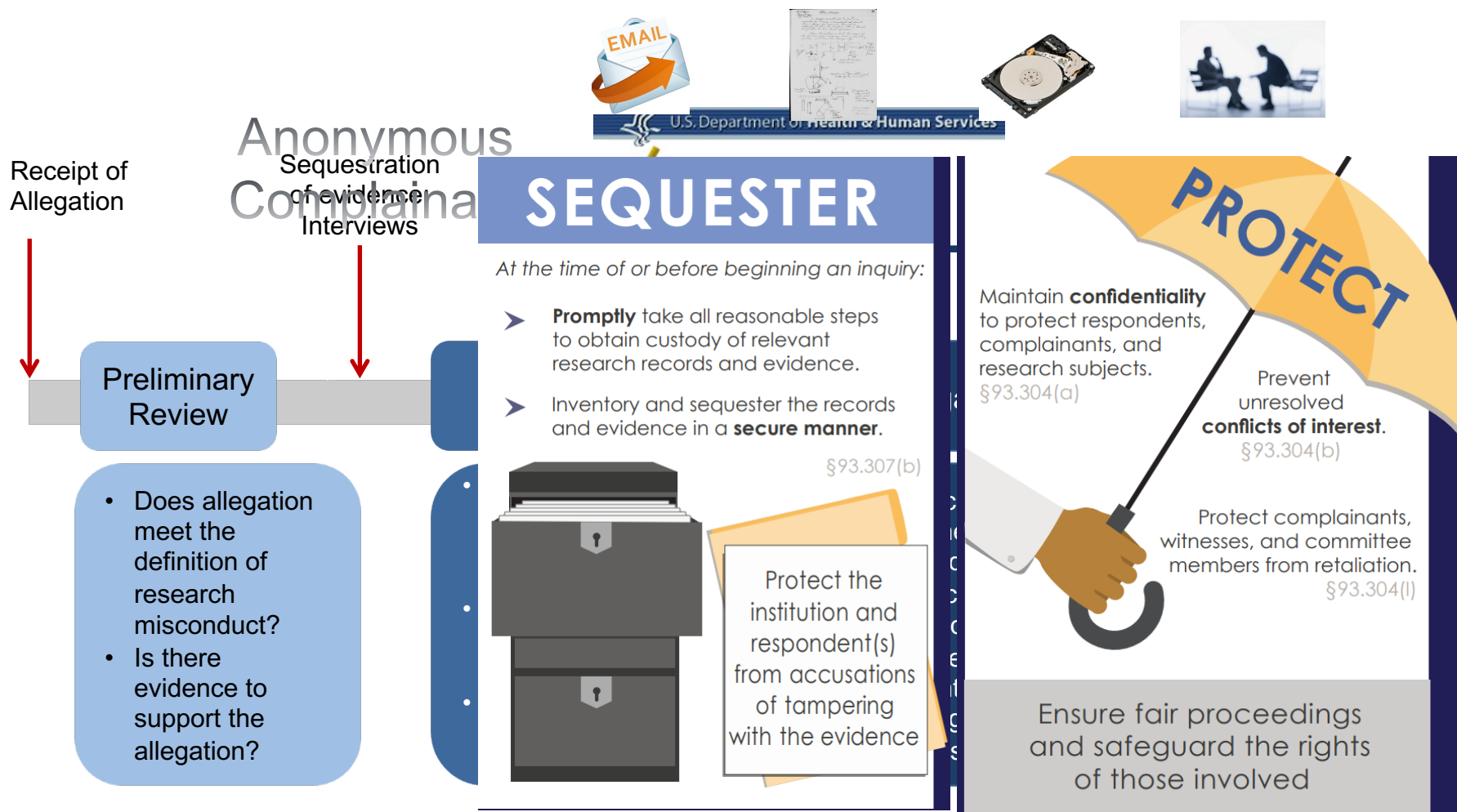
How do we investigate an allegation of misconduct?

