Good Research Practice

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Definitions

- Research – systematic search for knowledge
- Results in new knowledge
- Replication of previously published knowledge (not new) with the aim of confirming them (sound conclusions)
- Systematic-critical review and compilation of previous results in a certain area that can raise knowledge levels

Research misconduct

- Fabrication of evidence, data, results or consents
- Misrepresentation of evidence, data, results or consents
- Undisclosed duplication of publication Inappropriate attribution of work
- Failure to declare a conflict of interests
- Plagiarism - i.e. the copying of ideas, data or text without permission or acknowledgement
- Mismanagement of data or evidence
- Breach of duty of care to subjects/participants

The Woo Suk Hwang Case (2004)

Science
AAAS

Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst
Woo Suk Hwang *et al.*
Science **303**, 1669 (2004);
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Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst

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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.

RETRACTION

Post date 12 January 2006

The final report from the Investigation Committee of Seoul National University (SNU) (*1*) has concluded that the authors of two papers published in *Science* (*2*, *3*) have engaged in research misconduct and that the papers contain fabricated data. With regard to Hwang *et al.*, 2004 (*2*), the Investigation Committee reported that the data showing that DNA from human embryonic stem cell line NT-1 is identical to that of the donor are invalid because they are the result of fabrication, as is the evidence that NT-1 is a bona fide stem cell line. Further, the committee found that the claim in Hwang *et al.*, 2005 (*3*) that 11 patient-specific embryonic stem cells line were derived from cloned blastocysts is based on fabricated data. According to the report of the Investigation Committee, the laboratory "does not possess patient-specific stem cell lines or any scientific basis for claiming to have created one." Because the final report of the SNU investigation indicated that a significant amount of the data presented in both papers is fabricated, the editors of *Science* feel that an immediate and unconditional retraction of both papers is needed. We therefore retract these two papers and advise the scientific community that the results reported in them are deemed to be invalid.

As we post this retraction, seven of the 15 authors of Hwang *et al.*, 2004 (*2*) have agreed to retract their paper. All of the authors of Hwang *et al.*, 2005 (*3*) have agreed to retract their paper.

Science regrets the time that the peer reviewers and others spent evaluating these papers as well as the time and resources that the scientific community may have spent trying to replicate these results.

Donald Kennedy
Editor-in-Chief

References
1. Investigation Committee Report, Seoul National University, 10 Jan. 2006. (Members: Chairman Myung-Hee Chung, SNU, Uhtaek Oh, SNU, Hong-Hee Kim, SNU, Un Jong Pak, SNU, Yong Sung Lee, Hanyang University, In Won Lee, SNU, In Kwon Chung, Yonsei University, Jin Ho Chung, SNU).
2. W.-S. Hwang *et al.*, Evidence of A Pluripotent Human Embryonic Stem Cell Line Derived From a Cloned Blastocyst, *Science* **303**, 1669 (2004).
3. W.-S. Hwang *et al.*, Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts, *Science* **308**, 1777 (2005).

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10.1126/science.1124926

The Woo Suk Hwang Case (2004)

- **Claim:** Hwang *et al*. generated stem-cell lines from cloned human embryos, creating potential source of versatile, therapeutic cells that would be genetically matched to any patient.
- **Investigation, Retraction & Results**: The authors engaged in research/scientific misconduct and their two papers contained **fabricated data**.
  - With regard to Hwang *et al.* 2004, it was found that the data showing that DNA from human embryonic stem cell line NT-1 is identical to that of the donor are invalid because they are the result of fabrication, as is the evidence that NT-1 is a bonafide stem cell line.

The Woo Suk Hwang Case (2004)

- Furthermore, it was found that the claim in Hwang *et al.* 2005 that 11 patient-specific embryonic stem cells line were derived from cloned blastocysts is based on fabricated data. The laboratory did not possess patient-specific stem cell lines or any scientific basis for claiming to have created one.
- Because the investigation indicated that a significant amount of the data presented in both papers is fabricated, *Science* decided that an **immediate and unconditional retraction** of both papers was needed. They retracted the two papers and advised the scientific community that the results reported are invalid.
- Due to this case, the careers of the authors were devastated.

Scientific misconduct

Andrew Wakefield linked MMR (measles, mumps, rubella) vaccination to autism

- His hypothesis was that by combining the MMR into a single shot that it was somehow weakening the immune system, causing the measles part of the vaccine to travel to the gut and cause damage by theoretically traveling into the bloodstream and cause (theoretical) damage to the brain -- perhaps causing autism symptoms.

Scientific Misconduct

- The United Kingdom's General Medical Council concluded that Wakefield participated in "dishonesty and misleading conduct" when he conducted the 1998 case report of 12 children that questioned if a childhood vaccine caused a new form of autism.
- According to one of the findings against the doctor, Wakefield took blood samples from children at his own child's birthday party, and paid them five British pounds for their trouble.

