Cell Divisions

The announcement that a South Korean researcher created stem-cell lines from cloned embryos united scientists in hope. Now revelations of fraud have researchers investigating his work and pointing fingers.

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Article: A Nation's Pride Turns to Shame

By RICHARD MONASTERSKY

Biologists around the world moped through a dark holiday season, afraid to open their newspapers for fear of what news might emerge from the stem-cell scandal in South Korea — the biggest case of scientific fraud in decades.

"This is a stain on the honor and integrity of all scientists," said Robert Lanza, a stem-cell researcher and medical director of Advanced Cell Technology in Worcester, Mass. "It's a tremendous setback."

Late last month, an investigation by Seoul National University determined that an international scientific superstar named Woo Suk Hwang had fabricated data for a landmark paper in the journal Science in May. In that paper, Dr. Hwang reported that his team had created 11 lines of stem cells from cloned human embryos.

The stem cells were purportedly tailored from the DNA of individual patients, lending hope that researchers would soon be able to make personalized stem cells for patients suffering from diabetes, Parkinson's disease, and other illnesses. Such an individualized strategy would allow doctors to give patients therapeutic cells or tissues that would not be rejected by the patients' immune systems.

The hopes for quick progress were dashed last week, however. The investigation panel reported that DNA tests performed by three different labs did not support Dr. Hwang's claims from the May paper in Science.

"According to the results of three professional institutes, it is confirmed that the cell lines that Professor Hwang stored, and are now being cultivated, are not patient-tailored," the panel announced at a news conference in Seoul. The test results indicate that the stem cells actually came from fertilized eggs rather than cloned embryos.
The panel's full report is expected in mid-January. Last week *Science* editor-in-chief Donald Kennedy released a statement saying that his journal is "proceeding swiftly but appropriately" toward a full retraction of the May paper.

**A Difficult Process**

Two months ago, the subject of the current investigation was a national hero. Dr. Hwang had vaulted to that status in early 2004, when he claimed in a paper in *Science* that his team had been the first to successfully clone a human embryo and extract stem cells from it.

To make the clone, the team allegedly had sucked out an egg from a woman and extracted its nucleus. Then the scientists had inserted the nucleus of an adult cell from the same woman into the denucleated egg. The process is called nuclear transfer.

By shocking the egg, the researchers were able to get it to start dividing, even though it had never been fertilized by a sperm. The egg divided until it reached the stage of a blastocyst — a ball of cells from which Dr. Hwang's team extracted the highly prized embryonic stem cells.

From a biological perspective, those cells are blank slates that hold powerful potential. They have not yet grown and specialized to form the many different cell types in the human body. The hope is that researchers can learn how to coax embryonic stem cells to grow into any type of cell or tissue that is needed to treat a disease.

In 2001 Dr. Lanza's group at Advanced Cell Technology reported that it had cloned a human embryo using the nuclear-transfer procedure, but the embryo stopped growing after only a few divisions, too early for the scientists to extract stem cells. Dr. Hwang's reputed success in 2004 was to keep the embryo growing and to develop a line of stem cells from that cloned embryo.

Still, the process seemed inefficient. It took 242 eggs from 16 women to create the single line of embryonic stem cells reported in the 2004 *Science* paper. In May of last year, Dr. Hwang reported a huge leap forward. His paper described a tenfold increase in efficiency that led to the creation of 11 different stem cell lines from cloned embryos. The achievement made the day when the process would benefit patients seem that much closer.

**From Hero to Scapegoat**

But the amazing story told by Dr. Hwang and his fellow researchers started to unravel in November, when reports emerged that Dr. Hwang had lied about the source of the eggs donated for the 2004 *Science* paper. A South Korean television network reported that the eggs had been donated from junior researchers on the project and that Dr. Hwang's team had paid for eggs, a clear violation of scientific ethics.

Because of concerns about those reports, Gerald P. Schatten, a co-author of the 2005 paper and a stem-cell researcher at the University of Pittsburgh, severed his collaboration with Dr. Hwang in November. A month later, Dr. Schatten sought to retract his name from the *Science* paper when concerns came to light that some of the data might have been fabricated. Seoul National started
its investigation, as did a team at the University of Pittsburgh, which has yet to announce its findings. The Seoul investigation is still testing materials related to Dr. Hwang's 2004 paper to determine if he ever cloned a human embryo and extracted stem cells from the clone.

Some stem-cell researchers in the United States say they are convinced that Dr. Schatten did not know about the fabrication. But they say he can't avoid the fallout from the scandal. Dr. Schatten was listed as the last author, a prized position on biological papers. The last author is usually regarded as the most senior scientist on a team, who guides the overall direction of research.

"He is responsible," said Rudolf Jaenisch, a stem-cell researcher at the Whitehead Institute for Biomedical Research and a professor of biology at Massachusetts Institute of Technology. "No one can take the responsibility away from him."

"There are consequences for Dr. Schatten," said Donald Kennedy, editor of Science, during a news conference last month. "I think it's a sauce of the goose, sauce for the gander proposition. If you're going to be a full co-author and share in the credit for an accomplishment, then you have to take the fall if it's wrong."

Dr. Schatten has yet to respond to news-media requests for interviews, including requests from The Chronicle. Over the past few weeks, Dr. Hwang has denied fabricating data, but he has asked Science to retract his paper. He has also resigned from his post at Seoul National.

The journal Nature announced last month that it is investigating a paper that Dr. Hwang's team published in August which reported on the first successfully cloned dog. The Seoul National University panel is still testing material related to the dog to try to verify that claim.

Dr. Hwang, who once had to face mobs of autograph seekers when he ventured into public, has now become a national embarrassment and the butt of jokes. One South Korean newspaper reported that people had created a party game in which players drink from a line of 11 glasses, only a few of which contain real alcohol. The rest are shams, filled only with water.

Alan Brender contributed to this article.
Korean Team Speeds Up Creation Of Cloned Human Stem Cells

With speed and efficiency that will make waves in laboratories and legislatures around the world, scientists have created nearly a dozen new lines of human embryonic stem (ES) cells, ones that for the first time carry the genetic signature of diseased or injured patients. Last year, a group led by veterinarian Woo Suk Hwang and gynecologist Shin Yong Moon of Seoul National University reported the first—and until now the only—derivation of ES cells from human nuclear transfer experiments (Science, 12 March 2004, p. 1669). Those efforts yielded just one cell line from more than 200 tries, but the researchers report online in Science this week (www.sciencemag.org/cgi/content/abstract/1112286) that they can consistently derive a cell line in fewer than 20 tries.

The dramatic increase in efficiency suggests that creating genetically matched ES cell lines for patients needing some kind of cell transplant might not be impractical. “It’s a breakthrough that I didn’t think would happen for decades,” says developmental biologist Gerald Schatten of the University of Pittsburgh in Pennsylvania, an adviser to the Korean team and an author on the paper. Developmental biologist George Daley of Harvard University calls the work “spectacular.” And the work may influence the ongoing political debate over whether research with human ES cells, whether cloned or not, is ethically justified. “Some people will hate it, others will love it,” says Rudolf Jaenisch of the Massachusetts Institute of Technology. “But it puts the discussion on a very firm footing now. People will have to rethink the argument that it’s not efficient.”

The new ES cell lines were created by replacing an oocyte’s nucleus with one from a somatic cell and then chemically kick-starting development of the egg. Scientists similarly created Dolly the sheep in 1996 and since then have used nuclear transfer to clone thousands of cattle, mice, and other animals. Hwang and his colleagues had no intention of cloning a person, however. They only allowed the human embryos to develop for 6 days, just long enough to derive stem cells that, in theory, can form any cell type in the body.

One important factor in his team’s success, Hwang says, was the use of freshly harvested oocytes from fertile women instead of ones left over from fertility treatments. The age of donors may also be key. Whereas oocytes from women in their 30s yielded on average one ES cell line for every 13 tries, those from younger donors yielded one line for every 13 tries. In nine cases, it took only a single donation of oocytes from a woman to produce a new line. (Each donation yields about 10 oocytes.)

The Korean team developed several techniques to improve their efficiency. For example, instead of using a needle to suck out the egg’s nucleus, they make a small tear in the egg and gently squeeze out the chromosomes. They then insert a skin cell through the tear and apply an electric shock to fuse the two cells.

Most ES cells are derived by applying antibodies to a blastocyst-stage embryo that kill its outer cell layer and leave the inner cell mass. Hwang, Moon, and their colleagues simply put a blastocyst on a layer of human feeder cells and found that the blastocysts naturally formed colonies of ES cells. They exhibited key markers of ES cells and could form skin, muscle, and bone cells, among others.

Last year, because they had used a cell from the ovary of the oocyte donor as the nucleus donor, the Korean team could not rule out that the ES cell line was the result of parthenogenesis: an unfertilized egg starting to divide on its own. This time, except for one line, the oocyte and skin cell donors were different. In all 11 cases, the genetic fingerprint of each line matched that of the skin cell donor.

Nine of the 11 cell lines are derived from people, ranging in age from 10 to 56, who have suffered spinal cord injuries. The team has begun to test some of the lines in animal models of spinal cord injury, but Hwang cautions that they remain years away from transplanting the cells into people. “We have to be overconvinced” that the cells are safe, he says.

Another line is derived from a 2-year-old boy who has congenital hypogammaglobulinemia, a genetic immune deficiency. In theory, scientists could correct the genetic defect in the stem cells and then reinject them into the boy. Indeed, Jaenisch, Daley, and their colleagues have used such a strategy to treat mice with a similar genetic defect. Nevertheless, Hwang stresses that the boy’s parents and the spinal cord patients were explicitly told that the team’s research was unlikely to help them directly—even though the informed consent form used was, by Korean law, mandated to suggest such a possibility.