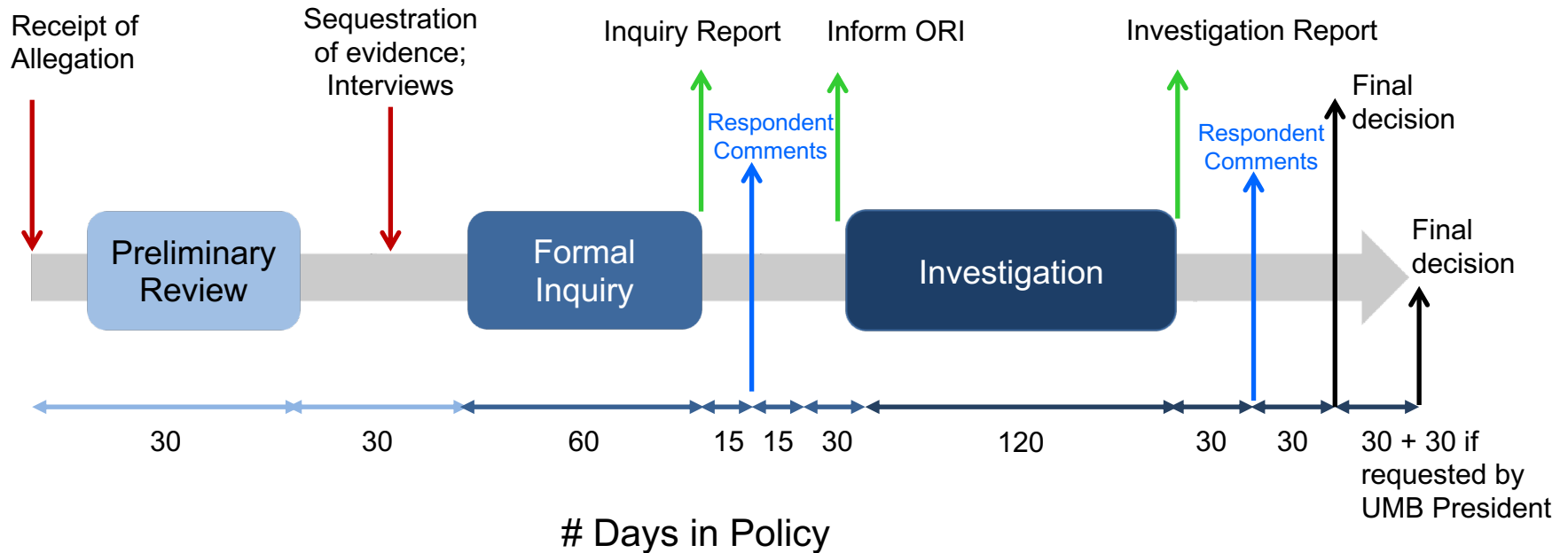




Requirements for a finding of Research Misconduct

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







Outcomes to findings of misconduct

Correct the scientific record!

- Paper corrections (in cases of honest error as well)
 - Retractions
 - Special training
 - Research oversight
-
- Prohibited from serving in an advisory capacity
 - Funding withheld (ORI)
 - Funding barred for X number of years (by ORI)
 - Money returned by institution
 - Termination of position



Research Misconduct involving Clinical Research

- Falsification
 - substituting subject records
 - altering the dates and results from visits and studies
 - altering the results of particular tests on blood samples to show that the test accurately predicted a disease or relapse
 - backdating to fit the time window determined by the study protocol
 - falsifying the times that samples were collected
- Fabrication
 - creating records of interviews of subjects that never occurred
 - making up progress notes for patient visits
 - preparing records for deceased subjects



Research Misconduct involving image manipulation

- Playing with contrast to remove unwanted data
- Changing raw data
- Falsification of blots
- Painting with Photoshop
- Cherry picking pictures
- Fabrication of controls

