

CONTEMPORARY CHALLENGES ON THE INTEGRITY OF SCIENCE:



The case of Hwang Woo-Suk

Who is Hwang Woo-Suk?

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- He was born in January 29th 1953. South Korea.
- He was a professor of theriogenology and biotechnology at Seoul National University (dismissed on March 20, 2006)
- Until November 2005, he was considered one of the pioneering experts in the field of stem cell research.
- Best known for two articles published in Science in 2004 and 2005.
- Both papers have been editorially retracted after being found to contain a large amount of fabricated data. He has admitted to various lies and frauds, but maintains he also was deceived by his collaborators.
- Government auditors have asked state prosecutors to file criminal charges against him.

Who was this man?

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“He was a national hero in South Korea, his research lab was probably one of the best funded in the world, and he flew first class anywhere he wanted, any time he wanted, for free, courtesy of Korean Air. He was treated like a rock star. His spectacular fall from one of the most envied positions in science plays out like a Greek tragedy.” [1]

[1] Dr Stephen Minger: *The Fall of a Scientific “Rock Star”*. BBC online: (Tuesday, 10 January 2006, 17:53 GMT) <http://news.bbc.co.uk/1/hi/sci/tech/4599974.stm>

The importance of the first publication

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- Hwang allegedly used the somatic cell nuclear transfer (SCNT) method and it was received as the first reported success in human somatic cell cloning.
- Hailed as a biotechnological breakthrough
- According to this publication, for the creation of a single cell line his research team used 242 eggs.

The importance of the 2nd publication

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- They claimed to have created 11 human embryonic stem cells (with somatic cells from patients of different age and gender) using 185 eggs.
- The team radically **improved the success rate** by 14 times.
- This would provide a method, a capability of creating biological material that are immunologically and genetically matched to patients.
- This brought significantly closer the **medical viability of the technology**;
- The prospect of providing patients with **custom-made treatments** without immune reactions;
- Moreover, it might be used for other **research purposes**, like making stem-cell lines that faithfully model human diseases.

Hwang first publication in *Science*

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Originally published in *Science Express* on 12 February 2004
Science 12 March 2004:
Vol. 303, no. 5664, pp. 1669 - 1674
DOI: 10.1126/science.1094515

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REPORTS

This article has been retracted

Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst

Woo Suk Hwang,^{1,2*} Young June Ryu,¹ Jong Hyuk Park,³ Eul Soon Park,¹ Eu Gene Lee,¹ Ja Min Koo,⁴ Hyun Yong Jeon,¹ Byeong Chun Lee,¹ Sung Keun Kang,¹ Sun Jong Kim,³ Curie Ahn,⁵ Jung Hye Hwang,⁶ Ky Young Park,⁷ Jose B. Cibelli,⁸ Shin Yong Moon^{5*}

Somatic cell nuclear transfer (SCNT) technology has recently been used to generate animals with a common genetic composition. In this study, we report the derivation of a pluripotent embryonic stem (ES) cell line (SCNT-hES-1) from a cloned human blastocyst. The SCNT-hES-1 cells displayed typical ES cell morphology and cell surface markers and were capable of differentiating into embryoid bodies in vitro and of forming teratomas in vivo containing cell derivatives from all three embryonic germ layers in severe combined immunodeficient mice. After continuous proliferation for more than 70 passages, SCNT-hES-1 cells maintained normal karyotypes and were genetically identical to the somatic nuclear donor cells. Although we cannot completely exclude the possibility that the cells had a parthenogenetic origin, imprinting analyses support a SCNT origin of the derived human ES cells.

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⁴ Gachon Medical School, Incheon, 417-840, Korea.

⁵ College of Medicine, Seoul National University, Seoul, 110-744, Korea.

The second in *Science*, 2005.06.17.

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RETRACTED 12 JANUARY 2006; SEE LAST PAGE

REPORTS

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grants EAR-9909225 and 9909565), the Petroleum

Research Fund (grants AC 37737 and AC 40735), and
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C. Dietl, and two anonymous reviewers for useful com-
ments on the manuscript.

