

**Science Editorial Statement Concerning
Stem Cell Manuscripts by Woo Suk Hwang, et al.**

--12 January 2006--

Note--As a service to reporters and the public, the AAAS Office of Public Programs and *Science* Editorial are providing the following chronology of events related to two stem-cell papers published in *Science*. This information is accurate to the best of our knowledge, as of this writing. The situation is complicated, however, and we reserve the right to correct or amend this chronology as new information comes to light. Please check back for any updates.

The following statement concerns two papers published in *Science* by Dr. Woo Suk Hwang *et al.*:

- “Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst” (February 12, 2004, *Science Express*; March 12, 2004, *Science*); and
- “Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts” (May 19 2005, *Science Express*; June 17, 2005, *Science*).

Dr. Hwang was the lead author on both of these papers. Dr. Gerald Schatten of the University of Pittsburgh Medical Center was a co-author on the 2005 paper only.

Science editors have been assessing a series of issues related to these papers.

The specific chronology of events, beginning with the most recent developments first, is as follows:

(25.) 12 January 2006, 5:00 pm U.S. ET – *Science* published an editorial retraction of the 2004 and 2005 Hwang *et. al* papers on the *Science Express* website (<http://www.scienceexpress.org>).

An excerpt from the editorial retraction is below. The full retraction is available at <http://www.sciencemag.org/cgi/content/abstract/1124926v1>.

“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.”

(24.) 10 January 2006, 2:00 pm U.S. ET – *Science*’s editor-in-chief Donald Kennedy has provided the following statement.

“The journal *Science* has received and reviewed the summary of last night’s report of the Seoul National University investigating committee, which charges the Hwang group that published two stem cell papers in *Science* in 2004 and 2005 with fraud resulting from serious research misconduct. The authors of the latter paper had earlier agreed to a retraction; since the other paper also is implicated in these misconduct findings, *Science* will be retracting it editorially as well.

“We have been providing, on *Science*’s Web site, a running chronology of this problem since it was first identified, along with editorial updates in an effort to provide the scientific community with information about the status of the research and our efforts to support investigations of its conduct at Seoul National University and at the University of Pittsburgh.

“We are doing a systematic review of the editorial history of both papers and our procedures for evaluating them, to search for ways in which we might improve those. I have pointed out in the past that even unusually rigorous peer review of the kind we undertook in this case may fail to detect cases of well-constructed fraud. To support this effort, we are calling on outside experts, including members of our Board of Reviewing Editors and our Senior Editorial Board.

“They and we will be considering options for providing additional procedural safeguards. These could include, for example, requiring all authors to detail their specific contributions to the research submitted, and to sign statements of concurrence with the conclusions of the work. We are implementing improved methods of detecting image alteration, although it appears improbable that they would have detected problems in this particular case.

“Fraudulent research is a particularly disturbing event, because it threatens an enterprise built on trust. Fortunately, such cases are rare -- but they damage all of us. Fraud is unlikely to be eliminated completely through the process of scientific publishing, and truth in science ultimately depends upon confirmation. But at *Science*, we are determined to do everything in our power to evaluate our own procedures for detecting research misconduct, and we will communicate the results of this effort to the scientific community when it is complete.”

(23.) 09 January 2006, 5:50 pm U.S. ET -- The journal *Science* continues to move as swiftly as possible toward the retraction of the Hwang *et al.* May 19, 2005 stem-cell article (May 19 2005, *Science Express*; June 17, 2005, *Science*). As of 5:50 p.m. U.S. ET on Monday, 09 January, however, *Science* editors were still awaiting the final results of an investigation conducted by a team at the Seoul National University (SNU).

Last Friday, *Science* editors e-mailed the head of the SNU investigation team, Dr. Roe Jung-hye, requesting an update on the committee's findings prior to a press conference that is expected to take place Tuesday, 10 January in Seoul. Editors have not yet received a response to that request.

Science editors also are taking other steps to try and gather as much information as possible. These steps have included e-mailing technical questions to co-authors of the 2004 Hwang *et al.* paper in *Science* (February 12, 2004, *Science Express*; March 12, 2004, *Science*); seeking advice from *Science*'s Senior Editorial Board; successfully urging Dr. Sung-Il Roh of MizMedi Hospital to institute an independent investigation looking into research procedures at the Medical Research Center of the hospital that are relevant to the two *Science* papers and papers in *Stem Cells*, *Biology of Reproduction* and *Molecules and Cells*; and asking the President of Hanyang University to conduct an independent investigation of activities of the Medical School staff and the Institutional Review Board related to the 2004 and 2005 Hwang *et al.* papers in *Science*.

