Placeholders:
An Honest Error Defense?

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OASH | Office of the Assistant Secretary for Health

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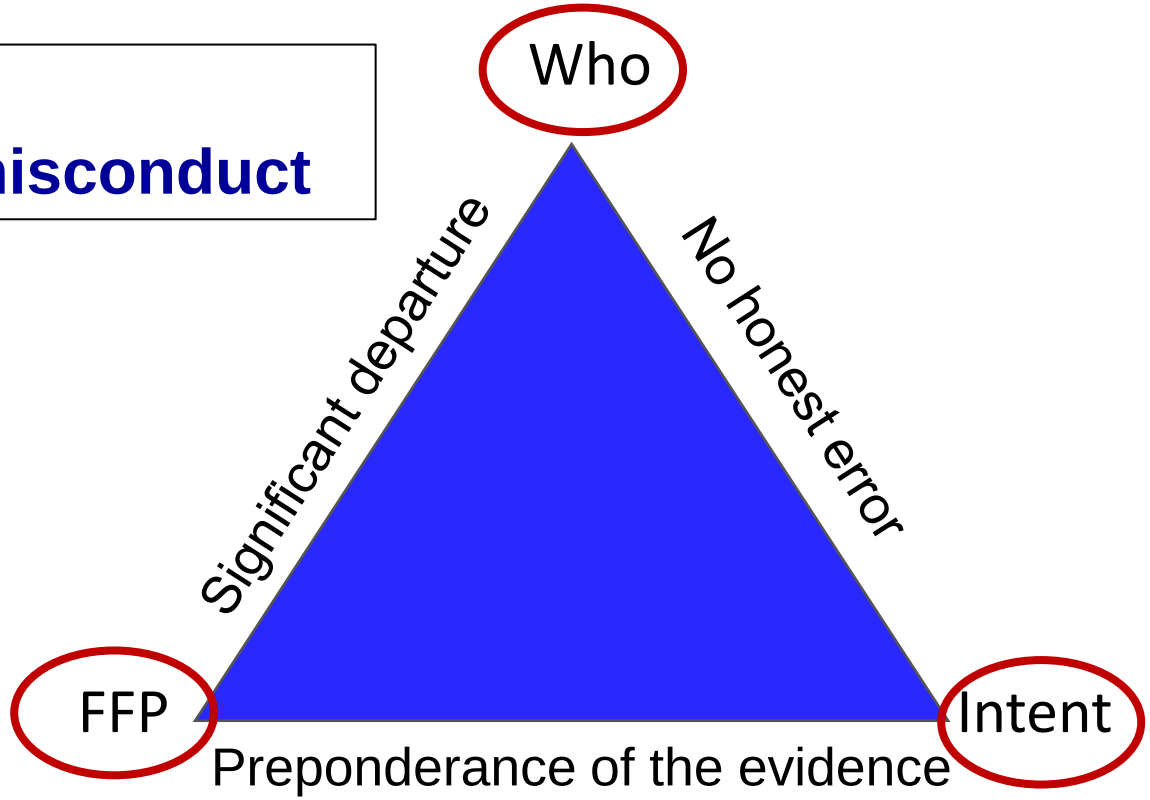
Disclosure

The opinions presented here are mine and does not reflect that of the Office of Research Integrity (ORI) and/or the Office of the Assistant Secretary of Health (OASH). I have no financial disclosures or incentives to declare. I have no actual or potential conflict of interest in relation to this program/presentation.