Supporting Online Material

[www.sciencemag.org/cgi/content/full/308/5729/1774/](http://www.sciencemag.org/cgi/content/full/308/5729/1774/DC1)
DC1

Materials and Methods

SOM Text

Fig. S1

Tables S1 to S5

References

8 April 2005; accepted 21 April 2005

10.1126/science.1113408

Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts

Woo Suk Hwang,^{1,2*} Sung Il Roh,³ Byeong Chun Lee,¹
Sung Keun Kang,¹ Dae Kee Kwon,¹ Sue Kim,¹ Sun Jong Kim,³
Sun Woo Park,¹ Hee Sun Kwon,¹ Chang Kyu Lee,² Jung Bok Lee,³
Jin Mee Kim,³ Curie Ahn,⁴ Sun Ha Paek,⁴ Sang Sik Chang,⁵
Jung Jin Koo,⁵ Hyun Soo Yoon,⁶ Jung Hye Hwang,⁶
Youn Young Hwang,⁶ Ye Soo Park,⁶ Sun Kyung Oh,⁴ Hee Sun Kim,⁴
Jong Hyuk Park,⁷ Shin Yong Moon,⁴ Gerald Schatten^{7*}

Retracted publications:

<http://retractionwatch.com/>

Retraction Watch

Tracking retractions as a window into the scientific process

IRB mishap costs MD Anderson team a paper on prostate cancer

with 3 comments

A group of researchers from MD Anderson Cancer Center in Houston has lost a 2013 paper in [BJU International](#) for running afoul of their institution's ethics review board, and of military reviewers, as well.

The paper, "Many young men with prostate-specific antigen (PSA) screen-detected prostate cancers may be candidates for active surveillance," looked at prostate cancer screening in men 55 and under — considered young for the older-man's disease. According to the abstract: [Read the rest of this entry »](#)



Written by amarcus41
February 18, 2014 at 2:27 pm

Posted in [BJU International](#), [freely available](#), [lack of IRB approval](#), [md anderson](#), [oncology retractions](#), [united states](#), [wiley retractions](#)

Retractions are useful for teaching science, say college profs

with 11 comments

From time to time, we find online college syllabi among those sites referring us traffic, and some professors have told us that they use Retraction Watch in their classes. We're pleased and humbled by that.

In a [new paper](#) published in the *Journal of College Science Teaching*, three professors at Clayton State University in Morrow, Georgia, discuss why retractions are good case studies for teaching ethics and examining the scientific process in class. [Stephen Burnett](#), [Richard H. Singiser](#), and [Caroline Clower](#) write: [Read the rest of this entry »](#)



Written by ivanoransky
February 18, 2014 at 9:30 am

Posted in [studies about retractions](#)

Failure to reproduce leads to retraction of Nature Chemical Biology herbicide paper

with 8 comments

A group of researchers at Emory has retracted a highly regarded paper after being



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Retracted! – experimental errors were found, the results could not be reproduced

Doing the right thing: Authors retract protein paper after finding experimental errors

with 11 comments

A group of researchers in the Netherlands has retracted a paper once they realized that the findings weren't reproducible and that there had been an error in the experiments.

Here's the [notice](#) for "Ubiquitin-specific protease 4 is inhibited by its ubiquitin-like domain," by MP Luna-Vargas, AC Faesen, WJ van Dijk, M Rape, A Fish, and TK Sixma: [Read the rest of this entry »](#)



Written by ivanoransky
January 10, 2014 at 12:30 pm

Posted in [cell biology](#), [crystallography retractions](#), [doing the right thing](#), [freely available](#), [investigator error](#), [not reproducible](#)

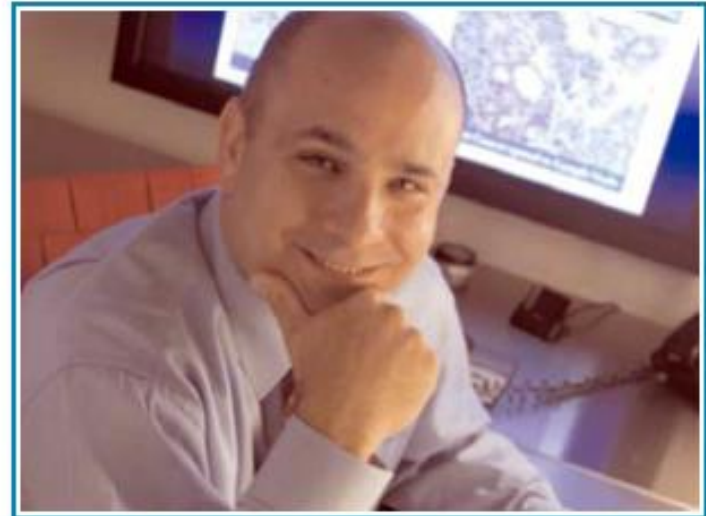
A John Hopkins University researcher: the 6th retracted paper

