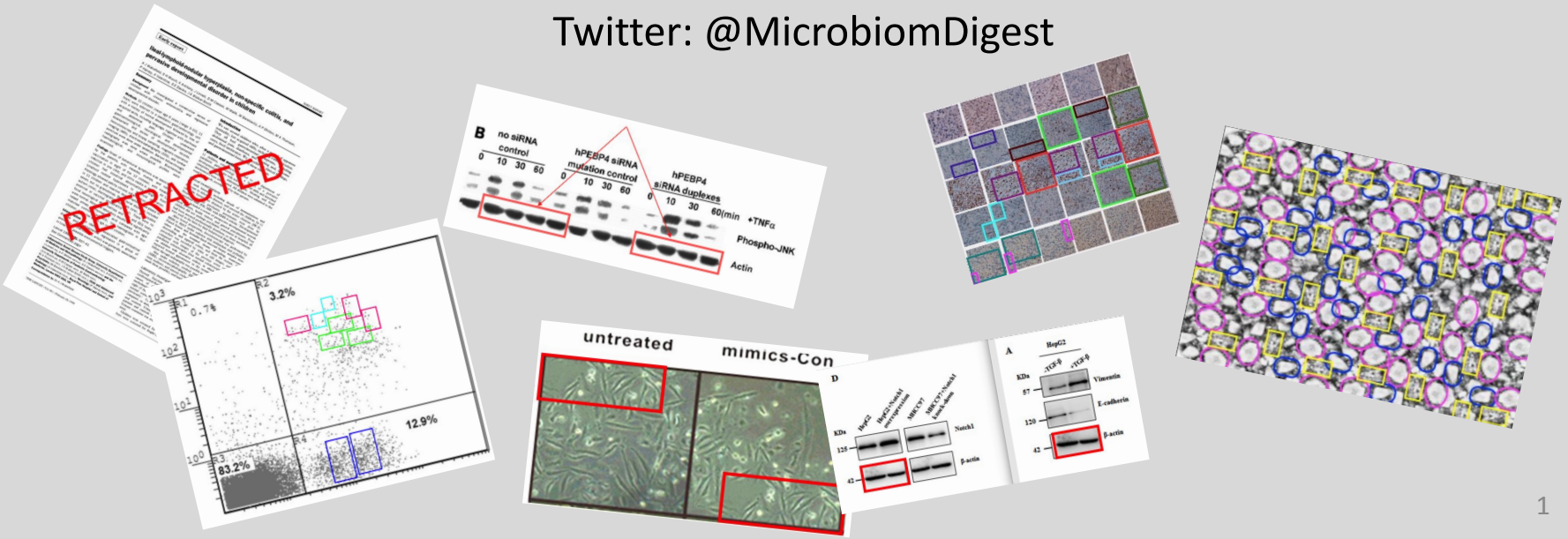
# The Dark Side of Science: Misconduct in Biomedical Research

Elisabeth Bik

www.ScienceIntegrityDigest.com

www.MicrobiomeDigest.com

Twitter: @MicrobiomDigest



# Disclosure Summary

- Consulting and speaker's honoraria:
  - *Universities, scientific publishers, lawyers*
- 4 uBiome / Psomagen Inc patents:
  - *US20190050534A1*
  - *US20180137239A1*
  - *US20190078142A1*
  - *US20200303070A1*
  - *uBiome founders are being charged with insurance fraud*
- Patreon account:
  - https://www.patreon.com/elisabethbik
- Most public work I do is unpaid

# Acknowledgements

*Many people are also searching for errors and concerns in scientific papers - often unpaid*





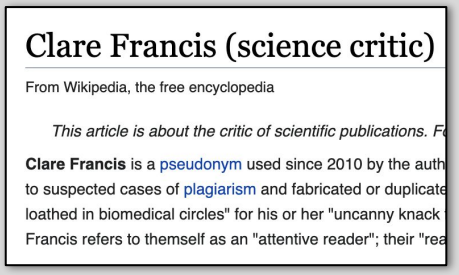




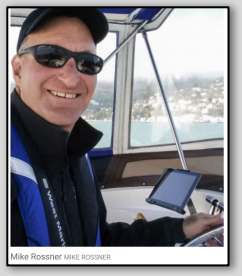






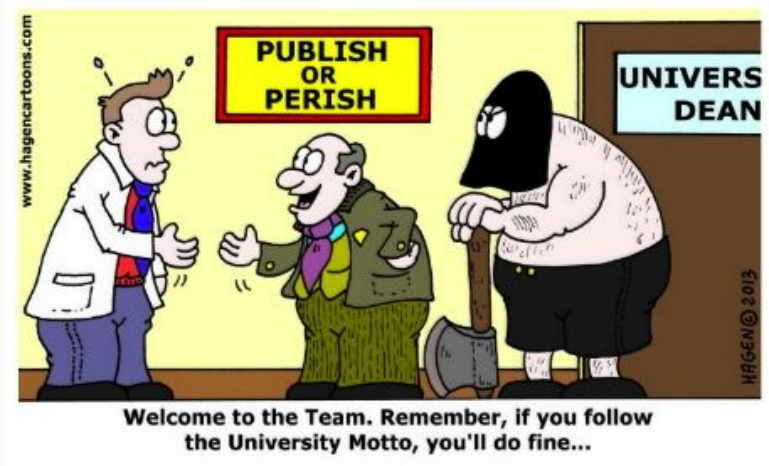






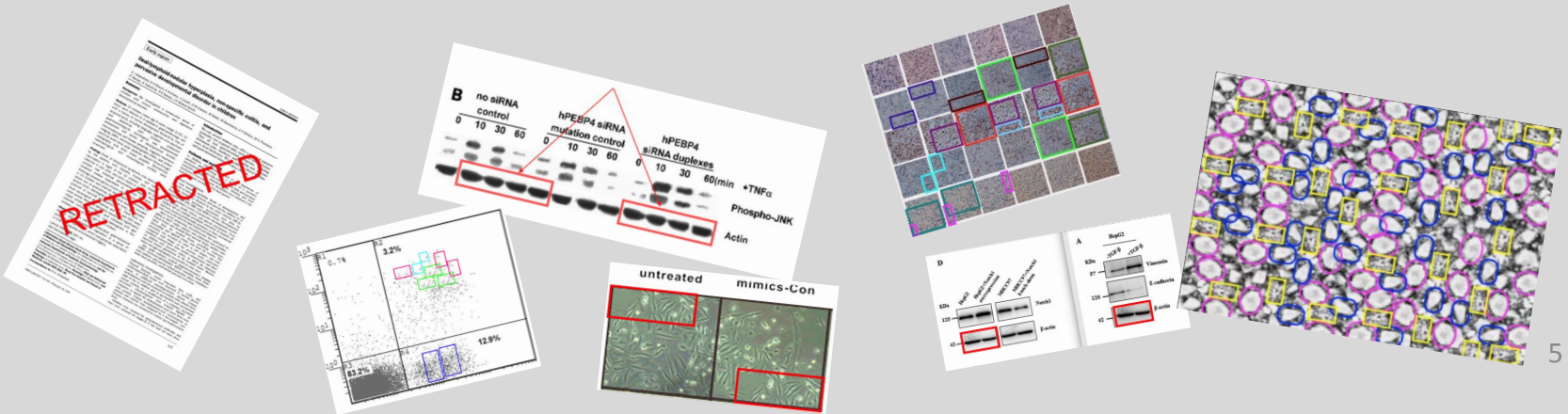

# Publications are the foundation of science

- Science builds upon science: Publications as building blocks
- Built on trust: Most scientists are honest and hard-working
- Science is not immune to fraud
- Science misconduct: plagiarism, falsification, fabrication (ORI)
- Behind each misconduct case, there is a sad story

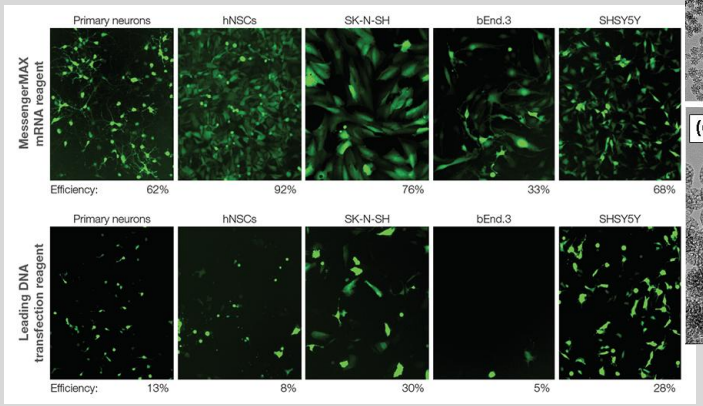


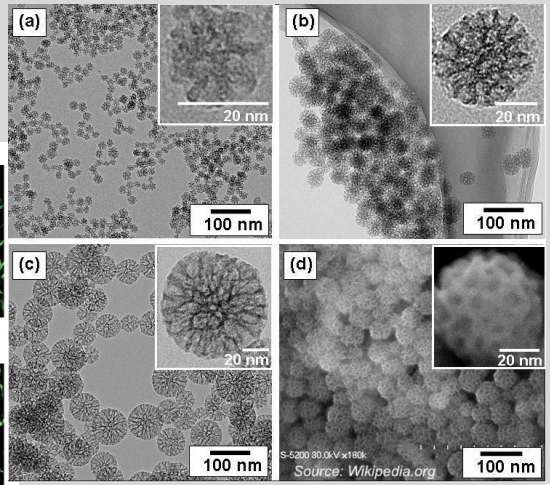

# Concerns about scientific papers

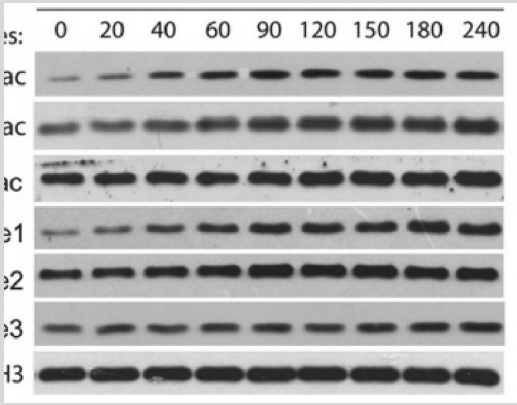
- Study set-up problems (e.g. control vs treatment group)
- Errors in statistics, calculations
- Undisclosed conflicts of interest (patents, company stock)
- Animal or human subject ethics (approval, lack of consent)
- Excessive self-citations
- Plagiarism
- Peer review concerns
- **Duplicated or altered photographic figures**