Why Claim Honest Error? - Not Misconduct

Honest error or differences of opinion is not research misconduct

42 CFR § 93.104:
Requirements for findings of research misconduct



Honest Error vs Intentional/knowing

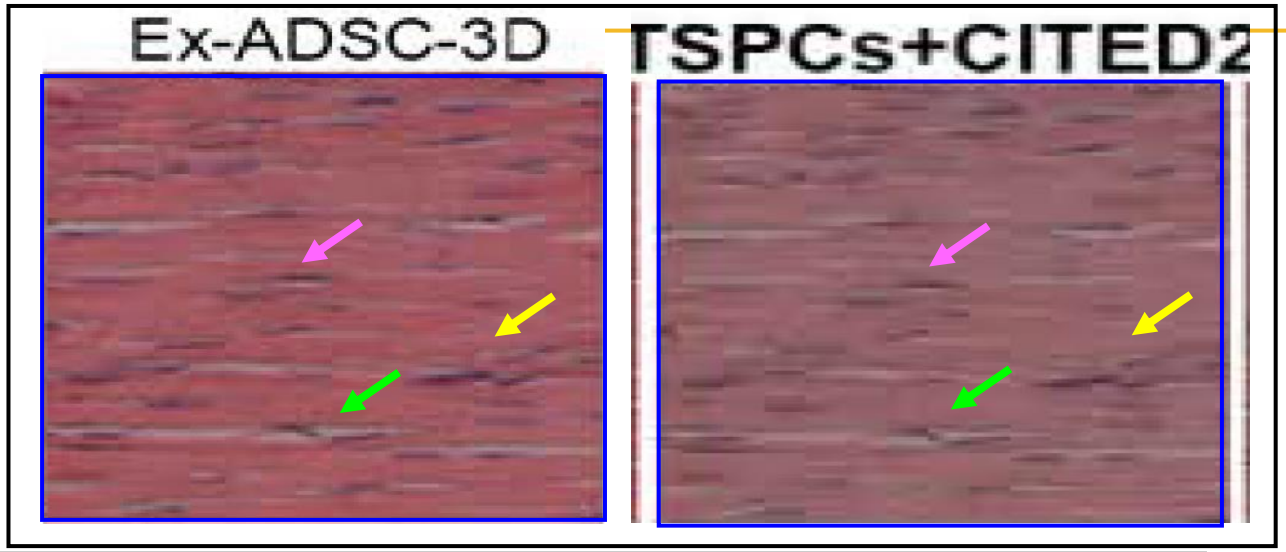
Honest Error	Intentional
Unaware of falsifications	Aware and deliberate
Occasional	Usually more than one occasion
No manipulations	Usually manipulated
Usually does not fit the intended hypothesis	Presented to fit the scientific message
Correct data available	No real data available

