

Publication Issues

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Introduction

Executive Yuan, Taiwan, "2 Trillion, Twin Stars" Plan

- Science & Technology Development Program (1979)
Promotion Plan for Biotechnology Industry (1995)
 - To position Taiwan as the center for human clinical trials in the Asia Pacific
 - to become a regional center for manufacturing of biotech products
 - to be the center for genomic R&D in Asia
 - to build the most vibrant biotech-focused venture capital industry in Asia

GCP is ...



- A standard by which clinical trials are designed, implemented and reported so that there is assurance that the **data are credible**, and that the rights, integrity & confidentiality of the **subjects are protected**

--ICH E6

Ethics is...

- Motivation based on ideas of right and wrong
- About
 - Minimizing harm
 - Maximizing benefit
 - Being fair
 - Being respectful of others



Study Results

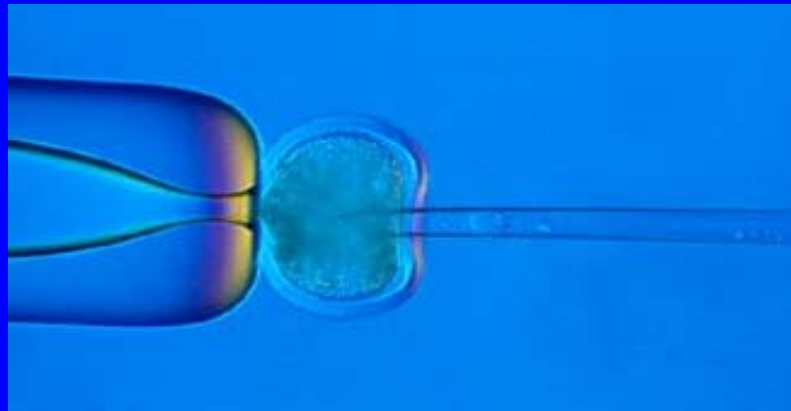
Publication

- Research: published in timely manner
- Data: presented accurately & clearly



Misconduct in Biomedical Arena

- Receives the most attention due to
 - greater public awareness & interest in health
 - more sponsored funding is available



Fraud definition

- “...when an author, editor or referee makes a false representation to obtain some unfair advantage or to injure deliberately the rights or interests of another person or group”