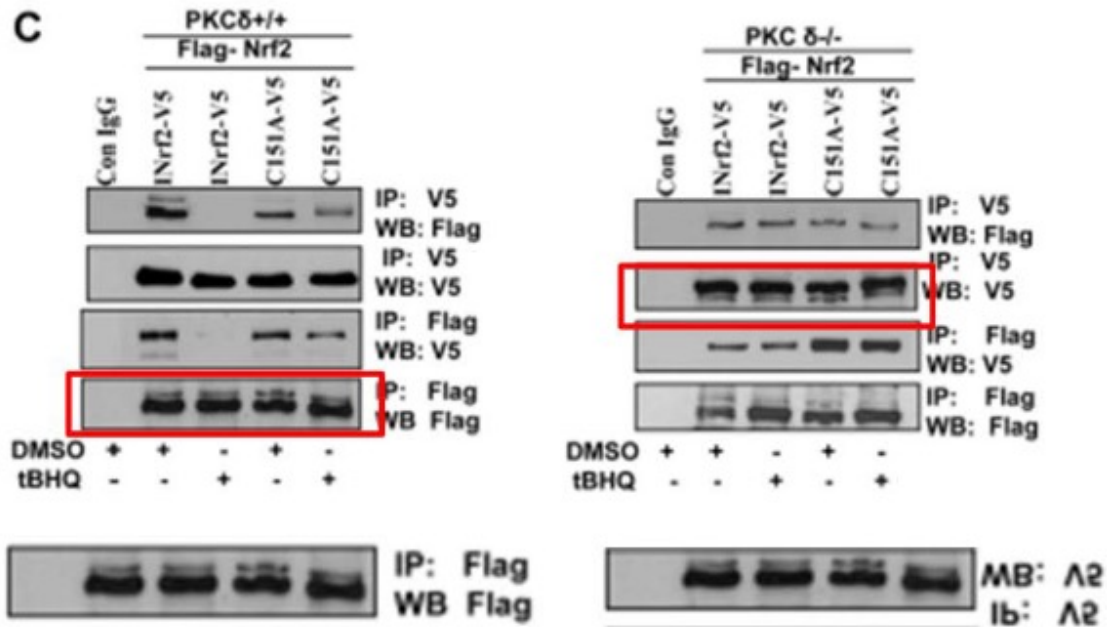
67%

ORI misconduct cases
involved image
manipulation 2011-2015



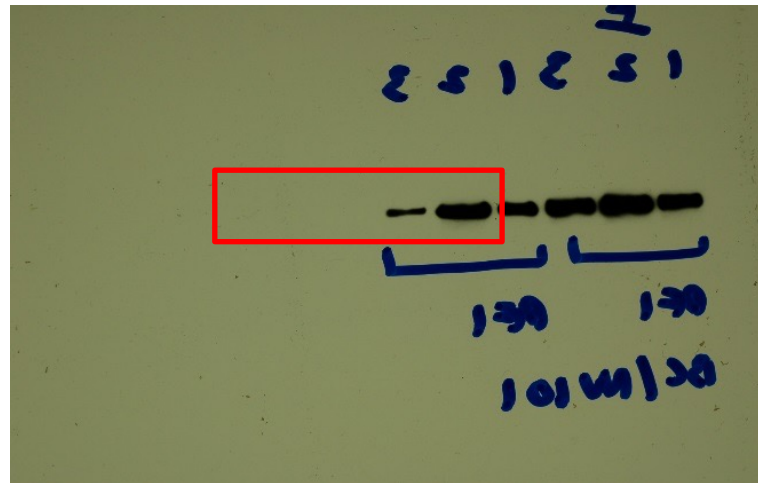
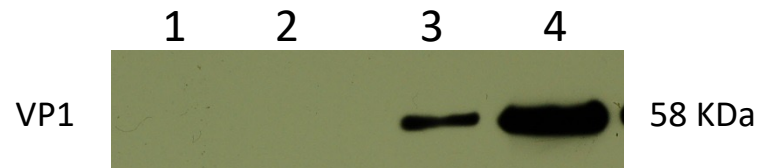


Falsifying blots



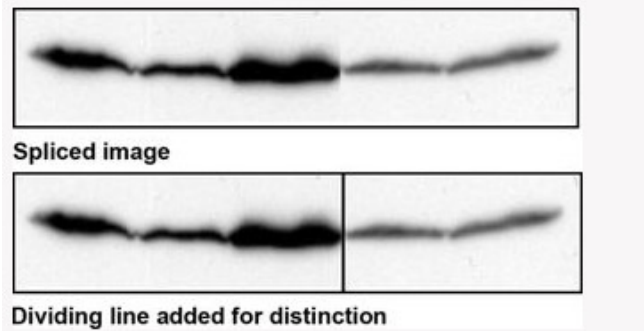
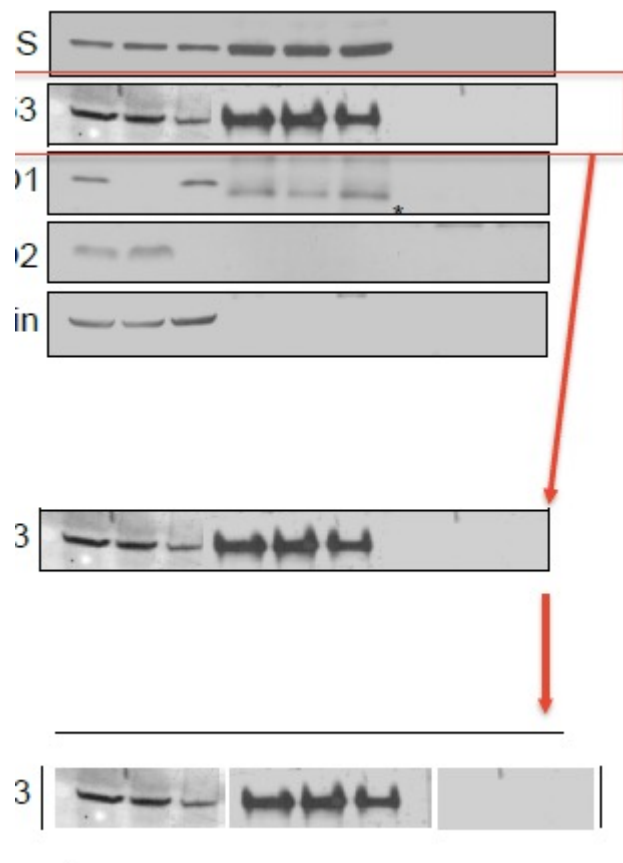