Reporters, please note: As previously indicated, *Science* editors don't anticipate further public comment until the retraction has been finalized. The *Science* Editor-in-Chief will have a formal statement at that time.

(22.) 04 January 2006, 9:00 am U.S. ET -- The journal *Science* issued the following statement regarding the South Korean stem cell probe.

“All authors have indicated a willingness to retract the 2005 paper (“Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts” May 19 2005, *Science Express*; June 17, 2005, *Science*)

“To ensure that the wording of the retraction reflects the final conclusions of the Seoul National University (SNU) investigation, *Science* will finalize the retraction text and proceed with the final steps of the retraction process only after the SNU investigation is completed next week.

“*Science* hopes this approach will yield a retraction that will convey accurately as much information as possible to the scientific community.”

Please Note: The Editors do not anticipate further media comment until after the Investigation Committee has communicated their final report to the journal. All *Science* press package recipients will receive e-mail notification prior to publication of the retraction.

(21.) 29 December 2005, 12:45 pm U.S. ET -- The journal *Science* today issued the following statement in response to news accounts of a press conference by a Seoul National University team that has been investigating the authenticity of stem-cell research article by Dr. Woo Suk Hwang:

“There is no question in our minds that the stem-cell paper published 19 May 2005 by the journal *Science* needs to be retracted, and we are proceeding swiftly but appropriately in that direction. As of this writing, however, editors at *Science* still have not received any official notification from Seoul National University regarding the interim findings just reported in the press, and so we have sent a message to the head of the investigation, Dr. Roe Jung-hye, seeking more information. *Science* also is continuing to try and gather all authors’ signatures for the retraction agreement.

“We feel it is important to note that retraction of a scientific paper is an editorial and bibliographic tool that is used to correct the permanent scholarly record, and it cannot be made based solely upon news reports. We are continuing, however, to proceed as quickly as possible toward a retraction of the 2005 paper.

“The latest news reports reinforce the authors’ previously received request to retract the 2005 paper. We continue to work with the authors on the wording

of the retraction and obtaining the signatures needed for publication. We have given them a deadline of tomorrow, Friday, 30 December. If we have not received all of the signatures by tomorrow, *Science* will be moving toward running an editorial retraction, or one signed by the investigation committee itself, possibly after the final investigative report is issued.”

-- *Science* Editor-in-Chief Donald Kennedy

(20.) 23 December 2005, 2:00 pm U.S. ET -- Statement by *Science* Editors on Korean Stem Cell Investigation.

“*Science* has now learned from the Seoul National University investigation committee, as transmitted by the head of the investigation, that some of the results of the 2005 Hwang *et al.* paper are the result of substantial research misconduct on the part of the authors. These involve portions of the DNA fingerprinting data, an exaggeration of the number of teratomas actually formed by embryonic stem cell lines, and unverifiable claims about the number of lines actually created.

“We are continuing to move forward with a formal retraction of the 2005 paper. If a statement is not provided in a timely manner by the authors or the investigation committee on behalf of Seoul National University, we will move forward with an editorial retraction. Both the committee and *Science* are also pursuing possible problems with the 2004 paper. We will continue to communicate the results as soon as they become available.

“We call renewed attention to the Editorial Expression of Concern issued on 22 December and updated today to reflect the preliminary findings of the investigation.”

The text is available at:

<http://www.sciencemag.org/cgi/content/abstract/1124185>

(19.) 22 December 2005, 3:30 pm U.S. ET -- The following Editorial Expression of Concern is published online at *Science* Express. It is now linked online to both of these papers, and it will be published in print in *Science* on 6 January 2006. This is an official notice to the readers of *Science* informing them that concerns have been raised about the validity of

the 2005 paper, and questions about the 2004 paper are being explored by *Science* Editorial.

(18.) 20 December 2005, 11:30 am U.S. ET - No additional communications or retractions have been received from the authors of the 2005 paper. The editors of *Science* are reviewing both the 2004 and 2005 papers from Dr. Hwang's laboratory in light of new questions about the authenticity of images in the 2004 paper. So far, there has been no substantiated charge. *Science* will act expeditiously and forcefully when the facts are known.

