

UNIVERSITY OF PITTSBURGH

**SUMMARY INVESTIGATIVE REPORT
ON ALLEGATIONS OF POSSIBLE SCIENTIFIC MISCONDUCT**

**ON THE PART OF
GERALD P. SCHATTEN, PH.D.**

February 8, 2006

Background and Summary of the Allegations

The allegations relate to the following paper (referred to below as the paper), of which Dr. Schatten, Professor of Obstetrics, Gynecology and Reproductive Sciences and Director, Pittsburgh Development Center, was co-corresponding and senior author:

W.S. Hwang, S.I. Roh, B.C. Lee, S.K. Kang, D.K. Kwon, S. Kim, S.J. Kim, S.W. Park, H.S. Kwon, C.K. Lee, J.B. Lee, J.M. Kim, C. Ahn, S.H. Paek, S.S. Chang, J.J. Koo, H.S. Yoon, J.H. Hwang, Y.Y. Hwang, Y.S. Park, S.K. Oh, H.S. Kim, J.H. Park, S.Y. Moon, G. Schatten, Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts. *Science* **308**: 1777 (June 17, 2005).

The experimental work underlying the paper was performed at Seoul National University (SNU) in South Korea in the laboratory of the other co-corresponding author, Woo Suk Hwang, D.V.M. The paper was considered to be a high-profile publication because it reported a relatively high efficiency in generating human nuclear transfer embryonic stem cells (NT-hES cells) by a cloning procedure which involved the implantation of donor somatic cells into an enucleated donated human oocyte. This result held promise of generating ES cells from a somatic cell of a diseased or injured patient that could in principle differentiate into a possible therapeutic cell or tissue with immunological compatibility with the patient and could be used for treating the diseased or injured individual.

This paper was published on-line by *Science* on May 19, 2005 and in print on June 17, 2005. On November 11, 2005 the authors of the paper submitted to *Science* corrections to one of the tables published in the paper, the effect of which was to reduce the number of confirmatory experiments supporting their overall conclusions. *Science* published a corrected table on its web site on November 12, 2005 and in print in *Science* **310**: 1769 (December 16, 2005). On December 4, 2005, Dr. Hwang contacted *Science* to report that unintentional erroneous duplications had occurred in some images published as part of the Supporting Online Material for the paper. On December 6, the University's Research Integrity Officer, Jerome L. Rosenberg, Ph.D., received a letter from a member of the University community reporting that an investigative affiliate of a Korean broadcasting company had received results of an independent analysis of DNA fingerprinting of some of the supposed NT-hES cells that called into question the existence of true NT-hES cells from some of the claimed 11 derived cell lines.

In accordance with the University's Research Integrity Policy (referred to below as the policy), Arthur S. Levine, M.D., Dean of the School of Medicine and Senior Vice Chancellor for the Health Sciences, appointed an Inquiry Panel of six senior investigators to examine various aspects of possible research misconduct on the part of Dr. Schatten. Dr. Schatten joined in the call for an inquiry.

Four separate allegations have been made in connection with the paper.

1. Table 2 in the above paper incorrectly listed 7 of the 11 described embryonic cell lines as having had pluripotency demonstrated by both embryoid body and teratoma confirmations. The authors themselves submitted a post-publication correction to *Science* on November 11, 2005, stating that although all seven of those cell lines had had pluripotency confirmed by embryoid bodies, only three of them were confirmed by teratomas.
2. In the supplementary on-line material for the above paper, four pairs of phase contrast photographs of cell lines appeared to be duplicates but were labeled as belonging to different cell lines. Dr. Woo Suk Hwang, the lead author of the above paper in whose laboratory the experiments were done, reported to *Science* on December 4, 2005, describing the error as unintentional.
3. DNA fingerprinting of some of the embryonic cell lines were compared with fingerprinting of samples from the respective donor's hair, both in the publication and in an independent investigation conducted in Korea. An individual familiar with the independent results alleges that the embryonic cell lines cannot all be assigned unequivocally as coming from the reported donors.
4. Reports from former members of Dr. Hwang's lab as well as independent investigations conducted in Korea alleged that there were only two stem cell lines, not the 11 claimed in the paper.

The initial task given to the Inquiry Panel was to determine whether the allegations appear sufficiently founded to warrant a formal investigation. With respect to the first two allegations they were to judge whether the admitted errors were honest mistakes that had no significant impact on the main conclusions of the paper or whether they constituted intentional deception. With respect to Allegation 3 and 4 the Panel was to judge whether it is possible to resolve this matter on the basis of the published data and any other material that might be gathered.