Although also unlikely to be employed for treatment, another ES cell line, derived from a 6-year-old type 1 diabetes patient, should interest scientists. “The possibility of being able to study disease in a culture dish is very exciting,” says Douglas Melton of Harvard University, who has recently received permission from the school’s ethics committee to derive ES cells from diabetes patients. “If we could make T cells and β cells in a dish—we’re not there yet, but we’re getting closer—then we could compare the diabetic cells to wild-type cells and ask what goes wrong,” he explains. “For ▶
Japan Bars Indian Physicists From Lab

Tokyo—Several Indian physicists have been blocked from visiting a Japanese research lab in the past year because of what appears to be an overzealous interpretation of rules aimed at restricting the spread of nuclear weapons. Two Japanese ministries are at odds over the unofficial policy shift, which is slowing research and raising questions about future collaborations between the two countries.

The snafu mostly involves visas for Indian scientists hoping to work at Japan’s High Energy Accelerator Research Organization (KEK) in Tsukuba, although there are reports of problems visiting other labs. KEK is the site of Belle, a 13-nation experiment to explore why the universe has more matter than antimatter. Last May, after making two trips to KEK, graduate student Garima Gokhroo of the Tata Institute of Fundamental Research in Mumbai learned that her visa application had been rejected. Over the next several months, at least one Tata colleague and at least three researchers from Punjab University in Chandigarh were also denied visas to visit KEK. Their plight has recently come to light.

The Indian scientists say they were never given a reason for their rejections, and Masanori Yamauchi, a KEK physicist and spokesperson for the Belle collaboration, says he has been unable to get an explanation from Japan’s Ministry of Foreign Affairs, which decides on visas. Contacted by Science, a spokesperson for the ministry declined to describe the criteria for granting or denying visas or say if Indian physicists are receiving special scrutiny.

But an official at the Ministry of Education, which recently started its own investigation, says the problem stems from concerns that India has declined to sign the Nuclear Non-Proliferation Treaty and other agreements intended to control the flow of sensitive weapons technologies. A change in agreements intended to control the flow of sensitive weapons technologies. A change in

Japan’s stance, says the official, who did not want to be identified. He says there could be a resolution “soon.”

KEK’s Yamauchi says that the 400-member Belle collaboration can continue without its Indian colleagues, but their absence is hurting data analysis from the experiments. “We are suffering there,” he says. Tata’s Gokhroo says her doctoral work “has definitely been delayed.”

There could also be long-term consequences, including Tata’s ability to play a role on a Belle upgrade and on the proposed Next Linear Collider. “I won’t be able to ask for funding if our researchers aren’t going to get visas,” says Aziz.

—DEAN NORMILE
The Seoul of Clones
Solving a biotech mystery: Why South Korea leads the world in stem-cell research.
By David Plotz
Posted Wednesday, Oct. 19, 2005, at 1:15 PM ET

The Chopstick Theory of Scientific Supremacy goes like this: Koreans eat with narrow, metal chopsticks. Nabbing grains of rice with slippery, steel sticks requires a surgeon’s dexterity. That’s why Koreans have mastered extraordinarily precise “micromanipulation” of eggs and embryos required for stem-cell and cloning research. Westerners with their clunky forks—and even other Asians with their thick, gripppy wooden chopsticks—can’t hope to compete with the dexterous Koreans.

The Chopstick Theory is how Hwang Woo-suk, the world’s greatest cloner, accounts for his nation’s stem-cell success. The theory has undeniable appeal: It’s exotic, it’s funny, and it’s even partly true. But it only begins to explain a peculiar anomaly of global science: how South Korea, a nation of only 48 million people and no history of biotech accomplishment, has emerged as the world capital of stem-cell and cloning research.

Yesterday Hwang and his colleagues announced that they are opening a stem-cell library in Seoul. The library, the first of its kind, will create 100 or so cell lines a year to supply the world’s scientists. Americans, whose stem-cell investigations have been hampered by Bush administration policies and funding restrictions, are expected to be the bank’s best customers. The bank is just the latest first from Korean stem-cell researchers, who make some new, jaw-dropping advance practically every month. In July, Hwang’s lab announced that it had cloned the first dog. This followed May’s disclosure that the lab had cloned the first customized embryonic stem cells. Last year, Hwang and his colleagues were first to clone human embryos and first to extract stem cells from them. Hwang was also first to clone a cow, and one of his former students was first to clone a cat. Even the cloning weirdos have South Korean ties: In 2002, scientists connected to the Raelian cult claimed (falsely) to have cloned the first baby, using South Korean embryos and mothers.

There is no clear reason why this future should be happening in Seoul. South Korea has only a few dozen stem-cell researchers, compared with more than 600 in the United States. The Korean government spends only $10 million or so a year on stem-cell and cloning research, less than one-hundredth of what the U.S. government disburses. Fellow Asian Tiger Singapore has spent $500 million to build “Biopolis,” a huge bioscience campus. By contrast, Hwang’s lab at Seoul National University, responsible for most of the Korean advances, gets by on only a couple million dollars a year.

And yet there they are in Seoul, cheerfully cloning for the brave new world.
Why?

For starters, the country is not preoccupied with moral questions about the beginning of life. Unlike its Asian neighbors, Korea has a huge and powerful Christian community, with strong ties to the evangelical American churches that have bollied up stem-cell research in the United States. Evangelical Protestants make up a quarter of the South Korean population, and Catholics are another 6 percent. Yet this has not translated into a moral movement against stem-cell research. Korean Protestantism is relatively new, only a century old. Prof. James Grayson, an expert in Korean religion at Sheffield University, says that Korean Christians—who have spent that century under occupation, at war, and then rebuilding a destroyed and colonized nation—have been busy with more practical moral questions of human rights, justice, and economic development. Whether life begins at conception, at implantation, at quickening, at birth—these abstract theological questions are distant from the daily demands of Christianity in Korea. (Non-Christian Koreans are not interested in these issues either.) The result is an entirely different approach to life issues. For example, despite a nearly absolute ban on abortion, Korea has one of the highest abortion rates in the developed world because the government looks away and no one protests. Similarly, the moral wrestling that has crippled American stem-cell research is absent. This liberates Korean scientists from exhausting debate and frees their research from condemnation. As Jose Cibelli, a Michigan State professor who collaborates with Hwang, puts it: "It really helps that every time [Korean scientists] give a talk, they don't have to have an argument about whether an embryo is a person."

In the nature-versus-nurture debate, Americans tend to come out for nurture. Our strong democratic ethos insists that anyone is capable of anything and that genes are secondary. This is much less true in Korea. Blood and genes are fundamental to Korean identity. Korea is the most ethnically homogeneous big country in the world. Practically everyone can trace their bloodlines, and a traditional clan system regulates marriage. Koreans think about themselves in explicitly genetic terms, and this makes them more sympathetic to genetic research than Americans, who tend to get queasy about such tampering. Similarly, Koreans are extremely open to medical self-improvement: Korean cosmetic-surgery rates are among the highest—the highest—in the world.

Korean fascination with bloodlines nurtures local stem-cell research in another way. Korean couples face enormous pressure to have their own genetic children, which has fueled one of the most vigorous assisted-reproduction industries in the world. According to Shin Young Moon, obstetrics professor at Seoul National and director of the Stem Cell Research Center, Korea has 95 IVF centers, and 4,000 IVF births occur every year. Korea's success rates for traditional IVF are as good as ours, says Shin, and its success rates for more specialized forms of assisted reproduction are even better. The IVF clinics have trained a generation of technicians with incredible lab skills. This outstanding technical ability—perhaps enhanced by steel chopsticks—explains why Korean stem-cell researchers can perform micromanipulations (such as gently squeezing DNA out of a single egg) that scientists in other countries struggle to master.

Korean scientists aren't just more technically skilled, they are also more diligent. Korean scientists work much harder than Americans. At Hwang's lab, everyone works every day of the week and holidays. This is not hyperbole. Hwang never takes a vacation, and neither do his underlings. In some branches of science—such as pure math or theoretical physics—this mania for work wouldn't matter much, but in stem-cell research, it's incredibly valuable. This research is repetitive, tedious, and factorylike. It rewards the persistent. Hwang's lab cloned and transferred more than 1,000 embryos into 123 dogs to make a single cloned puppy. "That tells you how single-minded they are. If it was me, I would have given up at the 10th transfer," says Hwang collaborator Cibelli.

The work culture is not merely relentless, it is also collectivist. In American and European labs, Cibelli says, researchers jockey to test their own hypotheses, run their own experiments,
and publish their own papers. At Hwang's lab, scientists take their orders from the top, work ferociously to carry them out, and let the glory fall to the boss. This is likely the product of Korea's Confucian tradition. Confucianism teaches that workplaces should be run as benevolent hierarchies, with younger and junior people obediently taking guidance from seniors. Stem-cell research depends much more on technical proficiency than blue-sky brainstorming. It fits well with a collectivist approach that focuses the entire scientific team on a single goal.

**Korea reveres scientists more than we do.** Science is trendy in Korea. It attracts the nation's best students. There's no nerd derision. Hwang Woo-suk is a celebrity in a way we can't imagine an American scientist could be. The national law-enforcement agency assigns officers to protect him. Korean Airlines flies him around the world for free. The minister of science and technology ranks at the top of the South Korean Cabinet—as high as the secretary of state or treasury in the United States. While most foreign scientists who study in the United States end up staying there, nearly 90 percent of Korean scientists end up returning home, despite much lower salaries.

