Recruitment of Egg Donors by South Korean Stem Cell Researchers – Case Summary

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I. Context

Stem cells are undifferentiated cells in the human body able to replenish themselves by dividing or capable under particular natural or medically-induced circumstances to develop into the more specialized cells forming bones, nerves, body tissue, brains, muscles and blood. Somatic ("adult") stem cells can be extracted from various body parts. Stem cells are interesting to scientists and physicians for three reasons. First, studying stem cells reveals more about the processes of normal and abnormal cell development, providing knowledge with potential for treating cancer and birth defects arising from faulty cell division. Second, stem cells offer the possibility of regenerative therapy for a range of diseases and conditions because they can develop into any body part. The goal is to develop regeneration in other organs where it does not occur naturally by using stem cells to develop healthy cells of the affected organ or tissue and inject those new cells into patients. Third, stem cells can be used in therapeutic cloning to correct life-threatening genetic defects.[1]

Stem cell research has provoked considerable ethical concern. Some observers worry that it will lead to cloning of humans or producing "designer babies" with traits their parents desire by using in vitro fertilization techniques. While many welcome the prospect of more effective treatments of birth defects or diseases, using human embryonic stem cells for such treatments or even in scientific research is very controversial. The embryo must be destroyed to secure its stem cells, and anyone who believes that

[1] Good internet sources of basic information on stem cells and stem cell research include www.isscr.org/public produced by the International Society of Stem Cell Researchers and http://stemcells.nih.gov produced by the US National Institutes of Health. The US government-run Medline Plus Encyclopedia at http://www.nlm.nih.gov/medlineplus/ency/ has good basic information about diseases, conditions, and treatments.

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human life begins at the moment sperm fertilizes egg to turn it into an embryo regards destroying embryos as committing murder.

Stem cells exist in all humans, and can be derived from adults', umbilical cords (which are discarded after birth), and embryos. Somatic ("adult") stem cells were first identified in bone marrow in the 1960s and used for treatments of leukemia, aplastic anemia, and some immune system deficiencies. Bone marrow transplants are also used to aid recovery from strong radiation treatments or chemotherapy. Embryonic stem cells were first derived from mouse embryos in 1981, and from human embryos in 1998. A process for "reprogramming" specialized adult cells to resemble stem cells was developed with mice during 2006 and extended to humans in 2007. The resulting induced pluripotent stem cells (iPCSs) have inspired considerable interest because they would not inspire the same ethical concerns inspired by derivation of embryonic stem cells. However, the methods for "reprogramming" are not yet routine and, because they involve use of viruses, may pose significant hazards. Various types of somatic stem cells have been used in certain medical treatments, and may have the advantage of being less likely to trigger rejection since they are grown from the patient to be cured, but they are shorter-lived and more difficult to increase through cell culture techniques than the embryonic stem cells derived from blastocysts (embryos in their 3rd through 5th day of development after fertilization).

Excitement generated by the first acquisition of human embryonic stem cells in 1998 spread around the world. In South Korea, where scientists and the government had been attuned to advances in genetics, bioscience, and biotechnology since the mid-1980s, there was strong interest in taking up the new possibilities. Four years earlier the South Korean government had adopted an ambitious Plan 2000 intended to make South Korea one of the leading sites of bioscience and biotechnology research in the world. In 1990, it provided its national Genetics Research Institute with ample facilities in the new Taedok Science town just outside Seoul; in 1995 it expanded the Institute and renamed it the Korea Research Institute for Bioscience and Biotechnology to better reflect its expanded areas of work. After 1998 South Korean government agencies were eagerly funding research on human embryonic stem cells and on somatic cell nuclear transfer (removing the nucleus of an unfertilized egg cell, replacing it with material from the nucleus of a specialized body cell, and stimulating this assembled cell divide), both of which promised to usher in a new range of medical therapies. In early 2003, the Ministry of Science and Technology reaffirmed its continuing interest by funding a project on xenotransplantation to be carried out by about 184 researchers in over a dozen Korean universities.[2]

Koreans became very excited about the therapeutic possibilities of stem cells as scientists suggested that it would not be long before stem cell-based treatments of various genetic defects and still-incurable diseases would be developed. Korean business leaders also saw considerable potential for industrial leadership in the field based on the apparent strength of local research.