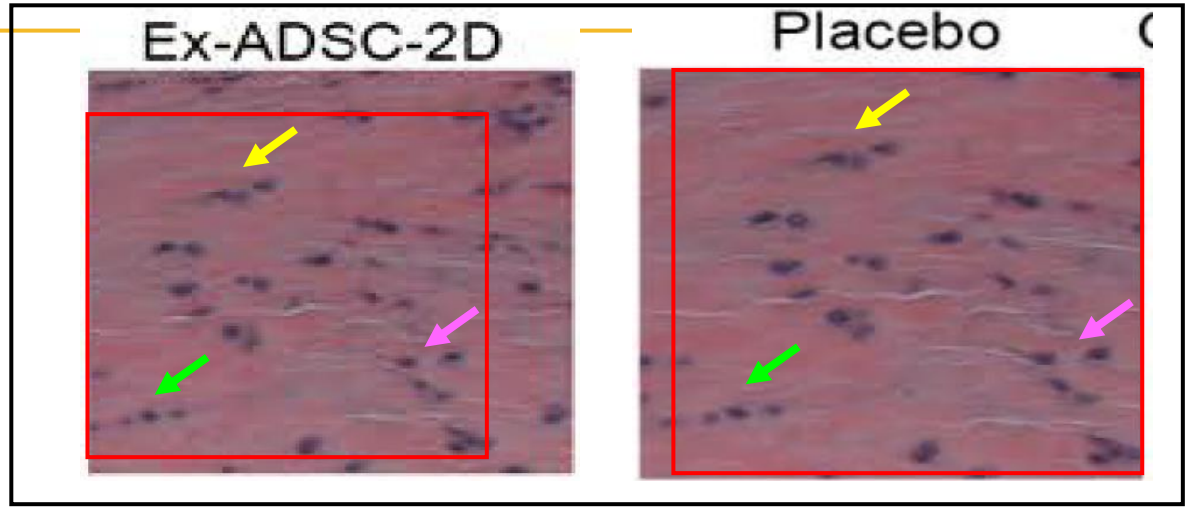
Allegations and Initial Findings

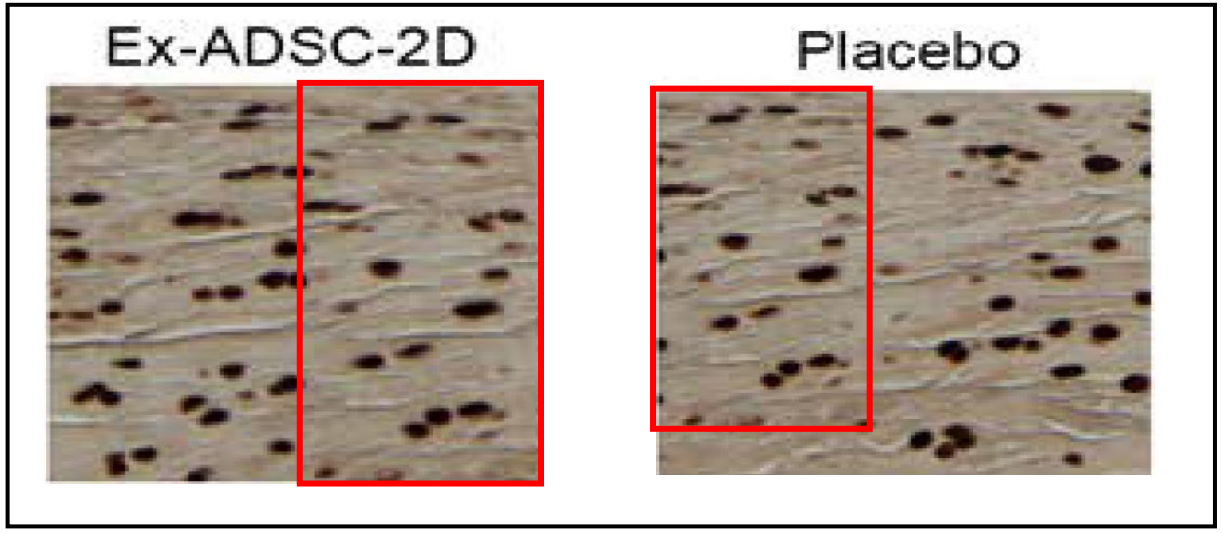
- **A grant reviewer complained to NIH**
  - Figures from a paper were reused in the grant application as data from unrelated experiments

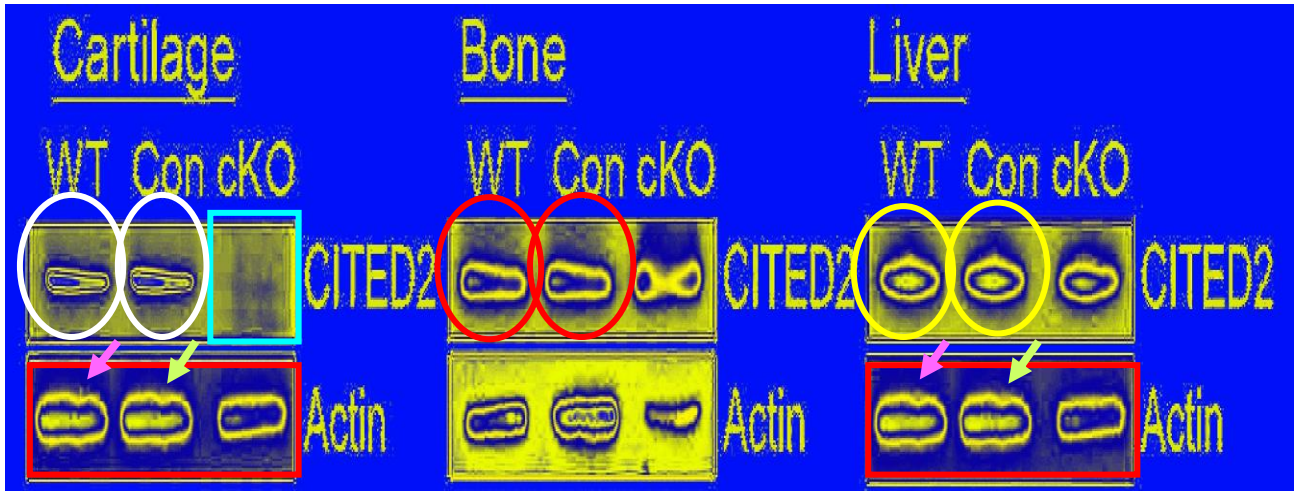
- **Initial Institutional Findings ….**
  - Postdoctoral Fellow knowingly and recklessly falsified/fabricated data, possibly by forgetting to replace placeholders, and therefore is guilty of misconduct
  - Principal Investigator (PI) recklessly failed to adequately review and oversee the assembly of data presented in grant applications and for publication, thereby preventing him from detecting the misconduct