The reverence for science helps cloning research, in particular, because cloning requires a huge supply of fresh human eggs. For one recent paper, Hwang and his colleagues used nearly 200 eggs collected from Korean women. To gather such a supply of eggs in the United States would be practically impossible, legally dubious, and financially ruinous. But Hwang has a waiting list of Korean women who have volunteered to donate eggs for free, to help his cause.

Korea had a rotten 20th century—occupied by Japan, split by war, driven into a miserable poverty. (At war's end, Korea was one of the world's poorest countries.) Koreans felt acutely the shame of being booted from the ranks of important nations, of being supplanted by China and Japan. It is hard to overstate just how driven Koreans are to make Korea a great nation. **This nationalism has helped Korea nudge aside whatever moral objections to cloning have popped up.** Though Korea has banned cloning for reproductive purposes, it has enthusiastically supported the research cloning that so troubles American conservatives. The ethical concerns in Seoul are minor, weighed against Korea's chance to become the world leader in the next great biotech industry.

Still, the most important reason why Korea leads the cloning race has nothing to do with the nation. The majority of Korea's stem-cell and cloning advances have been made by a single man, the profoundly brilliant, enthusiastic, and energetic Hwang. Korea's government, religion, culture, reverence for science, nationalism, and skinny chopsticks may make it possible for the nation to be a world leader in this research. But it is an individual genius who is turning his nation's potential into actual stem cells.

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**sidebar**

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The majority of Koreans practice Buddhism or "traditional" local religions. Neither Buddhism nor the traditional religions have theological concerns about when life begins.

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Stem-Cell Researchers
Under Fire for Source of Eggs

By GORDON FAIRCLOUGH
Staff Reporter of THE WALL STREET JOURNAL
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SEOUL, SOUTH KOREA -- Questions mounted this week about how women's eggs were obtained for use in experiments that produced stem cells from cloned human embryos for the first time.

On Monday, the head of a Seoul fertility clinic, Roh Sung Il, said he paid women who provided eggs used in the research, results of which were published in 2004. The experiments marked a significant advance toward the use of stem cells to treat diseases and put South Korea at the forefront of therapeutic-cloning work.

Then, late yesterday, an hourlong TV news show featured interviews with women who said they had sold their eggs because they needed the money.

The revelations deepened an ethics controversy surrounding the stem-cell-research program led by scientist Hwang Woo Suk, in which Dr. Roh collaborated. Dr. Hwang's team has made headlines around the globe for producing the first cloned dog, in addition to its advances in human cloning for the production of stem cells.

Stem cells have the potential to give rise to cells with specialized functions in the body, such as nerve and muscle cells. Scientists hope they can be used to repair spinal-cord injuries and treat illnesses. Dr. Hwang's work has come under renewed scrutiny since an American biologist, Gerald Schatten, severed a research alliance with Dr. Hwang this month and accused the Korean scientist of misleading him about the source of the eggs used for the research.

Shortly after Dr. Hwang's 2004 paper was published, an article in the journal Nature raised the possibility that some of the eggs used in the work had been provided by laboratory workers. Obtaining eggs from lab workers is considered unethical because they could feel pressured to donate them. On Monday, Dr. Roh declined to say whether any of the eggs came from lab workers; yesterday's news show also didn't say if any eggs were from lab workers.

Dr. Hwang repeatedly has denied those charges. Dr. Schatten said that he had initially accepted Dr. Hwang's word, but said new information had caused him to question his Korean counterpart's denials.
Dr. Hwang, who has become a national hero, has promised an explanation, and his lab has said it is conducting an investigation. But Dr. Hwang maintained his public silence yesterday. He didn't respond to a phone message seeking comment.

On Monday, Dr. Roh from the fertility clinic said that, faced with a shortage of eggs for use in therapeutic-cloning experiments, he decided to offer compensation to donors. He said he didn't tell Dr. Hwang about the arrangement. "I made a difficult decision, for which I alone am responsible," Dr. Roh said at a news conference.

Dr. Roh said that donors knew their eggs might be used for research. He also said that, since publication of the 2004 paper, researchers have had no problem finding donors and that eggs used in subsequent work haven't been obtained from people offered compensation.

Egg donation is time-consuming and can be unpleasant, involving more than a week of daily hormone shots. Eggs are extracted through a hollow needle inserted through the wall of the vagina. "For those who go through discomfort and sacrifice, it seemed natural to give some money as compensation for transportation" expenses and lost time at work, Dr. Roh said. He said he paid each woman 1.5 million won, or about $1,450, from his own pocket.

Dr. Roh said the compensation of donors took place in 2002. That was before the U.S. National Academy of Sciences published a recommendation that stem-cell researchers should avoid payments and before a Korean law outlawing payments for eggs took effect this year.

Write to Gordon Fairclough at gordon.fairclough@wsj.com
Women Offer Eggs to Doctor In South Korea
By GORDON FAIRCLOUGH
Staff Reporter of THE WALL STREET JOURNAL
November 25, 2005; Page B1

SEOUL, South Korea -- American scientists have responded to reports of ethics lapses at the labs of South Korean cloning researcher Hwang Woo Suk by severing ties and distancing themselves from him. But at home, Dr. Hwang is being embraced, and Korean women are lining up to donate eggs for his experiments.

Earlier this week, businesswomen and politicians in Seoul launched a nonprofit foundation to make it easier for women to provide eggs to support continued stem-cell research by Dr. Hwang and his colleagues. Several donors signed up on the spot, and the organizers say they have been deluged with calls.

"Professor Hwang is a Korean icon. Many people want to help," says Kim Yi Hyun, an industrial designer who volunteered to donate eggs. Ms. Kim, 46 years old, says the outpouring of support for Dr. Hwang reminds her of the aftermath of the Asian financial crisis in the late 1990s, when some Korean women handed over their gold jewelry to help pay the country's debts.

Dr. Hwang and his team have become a source of intense national pride here. The scientists were the first to produce stem cells from cloned human embryos, a major step toward using stem cells to treat an array of diseases. Those landmark results were published in 2004, and further advances followed in quick succession.

But after two weeks of allegations and revelations by other scientists, Dr. Hwang admitted yesterday that two junior researchers on his team provided eggs for use in his experiments. He also acknowledged that other eggs had come from donors who had been paid. Both actions raise ethical concerns, experts say.

"I am very ashamed," a grave and tired looking Dr. Hwang told reporters in a packed lecture hall at Seoul National University, where he works. Dr. Hwang said he would step down as chairman of the World Stem Cell Hub, an organization started last month in Seoul to foster international cooperation in therapeutic cloning. But he said he will continue doing stem-cell research.

South Korea's Ministry of Science and Technology rushed to the defense of Dr. Hwang, saying in a statement that the donations by the young researchers weren't unethical because the women
had voluntarily given their eggs. The ministry also said the payments to egg donors were not illegal, since they occurred before a new law, outlawing such compensation, took effect earlier this year.

Ethicists generally frown on donations by people in subordinate positions, such as junior researchers, since they can easily be pressured to participate. The science ministry statement, however, said that such a concern was unfounded in Korea and "has to be perceived as a cultural difference from the West."

Dr. Hwang said yesterday that he didn't know his researchers had been among the egg donors until after his 2004 paper was published. He said he then kept silent to protect the junior scientists' privacy. Dr. Hwang likewise said he was unaware that any egg donors had been compensated until shortly before another member of his team, the head of a fertility clinic, admitted to making payments on Monday.

The ethics controversy has dismayed supporters of stem-cell research in the U.S. and elsewhere, who fear the questions about Dr. Hwang's conduct will inspire more opposition to their entire field of inquiry -- which is already under attack by critics who say it is immoral to create embryos simply to produce stem cells.

But Koreans so far have stood by Dr. Hwang. Many Koreans think the international hand-wrangling over ethics is overblown and aimed at blocking the country's scientific progress. More than 65% of people in a public-opinion survey sponsored by the Hankyoreh newspaper - and published before Dr. Hwang's admissions yesterday -- said they didn't see any ethical problem with lab workers donating eggs.

Questions about the source of eggs used in Dr. Hwang's research received renewed attention after a University of Pittsburgh biologist withdrew from a research alliance with Dr. Hwang, saying he felt he had been misled. The biologist, Gerald Schatten, has since been attacked in the South Korean media.

In one conspiracy theory popular in press accounts, Dr. Schatten joined hands with Dr. Hwang to learn the secrets of his work and ride his coattails to a Nobel Prize. Then having learned Dr. Hwang's advanced techniques, this theory goes, Dr. Schatten decided to sideline his scientific rival.

A Web site dedicated to Dr. Hwang allows women to sign up to become donors. On Wednesday, there were 134 women on the list. By Thursday morning, the number had risen to 188. The Web site proclaims: "The people registered here are angels and are members of a patriotic army of national independence" who are protecting "the homeland at this time."

The site doesn't feature prominent warnings about the potential side-effects of donation, which involves more than a week of daily hormone injections and the insertion of a needle through the wall of the vagina to withdraw the eggs. But supporters say there is a description of the donation procedure and possible risks.
Many of the women are driven by the potential benefits of the stem-cell research. Scientists believe that stem cells may one day be used to treat spinal-cord injuries and illnesses ranging from Alzheimer's to diabetes.