Falsifying blots





Splicing together different experiments





Adjustments to make data disappear

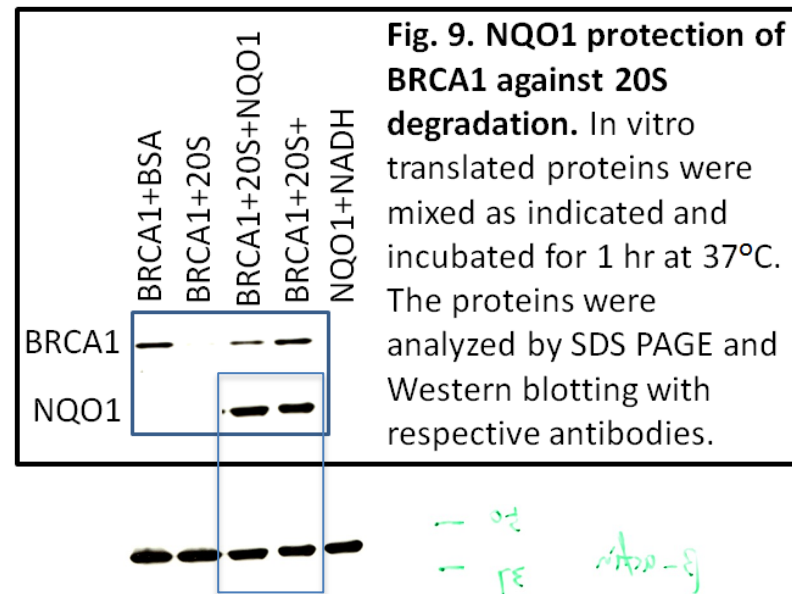
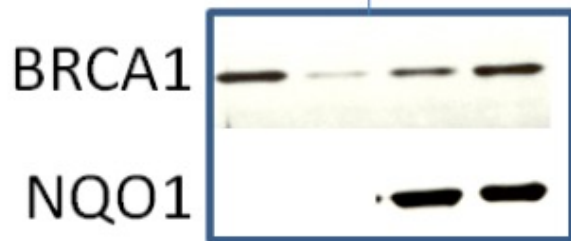
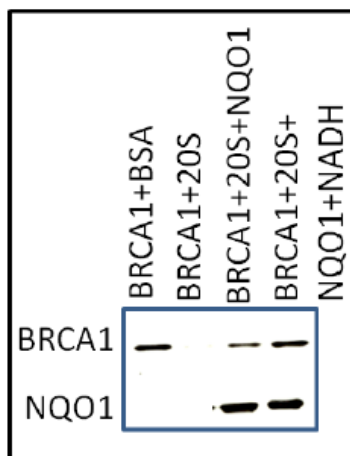
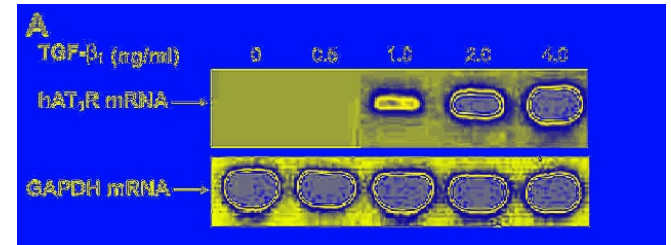
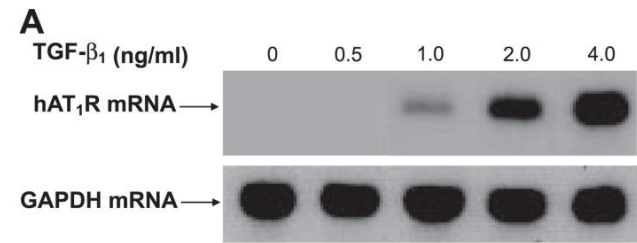
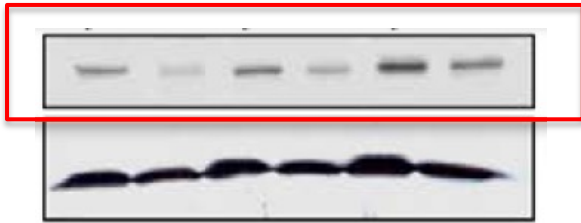


Fig. 9. NQO1 protection of BRCA1 against 20S degradation. In vitro translated proteins were mixed as indicated and incubated for 1 hr at 37°C. The proteins were analyzed by SDS PAGE and Western blotting with respective antibodies.