(17.) 16 December 2005, 2:30 pm U.S. ET – The journal *Science* and its publisher, AAAS, had a teleconference for reporters at 2:30 pm US Eastern Time on Friday, 16 December 2005. (To view an AAAS news summary of the teleconference and listen to the audio file, visit: <http://www.aaas.org/news/releases/2005/1216stemcellcall.shtml>)

(16.) 16 December 2005, 10:00 am U.S. ET -- Several hours prior to Dr. Woo Suk Hwang's press conference in Seoul, *Science* Editorial received direct communication, by telephone, from him and Dr. Gerald Schatten, the lead authors of the 2005 paper. They said they wish to retract the paper ("Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts," May 19 2005, *Science Express*; June 17, 2005, *Science*).

Science's stated policy is that all authors must agree to any retraction, and Dr. Hwang has assured us that he is contacting his coauthors. *Science* editors will honor the authors' request and assist them in preparing a retraction.

Science Editorial continues to follow and encourage the official investigations now underway and will have no comment on them until the investigations have been completed.

(15.) *Entry #15 was added on 28 December 2005 in an effort to provide as complete a chronology as possible.

Two corrections were published in the print *Science* on 16 December 2005, and can be found at: <http://www.sciencemag.org/cgi/content/full/310/5755/1769>.

There were two errors in Table 2 of "Patient-specific embryonic stem cells derived from human SCNT blastocysts" by W. S. Hwang *et al.* (17 June, 2005, p. 1777). The table has been corrected.

The second correction concerns "Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst" by W. S. Hwang *et al.* (12 Mar. 2004, p. 1669). Contrary to the statements in the second paragraph of text and first paragraph of the supporting online material, which indicated that there was no financial payment to oocyte and cumulus cell donors, some oocyte donors were financially compensated for their donation with a payment of approximately U.S. \$1,400. The correction has been added to the "Version History" of the paper.

(14.) 15 December, 11:20 am U.S. ET – All authors must formally request a retraction in writing for *Science* to retract a paper. Neither Dr. Hwang nor any of the co-authors have requested a retraction. *Science* editors have asked Dr. Hwang and his co-authors for clarification regarding unconfirmed news reports about requests for retraction.

(13.) 14 December 2005 – "The journal welcomes investigations being conducted by institutional authorities in Korea, as well as the inquiry now underway at the University of Pittsburgh," *Science's* Editor-in-Chief Dr. Donald Kennedy said 14 December 2005, in response to ongoing questions. "The journal itself is not an investigative body, but we await answers from the authors, as well as official conclusions, before we can come to any ourselves. We are doing our best to follow these fast-moving developments, and we will continue, as best we can, to keep the scientific community informed."

(12.) 13 December, 4:45 pm U.S. ET -- *Science* editors confirmed that they have now received a letter from eight scientists, stating that "accusations made in the press about the validity of the experiments published in South Korea are, in our opinion, best resolved within the scientific community." The letter, signed by Ian Wilmut of Edinburgh University and others, states: "We encourage Hwang's laboratory to cooperate with us to perform an independent test of his cell lines to determine their nuclear and mitochondrial genotype in comparison with the donors of the original cells." At 6:00 p.m. U.S. Eastern Time, *Science* published this letter on its *Science Express* site, <http://www.scienceexpress.org>.

(11.) 13 December – *Science* Editorial today confirmed that the journal *Science* has received a letter from Dr. Gerald Schatten of the University of Pittsburgh Medical Center. *Science* editors have chosen not to release this letter because it contains unsubstantiated allegations, along with Dr. Schatten’s request that he be removed as a co-author of Dr. Hwang’s 2005 paper. Retraction of a paper requires the agreement of all authors. There is no mechanism for retracting authorship. No single author, having declared at the time of submission his full and complete confidence in the contents of the paper, can retract his name unilaterally, after publication, and while inquiries are still underway by the Korean authors. Unlike Dr. Schatten, the Korean authors have direct contact with the conduct of the experiments. “We continue to take this issue seriously,” Dr. Kennedy said, “and we are following developments both in South Korea and at the University of Pittsburgh.”

(10.) 9 December -- *Science* Editorial was continuing to review and respond to inquiries about the papers by Dr. Hwang and colleagues. *Science* editors asked the authors for further information about questions regarding images and DNA fingerprinting records included as Supplemental Online Material. *Science* will disclose new information as that becomes possible. Contrary to reports that have come to editors’ attention, *Science* has never asked Dr. Hwang or anyone not to respond to press inquiries, nor has *Science* discouraged him from seeking independent replication of his findings.

(9.) On Monday 5 December, University of Pittsburgh officials said they had opened a preliminary inquiry after learning some high-resolution stem-cell images in the 2005 *Science* paper were duplicates, according to news accounts.

