

SCIENTIFIC MISCONDUCT

Investigations Document Still More Problems for Stem Cell Researchers

SEOUL—The accusations surrounding Woo Suk Hwang's discredited stem cell research have gone from bad to worse. Last week, a report from the South Korean National Bioethics Committee said that Hwang and his team seriously violated basic ethical rules in their collection of human oocytes and that some of the 119 donors became severely ill as a result of the procedure. The government's auditor also said on Monday that it so far could not account for \$2.6 million in research funds that Hwang had received. And there could be more to come: At least five investigations are continuing in South Korea and the United States.

The initial results of the audit have been referred to South Korean prosecutors, who are investigating potentially criminal aspects of the saga. Meanwhile, investigations are under way at *Science*, which published both of Hwang's now-discredited papers claiming to have derived embryonic stem cells from cloned human embryos, and at two U.S. universities where Hwang co-authors work.

On 6 February, the South Korean government's auditor said in a report that Hwang could not account for how he spent a significant sum of his research money, which included \$31.8 million (30.9 billion won) in public funds and \$6.2 million (6 billion won) from private sources. The Bureau of Audit and Inspection said Hwang could not prove how he used \$1.07 million from the state and \$1.6 million in private funds. Hwang also deposited public and private funds into his personal account and withdrew money for purposes "outside of research," the report says, although auditors do not know exactly how the funds were spent.

Some apparently went to lab members involved in the scandal. Shortly after questions were raised last fall about how Hwang obtained oocytes, news media reported that



Warm reception. Jong Hyuk Park, a member of Hwang's team, is mobbed by reporters when he returned to Seoul last week from the United States to talk to prosecutors.

two of his co-authors who were working at the University of Pittsburgh, Pennsylvania, Jong Hyuk Park and Sun Jong Kim, together received a total of \$50,000 from Hwang's associates. (Seoul National University officials said in December that Kim turned over \$30,000 that he had been given.) The auditors say this money came from the funds Hwang received from private sources.

In a separate investigation, the National Bioethics Committee said in an interim report released 2 February that Hwang's team received at least 2221 oocytes from 119 women between November 2002 and December 2005, 160 more than Seoul National University reported last month. (In their papers, Hwang and his colleagues reported using only 427 oocytes.) Citing "serious ethical violations," the panel also found that Hwang's team failed to fully explain the potential risks associated with oocyte donation and that the Institutional Review Boards at Hanyang University's medical center and Seoul National University provided insufficient oversight.

The panel says that a significant number of women who donated through MizMedi Hospital developed ovarian hyperstimulation syndrome, a side effect of the drugs given to oocyte donors. Fifteen out of the 79 MizMedi donors were treated for the syndrome, which can cause nausea in mild cases and liver and kidney damage in severe cases. The committee said two donors were hospitalized. The report also said that some women who suffered from health effects went on to donate again despite the risks.

Among the 119 donors, 66 received compensation. The committee said it is still looking into whether any of the payments occurred after 1 January 2005, when a law went into effect prohibiting such payments.

That is one of the questions the Seoul Central District Prosecutors' Office is trying to answer as a special team questions key figures associated with Hwang's fabricated research. As prosecutors try to pinpoint who did what in the labs, they are also looking into whether Hwang misused public funds and whether someone at

MizMedi Hospital, which collected oocytes for his research, switched his cloned embryonic stem cells with fertilized ones, as Hwang contends. The prosecutors continue to interview lab members, and they raided Hwang's home for a second time last week. They have also asked University of Pittsburgh professor and co-author Gerald Schatten to travel to South Korea for questioning. University spokesperson Jane Duffield said Schatten would seek legal advice on how to respond. She said the university's own investigation was likely to finish in mid-February.

Sung Il Roh, director of MizMedi Hospital, told *Science* that he expects to talk to the prosecutors by next week. Jong Hyuk Park and Sun Jong Kim have already been questioned, and prosecutors are expected to call co-author and former MizMedi researcher Hyun Soo Yoon, now a professor at Hanyang University.

The revelations about oocyte donations have triggered the retraction of yet another paper associated with Hwang's work (*Science*, 20 January, p. 321). On 31 January, the *American Journal of Bioethics* announced that it is ▶



retracting a paper about ethics and egg donation that appears in its January-February issue. The article, by ethics and legal expert Koo Won Jung of Hanyang University and bioethicist Insoo Hyun of Case Western Reserve University in Cleveland, Ohio, is based in part on visits to Hwang's lab last summer. Hyun says the article, which first appeared online in November, is being withdrawn because it contains descriptions of lab practices that it is now clear were not followed.