500s-11-A



Painting or “beautification” of blots





Falsifying controls

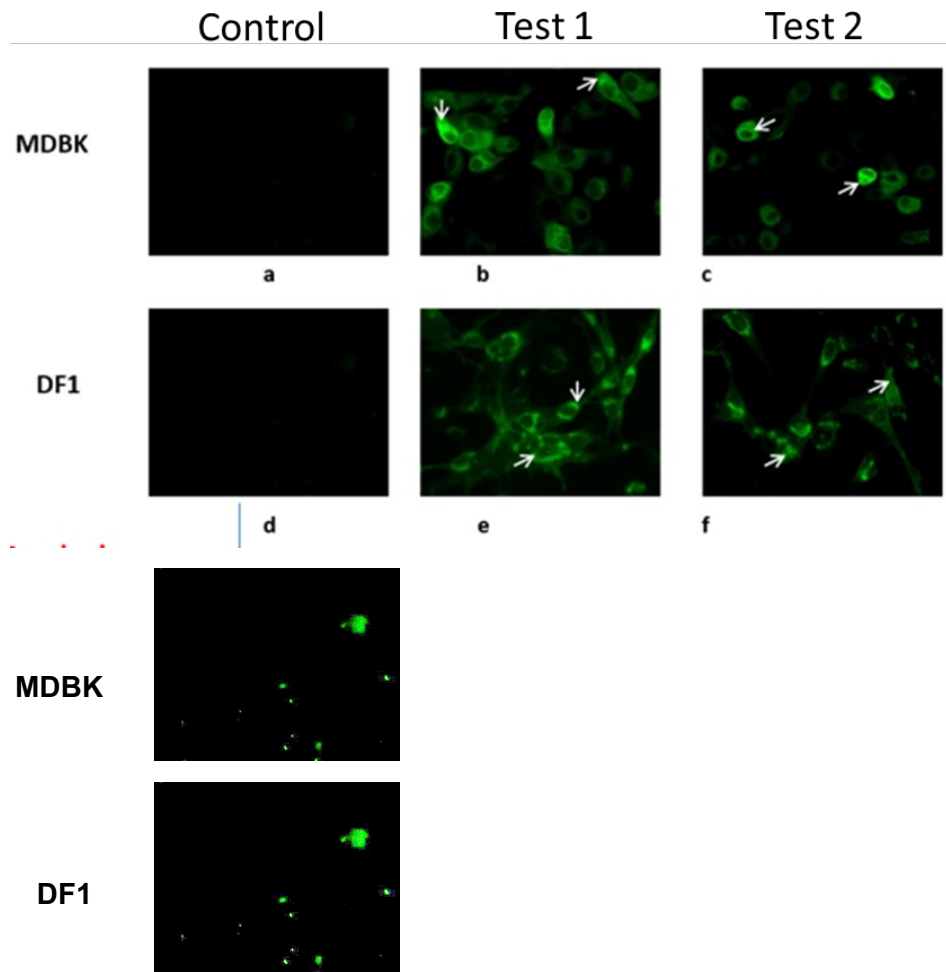


Image duplication

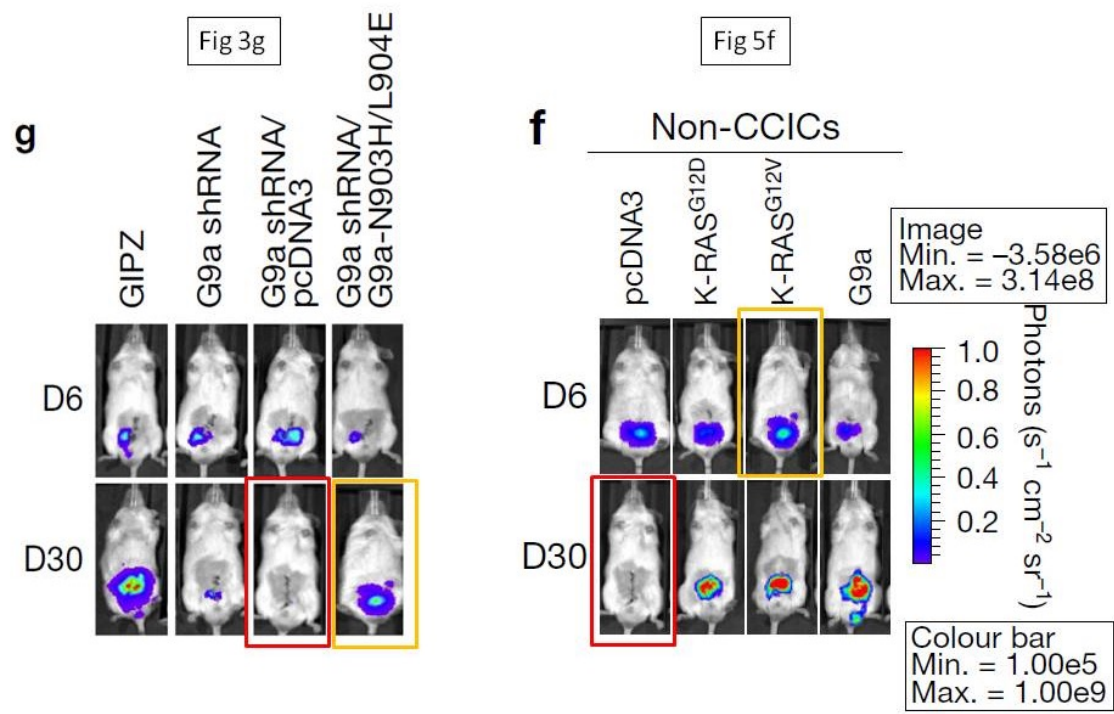


Fig 3g and Fig 5f, Nature Cell Biology 18:993



Image duplication

Figure 1A from JBC 2004a

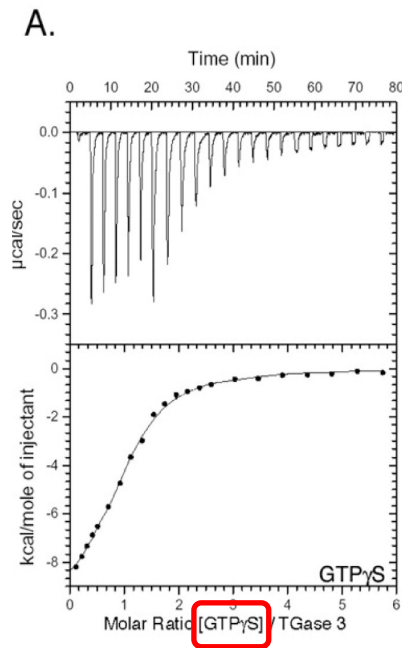
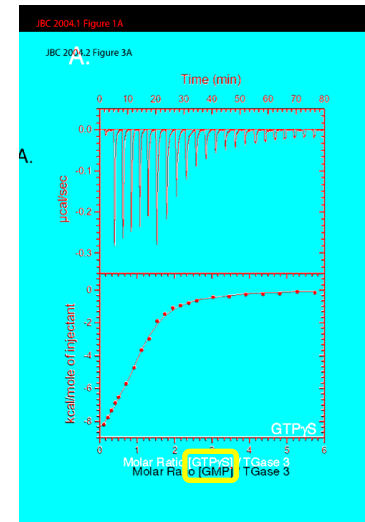
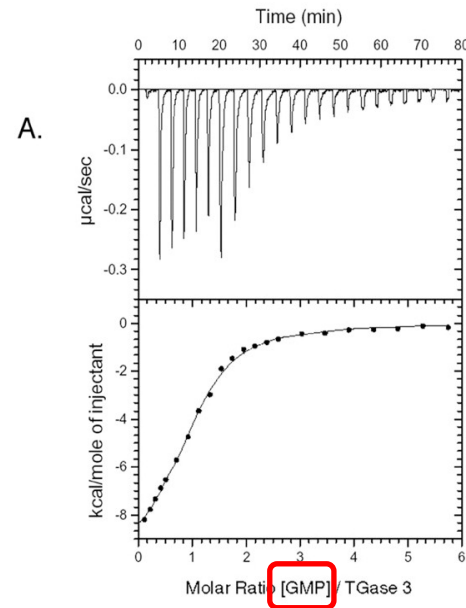