Former Hopkins and Pitt cancer researcher notches sixth retraction

leave a comment »

[Robert Getzenberg](#), a former researcher at Hopkins and Pitt, has retracted a sixth paper, this one in *Cancer Research*.

Here's the [notice](#) for "Mechanistic Analysis of the Role of BLCA-4 in Bladder Cancer Pathobiology:" [Read the rest of this entry](#) »



Written by ivanoransky
February 4, 2014 at 11:43 am

Posted in [cancer research](#), [freely available](#), [not reproducible](#), [oncology retractions](#), [robert getzenberg](#), [united states](#), [wrong reagents](#)

A Tokio University endocrinologists having his 23rd retracted publication...

Shigeaki Kato up to 23 retractions

with 8 comments

Shigeaki Kato, the former University of Tokyo endocrinology researcher found to have manipulated images in dozens of papers, has six more retractions, bringing his total to 23.

Five of them appear in *Molecular and Cellular Biology*. [Read the rest of this entry](#) [»](#)



Written by ivanoransky
February 7, 2014 at 2:28 pm

Posted in [corrections](#), [endocrinology](#), [freely available](#), [image manipulation](#), [japan retractions](#), [molecular and cellular biology](#), [nature publishing group](#), [oncogene \(journal\)](#), [shigeaki kato](#)

The authors were manipulating the citations in order to increase the impact factor of their own journal

Citation manipulation: Journal retracts paper because author boosted references to a journal he edits

with 5 comments

A group of researchers have lost a paper in a computer science journal because they were apparently using its references to help the impact factor of a different journal that one of them edits.

Here's the [notice](#) for "Impacts of sensor node distributions on coverage in sensor networks," a paper first published in 2011 and cited four times, according to Thomson Scientific's Web of Knowledge: [Read the rest of this entry »](#)



Written by ivanoransky
February 3, 2014 at 9:30 am

Posted in [citation manipulation](#), [computer science](#), [elsevier](#), [freely available](#), [greece](#), [j parallel distrib comp](#), [turkey retractions](#), [united states](#)

Hwang's cloned dog, Snuppy

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- On August 3, 2005,
- the first team to successfully clone a dog.^[1]
- after the series of investigations regarding Hwang's work, something that has proved to be genuine in January 2000.

[1] Hwang WS, *et al.* (2005). "Dogs cloned from adult somatic cells". *Nature* **436** (7051): 641. [PMID 16079832](#) [DOI:10.1038/436641a](#).

November 2005 the scandal broke out

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- Gerald Schatten has announced to cease his nearly two year long collaboration with Hwang.
- *"my decision is grounded solely on concerns regarding oocyte (egg) donations in Dr. Hwang's research reported in 2004."*
- G.S. Also requested the editors of Science to remove his name from their joint paper.
- This led to a chain of events:
 - from discussing ethical lapses,
 - to investigations on scientific validity and;
 - to an ongoing procedure of prosecution against Hwang.

Ethical lapses: the egg procurement procedure

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- November 2005 a close collaborator of Hwang, *Roh Sung-il*, admitted that he had paid women 1400 US\$ each. Members of his research lab also donated their eggs

- Informed consent given by the donors became questionable:
 - Coercive?
 - Voluntariness?
 - Fully informed about risks?

- At the end of November *Hwang* said he did not coerced his colleagues and he was unaware of payments, but resigned from his post:
„I was blinded by work and my drive for achievement”

The SNU investigative committee

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- Started their work on 2005 15th of Dec.
- It had to determine:
 - Hwang's and his research team's technical competence;
 - The scientific validity of both Science publications;
 - Snuppy's, the cloned dog's real status, and;
 - the details of the egg donations.