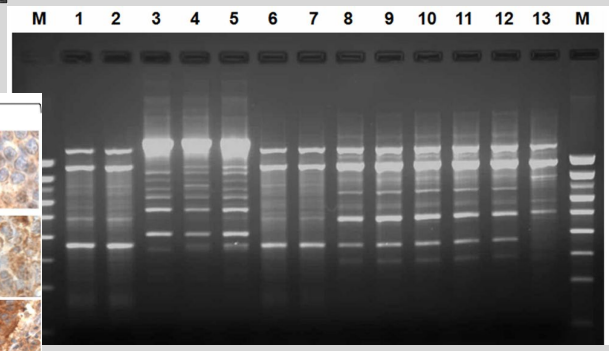


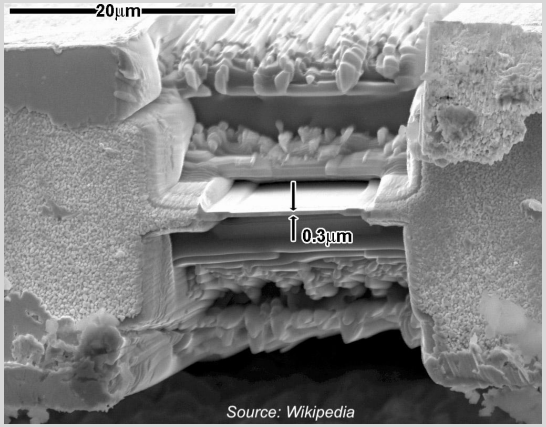
# Research images are unique

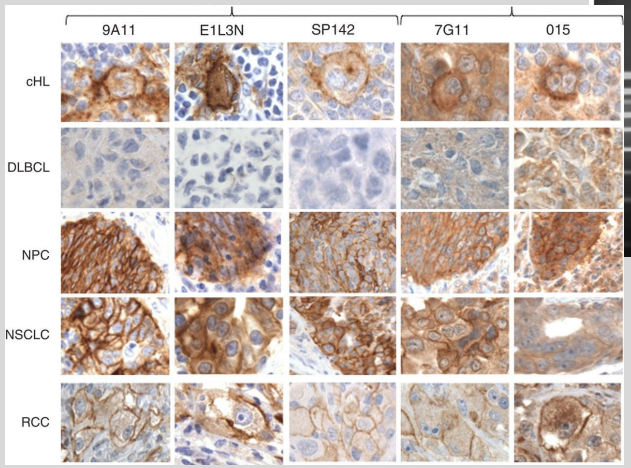


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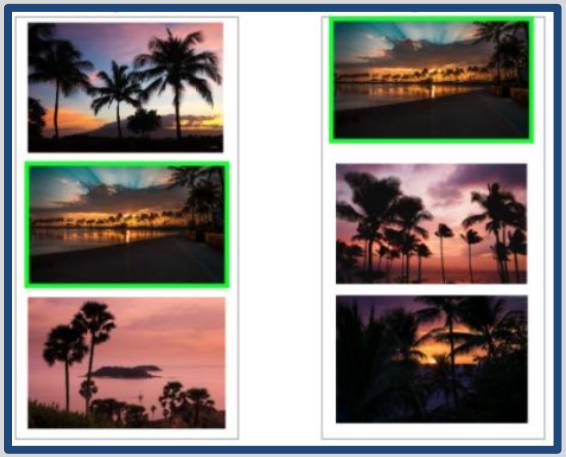
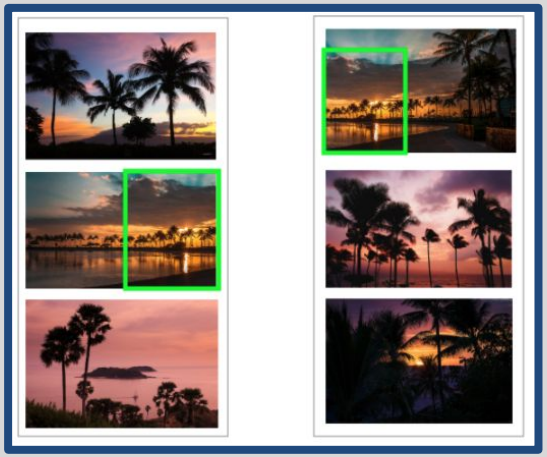
Category I
Simple duplication



Category II
Duplication with repositioning



Category III
Duplication with alteration

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*Michaela (@m_hampi), Jasper Boer (@jasperboer), Mikk Tõnissoo (@themikk), Mike Baker (@bike_maker), Chloe Leis (@tsunamiholmes), and Ethan Robertson (@ethanrobertson) at Unsplash.com*

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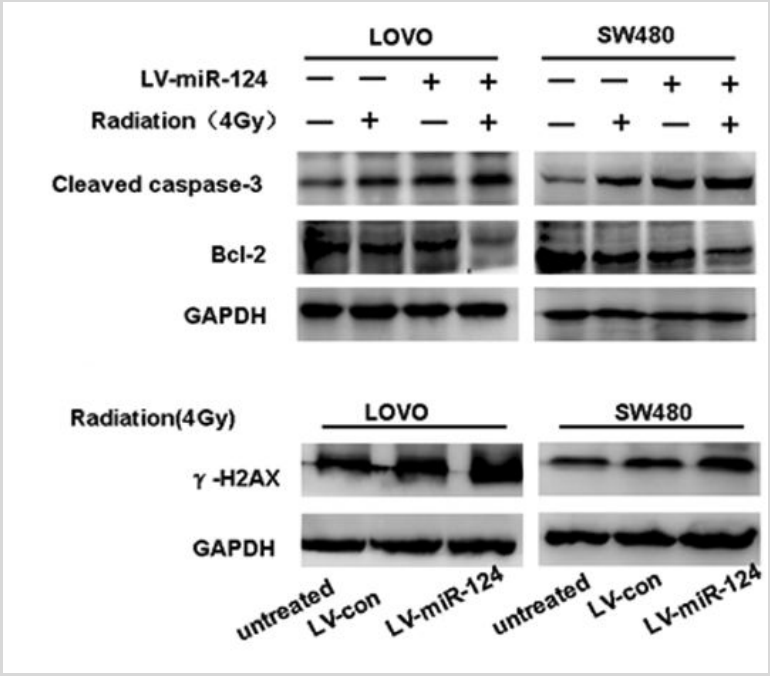


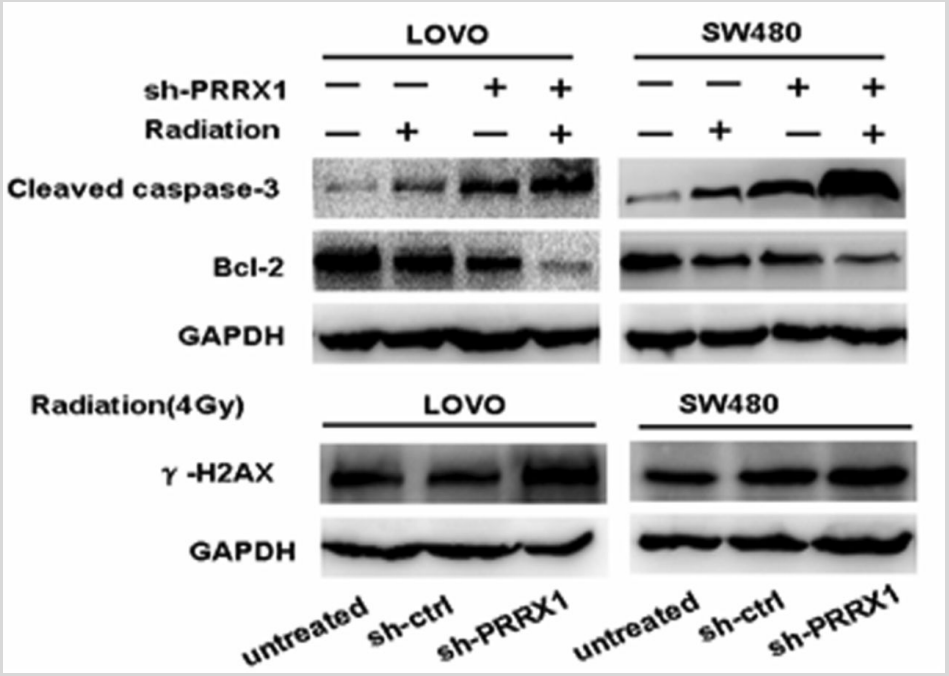


*PLOS ONE, April 2014 | Volume 9 | Issue 4 | e93917*
*Reported October 2015, not yet addressed*
*Cited by 106*

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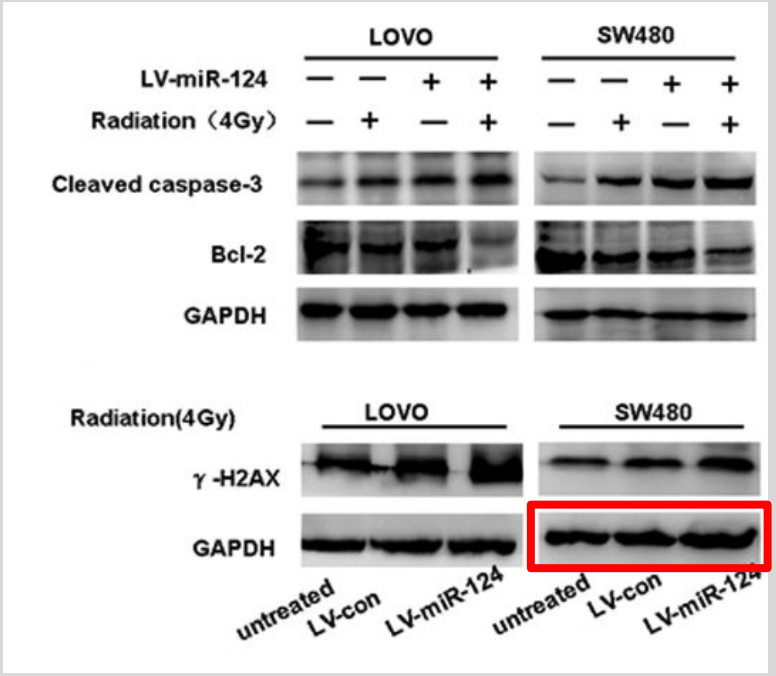


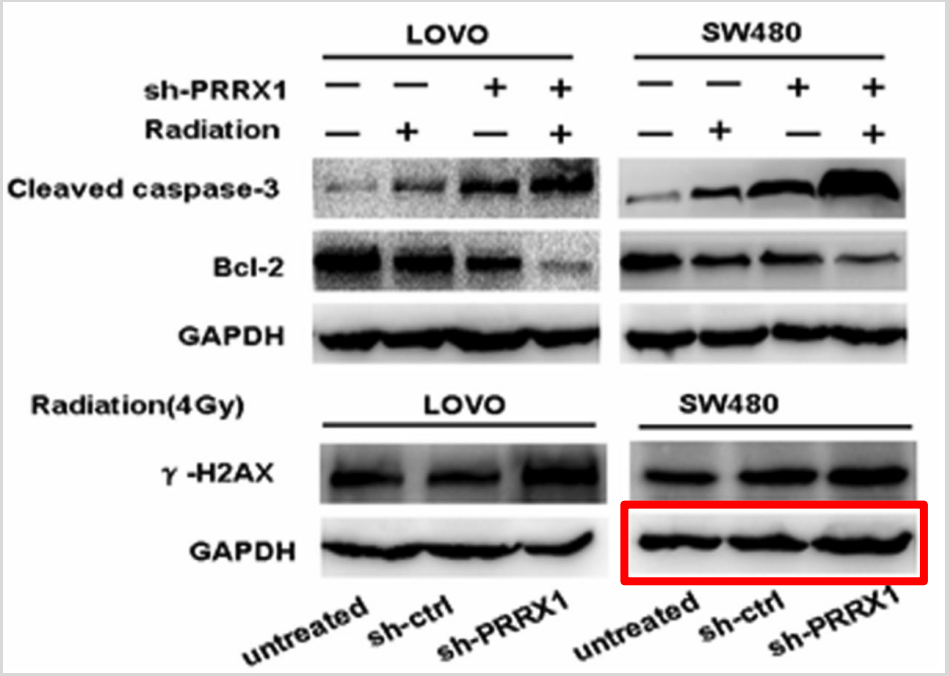


*PLOS ONE, April 2014 | Volume 9 | Issue 4 | e93917*
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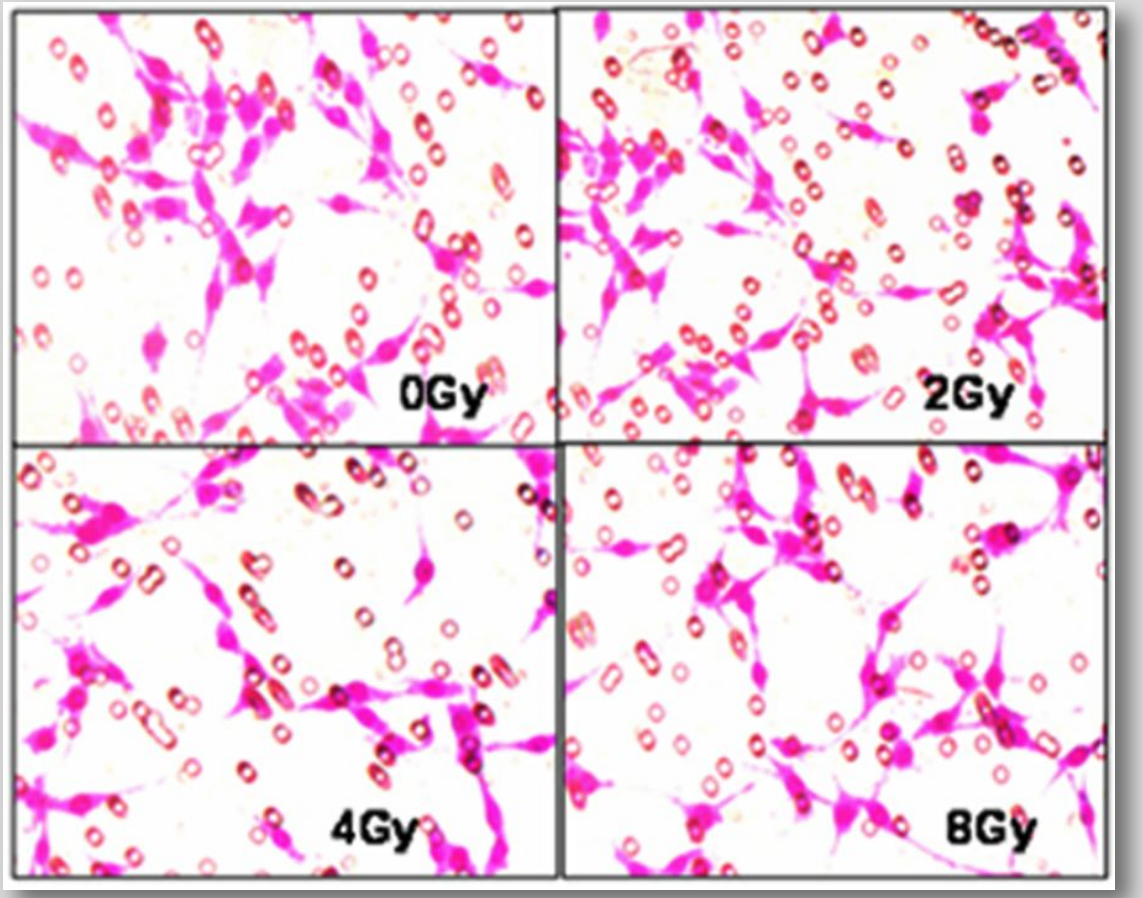