Lee Soo Young, chief executive of a computer systems-integration company, is one of the main backers of the new foundation, whose name roughly translates as "People's Foundation for the Donation of Ova for Research and Therapeutic Purposes." She says she wants to educate women about need for egg donations to ensure that Dr. Hwang's work can continue despite the current controversy.

"It would be very sad if Prof. Hwang's research is discredited or stopped because of this," says Ms. Lee, whose husband is paralyzed from the neck down as the result of an automobile accident. Ms. Lee says stem-cell research could help find a way to treat her husband and help him regain some mobility. "If this research stops, it will take away our hope," she says.

For others, there is also a strain of patriotism. Ms. Kim, the industrial designer, says: "I'm doing this for the love of the country and because I believe Dr. Hwang is a great man and an important person in human history."

Another woman who has signed up to donate, 46-year-old Hong Me Young, says: "We live in a country without power. We feel that we are strangled by the U.S." She adds: "I think Prof. Hwang empowers us. That is why I've decided to donate eggs."

Ms. Hong thinks the ethical concerns that have been raised are minor. "I think people aren't focusing on what really matters," which is the potential for further scientific breakthroughs, she says.

A Web site maintained by supporters of Dr. Hwang, titled "I Love Hwang Woo Suk," features a picture of the scientist, the dog his team cloned earlier this year and a South Korean flag. The site also broadcasts patriotic tunes. One man posted a message on the site this week, which said, "I fought with my wife because she doesn't want to donate her eggs."

--Lina Yoon contributed to this article.

Write to Gordon Fairclough at gordon.fairclough@wsj.com
The University of Pittsburgh has launched an inquiry into possible scientific misconduct by researchers involved in a highly publicized stem-cell finding.

On Monday, university officials said they had opened a "preliminary" inquiry after learning some stem-cell images in a prominent 2005 paper were duplicates. The paper, published by the journal Science, reported the creation of stem cells from cloned human embryos.

"The purpose of the inquiry is to determine if there is enough basis to launch an investigation," said Jerome L. Rosenberg, the university's research integrity officer.

The paper, based on experiments carried out by a cloning laboratory in Seoul, South Korea, included as a co-author Gerald Schatten, a University of Pittsburgh biologist who last month cut off his collaboration with the Korean lab.

The latest error brings to three the number of mistakes found in the Korean lab's high-profile research reports.

The claims of the Korean team, led by Hwang Woo Suk of Seoul National University, came under scrutiny in November after Dr. Schatten accused Dr. Hwang of misleading him about the source of human eggs used in an earlier result, published in 2004. In that paper, the Koreans wrote that women who donated eggs for the cloning project weren't paid. Dr. Hwang recently admitted that egg donors had been compensated. His admission set off a furor in Korea, where he is viewed as a national hero.

The stem-cell saga has since taken twists and turns, including allegations by producers of a Korean television program of wholesale scientific fraud by Dr. Hwang.

Dr. Hwang's team has denied those charges, and leading cloning researchers remain convinced the results are sound. In an email, Ian Wilmut, the British scientist who cloned Dolly the sheep, said "I have no doubts about the work."

But troublesome errors are keeping the issue alive. In November, Dr. Schatten informed Science that some supporting tests reported in the 2005 paper hadn't been carried out at the time.
Then on Monday, Dr. Hwang informed Science of an additional error, said Katrina Kelner, the journal's deputy editor for life sciences. According to Dr. Kelner, online material included with the paper contains four sets of duplicated images. The pictures, reported as different stem cells, are in fact identical. Dr. Hwang's request to correct the duplicate images was reported yesterday in the New York Times.

Dr. Hwang couldn't be reached for comment. His office said he was unavailable.

"Given the need for two corrections to the paper, and the huge publicity occasioned by this research, only an inquiry that vets, or fails to vet, all of the data will reassure the scientific community," said Arthur Levine, senior vice chancellor for the Health Sciences at the University of Pittsburgh.

According to university officials, Dr. Levine and Dr. Schatten requested the review to resolve any doubts about the research.

Dr. Kelner said the journal Science was looking closely at the paper, but so far considered the errors innocent mistakes. She said a review had shown the original Korean submission didn't contain the duplicate images. Instead, they had been submitted later when the journal requested high-resolution copies to publish on its Web site.

--Gordon Fairclough contributed to this article.

Write to Antonio Regalado at antonio.regalado@wsj.com
One of South Korea's top universities, confronted with growing doubts among scientists about the veracity of research published by cloning pioneer Hwang Woo Suk, said it would investigate the groundbreaking work.

Seoul National University, where Dr. Hwang works, said a team of faculty members and outside experts will probe whether researchers fabricated data indicating they had successfully produced stem cells from cloned human embryos.

During the past week or so, scientists at Seoul National and elsewhere in South Korea have started an online campaign questioning the validity of photographs of cell colonies and DNA "fingerprints" used to support the researchers' claims. They have called for independent tests to verify whether the lab actually succeeded in creating cloned cells.

The University of Pittsburgh, academic home of one of Dr. Hwang's co-authors, biologist Gerald Schatten, launched its own inquiry a week ago into the possibility of scientific misconduct by the researchers. Dr. Schatten last month cut off his collaboration with the Korean lab and accused Dr. Hwang of having misled him about the source of human eggs.

Seoul National said in a statement yesterday that "a basic function of an academic institution is to seek the truth," and that an investigation is "the only way that we can guarantee honor and the national interest."

Dr. Hwang is a hero in South Korea, and his cloning research has been held up as the leading example of the country's ability to do world-beating scientific work. If his results turn out to have been faked, it would be a huge blow to the nation's self-image. Dr. Hwang couldn't be reached for comment.

In 2004, Dr. Hwang's team reported producing stem cells from a cloned human embryo for the first time. In 2005, the team published another paper saying it had used cloning to produce stem-cell lines tailor-made for a series of patients. The team also created the world's first cloned dog.

When Dr. Hwang was admitted to the hospital last week for what his doctors said was extreme stress and fatigue, South Korean President Roh Moo Hyun offered public words of encouragement, and the science and technology minister made a pilgrimage to his bedside.
But as scientists have noted similarities between DNA fingerprints and photos submitted with a paper published in the journal Science earlier this year, some of his support, in academic circles at least, has started to waver.

Last week, postings on South Korean Web sites alleged that DNA read-outs in the experiments bore a suspicious resemblance to one another, with the implication that they had been fabricated. However, two U.S. experts on DNA analysis, including a forensic specialist, said the similarities posed no obvious reason for concern.

Several senior U.S. scientists indicated that doubts over the research might not easily be dispelled.

"I think after all this controversy, it would be important to have an independent laboratory confirm the finding," said Rudolf Jaenisch, a senior researcher at the Whitehead Institute in Cambridge, Massachusetts, whose laboratory has explored cloning technology using mouse cells.

Write to Gordon Fairclough at gordon.fairclough@wsj.com and Antonio Regalado at antonio.regalado@wsj.com
Clash Over Cloning Paper Deepens

The American co-author of a breakthrough cloning paper now under fraud investigation has asked to have his name removed from the 2005 report.

The imbroglio involves two papers, published by the journal Science in 2004 and 2005, which were the first to demonstrate the extraction of stem cells from cloned human embryos.

The scientific coup, by researchers at Korea's Seoul National University, began to unravel earlier this year.

In a letter sent to Science yesterday, University of Pittsburgh researcher Gerald P. Schatten asked that his name be removed from the paper. "My careful re-evaluations of published figures and tables, along with new problematic information, now casts substantial doubts about the paper's accuracy," Dr. Schatten's letter stated. In his letter, Dr. Schatten indicated a person involved with the experiments told him part of the result "may be fabricated."

Dr. Schatten was a co-author with the Korean laboratory of Hwang Woo Suk on the 2005 report, which detailed the creation of 11 cloned human cell lines. Some scientists trained by Dr. Hwang work for Dr. Schatten, including one who revealed some of the alleged problems to a Korean TV station in October.

Dr. Schatten had distanced himself from his collaborators after learning that Dr. Hwang had lied about the source of human eggs used in earlier experiments.

Science called Dr. Schatten's latest claims "unsubstantiated." The journal also said it could not withdraw Dr. Schatten's name unless all the authors of the paper agreed.

Late yesterday, no one answered the phone in Dr. Hwang's laboratory.

Write to Antonio Regalado at antonio.regalado@wsj.com
Cloning Scientist Falsified Data, Colleague Says

By ANTONIO REGALADO and GORDON FAIRCLOUGH
Staff Reporters of THE WALL STREET JOURNAL
December 16, 2005; Page B1

When South Korean cloning scientist Hwang Woo Suk strode onto the stage in a United Nations lecture hall in June of 2004, flashbulbs popping around him, he was treated like a hero.

Dr. Hwang launched into a detailed defense of the practice of cloning human embryos to make stem cells -- a feat his lab had reported accomplishing earlier in the year. He railed against a proposed U.N. ban on therapeutic cloning, saying it would dash the hopes of millions of patients with spinal-cord injuries and ailments from Parkinson's to diabetes. His supporters, including some in wheelchairs, applauded.

This week, it was Dr. Hwang who was in the hospital, suffering, his doctors say, from extreme stress and fatigue. And the scientific work that propelled him to the forefront of stem-cell research is in tatters.

Following weeks of escalating concerns about Dr. Hwang's blockbuster findings, one of his Korean colleagues yesterday charged that Dr. Hwang had largely fabricated evidence for the reported cloning breakthrough earlier this year.