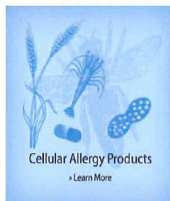
Figure 3a from JBC 2004b





Changing raw data

GLP-1 (Active 7-36) ELISA



Focus
Clinical Research
Application
Immunossays
Flow Cytometry
HPLC/LC-MS
Therapeutic Areas
Allergy & Infectious Disease
Bone Metabolism
CVD & Oxidative Stress

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Catalog Number: 43-GP1 HU-E01
Description: GLP-1 (Active 7-36) ELISA
Sample Types: EDTA Plasma, Plasma
Sample Sizes: 100 µL
Available Sizes: 96 Wells
Range: 0.64 - 48 pmol/L
Incubation: Overnight
Protocol: [GLP-1 \(Active 7-36\) ELISA](#)
Material Safety Data Sheet: [GLP-1 \(Active 7-36\) ELISA](#)
Regulatory Status: Research Use Only. Not for Use in Diagnostic Procedures.
Product Distribution: Available Worldwide

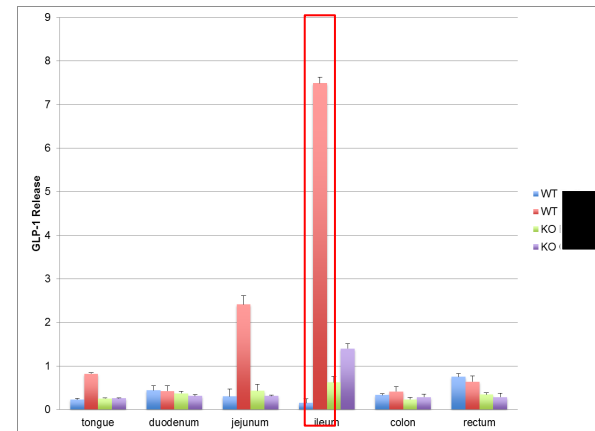
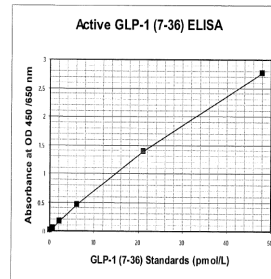


Table showing data for GLP-1 release, used for analysis and published.

Folder: T1R2 data and figures
File: T1R2 GLP-1 release.xlsx

	A	B	C	Blanco
tongue	0.199	0.28	0.206	
duodenum	0.654	0.381	0.295	
jejunum	0.63	0.245	0.036	
ileum	0.017	0.331	0.118	
colon	0.403	0.289	0.318	
rectum	0.866	0.606	0.784	

Sample #:

	A	B	C	D
Raw Data	1.696	1.226	0.364	1.677
Excel	7.696	7.226	7.364	7.677



Public contributions to the record



PUBPEER
The online Journal club

Retraction
Watch

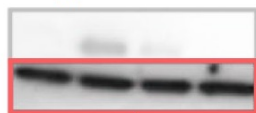


Public trust declines

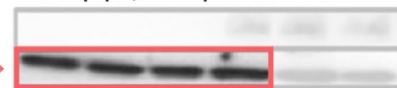
Two papers, three experiments, one image

These figures show western blots, which are used to detect the presence of a specific protein in tissues or bodily fluids.

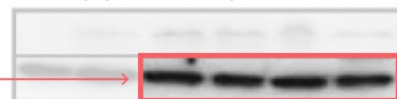
First paper



Second paper, first repetition



Second paper, second repetition

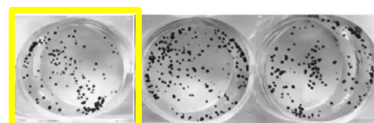


Stretched

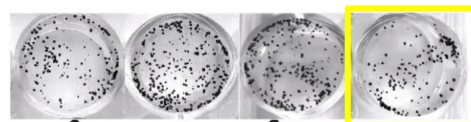
Flipped and tilted

2622 J. Ji et al.

Sources: "REDOX regulation of IL-13 signaling in intestinal epithelial cells: usage of alternate pathways mediates distinct gene expression patterns," by Debasmitha Mandal, Pingfu Fu and Alan D. Levine (first paper), "Elevated IL-13Rα2 in intestinal epithelial cells from ulcerative colitis or colorectal cancer initiates MAPK pathway," by Debasmitha Mandal and Alan D. Levine (second paper).



pcDNA3 pcDNA3 IRF1



pcDNA3 pri-miR-23a ASO-NC ASO-23a

Source: "miR-23a targets interferon regulatory factor 1 and modulates cellular proliferation and paclitaxel-induced apoptosis in gastric adenocarcinoma cells."