Scientific Misconduct

- The GMC panel also found Wakefield responsible for an ethics breach because he wrote that the children involved in the case report were referred to his clinic for stomach problems
- Wakefield knew nearly half of the children were actually part of a lawsuit looking into the effects of a measles-mumps-rubella (MMR) vaccine. Some children didn't have stomach issues at all.

Scientific Misconduct

- Lancet retracted Wakefield's paper from the publication
- Followed UK General Medical Council's Fitness to Practice Panel Jan 28, 2010 decision about incorrect elements Wakefield’s 1998 published paper
- Claims that children were 'consecutively referred' and that investigations were 'approved' by the local ethics committee have been proven to be false.

Conflict of Interest

- Parent autism advocacy groups supported Wakefield and filed a lawsuit against MMR vaccine provider
- The GMC also found that Wakefield failed to disclose he was paid in conjunction with the lawsuit
- Wakefield had a patent related to a new MMR vaccine in development when he submitted the 12-child case report to be published in a scientific journal

Scientific misconduct

“REPUTATION in science is EVERYTHING. Once gone, it’s extremely hard to get back.”

-- Alan Trounson

as cited by David Cyranoski (2014)

Ethical responsibilities of the investigator

Guidelines and Procedures for Good Research Practice. University of Worcester, UK, Revised 2013

1. Be honest

- Applies to the whole range of research, including experimental design, generating and analysing data, publishing results, and acknowledging the direct and indirect contributions of colleagues, collaborators and others.
- Refrain from plagiarism, piracy or the fabrication of results.

Ethical responsibilities of the investigator

2. Be open

- To discuss work with other researchers and with the public.
- Aim for widest dissemination of results possible, unless confidentiality agreements have been put in place and/or it has been agreed that sponsors will own a part or all of the intellectual property

Ethical responsibilities of the investigator

3. Document results clearly and accurately

- Keep clear and accurate records of the research methods used and of the results obtained, including interim results.
- This is necessary not only as a means of demonstrating proper research practice, but also in case questions are subsequently asked about methods used or results of the study

Ethical responsibilities of the investigator

4. Be critical of your results

- Academics should always be prepared to question the outcome of their research.
- The University expects research results to be checked before being made public.

Ethical responsibilities of the investigator

5. Ensure that data is stored securely and for the appropriate amount of time

- All personal data should be stored securely.
- Electronic data must be held on a secure server and/or be password protected.
- Hard copy of data must be kept in a locked filing cabinet
- Data must be stored in an appropriate format, normally for a period of at least 10 years from the date of any publication

Ethical responsibilities of the investigator

6. Acknowledge fully the role of collaborators and other participants

- The issue of authorship is an important aspect of GRP
- Anyone listed as an author of a research output should accept personal responsibility for ensuring that they are familiar with the contents of the output.
- The contributions of formal collaborators and all others who directly assist or indirectly support the research must be properly acknowledged.
- Support of funding bodies should be acknowledged in publications.

Ethical responsibilities of the investigator

7. To exercise a duty of care to all those involved in the research

- A researcher has a duty of care to all those involved in the research, whether as subjects/participants or as part of the research team, a duty which includes:
  - Ensuring that those involved are fully aware of all the risks and dangers in advance of that involvement
  - Protecting the confidentiality of those involved unless consent has been attained to reveal their identity or any other confidential information.
  - Ensuring appropriate informed consent is obtained properly, explicitly and transparently

Ethical role of investigator

8. Openly account for commercial interests and other associations.
9. Keep your research organized, for instance through documentation and archiving.
10. Strive to conduct your research without harming people, animals or the environment.
11. Be fair in your judgment of others' research.

Ethical Consideration Section

In a research protocol identify the ethical issues related to:

- Type of population involved: protection measures of vulnerable populations
- Research methods: interventional vs. observational
- Risks: measures to minimize them
- Benefits: measures to maximize them
- Informed consent: full disclosure
- Conflict of interest: disclosure and management

Ethics review of academic research

Ethics review of research projects

- It entails physical encroachment on the research subject, involving use of physical or psychological methods
- It carries an obvious risk of physical or psychological harm to the research subject,
- It entails studies on biological material that can be traced to specific individuals.
- It entails the handling of sensitive personal data

Ethics review of academic research

- Governed by international and national guidelines
- For post-graduate projects, it is the supervisor's responsibility to see that they are ethically reviewed
- Types of ethics review boards
  - Department/ Institutional
  - Regional/ cluster
  - Central/ National

Algorithm of Risk Determination

Assessment points

- Topic: Sensitive?
  - Yes No

- Intervention: Risky?
  - Yes No

- Population involved: Vulnerable?
  - Yes No

- Level of risk

- Low Medium High

Summary: Good Research Practice

Involves

- Use of sound scientific design
- Fair selection of participants
- Respect for participant autonomy
- Minimizing risks and maximizing benefits
- Management of conflict of interest

References

- Good Research Practice, Swedish Research Council, Revised 2011
- Guidelines and Procedures for Good Research Practice. University of Worcester, UK, Revised 2013