ORI Oversight Review - Additional Concerns in 17 Grant Applications









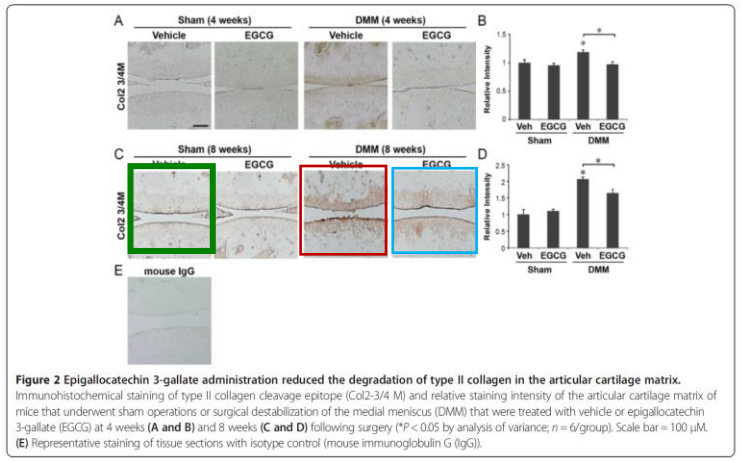
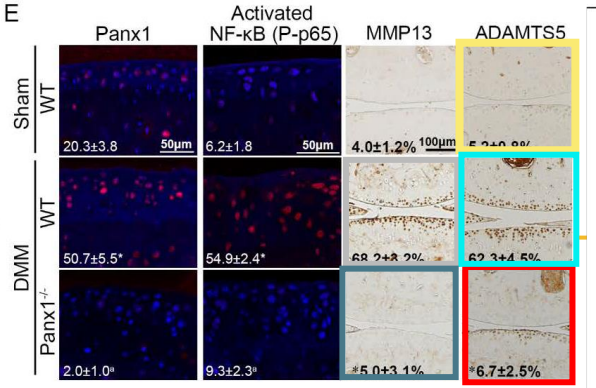
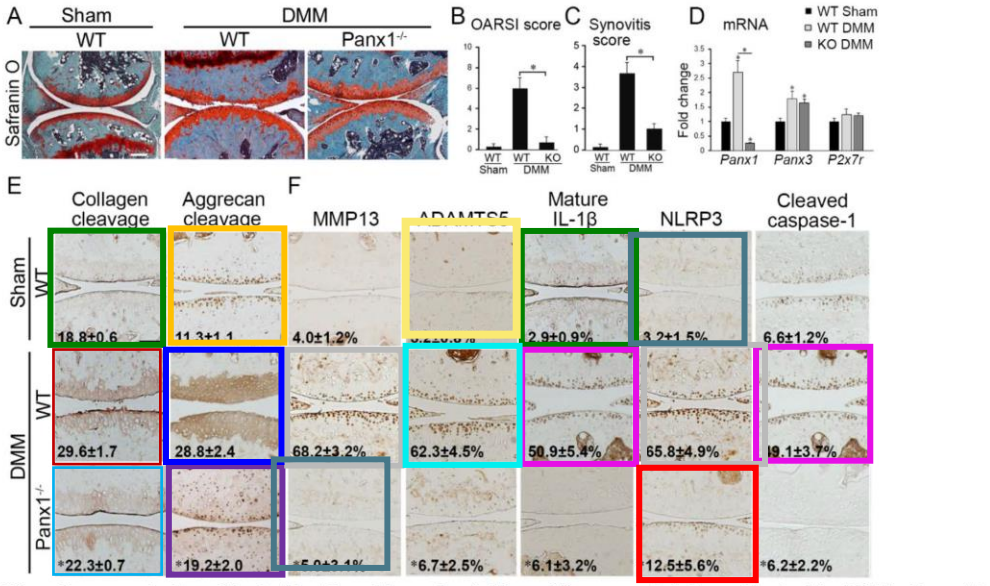