-- M. Laffollette

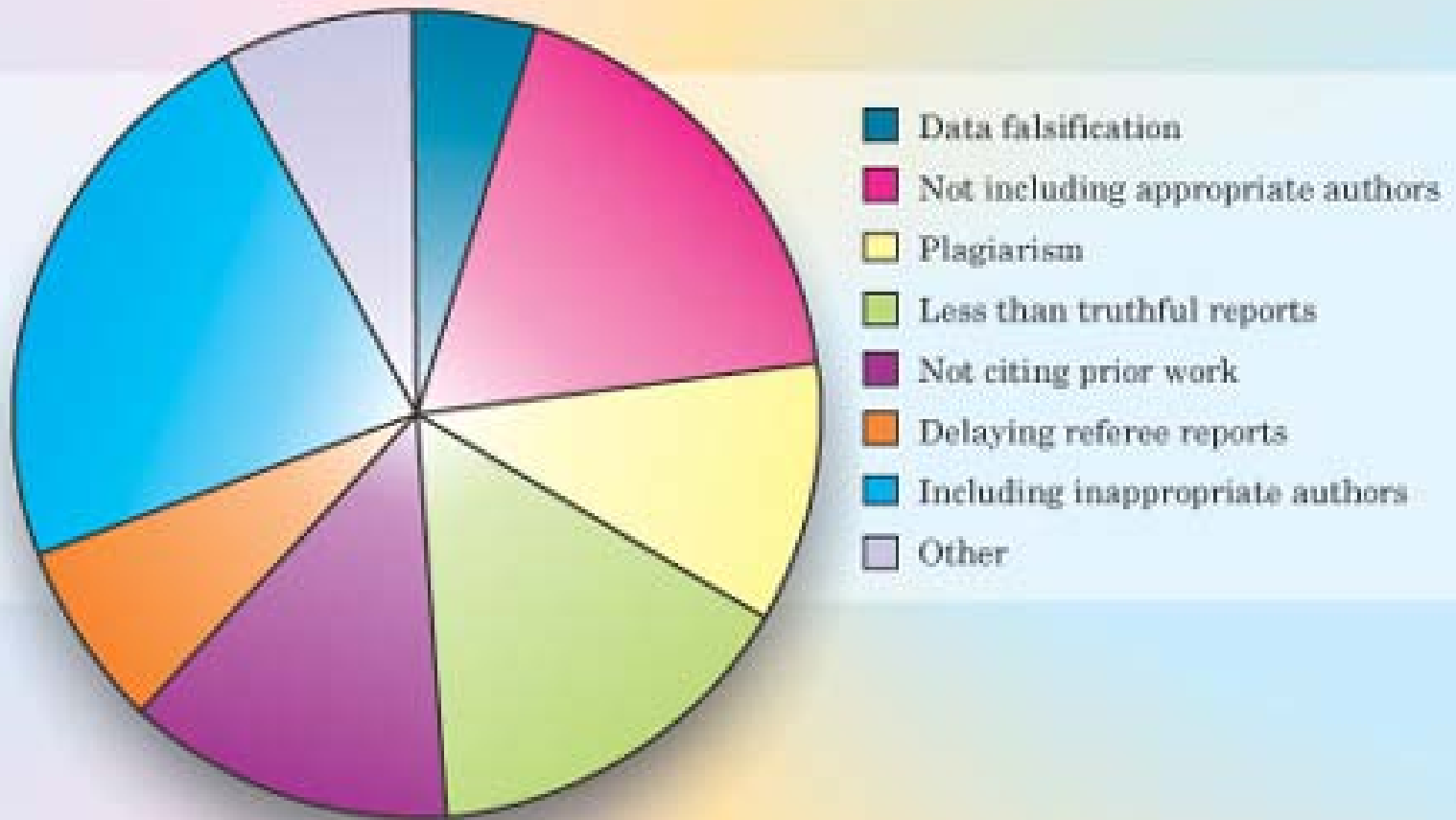


Fraud includes...

- Fabrication
- Falsification
- Plagiarism
- Misrepresentation of authorship
- Unreasonably delaying review or publication for personal gain



Scientific Misconduct

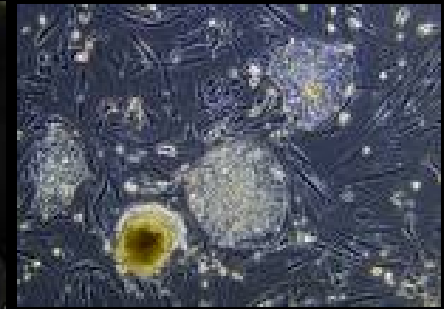


Source: <http://www.physicstoday.org/vol-57/iss-11/p42.html#cap1>

- Professionals receive most of their new knowledge by reading, especially the current peer-reviewed periodicals
- Research results should be published in a timely manner & in an appropriate venue



Fabrication



Woo Suk Hwang

- In 2006, Seoul National U delivered a damning report about Hwang's work on cloned human embryos, concluding it was all based on fraudulent data

Fabrication



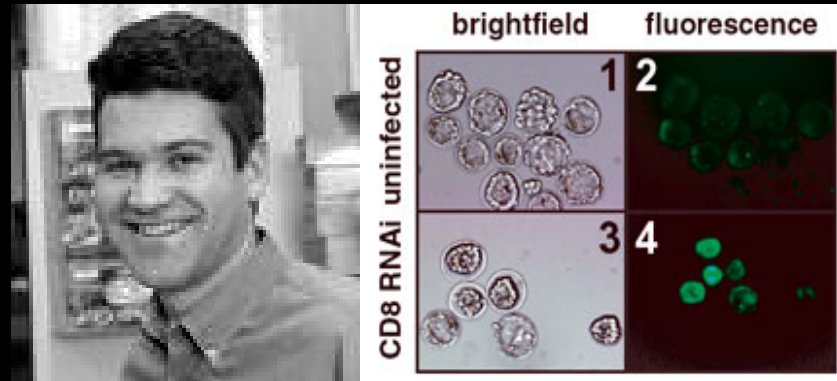
Jon Sudbo

- **BBC News**

Cancer study patients 'made up'

- A cancer expert invented patients for a study (published in Lancet) which concluded taking common painkillers could protect against oral cancer, it is alleged