The SNU committee published its report,

2006 9th of January

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- In the 2005 Science publication:
- all the data were fabricated, including:
 - tests results from DNA fingerprinting,
 - photographs of teratoma,
 - embryoid bodies,
 - MHC-HLA isotype matches and karyotyping.

The SNU report

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- Considering the 2004 paper:
- 23 samples were examined for DNA fingerprinting analysis
- by three independent centres, and all of these have obtained identical results
- that called forth the conclusion of the panel:
- *“results described in 2004 Science article including DNA fingerprinting analyses and photographs of cells have also been fabricated.”*

The SNU report

19 The number of donated eggs:

- *“From November of 2002 to November of 2005, a total of 2061 eggs from 129 females have been collected from four hospitals and provided to Professor Hwang's team”.*
- The number of used eggs in the published research is uncertain.
- Egg donations were voluntary.
- Hwang knew about the details of the procedure.
- Snuppy status as a cloned dog became confirmed:
“Results from analyses of 27 markers that allow distinguishing amongst extremely-inbred animals and of mitochondrial DNA sequencing indicate that Snuppy is a somatic cell clone of Tie”

Hwang's first reaction

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- Apologized for the fiasco, but denied cheating.
- Accused of the other members of deceiving him with false data.
- Conspiracy, sabotage, theft of materials involved.
- A certain part of the South Korean public still thinks about the issue in terms of a US conspiracy against their national hero.



Dr. Hwang Woo-suk, center, beside His junior researchers in the press Conference held at the National Press Center in Seoul on Jan. 12, 2006.

First reactions to the Hwang case:

21” “Problems with landmark paper may set field back by years.”

News

Nature **438**, 1058-1059 (22 December 2005) | doi:10.1038/4381058a

Special Report

Where now for stem-cell cloners?

Erika Check

Researchers assess their field after Woo Suk Hwang's revelations.

Scientists are surveying the wreckage left by the debacle involving stem-cell researcher Woo Suk Hwang after three co-authors on his landmark paper said that it could not be trusted. Researchers now face a long slog to rebuild the foundations of their field.

Evident consequences

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- Public trust
- Funding
- Financial harm
- Negative influence on the policy debate



South Korean Commemorative Stamps for Hwang's Research, Retracted in

Commentators are questioning...

23

- authorship in international mega-collaborations: who is responsible for what?
- the validity of scientific peer review;
- editorial practices of searching for the next big story;
- Authorship practices
- For profit science and conflicts of interests
- biomedical research is out of control (pace, competitiveness), „publish or perish“;
- the pressure from the Korean government: huge investments. In 1994 launched the *Biotech 2000 Project*

Inadequacy of the peer-review system?

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- Peer review is not the right tool to avoid the publication of fraudulent papers.
- Trust cannot be eliminated. (Although some journals started to check digital photo fabrication practices)
- Peer review alone cannot guarantee good scientific practice. (Although the Council of Science Editors insisting on changes)
- Peer-review is just one element in the larger system of science governance.

Inadequacy of the larger system of science governance?

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- Some points to consider in the case of South Korea:
- The distribution of grants and financial support is strongly based on government decisions, and strategies, rather than on review, competition, hearings and application.
- Park Ky Yong (advisor to the SK president for science and technology) was added to the list of authors to Hwang's 2004 *Science* paper.
- Yang Sam-Sung (the head of SK National Bioethics Committee) was Hwang's lawyer.
- Within this feudal framework Hwang became a leading figure in a national project that secured within few years considerable financial resources.
- After the 2005 *Science* paper Korean biotech stocks were rising threefold.

Research misconduct: under control?

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- Because of the mentioned harms, there is a tendency to pinpoint to the growing need „to do something” for promoting research integrity.
- What to do? E.g. Minimizing the number of reserach misconduct cases through education and oversight.
- Establishing international guidelines, regulations, standards. Harmonization of existing ones.

Defining research misconduct

27

- Most definitions include only (intentional!) **F**alsification, **F**abrication and **P**lagiarism.
- Some widen the scope to gross negligence in FFP cases.
- Research malpractice (Chubin, 1985): a wider definition that includes mundane misbehaviors.