The Panel was informed of the possibility that this inquiry may not be conclusive in regards to addressing the veracity of the specific allegation of fabrication and falsification, given that all of the experimental materials, e.g., donor and NT-hESC DNAs, are in Korea. However, the inquiry process might be complemented by information obtained from Korea. We soon learned that indeed SNU opened its investigation into allegations of research misconduct on December 15, 2005. In view of the fact that the Korean investigation had access to the suspect cell lines, they were in a better position than we to undertake independent analyses that could check the veracity of the claims in the paper. We decided to devote most of our attention to understanding what Dr. Schatten's role was and what steps he could have and did take to assure himself of the integrity of the data

According to relevant sections of the University of Pittsburgh policy,

Research misconduct is defined as fabrication, falsification, plagiarism, including misrepresentation of credentials, in proposing, performing, or reviewing research, or in reporting research results.

Fabrication is making up data or results and recording or reporting them.

Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

Misconduct does not include honest error or differences of opinion.

At our first meeting held on December 14, 2005, each investigative board member signed a confidentiality agreement declaring freedom from any close personal or professional association with the respondent, Dr. Schatten, or of other conflicts of interest that could bias their judgment in the Inquiry and possibly the Investigation. These statements were signed by all of us after a frank discussion in which several of us revealed that we had participated with Dr. Schatten in research projects and in funded grants and all members accepted the assurance that the natural professional contacts would not preclude an objective and dispassionate evaluation and interpretation of the evidence that we would encounter. At this first meeting, we quickly came to the conclusion that there was sufficient information to warrant a formal investigation, and we redefined our role as an Investigative Board in accordance with the mandate of Dr. Levine in the event that we should conclude that an investigation was warranted.

Structure of the Investigation

We planned a series of interviews with witnesses. Dr. Schatten waived his right to be present during the interviews with the other witnesses. He did exercise his right to be accompanied at the interview. In addition we invited several consultants to meet with us. Because of his interest in bringing this investigation to a prompt conclusion, Dr. Schatten did not insist on the 30-day notice of the interviews called for in the policy.

During the course of the investigation Dr. Levine asked us to consider two other publications, in which there were reports in the press of alleged falsifications.

Woo Suk Hwang, Young June Ryu, Jong Hyuk Park, Eul Soon Park, Eu Gene Lee, Ja Min Koo, Hyun Yong Jeon, Byeong Chun Lee, Sung Keun Kang, Sun Jong Kim, Curie Ahn, Jung Hye Hwang, Ky Young Park, Jose B. Cibelli, Shih Yong Moon.

Evidence of a pluripotent embryonic stem line derived from a cloned blastocyst. *Science* **303**, 1669-1674 (2004), referred to below as the 2004 paper

Byeong Chun Lee, Min Kyu Kim, Goo Jang, Hyun Ju Oh, Fibrianto Yuda, Hye Jin Kim, M. Hossein Shamim, Jung Ju Kim, Sung Keun Kang, Gerald Schatten, Woo Suk Hwang. Dogs clones from adult somatic cells. *Nature* **436**, 641 (2005), referred to below as the dog paper
Corrigendum to above. *Nature*. **436**, 1102 (2005)

Testimony about the Experiments

Much of the testimony served to inform us of the procedures that were used in this project for egg donation, somatic cell nuclear transfer, preparation of blastocysts at SNU, transport of blastocysts to MizMedi Hospital, development and maintenance of embryonic cell lines, extraction of DNA for fingerprinting analysis, and preparation of images for publication. Important parts of the testimony crucial for our investigation were the following.

We received direct testimony from a former staff member in Dr. Hwang's lab that one staff member had voluntarily donated oocytes for the 2004 paper. In fact, Dr. Hwang was aware of this since he drove the donor to the hospital on one occasion for the donation procedure. It was the report about this same donor that prompted Dr. Schatten to sever his collaboration with Dr. Hwang.

For the 2005 paper, we received testimony about the published DNA fingerprinting figures, pointing out that in some cases the DNA fingerprints of the alleged NT-hES cell lines and the donor did not agree and in other cases that the paired DNA fingerprints of stem cell and donor cell were so identical, including background noise that they must have come from a single source instead of from two sources.