PLOS ONE, June 2014 | Volume 9 | Issue 6 | e98448
DOI: 10.1371/journal.pone.0098448
Reported June 2014, corrected

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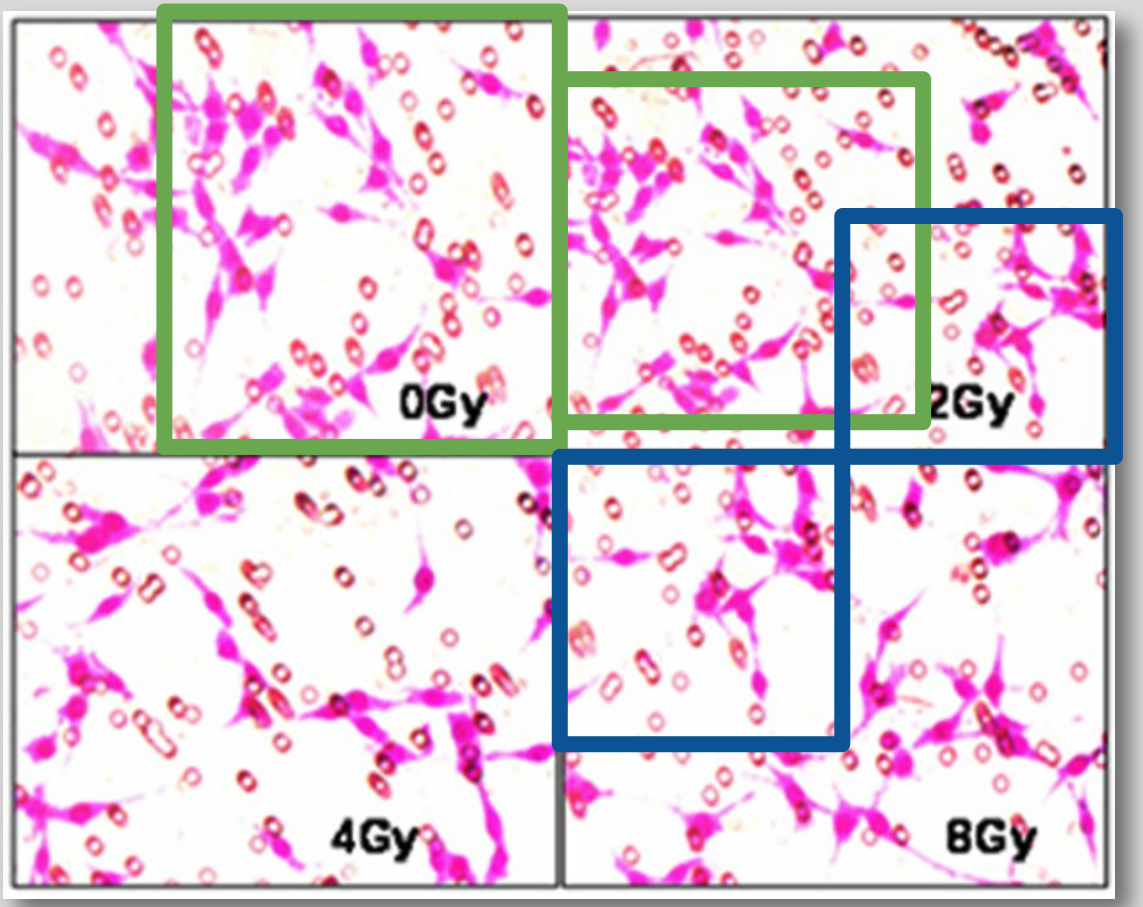


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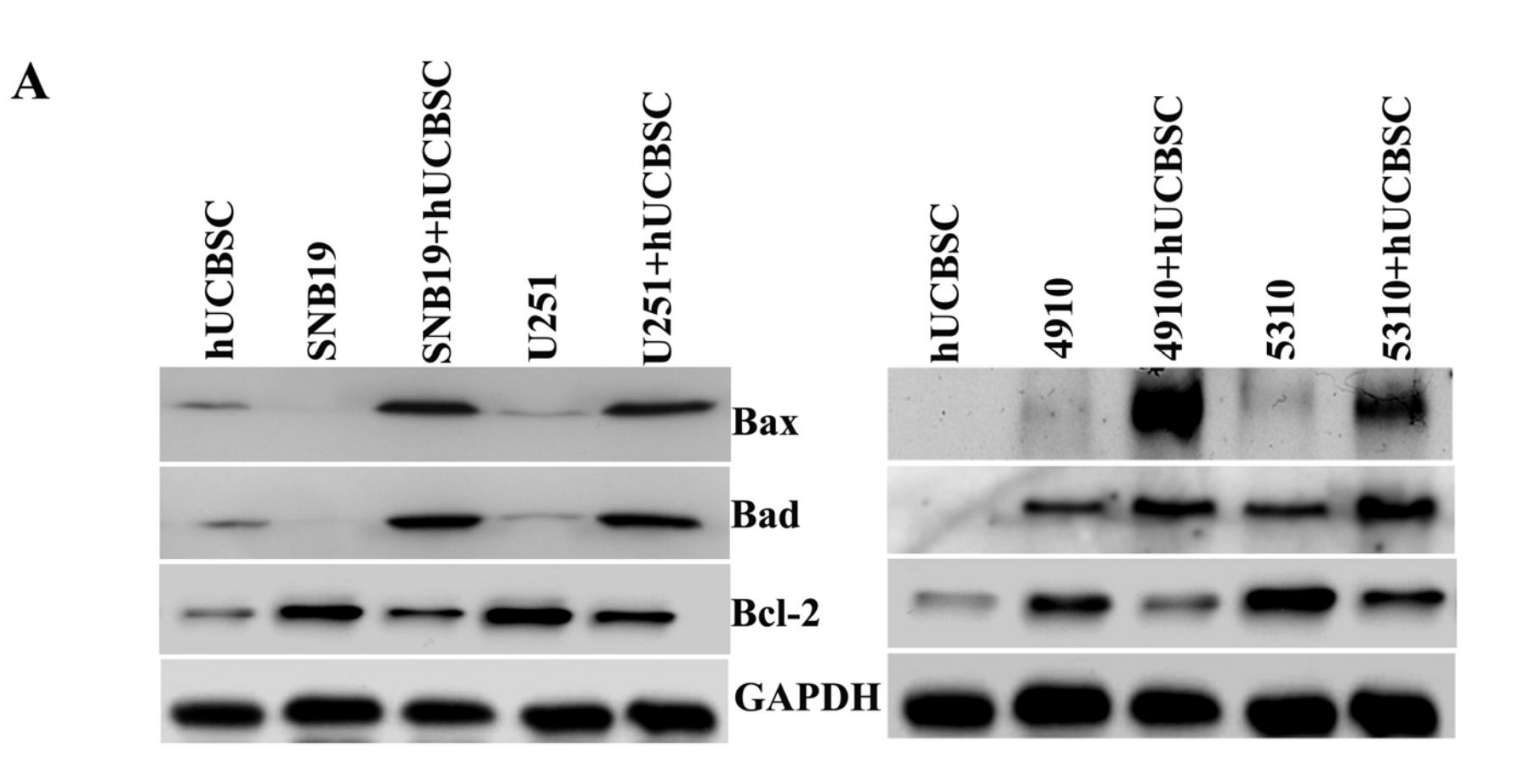
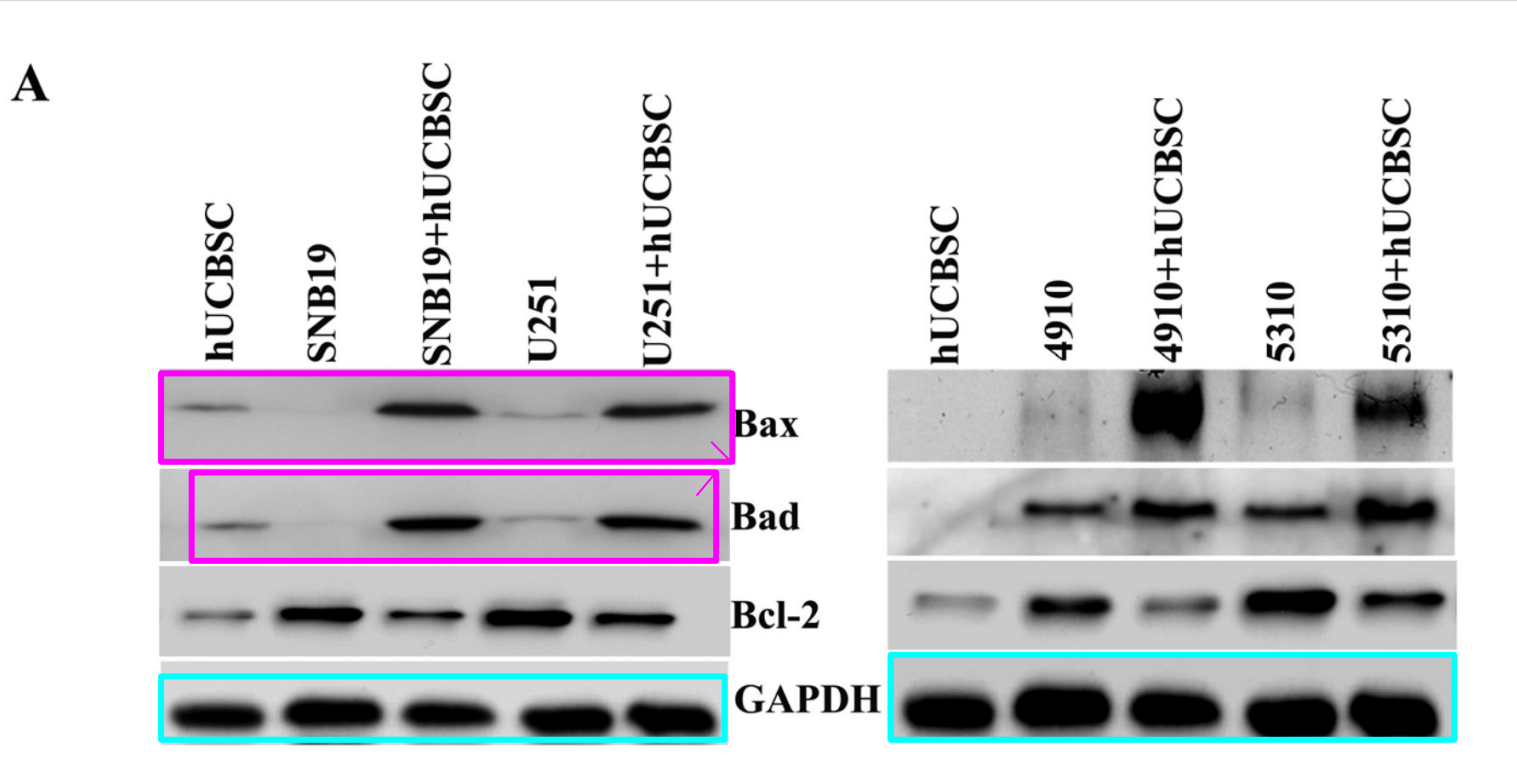



**Cord Blood Stem Cell-Mediated Induction of Apoptosis in Glioma**
**PLOS ONE (2010), DOI: 10.1371/journal.pone.0011813- Cited 86 times**
**Reported to institute and journal in**

