

SPECIAL REPORT

Korean scandal will have global fallout

The possibility that Woo Suk Hwang's cloning experiments were faked threatens to undermine confidence in stem-cell research.

In one of the biggest scientific scandals of recent times, South Korea's star cloner Woo Suk Hwang last week asked to retract his landmark paper on the creation of embryonic stem cells from adult human tissue. The request, along with new doubts about his earlier work, confirms what researchers in the field were already starting to realize — that the advance marked by Hwang's research, with all it promised for therapeutic cloning, may amount to nothing.

Worse, scientists fear that the episode will damage not only public perceptions of stem-cell research, but science's image as a whole.

The request for retraction of the paper (W. S. Hwang *et al. Science* 308, 1777–1783; 2005) came after three authors claimed the work was untrustworthy. Fertility expert Sung Il Roh of MizMedi Hospital in Seoul, claimed on 15 December that Hwang had admitted to him that data were fabricated, and there were no patient-specific cells. In a documentary aired the same day, Sun Jong Kim, formerly of Seoul National University (SNU), told the Seoul-based Munhwa Broadcasting Corporation (MBC) that Hwang had asked him to falsify images. And Gerald Schatten at the University of Pittsburgh asked for his name to be removed from the paper, claiming that information from a team member had caused him to doubt the work's accuracy.

And there are now concerns about earlier work. For example, in the paper in which

Hwang claimed to have extracted the first stem-cell line from a cloned human embryo (W. S. Hwang *et al. Science* 303, 1669–1674; 2004), figures supposedly showing cloned cell lines are identical to those in an earlier paper showing normal embryonic stem cells (J. H. Park *et al. Molecules and Cells* 17, 309–315; 2004). *Nature* has also announced an investigation into Hwang's paper on the first cloned dog (see 'Dogged by doubts', page 1059).

Hwang admitted on 16 December that there were errors in the 2005 stem-cell paper, but denied fraud. He maintains that 11 patient-specific stem-cell lines were created as reported, but six were never frozen, and subsequently became contaminated. He says five lines being thawed now will prove his success.

Culture of secrecy

Hwang's claims are meeting with increasing scepticism. "He was given a chance [to explain] but he didn't use it," says a molecular biologist at SNU, who asked not to be named. Robert Lanza of Advanced Cell Technology in Worcester, Massachusetts, who is also attempting to clone human cells, says it is difficult to believe that cell lines of such value weren't stored properly: "What stem-cell scientist doesn't freeze their cells?"

The SNU is investigating the team's work. The lab's atmosphere of pervasive secrecy and tradition of deference towards Hwang will make investigators' job difficult. But if there



At bay: Woo Suk Hwang maintains that further tests will prove his stem cells are genuine.

was fabrication, it will be hard for Hwang to plead ignorance. When *Nature* visited in 2004, he declined to show his first cloned stem-cell line, kept under lock and key. "Many lab members aren't allowed to see it either," he said.

Taken together, the concerns about Hwang's work leave biologists with no proof that stem cells can be extracted from cloned human embryos (see page 1058).

And the scandal's implications will reach further. There have been cases in which fraud has been established that have involved more papers: a 2002 investigation by Bell Laboratories in Murray Hill, New Jersey, found that Jan Hendrik Schön fabricated data in at least 16 papers while working there. But Schön's field of materials science has a lower public

12 February 2004

Woo Suk Hwang of Seoul National University (SNU) in South Korea and colleagues announce in *Science* they have cloned 30 human blastocysts and harvested stem cells from one of them.

6 May 2004

Nature raises ethical questions about Hwang's work after investigations suggest some of the eggs may have come from junior members of the lab. Hwang denies wrongdoing.

19 May 2005

Hwang's team reports in *Science* that it has established 11 embryonic stem-cell lines derived from the skin cells of individuals.

3 August 2005

Hwang and colleagues announce in *Nature* that they have cloned the first dog, an Afghan hound called Snuppy.

19 October 2005

South Korea's government launches the World Stem Cell Hub, an international network for exchanging embryonic stem-cell lines and cloning technology. Hwang is to run it.

12 November 2005

Gerald Schatten of the University of Pittsburgh, co-author on the 2005 stem-cell paper, cuts all ties to Hwang, saying he believes Hwang misrepresented consent issues relating to the 2004 paper. The authors of the 2005 paper correct their data, but say it doesn't alter their conclusions.

TIMELINE OF EVENTS ▶



K.-H. KIM/REUTERS

profile than cloning and stem-cell research.