Also for the 2005 paper, we received testimony from a former member of Hwang's group that at Hwang's insistence, images showing morphology and immunostaining of NT-hES cell lines 4 through 11 were made from cells in lines 2 and 3. This witness also testified that for lines 4-11 the paired tubes of reported donor cells and NT-hES cell lines given to him for extracting DNA for fingerprinting were really duplicate tubes of the same source (presumably DNA extracted from cells of the donor of the transferred nucleus) and that other members of the Hwang group knew this. Also, the witness reported severe contamination of NT-hES cell lines 4-7 on January 9th and these lines were all thrown away on January 10th, 2005. Six additional NT-hES cell lines were derived from February to the end of March 2005 but, in the opinion of this witness, there would not have been enough time for additional patient-specific embryonic cell lines between that date and March 15, when the paper describing 11 NT-hES cell lines was originally submitted for publication. This witness testified that teratoma experiments were carried out only for line 2 and 3. All the pictures of embryonic bodies from line 2 through 11 were fabricated from

IVF-derived ES cell lines and that mouse feeder cells, not human feeder cells, were used to derive NT-hES cell lines.

Another witness reported that one of the figures submitted for the 2004 paper was an unauthentic replacement for the correct figure that the witness had supplied. This replacement was carried out by Hwang or one of his close associates.

Conclusions about Falsification and Fabrication

From all the testimony we heard, we were convinced that falsifications and fabrications had occurred extensively in the 2005 paper and perhaps in the 2004 paper as well. Since the investigation that was underway at SNU could apply forensic techniques by reanalyzing the putative NT-hES cell lines, to which the investigation had access, we decided to wait for the outcome of the SNU investigation rather than rely on just witness reports. In fact, the SNU investigative report came out in three stages, December 23 and 30, 2005, and January 10, 2006. This very careful investigation found that not only did NT-hES cell lines 4-11 not exist, but lines 2 and 3 did not exist either. In fact, NT-hES cell line 1, reported in the 2004 paper, was found also to be non-existent. The reputed NT-hES cell lines turned out to have originated from fertilized cells preserved after IVF procedures. While we were not able to determine the origins of the falsification and fabrication in any detail, it seems likely that multiple members of Dr. Hwang's group either participated or were aware of the misconduct. This is supported by the confusion over the origins of cell lines 2 and 3, for which there was greatest experimental support at the time the paper was submitted and to the veracity of which witnesses testified, yet for which the SNU Investigation could find no verifying evidence. The details of the misconduct in Korea and the personnel involved is of interest since they could help to elucidate the role, if any, of Dr. Schatten in the fabrication and falsification of the data in the 2005 *Science* paper.

The Role of Dr. Schatten

We concentrated our attention on the possible role of Dr. Schatten in the fabrication and falsification of data in published papers from Dr. Hwang's laboratory, and on his overall role in the research on SCNT-derived hESCs performed in Dr. Hwang's laboratory. In particular, Dr. Levine had posed the following questions in his letter to Dr. Schatten of December 14, 2005, notifying him of the opening of the inquiry/investigation process.

What role did you play in the course of the research?

What oversight did you give to assure yourself of the integrity of the data?

When did you learn of the charge that only two cell lines had been isolated?

In his first meeting with us on December 15, 2005, Dr. Schatten described in detail the history of his association with Dr. Hwang and with the 2005 paper. The two had corresponded about the placement of a Korean post-doc in Schatten's laboratory. Subsequently, Dr. Schatten and Dr. Hwang met at an international stem cell meeting in Seoul in December 2003, where Dr. Schatten visited his host's laboratory, and Dr. Hwang told Dr. Schatten of his first cloned ES cell line, the subject of a manuscript that had recently been rejected by *Science*. Dr. Schatten volunteered to help steer the manuscript through acceptance by providing some editorial input into the revision which had already been written. We later learned from *Science* editors that Dr. Schatten had called them during the review process to lobby for the acceptance of the paper, which was published as the 2004 paper mentioned above.