# Type II: Duplication with repositioning




**Cord Blood Stem Cell-Mediated Induction of Apoptosis in Glioma**
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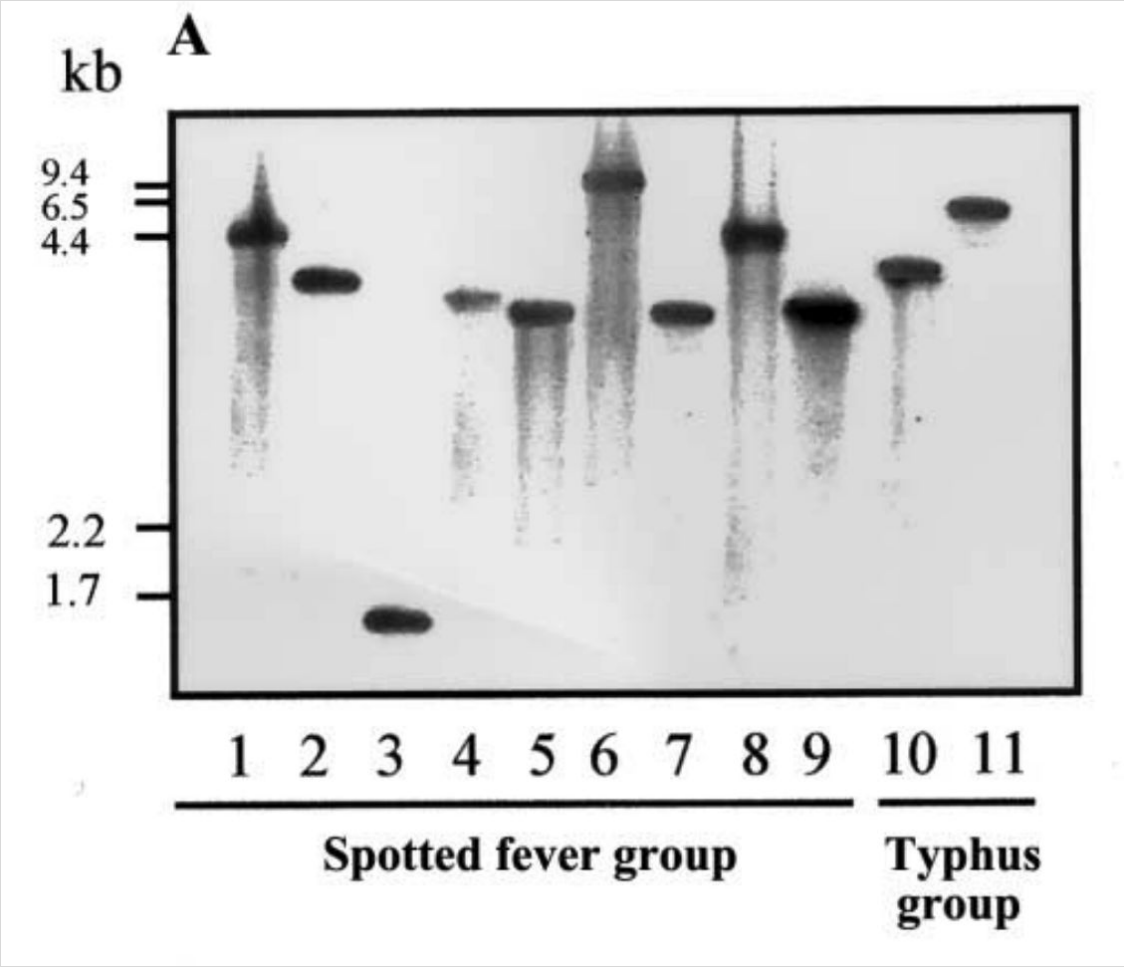


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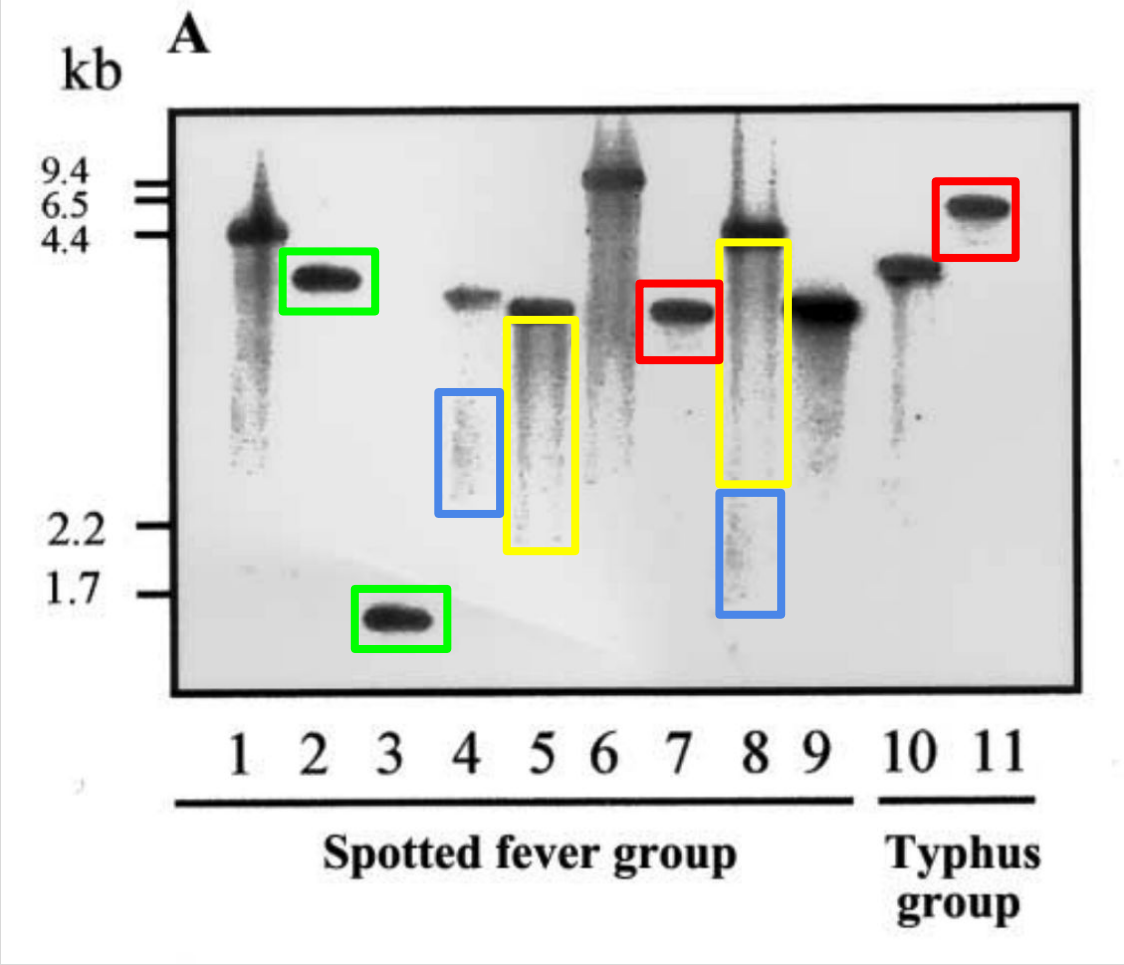


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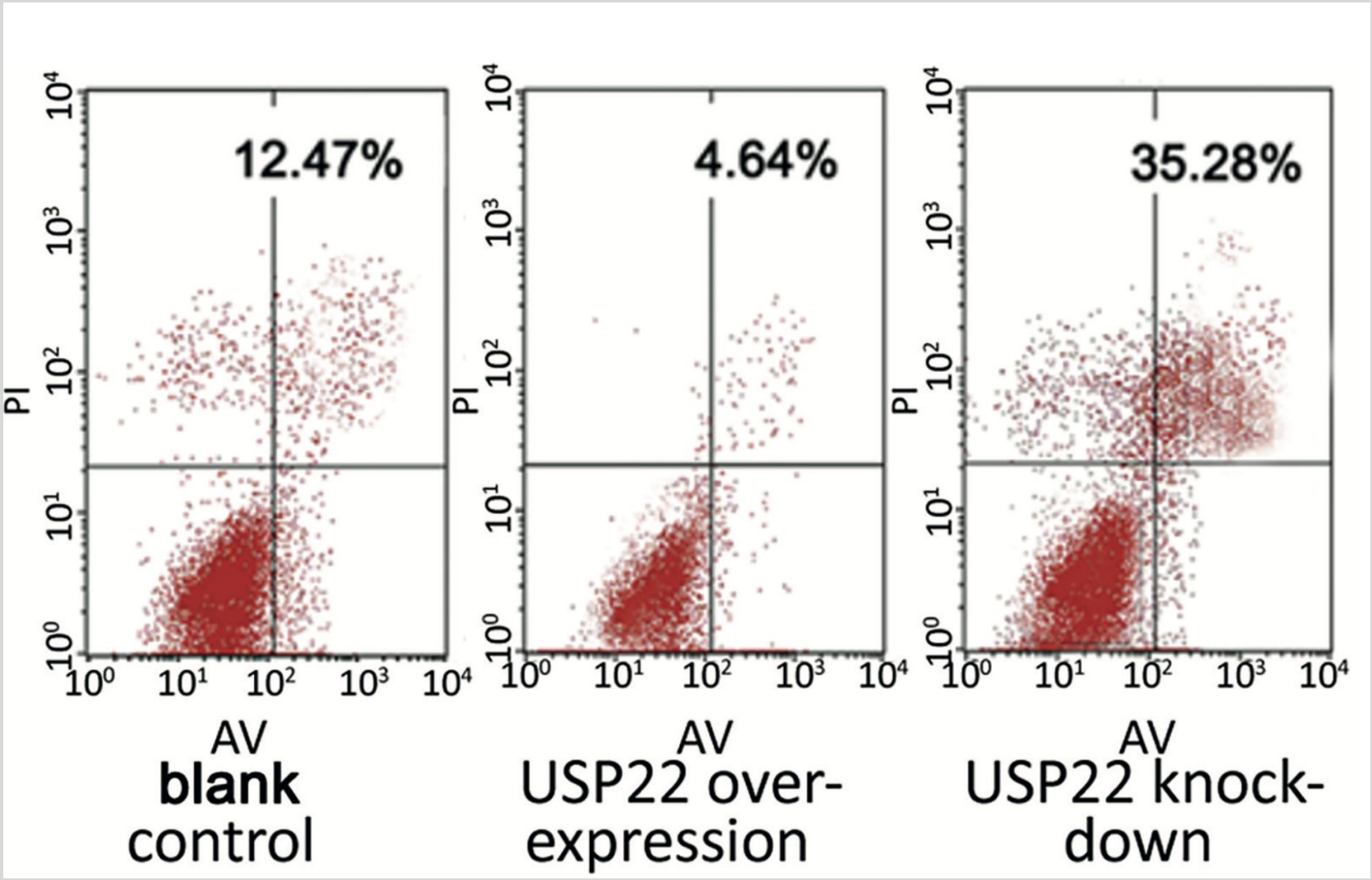

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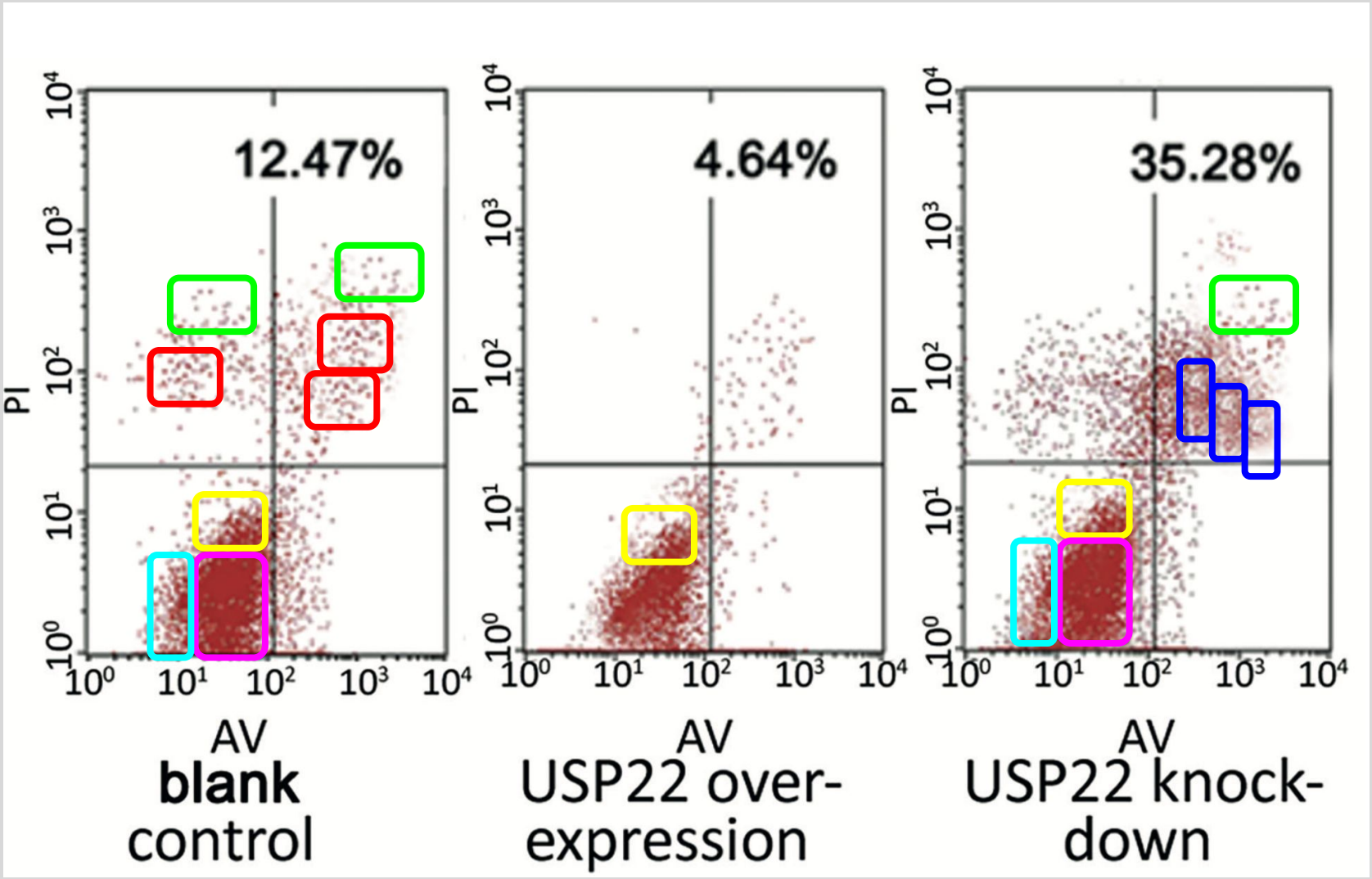