(8.) On 4 December, Dr. Hwang contacted *Science* editors at 11:29 p.m. Eastern Time to alert us to erroneous duplications in some images published as part of the Supporting Online Material for the 2005 paper. Specifically, Dr. Hwang reported that “we made some unintentional error by using about 4 pictures redundantly.” The images in question were labeled: SSEA-3 of NT-hESC-3 and NT-hESC-8; SSEA-1 of NT-hESC-5 and NT-hESC-6; SSEA-4 of NT-hESC-9 and TRA-1-60 of NT-hESC-11; and SSEA-1 of NT-hESC-7 and NT-hESC-11. After an investigation of the e-mail, database and paper trail between editors and authors, *Science* determined that the redundant images noted above did not appear in the PDF version of the paper accepted on 12 May. In preparation for publishing on *Science Express*

and in print, the editors had requested from the corresponding author, Dr. Schatten, high resolution images for all the figures. These author-provided high resolution images were received on 10 May and incorporated into a new PDF on 12 May for posting in the 19 May *Science Express* version. Some of the high resolution images did not match images that were in the version of the paper that peer-reviewers had seen and *Science* editors had accepted. On 13 May, the editor forwarded the new PDF with the high resolution images to the authors to ensure that the assembled files were correct. Unfortunately, the authors did not notice that the incorporated high resolution files contained the figure errors. *Science* has e-mailed Dr. Schatten and Dr. Hwang to request that they check their files to confirm this sequence of events and to shed light on the genesis of the high-resolution file. “There is no reason to believe at the moment that it is a problem that affects the scientific outcome of the paper,” Dr. Kennedy said in response to questions about the redundant images.

(7.) On 4 December, media outlets reported that the Munhwa Broadcasting Corporation (MBC) had publicly apologized for reporting tactics related to a 22 November, PD Diary program, “The Myth of Hwang Woo-suk and Suspicions over Eggs.” It was further reported that the Foundation of Broadcast Culture met the following day with Choi Mun-sun, the president of MBC, to discuss questions about the ethics of reporting methods associated with the segment on Dr. Hwang.

(6.) On 1 December, Dr. Moon-il Park, Director and Chair of the Institutional Review Board (IRB) on Human Subjects Research and Ethics Committees, Hanyang University Hospital, e-mailed Dr. Kennedy regarding the results of an investigation jointly carried out by the hospital IRB and the college of Veterinary Medicine, Seoul National University IRB. Dr. Park indicated that his findings had been submitted to the Ministry of Health and Welfare and National Bioethics Committee (NBC). Dr. Park’s e-mail concluded that, contrary to information originally given to *Science*: “After the investigation for the research conducted from late 2002 through late 2003 and published in issue of February 2004 of *Science*, we found out that 1) two researchers under Dr. Woo Suk Hwang’s supervision donated oocytes voluntarily without any coercion and 2) approximately US\$1,445 was paid for direct expenses.” Dr. Moon noted, however, that payment for ova donations was not illegal in Korea until January 2005, after the first paper was published. Further, the group concluded that Dr. Hwang’s research was conducted in accordance with the Helsinki Guidelines of 1964, which

prohibit coercion of research subjects. “We strongly believe that the identified concerns have no impact on the validity of the scientific conclusions,” Dr. Park concluded.

(5.) Beginning on 22 November, *Science*'s press office began to receive reporter calls regarding numerous different versions of charges that apparently had been made by a Korean television station, Munhwa Broadcasting Corporation's (MBC) “PD Diary” program. “None of these allegations have been credible,” Dr. Kennedy said in response to questions about the MBC broadcast. “Until a specific, scientifically based claim against Dr. Hwang's findings is reported to us, we will not offer speculations.”

(4.) Meanwhile, in an unrelated development, authors of the 2005 paper provided *Science* with corrections to data contained within one table (Table 2). The corrected table was promptly published on *Science*'s Web site, and was readied for print publication. *Science* Editor-in-Chief Donald Kennedy said at the time: “It is our understanding that the correction of the table does not significantly alter the paper's primary conclusion that patient-specific embryonic stem cells were derived from human SCNT-blastocysts.”

(3.) A formal statement by Dr. Schatten and the University of Pittsburgh was issued on November 12, 2005.

(2.) A day later, on 11 November, Dr. Schatten informed us that because he had come to believe that Dr. Hwang had misrepresented facts about consent issues related to the 2004 paper, he would not be able to work with Dr. Hwang in the future. Because this information was provided by Dr. Schatten, who had not been a co-author on the 2004 paper, *Science* Editorial asked Dr. Hwang to inform us of any concerns regarding his research. Dr. Hwang responded to say he was looking into the matter. We further urged Dr. Schatten to notify all appropriate institutional authorities about his concerns related to the 2004 paper.