Falsification

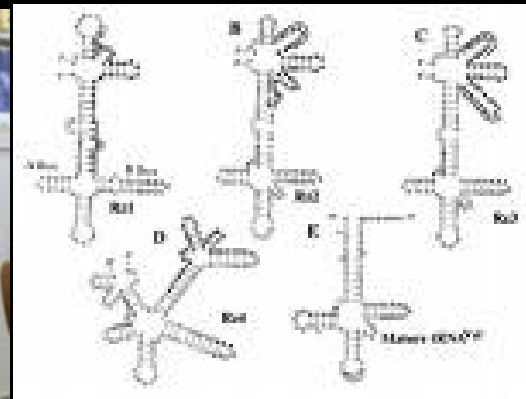


- MIT dismissed Van Parijs after his admission to fabricating & falsifying research data
- Van Parijs, whose research focuses on immune system functions and RNAi technologies, published that fraudulent paper in 2003 in Nature Genetics cited 247 times

Falsification

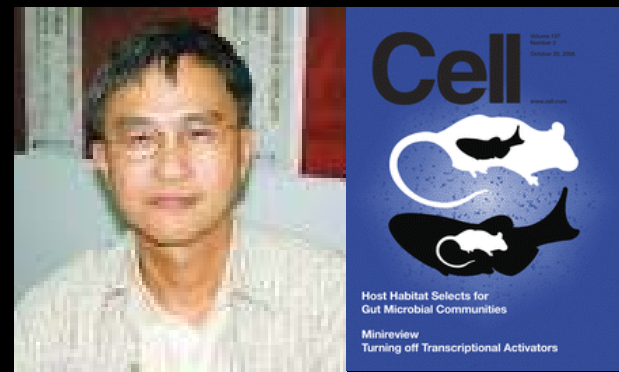


Kazunari Taira



- Tokyo U: the 2 RNA papers published in Nature by Taira is not reproducible
- Taira is known for his work on RNAi to intercept & regulate the process by which genes are turned into proteins
- 12 Taira's papers have been questioned

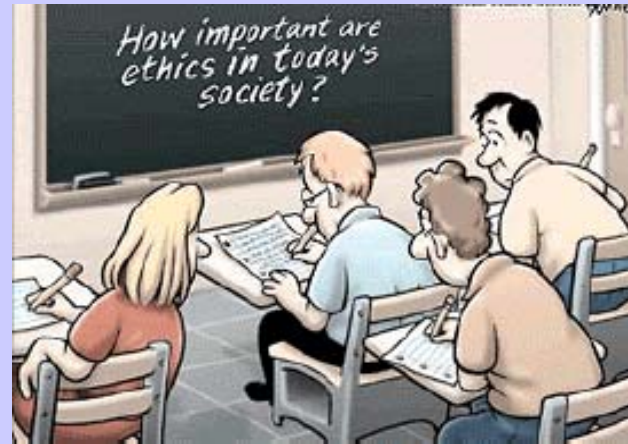
Falsification



Ban-Yang Chang

- Science. 2006, 314 (5806),1669
SCIENTIFIC MISCONDUCT: Online Sleuths Challenge Cell Paper
- CHU president, " Dr. Chang's findings will rewrite textbooks"
- Questions posted, "several dozen western lanes appeared to be copied and pasted"
- CHU, "The university will take this as a serious lesson for ethics education"

Plagiarism



- Use of sources from internet without proper documentation
- Undocumented use of sources from other written materials
- Use of other student's work as one's own
- To avoid plagiarism, quote and then cite the original source in a footnote

Why Fraud?

- Personal
- Financial
- COI between sponsor & PI



Conflict of Interest

- Financial
- Non-financial
- Might not be able to eliminate COI, but you can reduce, avoid, disclose



Prevention of Unethical Interpretation & Communication



FDA Concerns...

- FDA concerns for industry-sponsored studies
 - Independence
 - Timing of publication



FDA concerns about publishing
industry-sponsored studies most
frequently focus on independence
& how the sponsor may affect it



Case 1 B. Dong v. Boots

- Dong (UCSF), JAMA (1997): BE of generic & branded (Boots, sponsor) *l*-thyroxine
- Results
 - bioequivalence
 - \$356 M could be saved if substituted
- Trial finished in 1990. Why delayed?