*PMID: 28682440 - Eur Rev Med Pharmacol Sci (2017) - reported on PubPeer July 2020*

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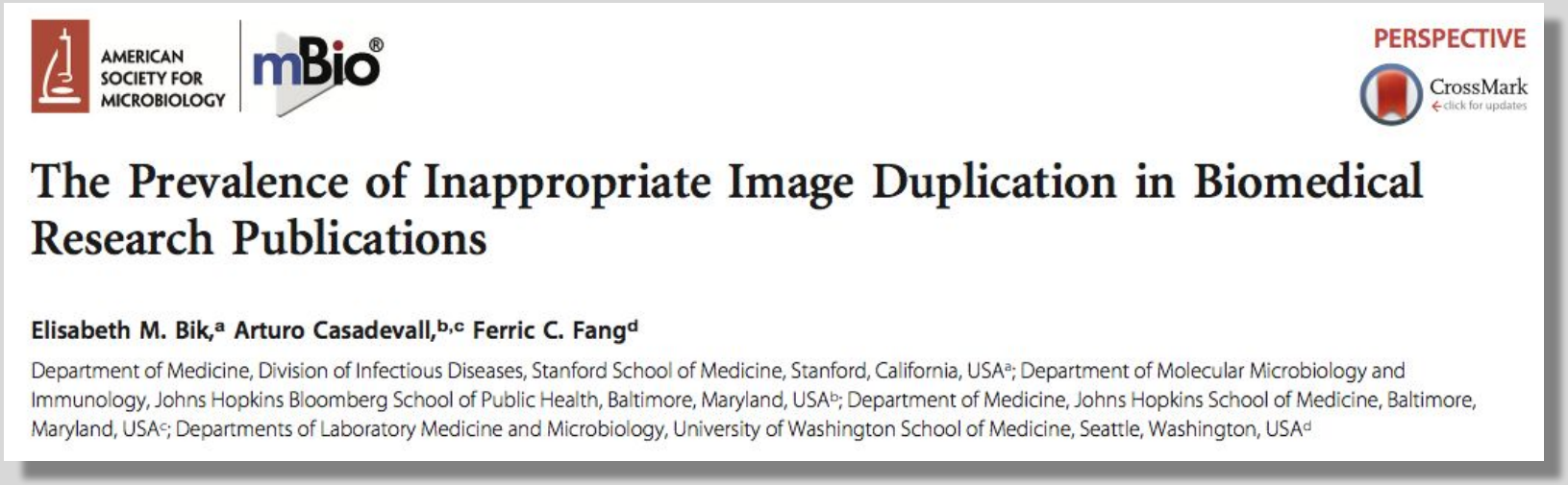

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PERSPECTIVE

CrossMark click for updates

**The Prevalence of Inappropriate Image Duplication in Biomedical Research Publications**

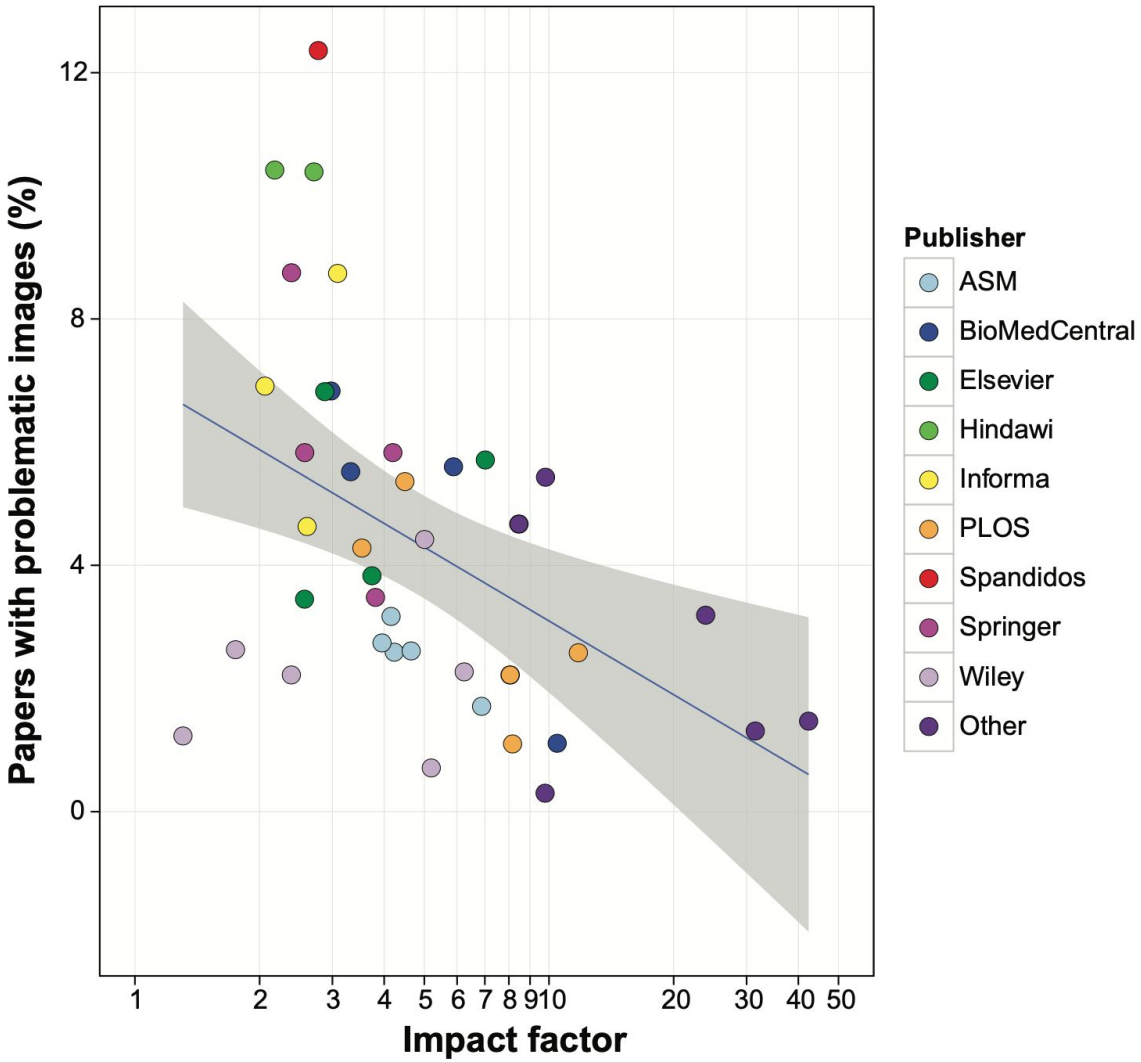
**Elisabeth M. Bik,[a] Arturo Casadevall,[b,c] Ferric C. Fang[d]**

Department of Medicine, Division of Infectious Diseases, Stanford School of Medicine, Stanford, California, USA[a]; Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA[b]; Department of Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland, USA[c]; Departments of Laboratory Medicine and Microbiology, University of Washington School of Medicine, Seattle, Washington, USA[d]

- I scanned 20,621 papers from 1995-2014 - by eye
- 40 journals from 14 publishers
- Found ~ 800 papers with duplicated figures (4%)
- 3 types: Simple - Repositioned - Altered
- Not all are misconduct! About half intentional: 2%
- Alteration in other data types much harder to detect

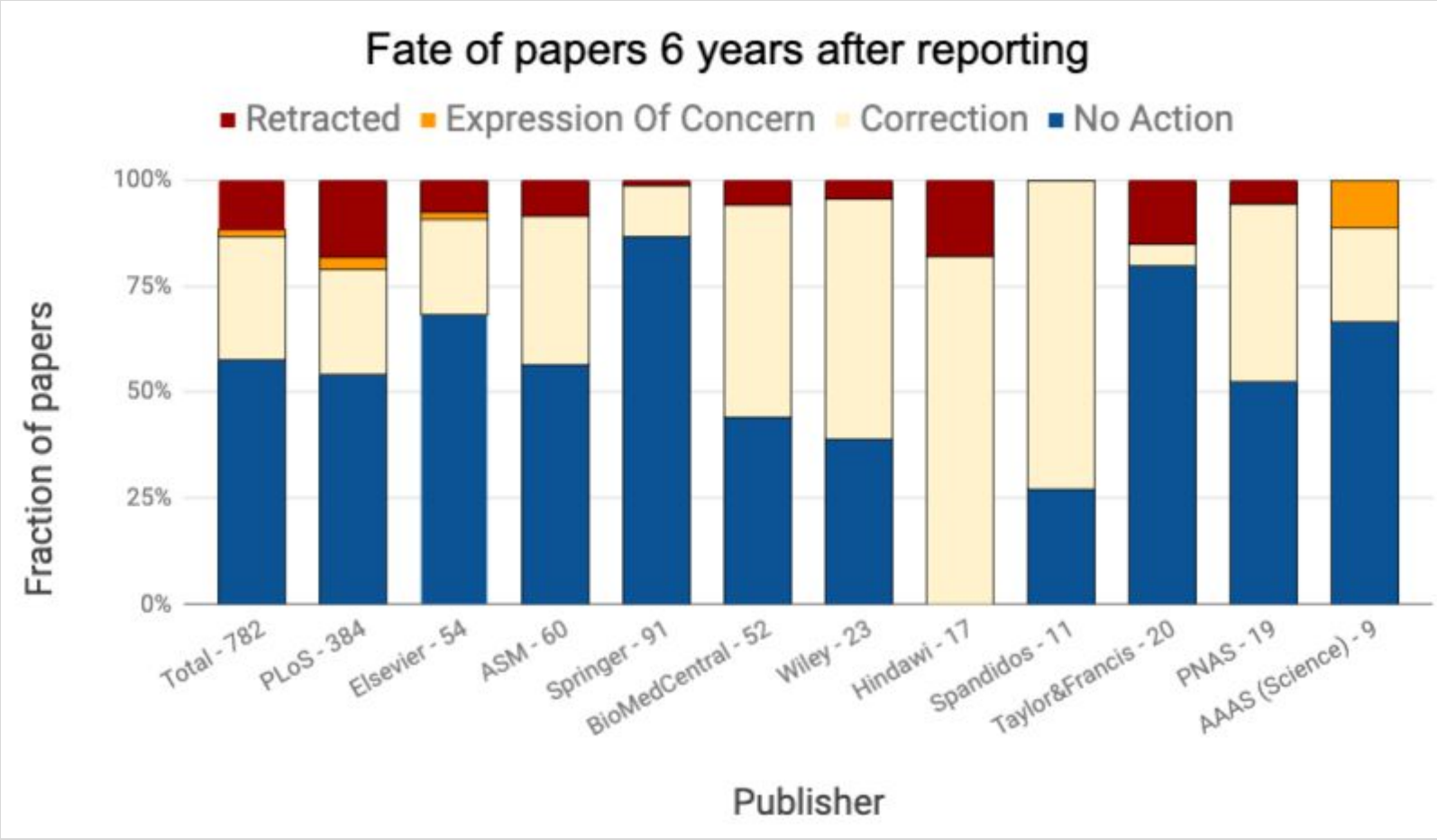
# High Impact Factor, fewer problems

*Bik EM et al. mBio 7(3):e00809-16 (2016), DOI: 10.1128/mBio.00809-16.*



# Journals are very slow to respond

*782 papers reported to journals - results after six years*
*60% of papers have not been corrected/retracted*