Throughout 2004, Dr. Schatten and Dr. Hwang met almost monthly, at one meeting or another, and they exchanged e-mails or phone calls almost daily to discuss scientific matters related to cloning. Dr. Schatten and Dr. Hwang first discussed the establishment of new embryonic stem cell lines by somatic cell nuclear transfer at some point in November 2004, and indicated an interest in preparing an article for *Science*. Early in January, 2005 the two began discussions of the scope and shape of what would be the 2005 paper. On January 1 Dr. Schatten sent Dr. Hwang by e-mail a detailed list of what should go into the figures, based on the characteristics of the already published 2004 paper. Two weeks later the two, while in India, drafted the first version of the paper. At that time Dr. Hwang asked Dr. Schatten to be senior author, but the latter deferred his response. Dr. Hwang began sending data, consisting largely of tables and figures, late in January and continuing into March. Many versions of the manuscript were exchanged by e-mail between Dr. Schatten and Dr. Hwang. To our knowledge, Dr. Schatten did not have any detailed phone conversations with anyone else in the Seoul research group other than Dr. Hwang, but did have limited discussions with co-author Dr. Jong-Hyuk Park who was then a researcher in Dr. Schatten's lab but had worked formerly with Dr. Hwang; we also learned that Dr. Kang frequently read and responded to Dr. Hwang's e-mail. Dr. Schatten reviewed the figures and tables and, in one instance, insisted on receiving the claimed teratoma plates. Although Dr. Schatten told us on December 15 that he did most of the writing of text, his response to one of the questions from the SNU investigating committee three weeks later was that he did not write the paper. The discrepancy lies in the subtlety of interpreting the word 'write'. A review of the e-mail exchanges between Dr. Schatten and Dr. Hwang revealed that Dr. Schatten composed the first and each subsequent draft of the text but did not generate the data or the figures and tables which underlay the text. In the published paper, the limitations of Dr. Schatten's role were described in footnote 32 of the paper as:

All experiments, and all results were obtained in Korea by Korean scientists, and all results were obtained in Korea, using Korean equipment and Korean sponsorship. G.S (Schatten) and J.-H.P. (Jong Hyuk Park) are grateful for the private philanthropy of the Magee-Womens Foundation, which supported their advisory roles in the analysis and for the interpretation and preparation for

publication of these results obtained in Korea. No U.S. federal or Commonwealth of Pennsylvania funds were used in any aspect of this report.

Similarly, there was a discrepancy in Dr. Schatten's use of the term 'senior author' in his two meetings with our Board. In the first interview, he described his original indecisiveness in accepting the role of senior author and told us that he first consulted with *Science* editors, his dean, his project officers at NIH, and University legal counsel about the appropriateness of his assuming that role, given the restrictions of his input described in footnote 32, before agreeing to be senior author. In his second interview, he denied that he was senior author, saying that his only specially designated role as a co-author was as one of the two co-corresponding authors. This second version does not correspond with the fact, for example, that he is the one who responded to reviewers' comments.

We believe that Dr. Schatten was disingenuous in his second interview in harping on strict definitions of 'writing' and 'senior author'. Furthermore, taken together with written comments to the committee, this appears to be part of a concerted and deliberate effort on the part of Dr. Schatten to further distance himself from Dr. Hwang and their joint publications. This is in sharp contrast to the full participation of Dr. Schatten in the media spotlight following publication of the paper. Also, from conversations we had with some of the people whose advice he sought, we were not able to confirm his interpretation of footnote 32 as precluding his inspecting the sources of raw data, such as going to Korea and looking down a microscope to see cells. The main restrictions according to these sources were on using federal funds or in having human embryonic stem cells within the borders of Pennsylvania. The permissible role for Dr. Schatten's involvement as senior author in the preparation of the manuscript in the context of Federal and State hESC policies cannot be used as an excuse for his lack of oversight and critical judgment.

Regardless of the adjective used to describe Dr. Schatten's co-authorship, whether senior or not, he did invest a tremendous amount of time and energy in working over the several drafts of the manuscript, more than in many papers of his own students, according to his testimony. We feel that he did not exercise a sufficiently critical perspective as a scientist. For example, he did not ask what event in Hwang's lab prompted the change in the reporting of some data differently in two successive versions of the same table. In another example, he reported that he was told by Dr. Hwang in the middle of January, 2005 that some contamination of the cells had occurred. Dr. Schatten's reaction was apparently to accept Dr. Hwang's assurance that this problem was a minor nuisance. Dr. Schatten did not extrapolate to conclude that if new cell lines had to be started in middle or late January there would not have been enough time to grow and analyze them by March 15, the date of the first manuscript submission.

A cover letter for manuscript submission was prepared by Dr. Schatten and sent to Dr. Hwang for review on March 6, 2005; Dr. Schatten logged the cover letter and accompanying manuscript into the *Science* database on or around March 15, 2005. The initial version of the cover letter was revised on several occasions by both Dr. Schatten and Dr. Hwang, but Dr. Schatten was the sole signatory on the submitted letter. In this letter, it was stated that all authors agreed that they had read and approved the manuscript. However, information communicated to

us suggests that the likelihood that only a few of the 25 authors read the manuscript prior to submission and that perhaps many did not read it until it was accepted and available online. As co-corresponding author and sole signer of the cover letter, Dr. Schatten must assume responsibility for including this false statement. We cannot rule out the possibility that if more authors had reviewed the manuscript they would have noted and reported the falsification and fabrication detailed by the SNU Investigation.