Roh Sung Il, a Korean researcher who co-wrote the paper, said in television and newspaper interviews in Korea that Dr. Hwang had told him that he had not succeeded in producing stem cells from 11 cloned human embryos as was claimed and instead faked the results.

It's not yet known whether the allegations are true. Dr. Hwang was not commenting yesterday, even after being released from the hospital. Seoul National University, home to Dr. Hwang's lab, said it will launch an investigation of his findings. The University of Pittsburgh -- where American scientist and co-author of the study, Gerald P. Schatten, works -- has started its own inquiry. In recent weeks, Dr. Schatten raised questions about the research, which was published in the June issue of the journal Science, at each stage further distancing himself until he asked Science on Tuesday to remove his name from the list of authors of the disputed paper, saying he had "substantial doubts about the paper's accuracy." Dr. Schatten declined to comment yesterday.

Dr. Roh said that Dr. Hwang has asked Science to retract his paper. But Daniel Kane, a Science spokesman in Washington, D.C., said that Science editors have received "nothing so far" from
the Korean researchers. A retraction would require all co-authors to agree, Science said in a statement.

If the results reported by Dr. Hwang and his co-authors were falsified, the case would rank as one of history's biggest scientific frauds. That could deal a blow to embryonic stem-cell research, which is already under fire from critics who say it is immoral to create cloned embryos to produce stem cells. A discovery that scientists aren't as far along in using cloning to treat a wide variety of ailments would be devastating to scientists and to patients.

It will also dent South Korea's national self-image. Dr. Hwang has been feted as personifying the country's aspirations to become a world leader in science and technology. Korean women have signed up in droves to donate eggs for his experiments. Dr. Hwang drew the most attention outside the genetic-research community when he announced last year that he had cloned a dog named Snuppy. Dr. Hwang's work on Snuppy could come under question: a spokesperson for the University of Pittsburgh said that Dr. Schatten, who was a co-author on the dog cloning paper, said he had not independently performed tests to confirm that Snuppy is a clone.

Regardless of the outcome, the case once again underscores the limitations of top scientific journals in verifying the results of the research they publish. Journals typically recruit independent reviewers to review papers. But such reviews don't involve actually repeating the experiments, which makes intentional fraud difficult to detect. Only the workers in Dr. Hwang's lab were in a position to know if the results were true. The journal says it relied on pictures of the cells, graphs of DNA readouts, and other data.

While all the details are not yet known, the case is certain to have political implications in Korea and the U.S. Conservative religious groups, with the support of President Bush, have long sought to have the technology made illegal, arguing it is unethical to destroy human embryos in research. With possible evidence of both ethical breaches and fraud in Korea, opponents will have new ammunition to make their case.

Advocates who had touted the Korean breakthrough sought yesterday to put their own spin on events. In a statement, the Coalition for the Advancement of Medical Research, a lobbying group backed by U.S. universities and disease-advocacy organizations, said "this is just another reason that this field of research should be allowed to be conducted in the U.S." under government supervision.

U.S. law prohibits the government from financially supporting research on human embryos, though it remains legal. Supporters have warned that U.S. rules could push the technology overseas to countries with less oversight and weaker scientific traditions.

Dr. Hwang's technology, sometimes known as therapeutic cloning, has been presented as a potential panacea for a host of diseases. The idea is to create powerful embryo stem cells that can grow into any other kind of cell, perfectly matched to a particular patient.
Cloning is the key step. Dr. Hwang's team said they took skin cells from sick patients, including some with spinal-cord injury, then injected their DNA into human eggs. The embryos that reportedly resulted were five-day old clones of these patients.

Dr. Hwang's team said it then extracted the embryos' stem cells. Those cells, in principle, might be used to treat a condition like paralysis or Parkinson's without triggering an immune reaction because they share a patient's DNA.

The episode is a potential disaster for what had been an astounding run for Dr. Hwang's Korean team. In 2004, his group reported in Science the first-ever cloned human stem-cell line. The American co-author on that paper, Jose Cibelli, a researcher at Michigan State University, said he now doubts whether it was true. "For reviewers and collaborators like myself, you look at the figures and the tables and you ask yourself, is this something that I believe they've done?" he says.

Dr. Hwang later teamed with Dr. Schatten of the University of Pittsburgh. Dr. Schatten helped the Koreans lodge a second major result in Science, in 2005. The report stated that Dr. Hwang's team had made 11 cell lines from people with a variety of ailments. The Koreans claimed a leap in efficiency, making all 11 lines from only 185 eggs instead of 242 eggs needed to make the first line.

Some scientists now say they should have seen the problems. In retrospect, the huge increase in efficiency was suspect. "We should have wondered how the efficiency improved 10 times in such a short time," said Dr. Cibelli.

The questions now put Dr. Schatten in an uncomfortable situation. Though he was listed as senior author of the paper, he has said he did little more than provide advice and edit the manuscript.

In October, Dr. Schatten announced he was severing ties with Dr. Hwang, citing possible problems with how human eggs were obtained for some of the team's early experiments. Dr. Hwang eventually admitted ethics lapses, acknowledging that some junior scientists had given their own eggs and that others had come from women who had been paid.

Allegations of fraud also began to circulate after a crew of TV journalists from Munhwa Broadcasting Corp. in South Korea traveled to Pittsburgh on the trail of a story about possible misconduct by Dr. Hwang's team. According to the TV station, a Korean scientist working at the Pittsburgh lab said that Dr. Hwang had ordered him to use two photographs of stem cells taken through a microscope to produce a series of 11 pictures which were later submitted to Science.

The repercussions are already being felt. Scientific American magazine, which had named Dr. Hwang as "Research Leader of the Year" in its 2005 ranking of top researchers, yesterday said it planned to withdraw the honor.

Write to Antonio Regalado at antonio.regalado@wsj.com and Gordon Fairclough at gordon.fairclough@wsj.com
South Korean Scientist Denies Falsifying Stem-Cell Research

By GORDON FAIRCLOUGH
Staff Reporter of THE WALL STREET JOURNAL

December 17, 2005; Page A4

SEOUL, South Korea -- South Korean cloning pioneer Hwang Woo Suk denied that he falsified the results of a landmark stem-cell research project, as alleged by a colleague, but said that his report on the work published in the U.S. journal Science was flawed and that he would seek to retract it.

A representative for Science said Thursday night Dr. Hwang and Gerald P. Schatten, an American co-author, asked that the article be retracted. The request was made during a conference call with the journal's editors, but a spokesman for Science said the journal can't retract the article until all the co-authors agree and that it was seeking their agreement.

Speaking to reporters here Friday, Dr. Hwang said, "I made a lot of mistakes." But, he said, his team had "indeed produced tailor-made stem cells for specific patients," adding that "I do have the technology to do this." Dr. Hwang's accuser, Roh Sung Il, a physician and co-author of the June study, responded in his own press conference by calling Dr. Hwang a liar who fabricated data.

Their bitter war of words is part of a larger battle over ethical lapses and fraud allegations engulfing what many scientists viewed as the most promising advance toward the use of stem cells to treat spinal-cord injuries and illnesses from Alzheimer's to diabetes.

It also highlights an important problem with science in South Korea and across much of Asia. As research has boomed, especially in cutting-edge and controversial areas such as cloning and nanotechnology, ethics guidelines and institutional-overight mechanisms have struggled to keep up.

Often, it is difficult to tell who, if anyone, is responsible for sorting out scientific disputes of the kind now plaguing Dr. Hwang's work. Seoul National University, home of Dr. Hwang's lab, said it would investigate the matter, but that was only earlier this week, about a month after the first allegations of improprieties -- and a week after the University of Pittsburgh, academic home of Dr. Schatten, took a similar step.

Friday, Seoul National University appointed a nine-person committee to look into the veracity of Dr. Hwang's assertions that he has produced stem cells from a series of cloned human embryos. Scientists have noted, among other things, what they say are odd similarities between DNA "fingerprints" used to support Dr. Hwang's claims.
On Thursday, Dr. Roh said Dr. Hwang admitted to him that stem-cell lines had been faked. News of Dr. Roh's statement pushed the South Korean stock market lower, and shares in biotechnology and pharmaceutical companies were hit as investors reassessed the risks of investing in South Korean science.

At his news conference, Dr. Hwang acknowledged what he called "human error" but asked for time to prove the accuracy of his work. He said that, within about 10 days, he should be able to show that stem cells he made came from cloned embryos. But he said there were some complications; some of the 11 stem-cell lines produced were destroyed by contamination in January, he said.

In addition, Dr. Hwang asserted that some of his stem-cell lines had been switched with stem cells drawn from noncloned embryos. He said he has asked law-enforcement authorities to investigate.

Dr. Roh said he met with Dr. Hwang on Thursday morning and advised him "that he should hold a press conference and tell everyone the truth. I told him that if he were to lie again, he would not be able to redeem himself."

Dr. Roh said he also recommended that he, Dr. Hwang and another co-author jointly retract the Science paper. He said that Dr. Hwang agreed. Dr. Roh also said that Dr. Hwang appeared driven to produce a large number of stem-cell lines to prove himself as a global player. "Professor Hwang said you need at least 10 lines to make it on the international level," Dr. Roh said. "It's difficult to make even one."
Cloning Pioneer Resigns Post Amid Stem-Cell Research Scandal

Associated Press
December 23, 2005 2:33 a.m.

SEOUL - Researcher Hwang Woo Suk apologized Friday and resigned from a South Korean university after the school said he had damaged the scientific community by fabricating results of at least nine of 11 stem-cell lines he claimed to have created.