# #BadEditorialDecision: Author is Associate Editor

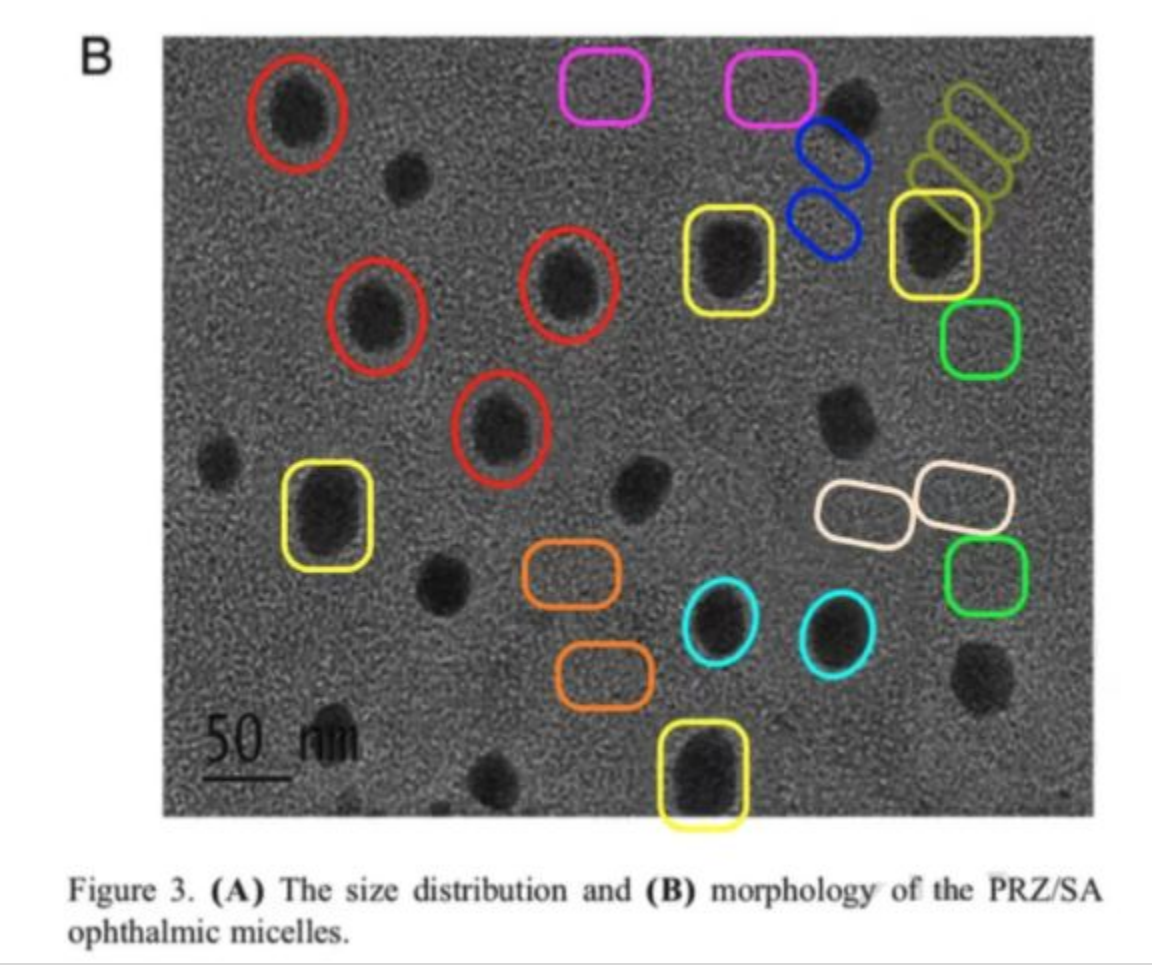
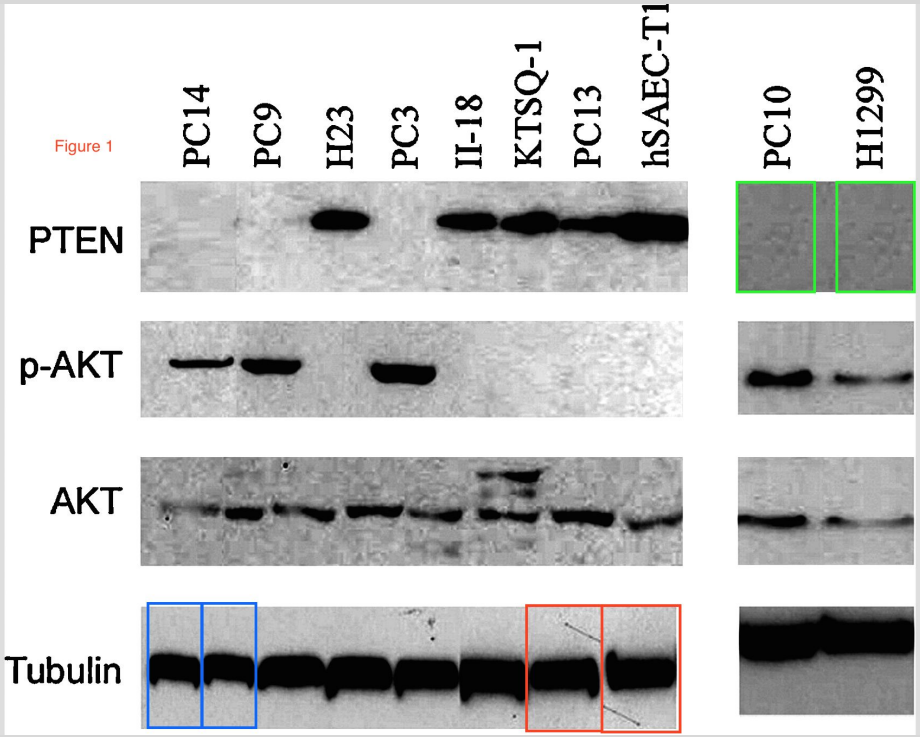


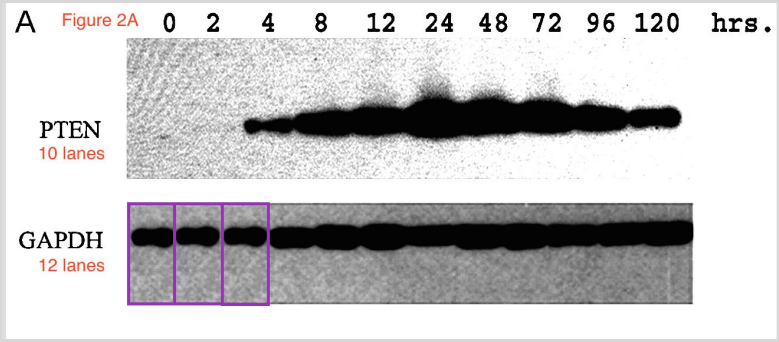

Figure 3. **(A)** The size distribution and **(B)** morphology of the PRZ/SA ophthalmic micelles.

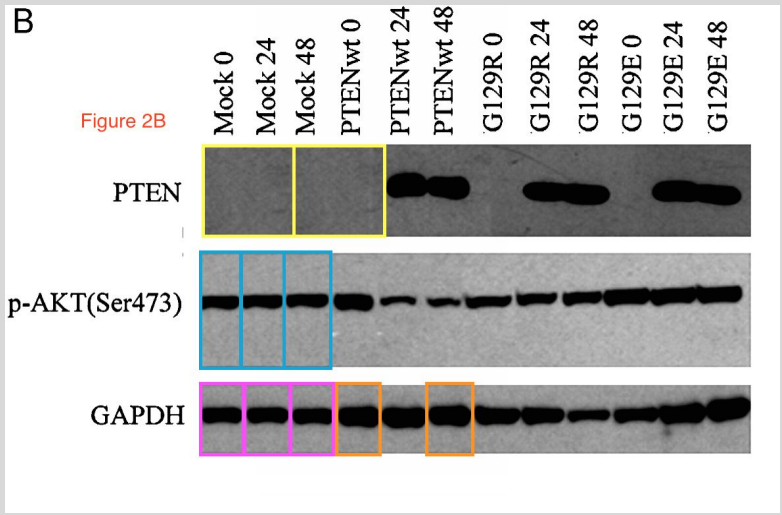
*Nanomedicine Nanotechnology Biology and Medicine (2017)*
*doi: 10.1016/j.nano.2017.05.001*
*Reported March 2020, Correction: October 2020*

# #BadEditorialDecision: The Naive Editor

"The publisher regrets that the authors mistakenly inserted the incorrect GAPDH line on Fig. 2A"




*Lung Cancer (2011)*
*doi: 10.1016/j.lungcan.2011.01.01*
*Reported October 2015, Correction: November 2016*

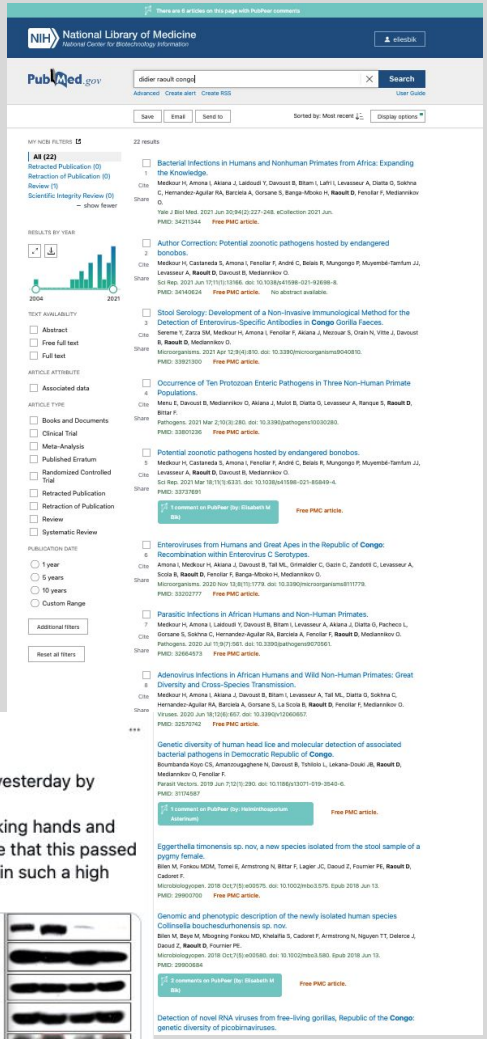
# Reporting concerns about research misconduct

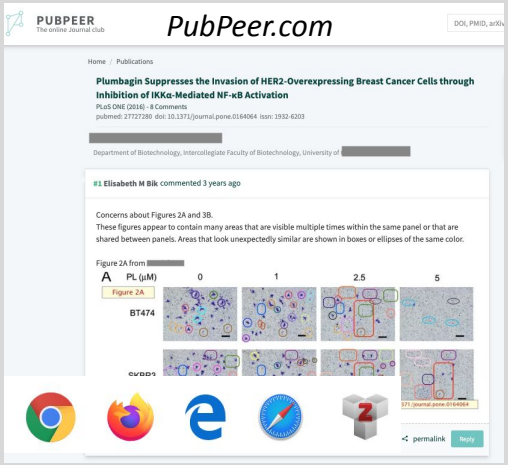
**The Official Professional Way:**

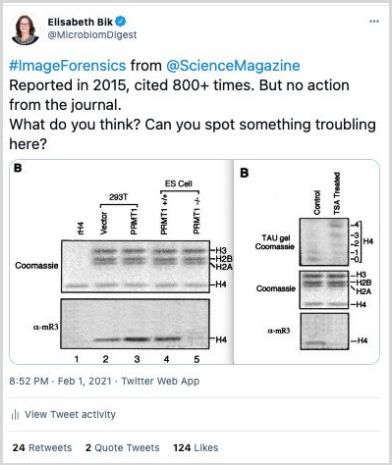
- Contact Editor-in-Chief of journal
- Contact Research Integrity Officer of the University
- Investigation might follow - or not

**The Experienced, Frustrated, and Proactive Way**

- Posting on PubPeer.com
- Posting on social media - Trial by Twitter?




# Scientific discussions in the courtroom

**Spider researcher uses legal threats, public records requests to prevent retractions**

Jonathan Pruitt

The case of Jonathan Pruitt, a spider researcher suspected of fabricating data in potentially dozens of studies, keeps getting weirder.

*Expression of concern turns into correction*

**Cancer researcher who once tried to sue critics is up to 40 retracted papers**

Welcome to the Top 10, Fazlul Sarkar.

Sarkar, the cancer researcher formerly of Wayne State University who once tried to sue critics on PubPeer, has had another seven papers retracted. That makes a total of 40, and places him in the Top 10 of our leaderboard of authors with the most retractions.