(1.) On Thursday, 10 November, *Science* was alerted by Dr. Schatten of reports in the Korean press, alleging that researcher Dr. Sung-II Roh had illegally traded ova. Dr. Roh is a co-author on Dr. Hwang's 2005 paper, and he is acknowledged for assisting with part of the research related to the 2004 paper. Dr. Schatten reassured us that “none of the oocytes used in Prof.

Hwang's 04 or 05 SCIENCE papers were obtained from reimbursed women donors."

Updates to this chronology, and the Science editor-in-chief's responses to ongoing developments, will be provided as they become available.

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Additional Questions and Answers

What were the conclusions and methods of the 2004 paper?

In 2004, the first Hwang paper described, for the first time, the development of versatile “pluripotent” human embryonic stem cells, potentially capable of becoming any cell in the body, from a cloned human blastocyst. The stem cells were harvested from a blastocyst produced by transferring the nucleus of a non-reproductive (“somatic”) cell, containing a woman's genetic blueprint, into a nucleus-free egg from the same donor. Following this transfer, factors within the host egg’s exterior, or cytoplasm, reprogrammed its new nuclear contents by activating versatile embryonic genes, while silencing the more limited adult somatic cell genes. Researchers were then able to collect embryonic stem cells from the resulting cell mass inside the cloned blastocysts.

Hwang and colleagues developed the stem cell line, SCNT-hES-1, after collecting 242 eggs from 16 people. (At the time, the researchers reported that the donors were unpaid volunteers who had signed informed-consent agreements. This information is now being corrected by *Science*.) From these eggs, scientists then cultured 30 blastocysts to obtain 20 suitable inner cell masses. By tweaking the amount of time that elapsed between the transfer of the nucleus and the activation of the newly transplanted genetic material, the team was able to optimize their results: A two-hour delay seemed to work best, so that 20 percent of all reconstructed eggs formed blastocysts. From the inner cell mass of these blastocysts, a single human embryonic stem cell line was obtained.

What were the primary conclusions of the 2005 paper?

In 2005, the second *Science* paper reported that scientists had isolated the first human embryonic stem cell lines specifically tailored to match the nuclear DNA of patients, both male and female of various ages, suffering from disease or spinal cord injury. The paper reported that these cell lines would enable the study of human disease in cells in the laboratory and move scientists one step closer to the goal of transplanting healthy cells into

humans to replace cells damaged by diseases such as Parkinson's and diabetes.

Hwang, Schatten and colleagues reported in the second paper that each of the 11 new human embryonic stem cell lines was created by transferring the nuclear genetic material from a non-reproductive cell of a patient into a donated egg, or "oocyte," whose nucleus had been removed. Next, oocytes with patient genetic material were allowed to grow to the blastocyst stage of embryo development. Stem cells were then derived from the inner cell mass of the blastocyst. In laboratory culture, these cell lines displayed signs of immunological compatibility with the patients' cells, the authors reported.

At the time of submission, authors provided documentation to show that oocyte donors were unpaid volunteers who signed informed-consent agreements. (This information is now being corrected by *Science*.) A related Policy Forum article in *Science* discussed international oversight and ethical issues in oocyte donation.

What consent-related information or supplemental materials were published along with these *Science* papers? What did *Science* do to ensure appropriate ethics guidelines were followed?

Science Editorial exercised unusually careful diligence prior to acceptance of this paper, by reviewing documentation stating that all egg donors were unpaid, un-coerced volunteers who had given prior consent.

Proper documentation -- in the form of a summary of the informed consent process for the 2004 paper, and donor consent forms and Institutional Review Board approval forms for the 2005 paper -- was published along with the research.

Specifically, the text of the 2004 paper and the related Supplemental Online Material (SOM) stated that only unpaid, un-coerced egg donations were used in the research. Specifically, the text and SOM stated:

Manuscript text read as follows: "Although expenses for public transportation and injections administered by medical personnel could have been provided, none of the donors requested this and therefore no financial reimbursement in any form has been paid."

Supplemental Online Material read as follows: “Donors understood that neither they nor their relatives would benefit from this research. Donations were made without coercion or financial payment. Although expenses for public transportation and injections administered by medical personnel could have been provided, none of the donors requested this reimbursement.”

Science editors have prepared a correction related to oocyte recruitment, related to the 2004 paper.