"I sincerely apologize to the people for creating a shock and disappointment," Dr. Hwang said as he was leaving his office at Seoul National University. "As a symbol of apology, I step down as professor of Seoul National University."

However, Dr. Hwang still maintained that he had created the technology to create patient-matched stem cells as he said he had in a May article in the journal Science. The article had raised hopes of creating tailored therapies for hard-to-treat diseases.

"I emphasize that patient-specific stem cells belong to South Korea and you are going to see this," Dr. Hwang said.

Earlier Friday, a panel of Seoul National University experts said Dr. Hwang had faked results of at least nine of 11 stem-cell lines he claimed to have created in the May paper the first confirmation of allegations that have cast a shadow over all his purported breakthroughs in cloning and stem-cell technology.

"This kind of error is a grave act that damages the foundation of science," the panel said.

The South Korean government, which has strongly supported Dr. Hwang and designated him the country's first "top scientist," said Friday it was "miserable" over the reported results of the investigation.

The government will consider ending Dr. Hwang's research funding, but still supports other similar research, the Ministry of Science and Technology said in a statement.

The university panel said Friday it found that "the laboratory data for 11 stem cell lines that were reported in the 2005 paper were all data made using two stem cell lines in total."

To create fake DNA results purporting to show a match, Dr. Hwang's team split cells from one patient into two test tubes for the analysis, rather than actually match cloned cells to a patient's original cells, the university said.

"Based on these facts, the data in the 2005 Science paper cannot be some error from a simple mistake, but cannot be but seen as a deliberate fabrication to make it look like 11 stem-cell lines using results from just two," the panel said.
"There is no way but that Professor Hwang has been involved," the university's dean of research affairs, Roe Jung Hye said, adding that Dr. Hwang "somewhat admits to this."

The panel said DNA tests expected to be completed within a few days would confirm if the remaining two stem-cell lines it had found were actually successfully cloned from a patient.

In light of the revelations, the panel said it would now also investigate Dr. Hwang's other landmark papers, which include another Science article in 2004 on the world's first cloned human embryos, and an August 2005 paper in the journal Nature on the first-ever cloned dog. The journals already are reviewing all the work.

Dr. Hwang has already asked Science to withdraw the May paper, citing "fatal errors," and saying he had created only some of the 11 stem-cell colonies at the time of publication but completed the work later.

The university panel said Friday that it found no records of two of the other stem-cell lines Dr. Hwang says he created. Four others died from contamination, and another three were in the nurturing stage and hadn't yet become full stem-cell lines.

Dr. Hwang's article this year had also been viewed as significant for his efficiency in cloning the stem-cell lines, claiming to use just 185 human eggs to create custom-made embryonic stem cells for the 11 patients.

But Mr. Roe said the investigation had "found that there have been a lot more eggs used than were reported" and were investigating the exact number.

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Fraud Allegations
Deal New Setback
To Cloning Effort

Touted Data on Stem Cells Were Faked, University Says; 'Why Didn't We See It?'
By GORDON FAIRCLOUGH and ANTONIO REGALADO
Staff Reporters of THE WALL STREET JOURNAL

The effort to clone human embryos, a promising but controversy-plagued endeavor, was dealt another setback Friday when South Korean investigators said scientist Hwang Woo Suk had falsified results of stem-cell research once hailed as a major breakthrough.

An expert panel at Seoul National University, where Dr. Hwang works, said he had fabricated much of the data for a widely noticed paper published by the journal Science earlier this year, in which he claimed to have produced stem-cell lines from cloned human embryos.

The findings cast doubt on Dr. Hwang's other work, including his 2005 claim of creating the world's first cloned dog, an Afghan hound named Snuppy.

Dr. Hwang, whose research had made him a national hero, said he would leave the university, adding, "I sincerely apologize to the people for creating a shock and a disappointment."

But he also said he had indeed produced stem cells from cloned embryos. "You are going to see this," he said.

Scientists are eagerly studying the prospects of embryonic stem cells, which have the potential to develop into many kinds of cells, such as nerve cells and muscle cells. The hope is that they could serve as a repair kit for damaged tissues, treating everything from spinal-cord injuries to diabetes.

As part of the effort, scientists are working to produce stem cells that are exact genetic matches to particular people. That involves using a person's DNA to produce a cloned embryo, from which the stem cells can be made.

The effort has sparked huge controversy. Some religious and ethics leaders say it is immoral to create human embryos solely for the purpose of producing stem cells. The criticism has made scientists sensitive about following ethical and scientific guidelines in their work.

Some stem-cell advocates and researchers worry that Dr. Hwang's work -- tarnished by alleged ethical and scientific lapses -- could further slow efforts world-wide to develop stem cells.
"Why didn't we see it? That is the question we all keep thinking," said Laurie Zoloth, a Northwestern University bioethicist. Dr. Zoloth was one of a large number of stem-cell advocates who joined Dr. Hwang in Seoul in October for the unveiling of the Stem Cell Hub, a plan to share the Korean cloning technology world-wide.

If fraud is proved, said Dr. Zoloth, it "means one person or more conceived of a massive international deception around one of humanity's most poignant hopes."

Cloning, one of biology's hottest and most controversial research areas, has for decades been plagued by a series of hoaxes and deceit.

"It's hard for me to think of an area of biomedical research which is more fraud-prone than this," said Arthur Caplan, a bioethicist at the University of Pennsylvania. "Eternal fame is a big motivator whether you are in a lab or in a cult."

Cloning remains a biological process with an almost mythic status -- a procedure long believed impossible but that may unlock the secrets of aging and reproduction. Like fusion in a bottle or perpetual-motion machines, it has drawn both kooks and ambitious scientists.

One of the highest-profile cases came in 2002, when a Montreal-based religious sect, the Raelians, claimed to have produced the first human clone, Eve. The claim was heavily covered by the media before being dismissed as a hoax. The Raelians, who never provided evidence Eve existed, have said since that another dozen cloned children have been born.

Reverberations from Dr. Hwang's alleged misconduct likely will be felt far beyond South Korea and may lead to cuts in the amount of money available to fund cloning research. In 2004, California voters approved $3 billion in spending on stem-cell research, an effort that has been delayed by legal challenges.

Among other steps, officials at Seoul National said they are conducting blood tests to determine whether Snuppy the dog actually is a clone. Time magazine chose the animal as its invention of the year this year.

Investigators said Dr. Hwang had used two stem-cell lines to fabricate data that made it appear he had produced a total of 11 lines matched to specific patients by using cloned human embryos. That means data for nine cell lines were fabricated. The panel said it still doesn't know if the other two stem-cell lines were produced by cloning or taken from existing human embryos.

To prove that he had succeeded in producing cloned cells, Dr. Hwang and his research team were supposed to compare the DNA of the stem cells with the DNA of each person whose genetic material was used to produce the cloned embryo. He didn't. Instead, the panel said, the team compared stem cells with each other to ensure a match.
Officials said it was too soon to tell what kind of disciplinary action they might pursue against Dr. Hwang.

The University of Pittsburgh, academic home of one of Dr. Hwang's co-authors, biologist Gerald Schatten, also is investigating whether intentional fraud occurred.

Jane Duffield, a spokeswoman for the university, said no disciplinary steps had been taken against Dr. Schatten or two Korean scientists working in his lab. She said an investigative panel had "secured" paper records, computer files and emails pertaining to the research. She said the Pittsburgh inquiry would not be completed until the end of January.

Dr. Schatten and several colleagues recently won a large grant from the National Institutes of Health to pursue stem-cell and cloning research, based in part on the claimed advances in South Korea. It is unclear whether Dr. Schatten's grant, which Ms. Duffield said is worth about $16 million, will be affected. Recently, Dr. Schatten has sought to distance himself from Dr. Hwang and the Science paper, flagging ethical and scientific concerns since November.

Some critics of embryo research said the evidence of fraud doesn't surprise them. Richard Doerflinger, Deputy Director of the Secretariat for Pro-Life Activities, U.S. Conference of Catholic Bishops, in Washington, said scientists willing to destroy human embryos in search of medical cures are driven by an "ends justifies the means" approach.

Some critics blame top science journals, which compete to publish breakthrough work. The review process at Science, which involves sending out manuscripts for expert review, now appears to have missed obvious red flags. For instance, Dr. Hwang and Dr. Schatten submitted their 2005 paper only seven weeks after winning ethics approval to collect human eggs.

That isn't enough time to have created and tested the 11 stem-cell supplies reported in that paper, said Jeanne Loring, a stem-cell biologist at California's Burhnam Institute.

In statement on Friday, the journal said, "We are continuing to move forward with a formal retraction of the 2005 paper."

Write to Gordon Fairclough at gordon.fairclough@wsj.com and Antonio Regalado at antonio.regalado@wsj.com
SEOUL, South Korea -- A South Korean university said Monday that it expected results next week on DNA testing that should prove whether there is any truth to the claim by disgraced scientist Hwang Woo Suk that he produced tailored stem cells.

A nine-member investigation panel at Seoul National University found last week that data in a much-heralded 2005 paper by a team led by Dr. Hwang was intentionally fabricated and had undermined the fundamentals of science. But the panel didn't reach any conclusion on whether the team had actually produced patient-specific embryonic stem cells that could one day be used to make genetically matched tissue to treat diseases such as diabetes and Alzheimer's.

Medical researchers have said it would be one of the biggest scientific frauds in recent history if Dr. Hwang's team hadn't produced tailor-made stem cells, as they claimed in the paper published in the journal Science.