Case 1 B. Dong v. Boots

Continued

- Conflicting views
 - PI: the results had important clinical implication & should be shared
 - Sponsor: concerned the market share
- UCSF: the study conducted in a way complied fully with the contract



Case 1 B. Dong v. Boots Continued

- UCSF's conclusion
 - No reason to suppress the manuscript, and to do so would be “an unprecedented intrusion upon academic freedom”



Suppressing publication of study results can be viewed as an intrusion upon academic freedom. However, industry sponsors may have other concerns e.g. patent infringement, commercial interests, liability issues



Case 1 B. Dong v. Boots

Continued

- 1994: MS submitted
- 1995: withdrawn due to “impending legal action by Boots against UCSF & Dong”
- ...
- 1997: published



Case 1 B. Dong v. Boots Continued

- Dong's contract clauses
 - All information contained in this protocol is confidential & used by the investigator only for the conduct of this study
 - Data obtained by the investigator while carrying out this study is also considered confidential & not to be published or otherwise released without written consent



Case 1 B. Dong v. Boots

Continued

- UCSF prohibits restrictions on publishing rights

“... the University will undertake research or studies only if the scientific results can be published or otherwise promptly disseminated” (signed by Dr. Dong)



Case 1 B. Dong v. Boots

Continued

- Fact

Protocol contracts with pharma sponsors often contain restrictive clauses, yet rarely have they prevented publication

- Dr. Dong believed these contracts, regardless of content, could not prevent publication



Protocol contracts with industry sponsors may contain restrictive clauses prohibiting publication without permission from the sponsor



Case 1 B. Dong v. Boots Continued

- 1996: came to the attention of the public
- 1994: FDA letter to Boots stated a Boots's article was misleading; its dissemination should cease. The study design (normal volunteers, studied 48 h) should be patients, chronic administration (precisely the one used by Dong)



Case 1 B. Dong v. Boots Continued

- Boots referred to the work by Dong, but dismissed it as “worthless”
- FDA: Dong study was appropriate to test BE & cited Boots for not previously disclosing the Dong results



Case 1 B. Dong v. Boots

Continued

- Boots ultimately agreed to publication of the manuscript
- JAMA published the paper along with apology letters from Boots



Case 2 D. Kern v. Microfibres Continued

- 1994: Dr. Kern (Brown U) observed a worker at Microfibres with ILD & visited the plant & signed a trade secret agreement
- 1996: learning of another worker with ILD & several cases afterward, Kern notified the company & NIOHS



Case 2 D. Kern v. Microfibres Continued

- Began to study the ILD “outbreak”. The company agreed but did not bring up the agreement signed in 1994
- Kern’s ensuing investigation identified another 6 “work-related” ILD cases



Case 2 D. Kern v. Microfibres Continued

- 1996: prepared an abstract to submit to 1997 ATS meeting
- Microfibres asked the draft not submitted, stating the publication would violate the agreement signed
- Kern notified administrators at both the hospital & the medical school



Sponsors & investigators may have conflicting perspectives on what constitutes a “trade secret.” Open communication before signing agreements is important



Case 2 D. Kern v. Microfibres Continued

- Submitted & presented the abstract at ATS meeting
- Got pressure from the company; at the same time, support from all over
- Published in *Annals of Internal Medicine*
- Microfibres never filed a lawsuit against any of the involved parties



Withholding Data

- Publishing the data > 6 M after completion of the study
- Most often the investigator (~20%) delay the dissemination of data, not the sponsor
- Major reason given: patent application
- Only 4% due to formal agreement with an industry sponsor



Tension btw investigators & industry
may occur due to

- Different interpretations of contractual text
- Different expectations of what will happen to the data



Learn Lessons from the Cases

- The research contract
 - Before signing, make sure you have the authority to do so for your institute
 - Read the contract!
 - Obtain the proper institutional reviews/approvals of the grant/contract prior to signing it
 - Ask the sponsor questions



Learn Lessons from the Cases

- Know your rights
- Review your employment contract before signing
- Recognize the different concerns of all parties involved
- Remember if you sign a contract without carefully reviewing it, you may be signing away certain rights



3 steps to prevent contract conflicts

- Read the contract. Know exactly what you are signing
- Ask questions. Clarify all issues & terminology
- Know your rights



The Data

- It is important to clarify
 - What data are
 - Who controls the data
- Different institutions have different definitions of what data are, for legal reasons



All contracts must be approved by
the institution **before** you sign them



The Data

- Regardless of the funding, the institution usually “owns” the data produced
- The “creator” of the data & the sponsor retain rights to access & use data
- Know how your institution defines data & what the institution’s perspective is regarding publication & presentation



The Data

- Read the contract carefully
- Do not assume the sponsors will encourage (or even permit) publication of unfavorable results
- Do not allow sponsors veto power for publication of data
- Know the position of your institution regarding restrictive clauses relating to the publication & dissemination of data



The Data

- Do not assume your institution will defend your academic freedom
- Ask questions about intentions of the sponsor regarding publication & dissemination of the results
- Be honest about your expectations regarding the presentation & publication of study results



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Thanks



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