

NEWS

Stem-cell brothers divide

Stem-cell researchers worldwide have been dismayed and confused by the abrupt end of the highest-profile collaboration in their field.

Over the weekend, the University of Pittsburgh's Gerald Schatten suddenly accused Woo Suk Hwang of possible irregularities in the donation of eggs used for his research. Schatten cut all ties to Hwang and his team at Seoul National University in South Korea. Researchers in the field, many of whom were considering collaborating with Hwang through his World Stem Cell Hub, say their plans are now on hold.

Hwang and Schatten's 20-month collaboration produced two landmark papers — the first examples of patient-specific human embryonic stem cells (W. S. Hwang *et al. Science* 308, 1777–1783; 2005) and the first cloned dog (B. C. Lee *et al. Nature* 436, 641; 2005). But Schatten's accusations relate to the earlier work that shot Hwang to fame, in which he established the first stem-cell lines from a cloned human embryo (W. S. Hwang *et al. Science* 303, 1669–1674; 2004).

In a statement issued by the University of Pittsburgh, Pennsylvania, on 12 November, Schatten said: "Yesterday information came to my attention suggesting that misrepresentations might have occurred relating to [egg] donations. I have...accordingly suspended my collaboration with Professor Hwang."

Hwang has yet to respond formally. On Tuesday, he e-mailed *Nature* stating: "I have begun an investigation to find out what happened. I will inform you of the result as soon as it comes."

In May last year, an article in *Nature* presented claims that Hwang's procedures were ethically tainted by the use of eggs from two junior members of his lab (*Nature* 429, 3; 2004). One of them, a graduate student of Hwang's, told *Nature* that she had donated eggs for the lab's research at MizMedi Hospital in Seoul. She later retracted her statement.

Egg donation is a painful and invasive procedure that requires multiple hormone injections. Donation by junior researchers is ethically suspect, because it raises the possibility that senior researchers could pressure graduate students into undergoing the procedure.

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Fractured: Woo Suk Hwang (left) and Gerald Schatten's close partnership has split over ethical concerns.

Last week, Korean newspapers reported that Sung Il Roh, a fertility doctor at MizMedi Hospital who has worked with Hwang since 1995, had used illegally traded eggs to treat infertile couples. Roh refused *Nature's* request for an interview, but has so far denied that any such eggs were used for Hwang's experiments.

Hwang himself has continuously denied using either illegally traded eggs or eggs from graduate students. And Schatten had staunchly defended him. In May 2005, Schatten told *Nature* that the internal review board overseeing Hwang's research "had made it clear that no students have ever donated".

Support crumbles

Schatten's sudden statement regarding possible ethical irregularities in Hwang's work, and the fact that he has withheld related details, have shaken the world of stem-cell research. Jose Cibelli of Michigan State University in East Lansing was a co-author on the 2004 paper. He says he will await clarification of the allegations and a formal response from Hwang. But he is worried about the field. "This is a setback," he says. "We are all very confused."

Kevin Eggan, a developmental biologist at the Harvard Stem Cell Institute in Cambridge,

Massachusetts, says the allegations are difficult to weigh, because they come without any public explanation of their origins. "We have to wait and see, because there is no evidence proving them."

This has led to calls that Schatten present the reasons behind his charge. "At this stage, it is Dr Schatten's and others' responsibility to come forward with evidence," says bioethicist Insoo Hyun of Case Western Reserve University in Cleveland, Ohio.

But the allegations themselves are sufficient to cast doubt on the future of the World Stem Cell Hub. This network, launched last month, is meant to serve as a stem-cell bank and a research facility where scientists from any country can study cell lines created to order by South Korea. Many scientists in the United States, Britain and elsewhere had planned to participate, but are reconsidering their position.

Eggan, for example, says his plans are now on hold. "The allegations are serious and would have to be completely resolved for us to continue to consider collaborating with them."

And the Korean media is starting to criticize Hwang, who until now has been treated like an idol. An editorial in *JoongAng Ilbo* calls on Hwang to "prove that cloning is clean".



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Japan's embryo experts beg for faster ethical reviews

TOKYO

Zealous review committees are crippling Japanese research on human embryonic stem cells, according to a plea about to be lodged at the country's science ministry.