The Korean Medical Association said Monday that it was starting its own probe into the affair. The association will fine and/or suspend any medical professionals who violated legal or ethical guidelines, it said in a statement.

The investigating panel has asked three laboratories to conduct DNA testing on cells that were part of work by Dr. Hwang's team to see if they are stem-cell lines with DNA that matches that of the donors.

"Taking into account time we need to review the results, the announcement on the test results is unlikely to come this week," the panel said in a statement.

Several South Korean media outlets reported that much of the DNA testing has already been completed, citing people close to the probe.

The panel also questioned a junior scientist with Dr. Hwang's team over the weekend. Researcher Kim Sun Jong told South Korean media that he was ordered to alter photographs to make it appear as if Dr. Hwang's team had produced several lines of stem cells. The panel found the team had produced only two-stem cell lines, not 11, as the authors had claimed in the fraudulent study.
Prosecutors are expected to question Dr. Hwang this week over his allegation that someone in his team might have undermined his work by switching data, the daily Chosun Ilbo newspaper reported. Prosecutors have said Dr. Hwang could face a criminal probe for misappropriation of state funds if his work is proved fraudulent.

Dr. Hwang resigned his position at the university last week and apologized for the scandal. But he has insisted it would be confirmed that he did produce patient-tailored embryonic stem cells.

The panel is also testing the veracity of other work by Dr. Hwang's team, including a 2004 paper on producing the first cloned human embryos for research and a claim that it produced the world's first cloned dog, an Afghan hound named Snuppy.
University Says Hwang Produced No Patient-Specific Stem Cells

South Korea's top university said Thursday that Hwang Woo Suk fabricated results for all the stem cells he said were tailored to individual patients - a shattering blow to the disgraced scientist's already damaged reputation as a cloning pioneer holding the key to medical breakthroughs.

Seoul National University's investigative panel, which said last week that at least nine of the 11 patient-specific stem-cell lines Dr. Hwang reported in May in the journal Science were fabricated, announced the remaining two were also faked.

"The panel couldn't find stem cells that match patients' DNA regarding the 2005 paper and it believes that Hwang's team doesn't have scientific data to prove that [such stem cells] were made," Roe Jung-hye, the university's dean of research affairs, told reporters.

Mr. Roe said that an investigative panel found that stem cells Dr. Hwang claimed to have established in a 2005 paper published in the prestigious journal Science actually came from fertilized eggs and weren't designed specifically for patients.

Stem cells are master cells that can grow into any body tissue. Creating patient-specific ones would be a breakthrough because they would not be rejected by patients' individual immune systems. Stem cells taken from a fertilized egg would not be an identical match to a patient's DNA.

Last week, Dr. Hwang, who had been lionized in South Korea for his purported breakthroughs, apologized for the fabrication and stepped down as professor at the university. He insisted, however, that his team has developed the technology to create patient-matched stem cells.

The university panel's interim results suggested, however, that even the stem cell lines that Dr. Hwang claimed to have developed though not reported in the 2005 paper were also not patient-specific casting doubt on whether the veterinarian ever developed the technology.

Still, Seoul National University's Ms. Roe said the panel remains in consultation with outside experts to determine if Dr. Hwang possesses the technology to produce such stem cells.

The final results of the investigation will be released in mid-January and will also include results of the panel's investigation into Dr. Hwang's earlier purported breakthroughs, including the world's first cloned dog Snuppy and stem cells from the world's first cloned human embryo reported by Dr. Hwang last year in Science.

Dr. Hwang filed a complaint with prosecutors that some of the stem cell lines his team created were replaced by those created at Mizmedi Hospital, which had collaborated with his research team.
Ms. Roe said that while the investigation found that the fertilized eggs came from Mizmedi, probing into any possible switch is beyond the scope of the panel.

Dr. Hwang's whereabouts weren't known and he couldn't immediately be reached for comment.

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Hwang, Drawn and Quartered?
By SUKI KIM
December 29, 2005; Page A10

The current investigation of the South Korean scientist Hwang Woo Suk has not only cast doubts on the authenticity of his breakthrough cloning of the first human embryos, but is also providing a glimpse of the chasm beneath the inner workings of a country that is ranked the world's 11th-largest economy.

Dr. Hwang resigned last Friday after it was proven that he fabricated nine of the 11 cloned stem cells, and sadness seems to be the uniform emotion. An American journalist friend asked me if this was not indeed a very disappointing time for Koreans. A writer who had recently traveled to Seoul to visit Dr. Hwang's lab for her now-to-be-revised manuscript on stem cells called to say that the science world was in mourning. The sadness was most palpably witnessed on the Korean Biological Research Information Center's Web site, where its young scientists first posted their concerns about Dr. Hwang's claims long before the scandal broke, along with Daum.com and Naver.com, the leading chat sites in a nation where over 70% of the people are connected to the Internet at cable speed.

When I visited Seoul a few months ago, Dr. Hwang's name was mentioned in almost all contexts. An editorial in the leading newspaper Donga Ilbo lamented that no Koreans were chosen in the list of the 100 global intellectuals compiled by the journals Foreign Policy and Prospect; the editorialists suggested Dr. Hwang as Korea's nearest hope. Everywhere, people excitedly showed me the state-issued Hwang Woo Suk commemorative postage stamps, which depicted the image of growing stem cells against the silhouette of a man rising from a wheelchair. I met up with a friend, whom I had not seen since I emigrated from South Korea over 20 years ago, and whose first words had something to do with Dr. Hwang. Only after a little while did I understand that my childhood friend was now a proud yoga teacher at a center that had once been visited by the scientist.

In the charismatic and brilliant Dr. Hwang, South Koreans found the heroic symbol of their zealous nationalism. His popularity was akin to that of the Beatles, to whom the scientist had once likened himself. Earlier this month, as he ensconced himself in a hospital in order to avoid the hounding media, some of the 47,000 members of his fan club, "I Love Hwang Woo Suk," decorated the 80-meter-long stairs to his office with azalea, the flower traditionally reserved for the beloved. Even the president of MBC, the TV network which aired the program that was ultimately responsible for breaking the cloning story open, was forced to make a national apology for questioning Dr. Hwang's truth.
But it was not only the South Koreans who were quick to hail Dr. Hwang as one most likely to win a Nobel Prize. Time magazine named him "one of the 10 people who mattered in 2004" for his first-ever cloned dog, Snuppy, whose legitimacy is now under investigation. Science, arguably the world's foremost scientific journal, took less than two months -- rather than the usual four months -- to examine and approve his report before publishing it in May. The BBC ran a special feature, detailing everything from his childhood to his favorite hobby to his favorite film -- which, incidentally, is "Gone with the Wind." This seems to resemble the fate of his debated stem cells, most of which he now claims died from a contamination caused by bacteria that had been carried by the wind from the kennel across the street from his lab.

As Seoul National University's investigation panel digs deeper, the newspapers are publishing claims by Dr. Hwang that are immediately rebuked by experts. He now blames a blackout for the absence of six of the stem cells. The ones at his lab appear to have been switched by someone, he conjectured recently, with those from the fertilized eggs that belonged to his partner's hospital. Then there was the move of his office that caused the loss of Snuppy's DNA reports, leaving no other copy. Fueling the confusion are the conflicting statements made by his former colleagues and subordinates, including University of Pittsburgh researcher Kim Sun Jong, who accepted $30,000 from Dr. Hwang's team, probably as hush money, before finally admitting that he was coerced by his former boss to help fudge the number and photos of stem cells for the report published in Science.

Dubbed the "tale of the boy who cried wolf," the case of Dr. Hwang has become South Korea's headache and pain. What is sad, however, is the curious acquiescence with which its people seem to accept the chaotic unfolding of what appear to be improbable lies. Many are not surprised that such a world-class mishap could happen in their highly competitive society, where step-by-step procedures can be overlooked or even circumvented at times to get to the results faster. South Koreans often describe their national spirit as "saucepan," suggesting a temperament that boils fast and cools even faster.

Having seemingly become an overnight superstar, Dr. Hwang was said to have been under unprecedented pressure to deliver a major scientific discovery to the people for whom no speed was quick enough. One of his former associates was quoted, "He wanted to bypass 10 years of research, because people couldn't wait 10 years."

After all, this is a country that transformed, in mere decades, its faltering postwar economy into a leading manufacturer of cars, cell phones and digital TVs, as well as a hub for cosmetic surgery. Obsessed with ranking, South Koreans claim to have the world's largest bookstore, church congregation and Starbucks. The divorce rate has skyrocketed, while the birth rate has plummeted, despite their insistence on Confucian family values. The pursuit of modernity has not only affected their skills and lifestyles but has also infiltrated their beliefs. Although shamanism, Buddhism and Confucianism have been at the root of their tradition for thousands of years, almost half of all South Koreans have converted to Christianity in the last century.

Yet the Confucian-based hierarchy remains in the way that Koreans think, live and conduct business. Growing up, one thing for which I was reprimanded always was talking back to my parents. I didn't then understand why, but I now can see the inadequacy in the way that Dr.
Hwang's researchers have been portrayed in the world's media as con artists. This is not to excuse the lies they might have told, but I also know that in that society, you do not question your senior, especially one as revered as Dr. Hwang.

This morning, when I checked their Internet forums, the majority of South Koreans seemed tired. They have spent the past few weeks trying to decipher the numbers and statistics that were thrown at them by the clone experts in their seemingly coded scientific language. They have pretty much given up hope on their rapidly tumbling hero, who has changed his story so many times that everything is even murkier than before. One clear fact is that he is no longer going to bring them a Nobel Prize, or an inclusion in the world's 100 top intellectuals.