"This is such an important experiment and there was so much publicity around it," says Rudolf Jaenisch, a mouse-cloning expert at the Massachusetts Institute of Technology. "It is shocking to think that it might have been fabricated."

"It will probably affect the general perception of scientists and what we do," says Theodore Friedmann, a gene-therapy researcher at the University of California, San Diego, who has chaired the US Recombinant DNA Advisory Committee. "There's a climate of mistrust of science now that's stronger than in the past. That will be exacerbated by this sort of event."

The debacle may well strengthen the hand of those trying to ban stem-cell research in the United States. "This is an example of the corruption of science that this whole cloning field

has been tending toward, with its end-justifies-the-means mentality," says Gene Tarne of Do No Harm, a Washington DC-based coalition that coordinates opposition to stem-cell research. "For almost a decade now, we've heard these overhyped claims about therapeutic cloning. Somebody took the first step in providing any evidence for these claims and it turns out the evidence simply wasn't there."

Lessons to learn

Researchers are left wondering how such a fiasco happened. The journal *Science*, which published two of Hwang's high-profile papers, has defended its peer-review process. Donald Kennedy, *Science's* editor-in-chief, says the journal typically takes 120 days to review and publish biology manuscripts. Hwang's 2005 paper took 58 days, leading some to wonder whether it was rushed. "If it's a really hot paper

and you want to get it out quickly, how many shortcuts do you take?" says Nobel laureate Paul Berg of Stanford University, California.

In a press conference on 16 December, Kennedy insisted the journal does not rush papers. "I think we were appropriately suspicious in this case. I don't think this points to a generic fault in the peer-review system," he said.

Asked whether *Nature* could have been caught out in the same way, editor-in-chief Philip Campbell agrees. "We would hope the errors would have been noticed," he says. "But usually reviewers have to take on faith that the authors are presenting what they say they are." He suggests that in future some important claims should be independently tested.

Others are questioning Schatten's role. He promoted the South Korean group in the West, and was senior author on the 2005 paper, although he did not perform any of the experiments it describes. "The lesson I've learned is that I would not be a co-author on a paper unless I was essentially willing to stake my entire career on every piece of data in that paper," says cloning researcher Kevin Eggan of Harvard University in Cambridge, Massachusetts.

Schatten referred *Nature's* inquiries to Jane Duffield at the University of Pittsburgh Medical Center's news bureau. "He is still not doing interviews with reporters," Duffield wrote in an e-mail.

But some have sympathy for Schatten. "Many scientists would be tempted to do similar things if someone offered them authorship on what seemed like an important breakthrough," says Friedmann.

The field as a whole should tone down its rhetoric, he adds. "I have been very concerned about some of the language used. It seems reminiscent of the gene-therapy experience, where so much promise was obvious, but it was hyped and exaggerated to the detriment of the field. We should be more circumspect" ■

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Read more on the Hwang case at:

▶ www.nature.com/news

21 November 2005

Sun Il Roh, a fertility expert at MizMedi Hospital in Seoul and co-author on the 2005 study, admits that 20 of the eggs he gave to Hwang for his 2004 study were paid for. The next day, Munhwa Broadcasting Company (MBC) airs evidence that Hwang used eggs from junior lab members.

1 December 2005

Two review boards say that donations by researchers did not violate ethical guidelines, as they were not coerced. MBC releases results of tests on five samples of Hwang's cell lines. DNA can only be extracted from one line, and MBC says this doesn't match the corresponding tissue sample. Hwang stands by his results.

4 December 2005

Hwang alerts *Science* to wrongly duplicated images published in supplementary information for the 2005 paper. Over the next week, the University of Pittsburgh and SNU announce investigations.

13 December 2005

Science publishes calls for Hwang to cooperate with independent tests. Schatten asks Hwang to retract their 2005 stem-cell paper, claiming allegations from a team member have made him doubt its accuracy. Two days later, news stations across Korea report allegations from Roh that the 2005 paper was faked.

16 December 2005

Hwang says there were mistakes in photographing and preserving his cloned stem-cell lines. He says he will seek to retract the paper, and that he is thawing frozen stem-cell lines to prove the study's validity. *Science* announces that Hwang and Schatten have requested a retraction, but says the entire team's consent is needed.

19 December 2005

Claims circulate that Hwang's 2004 study includes images taken from other papers. *Science* says it is investigating the 2004 and 2005 stem-cell papers. Doubts are also raised about whether Snuppy is really a clone. *Nature* announces an investigation of the Snuppy paper.