Figure 2 Epigallocatechin 3-gallate administration reduced the degradation of type II collagen in the articular cartilage matrix. Immunohistochemical staining of type II collagen cleavage epitope (Col2-3/4 M) and relative staining intensity of the articular cartilage matrix of mice that underwent sham operations or surgical destabilization of the medial meniscus (DMM) that were treated with vehicle or epigallocatechin 3-gallate (EGCG) at 4 weeks **(A and B)** and 8 weeks **(C and D)** following surgery (*$P < 0.05$ by analysis of variance; $n = 6$/group). Scale bar = 100 μM. **(E)** Representative staining of tissue sections with isotype control (mouse immunoglobulin G (IgG)).





e 2. OA pathogenesis is mitigated in Panx1 knockout (Panx1$^{-/-}$) mouse joints subjected to DMM. Panx1$^{-/-}$ with DMM injury (bred from heterozygous Panx1$^{tm1a(KOMP)Wtsi}$ mice, male, 3-6 months old[48]) displayed reduced age degradation by **(A)** Safranin O, **(B)** lower OARSI score, and **(C)** synovitis score, when compared to age- and er-matched wild-type (WT) controls. **(D)** Panx1 mRNA expression or alteration of Panx3 and P2X7R were not table in Panx1$^{-/-}$ mice. **(E)** Panx1-mediated mitigation of OA was associated with reduced cleavage of type II gen and aggrecan. **(F)** Reduced numbers of chondrocytes staining positive for MMP-13, ADAMTS5, IL-1β, NLRP3 cleaved caspase-1. (DMM: 8 weeks after DMM surgery in male, 3-6 months, mice on C57BL/6 background, group). Scale bar=100μm. Immunohistochemistry staining intensity (for collagen and aggrecan cleavage) and ntage of positive chondrocytes indicated. *D*: *p<0.05 vs. WT Sham control; *E, F*: *p<0.05 vs WT DMM mice. No icant differences between the WT Sham and Panx1$^{-/-}$ DMM groups (p>0.05).

Figure 3

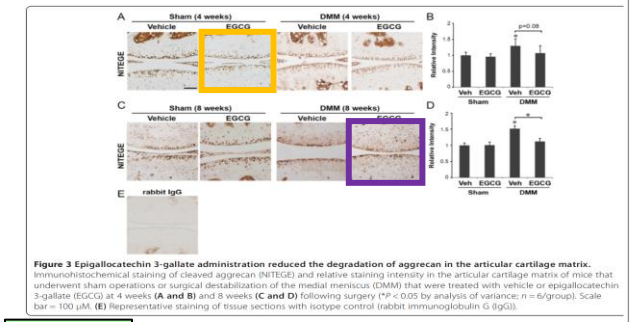


Figure 3 Epigallocatechin 3-gallate administration reduced the degradation of aggrecan in the articular cartilage matrix. Immunohistochemical staining of cleaved aggrecan (NITEGE) and relative staining intensity in the articular cartilage matrix of mice that underwent sham operations or surgical destabilization of the medial meniscus (DMM) that were treated with vehicle or epigallocatechin 3-gallate (EGCG) at 4 weeks **(A and B)** and 8 weeks **(C and D)** following surgery (*$P < 0.05$ by analysis of variance; $n = 6$/group). Scale bar = 100 μM. **(E)** Representative staining of tissue sections with isotype control (rabbit immunoglobulin G (IgG)).