But mostly, they were exhausted from an investigation that was not reaching a quicker conclusion. The holidays were here. They were looking forward to the New Year. The snow was covering the country. What has made South Korea the country of an economic phenomenon, and for a brief, exhilarating period, a scientific miracle, is its people's ability to move on faster than expected. Already, the most searched term on Naver.com has changed from Hwang Woo Suk to Naomi Watts, the blond actress from the newly premiered blockbuster, "King Kong."

Ms. Kim is the author of "The Interpreter" (Farrar, Straus & Giroux, 2003).
Korean Scientist Gets Another Hit
Over Stem-Cell Research Claims

Associated Press
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SEOUL, South Korea -- An already disgraced scientist has suffered a new jolt to his shattered reputation. Investigating researchers said yesterday that Hwang Woo Suk lied about all of the stem-cell lines he claimed were matched to different patients through cloning.

Yesterday's announcement all but ends the fraud investigation into one of three major cloning breakthroughs claimed by the onetime scientific superstar and national hero. Probes of Dr. Hwang's two other groundbreaking experiments are still under way at Seoul National University, where he worked before resigning in disgrace last week.

The latest news was one more disappointment to the scientific world, which had viewed Dr. Hwang's achievements as holding great promise for treating people with a variety of ailments, from spinal-cord injuries to Parkinson's disease.

One researcher bemoaned the most recent development. "The bottom line is that it's a major disaster to our whole field because the expectations were so high and now we are back to square one," said stem-cell scientist Joseph Itskovitz, director of the department of obstetrics and gynecology at Rambam Medical Center in Haifa, Israel.

In the experiment deemed fraudulent, Dr. Hwang, 53, had claimed in a paper published in May in the journal Science that he had created 11 colonies of human embryonic stem cells genetically matched to specific patients.

An investigative panel at the university reported last week that Dr. Hwang had faked the research on nine of the stem-cell lines. Yesterday, it confirmed he also fabricated his research for the two remaining cell lines as well. "The panel couldn't find stem cells that match patients' DNA regarding the 2005 paper and it believes that Hwang's team doesn't have scientific data to prove that [such stem cells] were made," said Roe Jung Hye, the university's dean of research affairs.

The university said that by next month it expected to wrap up all work on that case and have findings on two others: Dr. Hwang's first blockbuster claim in 2004 in the journal Science that he created the world's first cloned human embryo and extracted stem cells from it; and his research published in Nature last August claiming to have produced the first cloned dog.
Prosecutors said last week that they are waiting for the university investigation into all of Dr. Hwang's research before launching their own probe. The scientific journals also await those findings.

"We were already worried about the 2004 paper and this doesn't make us any less worried," said Katrina Kelner, an editor at Science, who said the 2005 paper would be retracted.

Yesterday Dr. Hwang's whereabouts were unknown and he couldn't be reached for comment.

Despite Dr. Hwang's fall from grace, some weren't ready to give up the dreams that his claims inspired. "Our confidence in Hwang remains unchanged," said Jung Jin Owan, 40, secretary general of the Korea Spinal Cord Injury Association.

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Stem-Cell Claims
By Korea Scientist
Found to Be Untrue

SEOUl -- Disgraced Korean cloning expert Hwang Woo Suk never produced any stem cells from cloned human embryos, according to findings released yesterday in a continuing fraud investigation by officials at Seoul National University.

"We could not prove the stem cells were ever made," said Chung Myung Hee, chairman of the university's investigation committee.

In two prominent studies published by the U.S. journal Science in 2004 and 2005, Dr. Hwang's laboratory claimed to have mastered the technology of therapeutic cloning, or cloning embryos to extract their stem cells.

After the 2005 report was labeled fraudulent by investigators late last year, Dr. Hwang and more than a dozen co-authors agreed to retract it.

Investigators say the initial discovery reported in 2004 of the world's first human stem cell from cloning was faked using manipulated photographs and phony DNA evidence.

The stem-cell line reported wasn't created by cloning, said investigators, but via a different method.

Altogether, investigators said, Dr. Hwang had used more than 2,061 eggs from 129 women volunteers, not the less than 500 he had reported using.

The investigating panel said that Dr. Hwang's claim to have created the world's first cloned dog was borne out by detailed DNA tests, and appears to be true.

The scandal's repercussions continue to be felt in the U.S. Officials at Science said they hadn't seen a copy of the investigating committee's report, and couldn't comment on
whether they would seek a retraction of the 2004 study, although that step seems
inevitable. Science editors are in the process of retracting the 2005 study.

The 2004 study included an American co-author, Jose Cibelli of Michigan State
University. Jeffrey Armstrong, dean of Michigan's school of agriculture and natural
resources, said Dr. Cibelli's contribution to the paper was limited to providing technical
advice and some chemicals used in DNA tests.

Michigan hasn't opened a formal inquiry into whether Dr. Cibelli was involved in any
scientific misconduct. "I won't speculate if we'll have an investigation," said Mr.
Armstrong.
Crumpled Papers

Lowering Expectations at Science's Frontier

Jeon Kyung Woo/Newsis via Reuters

**DISGRACED** Hwang Woo Suk, whose claims to have created tailored embryonic stem cells were declared fraudulent by a scientific panel, apologized for his actions.

By **NICHOLAS WADE**
Published: January 15, 2006

THERE is considerable disorder in heaven when stem-cell scientists are chided by the Roman Catholic Church for the folly of pursuing "miracle cures." But such are the paradoxes generated by the implosion of a South Korean researcher's widely believed claims to have created human embryonic stem cells from patients.

Of course, miracles like the Shroud of Turin are also widely believed. But scientific claims are meant to belong to a different category of truth: They are the certified knowledge of a community of scholars who have rigorously tested their ideas through experiment and mutual criticism.

How then can the fraudulent claims by **Dr. Hwang Woo Suk** have been accepted by Science, a leading journal that rejects most papers submitted to it? How can the community of stem-cell scientists have allowed a very visible claim to have stood unchallenged in their field for 20 months? Little wonder that Richard Doerflinger, an official of the United States Conference of Catholic Bishops, ridiculed the dreams of therapeutic cloning in a statement last week, scoffing that scientists were chasing miracle cures "in pursuit of this mirage."
The contrast between the fallibility of Dr. Hwang's claims and the general solidity of scientific knowledge arises from the existence of two kinds of science - a distinction that is often blurred when new advances are reported first by scientific journals and then by the news media. There is textbook science and frontier science, and the two types carry quite different expiration dates.

Textbook science is material that has stood the test of time and can be largely relied upon. It may include findings made just a few years ago, but which have been reasonably well confirmed by other laboratories.

Science from the frontiers of knowledge, on the other hand, is wild, untamed and often either wrong or irrelevant to future research. A few years after they are published, most scientific papers are never cited again.

Scientific journals try to impose order on the turbulent flow of new claims by having expert reviewers assess their merit. But even at the best journals, reviewers provide only a rough screen. Many papers slip through that later turn out to be innocently wrong. A few, like Dr. Hwang's, are found to be fraudulent.

This rough screening serves a purpose. Tightening it up, in a vain attempt to produce instant textbook science, could retard the pace of scientific advance.

But the roughness of the proceedings is not prominently advertised by journal editors, except when cases of blatant fraud are detected, whereupon they proclaim that peer review cannot reasonably be expected to detect fraud. They do not protest so much when newspapers report their journals' claims as if they were certifiably true. Because of Science's authority, Dr. Hwang's claims to have cloned human embryonic cells were prominently reported and presented to the public as if they were important breakthroughs.

But any new advance belongs to frontier science, which is inherently fallible, and a journal's imprimatur, though worth something, is no guarantee of truth. An advance only becomes solid when other laboratories have confirmed it, by which time it is no longer news. This presents a serious problem for journalists: many scientific claims, including those in leading journals, turn out to be overstated or wrong, and science reporting that presents these journals' products as gospel is likely to be misleading.

Scientists and journal editors are, of course, well aware of the tentative nature of frontier science. As Donald Kennedy, the editor of Science, observed when the Hwang case first broke, journals often publish work that is innocently wrong. "The public needs to understand that the journals and peer review are not perfect," he said.

But last week Dr. Kennedy announced he was considering revising the journal's publication procedures, though not with any great hope of preventing future cases of fraud. He suggested that authors would be required to state in writing their specific contributions to a report, a reform perhaps aimed at Dr. Gerald Schatten of the University of Pittsburgh. Dr. Schatten accepted senior authorship of - and thus responsibility for - one of Dr. Hwang's papers, even though Dr.
Schatten had performed none of the experiments and was not in a position to vouch for them. All the work was done in Seoul.

A second proposed change is to have all authors state that they agree with an article's conclusions.

Both procedures may seem to include a certain potential for generating strife. Each author could overstate his or her contribution, arousing the wrath of all the others. Some authors may think a conclusion too timid, while others consider it an overstatement.

But some medical journals, like The Journal of the American Medical Association, already require authors to state who did what. The system works very well, said Drummond Rennie, the journal's deputy editor and the instigator of the idea. Requiring authors to specify that they agree with the conclusions leads to conservative statements, a result that is also beneficial, in Dr. Rennie's view.

Tightening up the reviewing system may remove some faults but will not erase the inescapable gap between textbook science and frontier science. A more effective protection against being surprised by the likes of Dr. Hwang might be for journalists to recognize that journals like Science and Nature do not, and cannot, publish scientific truths. They publish roughly screened scientific claims, which may or may not turn out to be true.