Japan is a world leader in embryonic stem-cell research involving mice and monkeys, but work involving human cell lines is another matter. That is because review committees regularly take far longer to approve such projects than other countries do, researchers charge.

Norio Nakatsuji of Kyoto University will send anecdotal data about Japan's lag to the science ministry this month, with a request to simplify the system. "We cannot wait long, because already Japan is greatly behind other countries," he says.

In 2001, Japan decided to allow research on human embryonic stem cells and issued guidelines for researchers. Three years later, Nakatsuji, who created all three of Japan's current cell lines, began distributing them. Yet so far only 15 laboratories in Japan work on human embryonic stem cells. In a rough survey of the scientific literature for 2004 and 2005, Nakatsuji found that, of 259 papers with titles mentioning human embryonic stem cells, only three had Japanese first authors. The United States had 90 first authors and Britain had 25.

Scientific expertise with stem cells does not seem to be the problem. Japanese researchers account for more than a quarter of first authors on the 204 papers involving mouse embryonic stem cells, and more than a third of the 21 involving primates that Nakatsuji looked at. There is also no lack of funding — for example, the Ministry for Economy, Trade and Industry recently promised annual sums of ¥250 million (US\$2.1 million) for the next five years to investigate the use of human embryonic stem cells in clinical work.

Nakatsuji blames the review process, which requires approval first by an institutional review board (IRB) and then by the science ministry.

Last month he sent an informal questionnaire to 20 researchers, all of

whom complained of the time-consuming approval process, which averaged 12.5 months. Most vexing, it seems, were the questions about researchers' personal beliefs. "The boards want to know exactly how important you think the cells are. It's as if they have a soul, but they are just a bunch of cells in culture," Nakatsuji says.

"The people on the IRB seem to think of the cell lines as just as sacred as the embryos used to establish cell lines," adds Issei Komuro, a cardiovascular specialist at Chiba University. It took a year for his review board to tell him that he needed to exhaust all relevant mouse and monkey studies before moving on to humans. Eventually he gave up his plans and

decided to stick with mice.

"Review boards want to know exactly how important you think stem cells are — as if they have a soul."

Researchers contacted in other countries, where there is usually only one level of approval, say it generally takes a fraction of the time — two to three months in Singapore, South Korea,

Australia and Britain. In the United States, despite its reputation for restrictive policy, approval to work with permitted stem-cell lines can take as little as a few weeks.

Officials at Japan's science ministry say they are trying to improve the system. "Ministry guidelines were not clearly communicated to the institutional review boards," says Yasuhiko Ishii, director of the ministry's bioethics and biosafety office. At a meeting on 11 November he says officials discussed ways to streamline the process. They also decided to make it clear that thorough monkey studies are not always necessary before moving to human cells. "We don't want to be an obstacle to research," says Ishii. "But we need to know that proper ethical considerations are being made."

Meanwhile, Nakatsuji, who is co-hosting an international symposium on embryonic stem cells in Kyoto this week, is undeterred. He plans to create ten more human embryonic stem-cell lines in the next year, and to build a cell-processing centre to produce clinical-grade lines in the next five years. ■
David Cyranoski

Korean scientists are calling for an independent investigation, but it is not clear whether this will happen (see page 257). In the meantime, researchers are left wondering what caused Schatten's sudden change of heart.

Until recently, Hwang and Schatten had been getting on famously. "They seemed as close as they could be," says Hyun, who spent this summer studying the Korean team's ethical practices. "Gerry kept referring to Dr Hwang as his brother, and Dr Hwang's public toast to Gerry at a formal dinner was so effusive, it was almost embarrassing."

Eggen adds that just last week the two were as chummy as ever at a conference in New York. "They seemed to have every intention of continuing to collaborate in the future," he says.

Evan Snyder, a neuroscientist from the Burnham Institute in La Jolla, California, says that he received an e-mail from Schatten just before he issued his statement. "Whatever prompted this he found so exceedingly disturbing, he could not sit on it," says Snyder. "You have to realize this is a major part of his research programme as well, so to do something this precipitously, it must have been terribly shocking." ■

David Cyranoski and Erika Check