Figure 4

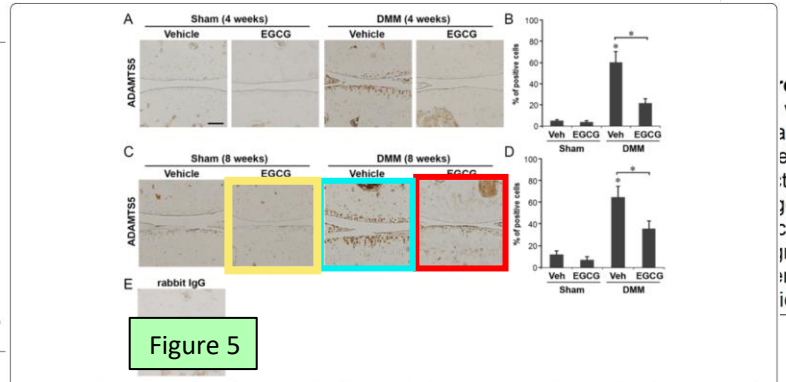


Figure 5

Figure 5 Epigallocatechin 3-gallate administration reduced ADAMTS5 levels in the articular cartilage. Immunohistochemical staining of A disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS5) and percentage of ADAMTS5-positive cells in the articular cartilage of mice that underwent sham operations or surgical destabilization of the medial meniscus (DMM) that were treated with vehicle or epigallocatechin 3-gallate (EGCG) at 4 weeks **(A and B)** and 8 weeks **(C and D)** following surgery (*$P < 0.05$ by analysis of variance; $n = 6$/group). Scale bar = 100 μM. **(E)** Representative staining of tissue sections with isotype control (rabbit immunoglobulin G (IgG)).

ORI findings included …..

106 figure panels in 50 figures included in 3 papers, and 16 PHS grant applications

Honest Error *vs* Intentional/knowing

Honest Error

- **Unaware of the falsifications**
- **Occurs occasionally**
- **No manipulations**
- **Not usually fit the intended hypothesis**
- **Correct data is available**

Intentional

- **Knowing and intentional**
- **One or more research records**
- **Usually manipulated**
- **Presented to fit the scientific message**
- **No real data available**

Postdoctoral Fellow - Acknowledged that he made the figures

- But still claimed that:
  - **The reused images are "placeholders" and he forgot to replace the placeholders; "Honest Error," not intentional falsification/fabrication**
  - **He was not responsible; the PI, who oversaw the work was responsible**
  - **The affected data are not scientifically significant**
  - **The replacement data are available for some but not all questioned figures**

Principal Investigator - Did not challenge the figure reuse

- But he:
  - **Denied culpability**
  - **Blamed the Postdoctoral Fellow**
  - **Claimed honest error of forgetting to replace the "placeholders"**

However, the PI's actions were knowing and reckless

- ORI also found:
  - **PI was involved in two prior misconduct cases, though no findings against him**
  - **Blamed other laboratory members for the issues, as in this case**
  - **During the current proceedings, he continued to submit grant applications with falsified data**

When Presented with Evidence - Respondents did not challenge

- **Both respondents signed voluntary settlement agreements with ORI**

ORI Findings – Research Misconduct:

- **The Postdoctoral Fellow knowingly, intentionally, and/or recklessly falsified and fabricated data**

- **PI knowingly and/or recklessly reported falsified and fabricated data**

- **In the absence of reliable image data, the respondents falsified or falsely reported figures and quantitative data in associated graphs purportedly derived from those images, statistical analyses, and related text are also false.**

Outcome of ORI's Efforts – Protect PHS Funds, Correct Affected Literature, Deterrence of Misconduct

- Postdoctoral fellow:
  - **Debarred from receiving federal funding for four (4) years and supervised for another 4 years**
- Principal Investigator
  - **Research supervised for a period of twelve (12) years.**
- Affected Papers have been retracted
  - https://www.nature.com/articles/s41598-018-34658-3
  - https://www.nature.com/articles/srep13149
- Findings are published on ORI website and Federal Register Notice
  - **https://www.federalregister.gov/documents/2022/03/24/2022-06246/findings-of-research-misconduct**
  - **https://www.federalregister.gov/documents/2022/08/05/2022-16867/findings-of-research-misconduct**

Thank you

“Placeholder claims” are a red flag - necessary to rule out intent.

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ORI THE OFFICE OF RESEARCH INTEGRITY

ORI's Mission & Vision

Mission

ORI's mission is to advance research integrity, protect taxpayer funds for Public Health Service-supported research, and support research integrity communities.

Vision

Promoting a world where we build trust in science together for future generations.