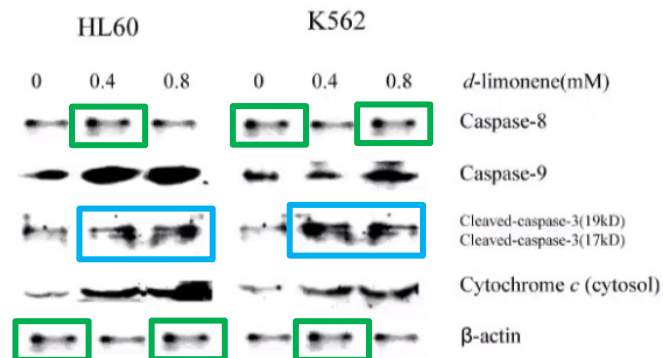
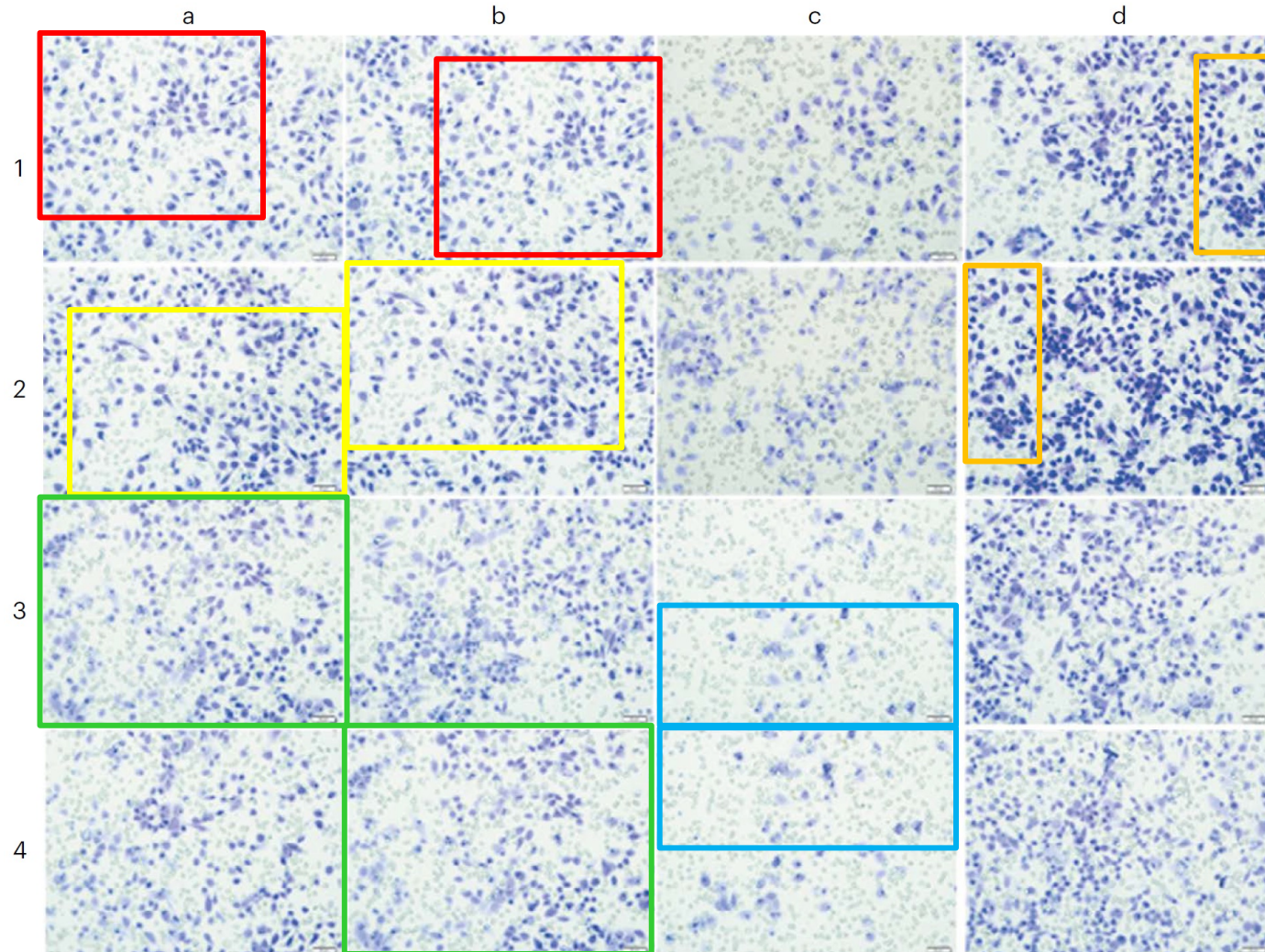


Figure 4. d-Limonene induces increased expression of caspase-9 and cleaved caspase-3, but not caspase-8, in a dose-dependent manner in both K562 and HL60 cells. Cytochrome c protein content of the cytosolic fraction was measured by western blotting. Cells were treated with 0.4 or 0.8 mM of d-limonene for 24 h. β-actin was used as an internal control to monitor equal protein sample loading.