Fazlul Sarkar

*77 papers on PubPeer*
*40 retractions*
*tried to sue PubPeer*

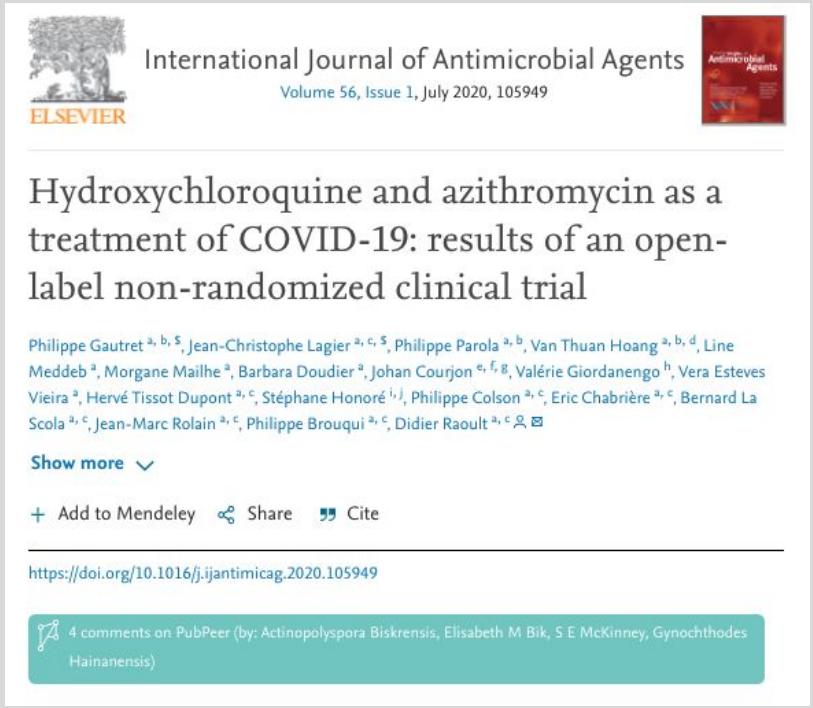
**Litigious OSU professor loses appeal in federal defamation case**

Carlo Croce

Carlo Croce, a cancer researcher at The Ohio State University who has had 10 papers retracted and at least as many subject to corrections or expressions of concern, has lost another court appeal.

*90 papers on PubPeer*
*10 retractions*
*Sued New York Times*
*Still a professor*

# Small study, many concerns, no action



International Journal of Antimicrobial Agents
Volume 56, Issue 1, July 2020, 105949

ELSEVIER

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret [a, b, $], Jean-Christophe Lagier [a, c, $], Philippe Parola [a, b], Van Thuan Hoang [a, b, d], Line Meddeb [a], Morgane Mailhe [a], Barbara Doudier [a], Johan Courjon [e, f, g], Valérie Giordanengo [h], Vera Esteves Vieira [a], Hervé Tissot Dupont [a, c], Stéphane Honoré [i, j], Philippe Colson [a, c], Eric Chabrière [a, c], Bernard La Scola [a, c], Jean-Marc Rolain [a, c], Philippe Brouqui [a, c], Didier Raoult [a, c]

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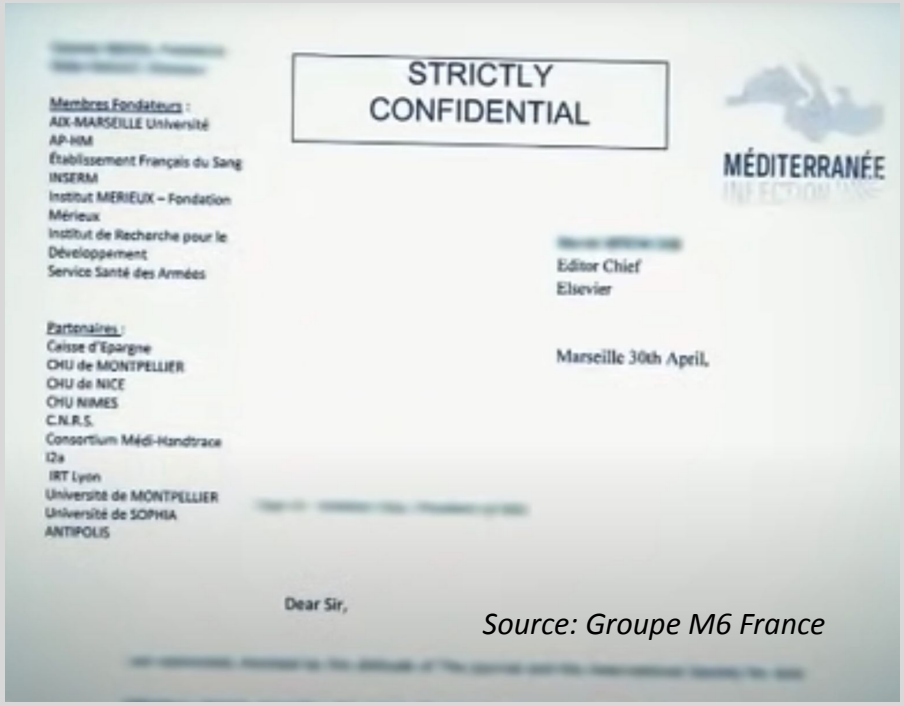
https://doi.org/10.1016/j.ijantimicag.2020.105949

4 comments on PubPeer (by: Actinopolyspora Biskrensis, Elisabeth M Bik, S E McKinney, Gynochthodes Hainanensis)



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MÉDITERRANÉE INFECTION

Editor Chief
Elsevier

Marseille 30th April,

Dear Sir,

Source: Groupe M6 France

*Expression of concern disappeared*

*"We consider this decision to be based exclusively on political and financial arguments and this dishonours you [...]*
*I'll send this file to my lawyer for harassment and defamation."*
*"I have no doubt that you will relinquish your decision to retract this study."*

# Legal threats for science whistleblowers

AAAS Become a Member

Science Contents News Careers Journals

Scientists rally around misconduct consultant facing legal threat after challenging COVID-19 drug researcher

By Cathleen O'Grady | May. 27, 2021 , 5:05 PM


Le Monde Se connecter S'abonner

SCIENCES · CORONAVIRUS ET PANDÉMIE DE COVID-19

Didier Raoult entame un bras de fer judiciaire contre une spécialiste de l'intégrité scientifique

L'infectiologue marseillais et un de ses lieutenants portent plainte pour « harcèlement, tentative de chantage et d'extorsion » contre la biologiste Elisabeth Bik, qui s'est interrogée sur plusieurs de leurs travaux sur le site PubPeer.

Par David Larousserie

# Paper Mills: Fake Papers

- Scientific paper mills sell fake papers to authors who need them
- China: Publication needed for promotion/raise medical doctors
- No time / lab to do research
- "Paper Mills" offer papers for US$ 5,000-10,000
- Written by ghostwriters based on a template



# Tadpole paper mill titles

| Insert the name of a molecule | Pick a verb (present tense, third person singular form) | Choose one or two cellular processes | Pick a cancer or cell type | Pick your connector word | Choose a verb (present particle form) for the mechanism | Insert name of miRNA or pathway |
|---|---|---|---|---|---|---|
| <protein name><br><drug name><br><RNA name> | alleviates<br>attenuates<br>exerts<br>governs<br>inhibits<br>prevents<br>promotes<br>protects<br>relieves<br>remits<br>retards<br>suppresses | apoptosis<br>autophagy<br>inflammation<br>invasion<br>migration<br>proliferation<br>viability | lung cancer<br>medulloblastoma<br>renal carcinoma<br>ovarian cancer | by<br>via<br>through | activating<br>attenuating<br>declining<br>downregulating<br>inhibiting<br>interfering with<br>modulating<br>targeting<br>regulating<br>upregulating | <miRNA name><br><pathway name><br><protein name> |

**Tripterine inhibits proliferation, migration and invasion of breast cancer MDA-MB-231 cells by up-regulating microRNA-15a**

**Ganoderic acid A alleviates hypoxia-induced apoptosis, autophagy, and inflammation in rat neural stem cells through the PI3K/AKT/mTOR pathways**

**Sinomenine exerts antitumour effect in gastric cancer cells via enhancement of miR-204 expression**

**Bifidobacterium plays a protective role in TNF-α-induced inflammatory response in Caco-2 cell through NF-κB and p38MAPK pathways**

**Knockdown of lncRNA HULC inhibits proliferation, migration, invasion and promotes apoptosis by sponging miR-122 in osteosarcoma†**

**The circular RNA ZNF292 alleviates OGD-induced injury in H9c2 cells via targeting BNIP3**

# Stock Photo Paper Mill: two of the 125 papers



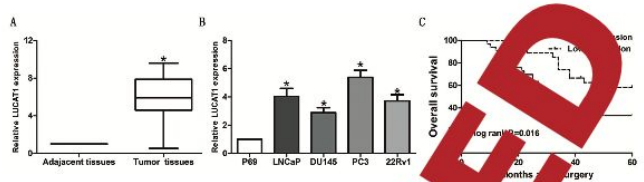



**Figure 1.** The expression levels of LUCAT1 increased in prostate cancer tissues and cell lines. LUCAT1 expression significantly increased in the prostate cancer tissues compared with adjacent tissues. The expression of LUCAT1 relative to β-actin were determined in the human prostate cancer cell lines and P69 (normal human prostate epithelial cell lines) by qRT-PCR. ***C,*** High level of LUCAT1 was associated with worse overall survival of prostate cancer patients. Data were presented as the mean ± standard error of the mean. *$p<0.05$.

method was performed for evaluating the prognosis. $p<0.05$ was considered statistically significant.

## Results

### *LUCAT1 Expression in Prostate Cancer Tissues and Cells*

QRT-PCR was performed to detect the expression of LUCAT1 in 56 tumor tissues and adjacent normal tissues. The result revealed that LUCAT1 was significantly upregulated in tumor tissue samples (Figure 1A). Identically, LUCAT1 expression in prostate cancer cells was significantly higher than that of HK-2 (human kidney epithelial cell) (Figure 1B).

### *LUCAT1 Expression was Related to Overall Survival of Prostate Cancer Patients*

After the surgery, the Kaplan-Meier method was utilized to analyze the survival time of prostate cancer patients. The prostate cancer patients were divided into two groups, the high-LUCAT1 group and the low-LUCAT1 group, based on their expression level of LUCAT1. The result of Kaplan-Meier analysis showed that prostate cancer patients with low LUCAT1 level had a better overall survival compared to those with high level (Figure 1C).

### *Overexpression of LUCAT1 Promoted Cell Migration and Invasion of Prostate Cancer Cells*

PC3 and DU145 prostate cancer cell lines were chosen in this study. First of all, the transfection efficacy of overexpression lentivirus targeting LUCAT1 was verified (Figure 2A). Moreover, the results of wound healing assay indicated that migrated ability of prostate cancer cells was significantly facilitated after LUCAT1 overexpression (Figure 2B). Furthermore, transwell assay also revealed that the number of

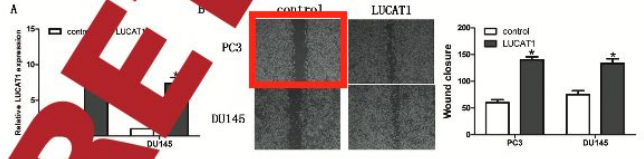



**Figure 2.** Overexpression of LUCAT1 promoted prostate cancer cell migration. ***A,*** LUCAT1 expression in prostate cancer cells transfected with LUCAT1 lentiviruses (LUCAT1) and the empty vector (control) were detected by qRT-PCR. β-actin was used as an internal control. ***B,*** Wound healing assay showed that the overexpression of LUCAT1 significantly increased cell migration in prostate cancer cells. The results represent the average of three independent experiments (mean ± standard error of the mean). *$p<0.05$.