We believe that Dr. Schatten entered into this relationship with Dr. Hwang on the 2005 paper not only to help a colleague whom he admired, but also to gain some authoritative input and reputational enhancement from a paper which he thought had high potential of being a major breakthrough. He obviously had high expectations of the impact the paper would have. For example, he nominated Dr. Hwang for foreign membership in the United States National Academy of Sciences and, with others, for a Nobel Prize. He was not averse to accepting honoraria totaling \$40,000 within a 15-month period from Dr. Hwang – including \$10,000 paid in cash while attending a press conference following publication of the 2005 paper – amounts that seems to us as far above normal honoraria for consultation. Nor did he hesitate to help to relieve Magee's financial responsibilities in supporting his work, when he could not call on federal funds for his activities with human embryonic stem cells, by submitting a proposal to Dr. Hwang for laboratory support amounting to \$200,000 for the last four months of 2005, an amount which he hoped would turn out to be the amount of an annual subsidy in subsequent years. Also, Dr. Schatten's patent application of 2004, submitted through Magee, presents claims that likely could not be fulfilled by inventions developed at Magee alone, but might plausibly be supported by technologies reportedly developed by Dr. Hwang's group between the filings of provisional and actual patents.

We comment just briefly on the 2004 paper and the 2005 communication to *Nature* about the cloning of the dog. Dr. Schatten was not a co-author of the 2004 paper and, at his own request, he was not even acknowledged. A full manuscript had already been written, and rejected, before Dr. Schatten became involved. He may have contributed with suggestions and with political influence to help the paper through to acceptance, but we have no basis to associate him with any of the substantive work described in the paper. Nonetheless, he lobbied hard for publication of this paper in *Science*, without any direct knowledge of the veracity of the data. Dr. Schatten's role in successfully getting the 2004 paper published in *Science* is likely to have provided considerable encouragement to Dr. Hwang to offer him authorship on the 2005 paper. As for the brief communication to *Nature* about the cloning of the dog Snuppy, for which Dr. Schatten was a listed co-author, we have no reason to doubt Schatten's statement to us that his major contribution to the paper was a suggestion that a professional photographer be engaged so that Snuppy would appear with greater visual appeal. It is less clear that this contribution fully justifies co-authorship.

Conclusions

We conclude that Dr. Schatten likely did not intentionally falsify or fabricate experimental data, and that there is no evidence that he was aware of the misconduct reported to have occurred in Dr. Hwang's group in Korea. Given his dominant role in the writing of the 2005 paper his authorship is not unreasonable, but his positions as co-corresponding author and senior author were determined with considerable care and deliberation. Dr. Schatten's listing as the last author not only conferred considerable credibility to the paper within the international scientific community, but directly benefited Dr. Schatten in numerous ways including enhancement of his scientific reputation, improved opportunities for additional research funding, enhanced positioning for pending patent applications, and considerable personal financial benefit. However, these benefits are accompanied by responsibilities for the manuscript as a whole, approval of the manuscript by all co-authors, and the veracity of the data reported. Dr. Schatten shirked these responsibilities, a serious failure that facilitated the publication of falsified experiments in *Science* magazine. While this failure would not strictly constitute research misconduct as narrowly defined by University of Pittsburgh policies, it would be an example of research misbehavior.

Finally, we would like to acknowledge Dr. Schatten's expeditious and appropriate actions upon learning of allegations of Dr. Hwang's misconduct. The first instance was his finding on Friday, November 11, that at least one of Dr. Hwang's staff had been an egg donor, although Dr. Hwang had forcibly denied this only three days earlier. Dr. Schatten publicly dissociated himself from his collaboration with Dr. Hwang on the next working day. The second instance occurred on December 10, when Dr. Schatten first received direct testimony that NT-hES cell lines 4-11 did not exist. This discovery prompted Dr. Schatten to write to *Science* on December 12 to initiate retraction of the paper.

Recommendations

We recommend that the University administration implement whatever corrective or disciplinary actions are commensurate with this finding of research misbehavior. We also recommend that the University consider amending its Guidelines for Ethical Practices in Research to include a specific statement regarding the responsibilities of senior or corresponding authors of scientific publications. While these responsibilities may be generally recognized as routine procedures within the scientific community, this investigation has discovered how easily this responsibility can be disregarded, and the sad and unfortunate consequences that can result.

Submitted by the Investigative Board