Research misconduct statistics

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- No data before the 1990's.
- USA, estimation: 1 case in 100.000,
2 million active researchers.
- Between 1990 and 2002 the Office of Inspector General at the NSF investigated 800 allegations of misconduct in 600 cases.
- In 2002, the ORI reported that 99 institutions had 83 cases of misconduct, with 71 institutions reporting a new allegation.
- Both institution agrees that the cases were underreported: resolving allegations without reporting.

Scientists behaving badly ^[1]

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- Collecting data about everyday misbehaviour, beyond FPP.
- Letting scientists define what count as misbehaviour (focus groups)
- Six compliance officers assessed the seriousness of the specified behaviours to form a rank.
- Using self reports: „Have you engaged in the listed behaviours in the last three years?“ (anonymity)
- Large random samples of US scientists funded by NIH

Table 1 | Percentage of scientists who say that they engaged in the behaviour listed within the previous three years (n = 3,247)

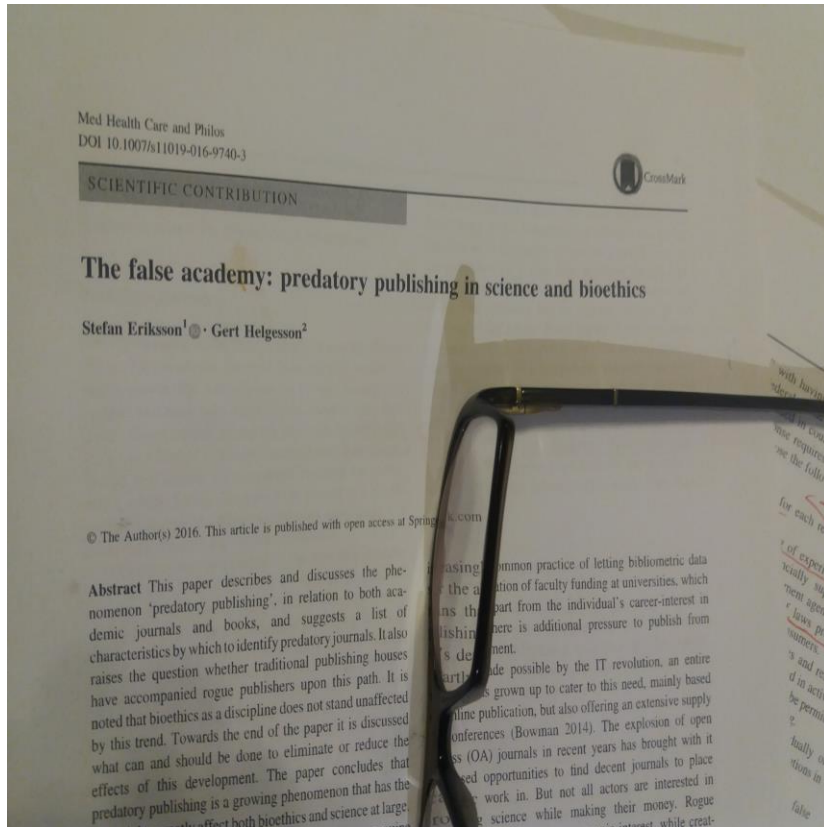
Top ten behaviours	All	Mid-career	Early-career
1. Falsifying or 'cooking' research data	0.3	0.2	0.5
2. Ignoring major aspects of human-subject requirements	0.3	0.3	0.4
3. Not properly disclosing involvement in firms whose products are based on one's own research	0.3	0.4	0.3
4. Relationships with students, 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 *** ($P < 0.001$).

Looking
Beyond FFP
(Fabrication
Fasification
Plagiarism)

Percentage of s scientists who say that they engaged in the behaviour listed within the previous three years (n=3247)

The False Academy



Open Access Scholarly Publishers Association <http://.oasp.org/> 2008

Blacklist, <http://scholarlyoa.com/> 900 journals

+ others = cc. 8000 scientific journals globally

White list: Directory of Open Access Journals, www.doaj.org

Authorship for sale: China's Publication Bazaar, Int Jor Biochem Cell Biol. 1 4800 USD.

False review, Books: „vanity publishing” Conferences

Blacklist: <http://scientificspam.net/>

Thank you for your attention!