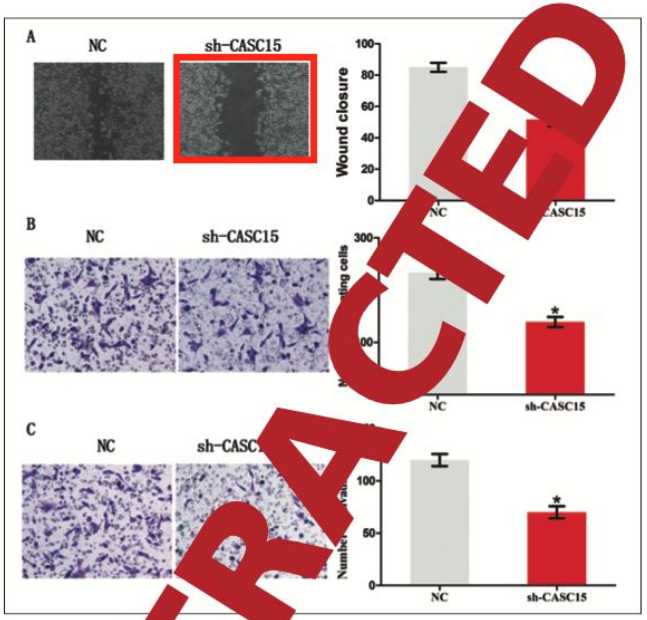


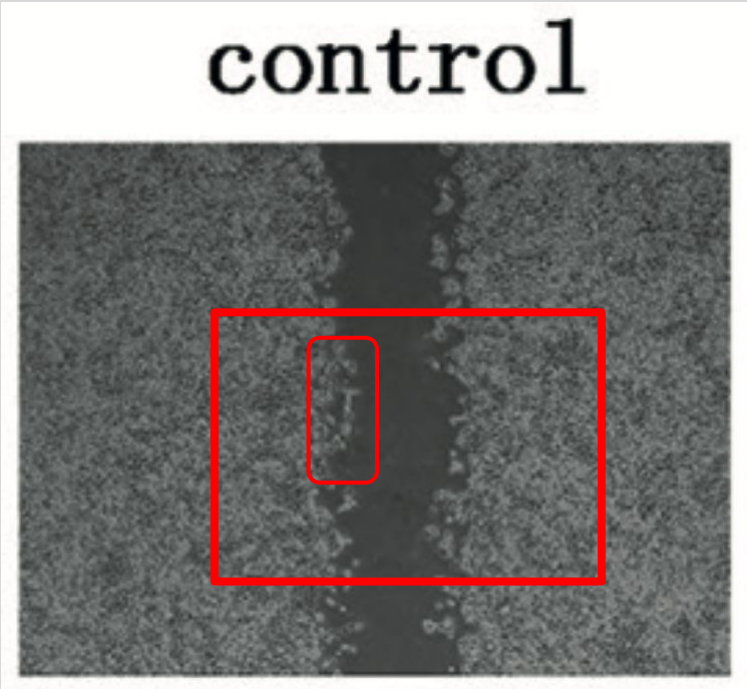

**Figure 2.** Functional assay showed that silenced CASC15 inhibited PC cell migration and invasion. **A,** Wound healing assay showed that wound closure was significantly decreased via silence of CASC15 in PC cells (magnification: 40×). **B,** Transwell assay showed that migrated cells was significantly decreased via knockdown of CASC15 in PC cells (magnification: 40×). **C,** Transwell assay showed that invaded cells was significantly decreased via knockdown of CASC15 in PC cells (magnification: 40×). *$p<0.05$, as compared with the control cells.

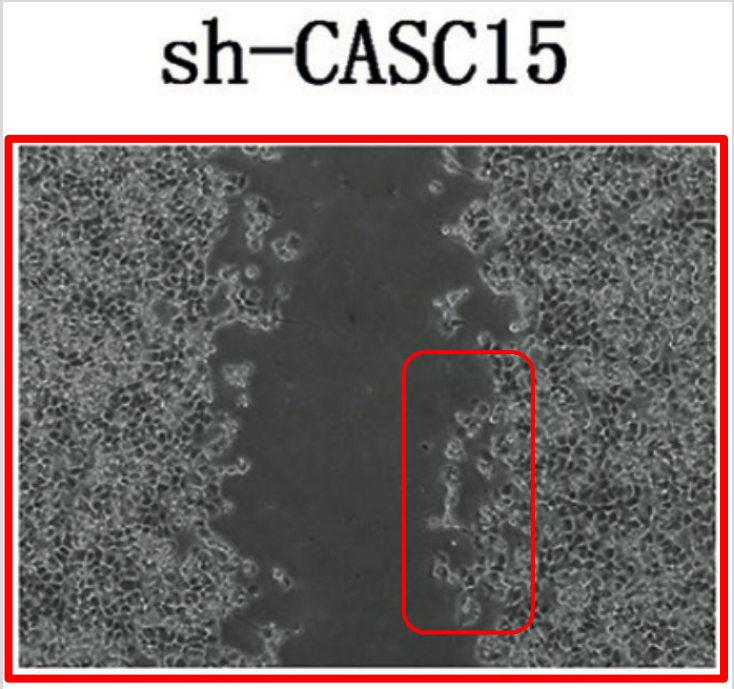
fection of CASC15 and miR-200a-3p had no effect on the activity either (Figure 3C). Further found a negative correlation between miR-200a-3p and CASC15 expression level in PC (Figure 3D).

### *The Interaction Between CASC15 and MiR-200a-3p in PC Migration and Invasion*

To further identify the association between CASC15 and miR-200a-3p in the metastasis of PC, we conducted rescue experiments in PC cells. Wound healing assay revealed that knockdown of miR-200a-3p could reverse the inhibition of cell migration by silence of CASC15 in DU145 cells (Figure 4A). Besides, results of transwell assay showed that knockdown of miR-200a-3p could reverse the inhibition of cell migration and invasion by silence of CASC15 in DU145 cells (Figure 4B and 4C).

# Stock photo paper mill: detail

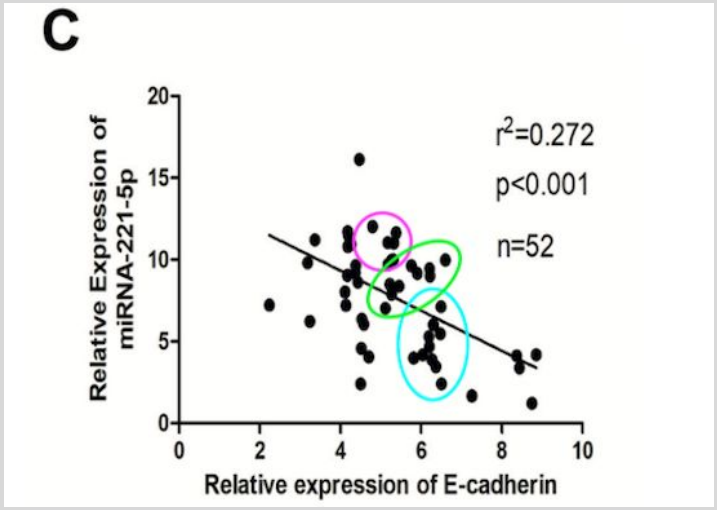


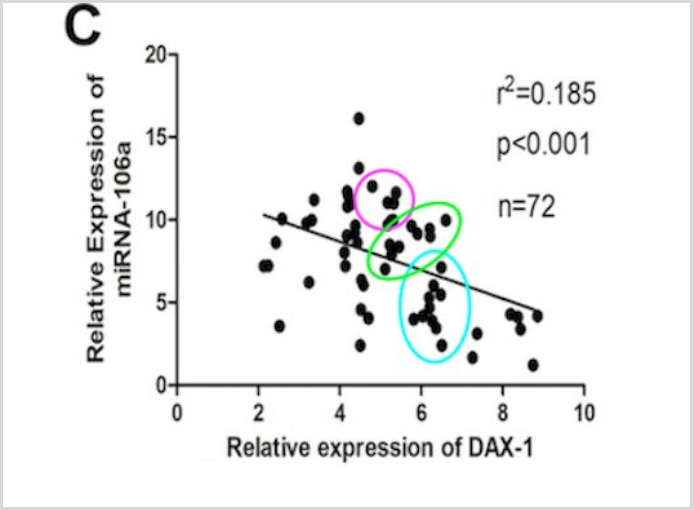



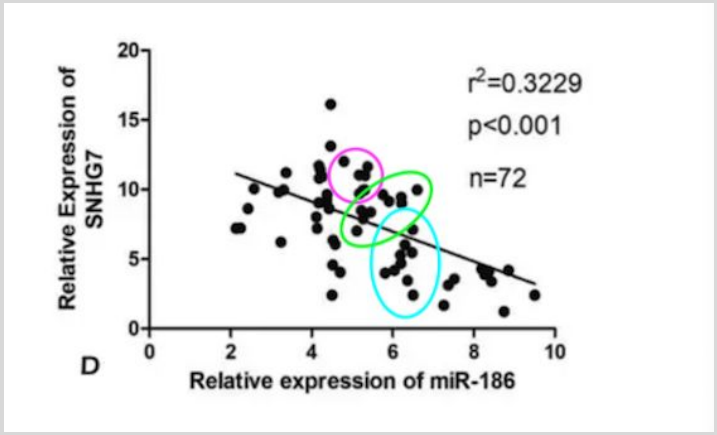

Stock photo paper mill: ~125 papers

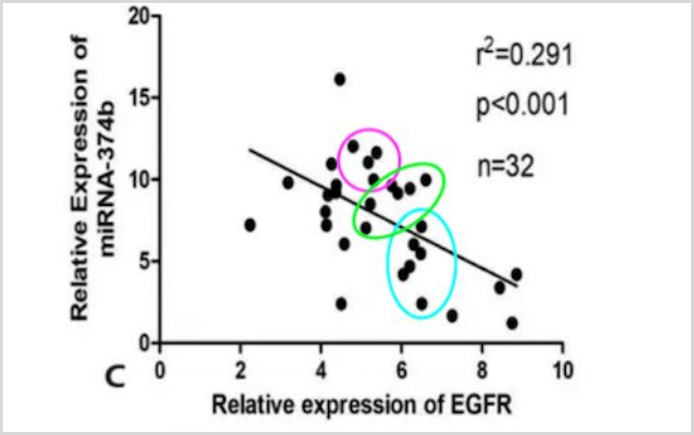
# Comb Paper Mill (200 papers): correlation plots

*Each of these four correlation plots came from a different paper. They represent different experiments. The papers came from different authors in different hospitals. But the graphs look unexpectedly similar.*



# Unexpected findings - can you spot it?

MiR-605-3p inhibits malignant progression of prostate cancer by up-regulating EZH2

**Table I.** Association of miR-605-3p expression with clinicopathologic characteristics of prostate cancer.

| Parameters expression | Number of cases | miR-605-3p | | *p*-value |
|---|---|---|---|---|
| | | High (%) | Low (%) | |
| Age (years) | | | | 0.964 |
| <60 | 20 | 12 | 8 | |
| ≥60 | 32 | 19 | 13 | |
| Gender | | | | 0.236 |
| Male | 25 | 17 | 8 | |
| Female | 27 | 14 | 13 | |
| T stage | | | | 0.043 |
| T1-T2 | 31 | 22 | 9 | |
| T3-T4 | 21 | 9 | 12 | |
| Lymph node metastasis | | | | 0.002 |
| No | 33 | 25 | 8 | |
| Yes | 19 | 6 | 13 | |
| Distance metastasis | | | | 0.033 |
| No | 38 | 26 | 12 | |
| Yes | 14 | 5 | 9 | |

# "Tortured phrases": Synonymized text

*A recent preprint describing papers that use unexpected, synonym terms. Often, these are plagiarized papers, in which text is "translated" to go undetected in plagiarism scanners.*

arXiv:2107.06751 Preprint, July 2021

**Tortured phrases: A dubious writing style emerging in science**

**Evidence of critical issues affecting established journals**

**Guillaume Cabanac · Cyril Labbé · Alexander Magazinov**

**Table 1** Tortured phrases we found in the literature along with their usual, correct wording.

| Tortured phrase found in publications | Correct wording expected |
|---|---|
| profound neural organization | deep neural network |
| (fake \| counterfeit) neural organization | artificial neural network |
| versatile organization | mobile network |
| organization (ambush \| assault) | network attack |
| organization association | network connection |
| (enormous \| huge \| immense \| colossal) information | big data |
| information (stockroom \| distribution center) | data warehouse |
| (counterfeit \| human-made) consciousness | artificial intelligence (AI) |
| elite figuring | high performance computing |
| haze figuring | fog/mist/cloud computing |

# Example of "tortured phrases" abstract

**Abstract:**
In the nonexistence of helpful discovering substantiations, it is mistaken for the ace to stand up about the survey of disease with authentication. All things considered many tests are done that incorporate gathering or portrayal of generous scale data. However many tests could befuddle the standard assurance process and incite to the inconvenience in procuring the last items, particularly for the circumstance where many tests are performed. This kind of inconvenience could be settled with the guide of machine learning strategies. In this paper study on three differing procedure are taken into the idea. The Data set, Cloud security and the Diabetes Disease are dismembered and seen with existing works. This review paper reveals distinctive existing approach that need managed for to certification the issue utilizing information mining framework.

**Published in:** 2017 Third International Conference on Science Technology Engineering & Management (ICONSTEM)

**Date of Conference:** 23-24 March 2017 **INSPEC Accession Number:** 17507400

**Date Added to IEEE *Xplore*:** 18 January 2018 **DOI:** 10.1109/ICONSTEM.2017.8261260

**ISBN Information:**



*The text of this abstract does not make much sense. The text was taken from a 2013 paper and run through a Synonym converter tool, probably to hide the plagiarism.*

# Science Misconduct: Discussion

- Why do people commit science misconduct?
- Are we focusing too much on publications/productivity?
- Conflicts of interest *(publishers, institutions)*
- Whose role is it to detect science misconduct?
- Legal protection for whistleblowers
- Tremendous cost of science misconduct *(scientists, science)*