Source: "Induction of apoptosis by d-limonene is mediated by a caspase-dependent mitochondrial death pathway in human leukemia cells."



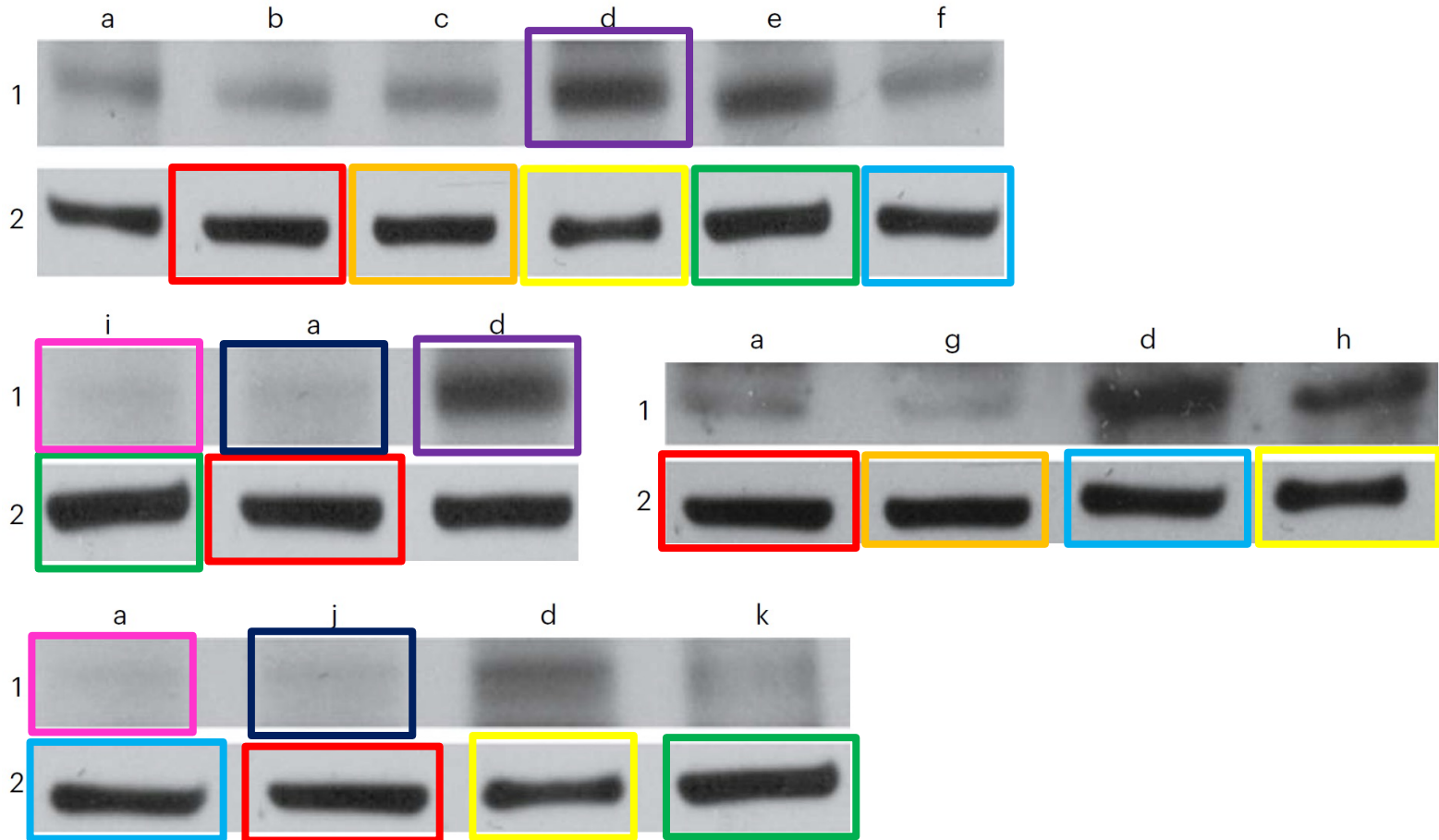
Image duplication



SOURCE: S. GENGET AL. PLOS ONE 9, E91566 (2014); RETRACTION 14, E0214018 (2019).



Fabricating blots



SOURCE: Y. TAN ET AL. PLOS ONE 9, E102195 (2014); RETRACTION 14, E0220600 (2019).



Ways to minimize misconduct

- Changing publish or perish culture
 - Be open to criticism and engage in constructive conversation
- Recognize pressures in lab
 - Research should be exciting for everyone!
- Oversight while mentoring
 - PIs, trainees, staff are all capable of misconduct
 - Look at the source data!
- Provide adequate training
 - Do not assume people know how to analyze or interpret data
 - Controls, controls, controls!





Ways to minimize misconduct

- Saving organized source data
 - Notebooks
 - Lab server
 - No personal laptops!
 - Be able to link publication figures to raw data
- **Having data helps protect YOU against misconduct allegations**





Report Misconduct:

- Hotline 866-594-5220
- <http://www.ethicspoint.com>
- Email
- In person

UMB OAC

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Baltimore, MD 21201

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