Jose Cibelli, who was a co-author on Hwang's 2004 paper, has also requested that Michigan State University investigate his role in the work.

Science will be conducting an internal review this month, and an external review led by outside scientists will take place in March and report its findings in April. John Brauman, a chemist at Stanford University in Palo Alto, California, and chair of *Science*'s senior edi-

torial board, will head the external panel, which will examine both how the Hwang papers were handled and *Science*'s policies in general. "They will be given whatever they want," says Monica Bradford, *Science*'s executive editor.

—SEI CHONG

Sei Chong is a freelance writer in Seoul. With reporting by Jennifer Couzin, Constance Holden, and Gretchen Vogel.

WOMEN'S HEALTH

Study Yields Murky Signals on Low-Fat Diets and Disease

An 8-year study of nearly 49,000 postmenopausal women that explored links between a low-fat diet and health is leaving confusion in its wake. The study, run by the Women's Health Initiative (WHI), found that individuals asked to adhere to a low-fat diet had roughly the same risk of breast cancer, colorectal cancer, and cardiovascular disease as those whose diet didn't change. But methodological problems have left researchers stymied about what the message of the three-pronged study, published this week in the *Journal of the American Medical Association*, should be. "We have a very sobering situation," says Harvard University epidemiologist Walter Willett. While praising the dedication of WHI investigators, he notes that "this was the biggest and most expensive [diet] study ever done," and it arrived at "a very crude result."

The study is the second of three from the WHI (*Science*, 10 June 2005, p. 1570). The first, whose results were reported in 2002 and 2004, was controversial. It found that hormone replacement therapy could raise the risk of breast cancer and heart disease, prompting a stampede away from the drugs. The third, examining the effects of calcium and vitamin D on bone health, will be published next week.

The diet study randomized more than 19,000 women to a diet low in fat and high in fruits, vegetables, and grains. A comparison group included 29,000 others. It was hoped that the first group could slash its fat intake to 20% of calories, while the second would hover around 40%. Study leaders predicted

that even if the difference in fat intake was just 11% at the study's end, they would see 14% fewer cases of breast cancer among the dieters. The study also examined whether the low-fat diet could avert colorectal cancer and cardiovascular disease.

But, as is common in nutrition studies, participants had difficulty sticking to the diet.

After 6 years, dieters were consuming 30% of their calories from fat, compared with 38% in the control group. There was no

whether targeting certain types of fat would be a more effective approach," says JoAnn Manson, a WHI principal investigator and chief of preventive medicine at Harvard's Brigham and Women's Hospital in Boston.

In addition to dietary adherence, the study may have been limited by its length, says Willett. Although impressive by most standards, 8 years is relatively brief where diet's effects on slow-growing cancers are concerned. The results could also have been influenced by the fact that participants started the diet late in life: Researchers don't yet know whether diets begun earlier are more powerful than those begun at older ages.

Norman Boyd, a cancer epidemiologist at Princess Margaret Hospital in Toronto, Canada, notes that diet data were collected through food-frequency questionnaires; they were given to participants at the study's launch, after the first year, and every 3 years thereafter. Such questionnaires rely heavily on memory and are "not a very good way of addressing diet," says Boyd. He's finishing a breast cancer prevention study of 4700 women that also tests a low-fat diet followed for at least 8 years. His participants are at risk of the disease and also younger—their average age is 42. Results of Boyd's trial are expected later this year.

Despite the WHI study's mixed results, critics and supporters alike agree that when it comes to disease, diet matters. Although its dieters can now hop off the low-fat bandwagon, WHI investigators will follow them for another 5 years, searching for additional clues about fat's role in health.

—JENNIFER COUZIN



Women's Health Initiative Study

	% calories from fat	
	Dieters	Nondieters
Original study goal	20%	40%
At 1 year	24%	35%
At 6 years	30%	38%

difference in colorectal cancer or cardiovascular disease rates. Dieters did suffer 9% fewer cases of breast cancer, but that result failed, just barely, to reach statistical significance, meaning it could have occurred by chance. Still, "I don't think it can be dismissed," says Lynn Rosenberg of Boston University School of Public Health.

The study's diet was designed with breast cancer in mind, says Ross Prentice, a biostatistician at Fred Hutchinson Cancer Research Center in Seattle, Washington, and a leader of the WHI trial. Although cardiovascular disease can be prevented by replacing saturated fats with polyunsaturated ones, "for breast cancer, it remains unclear