Dr. Hwang Woo-suk, a member of the veterinary faculty at Seoul National University, emerged as one of South Korea's leading stem cell and cloning researchers in 1999 after claiming to have cloned cows. In 2002-05 he and several teams of collaborators were pursuing research on human and animal cloning and on embryonic stem cells. The human stem cell research raised three ethical concerns. The first arose from Hwang's plan to clone human embryos to provide stem cells from which he hoped to make "tailored"

[2] "Biotech powers Korea," Korea Herald, 2 October 2003 available via http://www.digital-bio.com/board/kboard.php?board=eng_news&act=view&no=227 (accessed 15 September 2009).

or "patient-specific" stem cells. Stem cells had already been derived from human embryos – "spares" remaining in storage at fertility clinics after *in vitro* fertilization of an egg then implanted into a woman's uterus. Even this use of embryos had aroused serious controversies in some countries. Religious conservatives and philosophers treating embryos as fully human, and therefore, entitled to complete respect of their human identity, condemned using the "spare" embryos as a source of stem cells. Many more people were uneasy about the notion of cloning human embryos for any purpose, including the derivation of stem cells. As Dr. Hwang and his colleagues set to work, 12 countries had already banned all forms of human cloning[3] and other scientists in South Korea criticized Hwang for pressing forward with embryo cloning when the question of its propriety had not been debated or settled.[4] The second ethical concern arose when other scientists charged in late 2005 that at least two, and possibly as many as five, papers published by Hwang and collaborators contained fabricated data.[5] The third, which is the subject of this case, arose from questions about how Hwang and his collaborators recruited women to donate eggs (oocytes) for the research. This controversy involved basic issues about treatment of human research subjects that had been debated at length in many countries.

Concern about protecting humans, whether patients or healthy persons, from abuse by medical researchers became acute in the wake of revelations about experiments on prisoners in Nazi concentration camps. The Nuremberg War Crimes Trials resulted in convictions of several of the participating physicians of crimes against humanity.[6] The detailed revelations of the trial also inspired the earliest internationally agreed statement of ethics relating to human subjects, the Nuremberg Code of 1947. It set forth the principles of informed consent, absence of undue influence in securing that consent, humane conditions, avoidance of unnecessary pain, and clear scientific benefit. Continuing abuses, including the deliberate infection of unknowing human subjects with serious diseases that had been a central part of the charges against the Nazi physicians, were known to medical researchers.[7] In 1964 the World Medical Association adopted the first version of the Declaration of Helsinki outlining ethical standards to guide use of human subjects in medical research. General public attention was revived in the USA and other countries during 1972-73 by extensive newspaper discussion and Congressional Hearings on the Tuskegee Syphilis Study (1932-1972). It involved two clear violations of the Nuremberg Code: the African-American males selected for the study were given incomplete and misleading information about the goals and duration of the experiment, and were denied adequate treatment for the disease even after highly effective penicillin cures were developed in 1947 so researchers could continue observing the natural course of the disease.[8]

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[3]R.M. Isasi and B.M. Knoppers, National Regulatory Frameworks regarding Human Cloning for Reproductive and Therapeutic/Research Purposes, August 2005 available at http://www.dnapolicy.org/pdf/cloning.pdf (accessed 14 Sept 2009).

[4] Letter to the editor by Song Sang-yong, President of the Korean Bioethics Association, and response by Hwang Woo-suk and Moon Shen-yong defending their work as conforming with all requirements of South Korean law in Science 305: 944-945 (13 August 2004).

[5]Rowan Hooper, "Rise and fall of the stem cell king," *New Scientist* 188 (No. 2531/2532): 24 December 2005.

[6] George J. Annas and Michael A. Grodin, eds., *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*. New York: 1992; Paul Hoedeman, *Hitler or Hippocrates: Medical Experiments and Euthanasia in the Third Reich*, Ralph de Rijke, trans. Lewes 1991.

[7] Henry K. Beecher, "Ethics and clinical research," *New England Journal of Medicine* 274: 1354-1360 (1966).

[8]James H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment*. New York: The Free Press, 1981.

Reports of severe maltreatment of patients in psychiatric hospitals later in the decade kept the issue in view, with later revelations inspiring the World Medical Association to revise the Helsinki Declaration several times. In 2002 when Hwang's research teams first recruited egg donors, the 2000 revision was the most recent statement. While the Helsinki Declaration was the statement of an international professional group, similar standards had been incorporated into national law or regulations governing the conduct of medical research on humans in many countries.

South Korean law did not address the question of permissible and impermissible types of genetic research, cloning, or stem cell research in 2002, but it did include provisions for protection of human subjects. Korean universities and research hospitals were required to have an Institutional Review Board and researchers were required to submit their plans for all research using human subjects, a description of how they will select human subjects, and copies of the consent forms they intend to use for the IRB's approval before starting their experiments. South Korean law also required that an IRB include non-researchers, specifically "more than one attorney or religious representative, not from the fields of medicine, dentistry, oriental medicine, pharmacy, or nursing sciences."[9]

Paragraph 1 of the Helsinki Declaration specifies that, "medical research involving human subjects includes research on identifiable human material and identifiable data." Thus its guidance applies to any form of stem cell research that begins with securing stem cells from human body parts or embryos. The Nuremberg Principles and the Helsinki Declaration also cover the process of securing eggs and sperm needed to produce embryos since these require human participants. The stimulation of erection and ejaculation needed to secure sperm do not require any drugs or surgery; egg donation involves hormone injections and a surgical procedure, so most of the attention devoted to questions of protecting donors has focused on the women providing eggs.

The basic surgery for egg donation is minor, and can be performed in a clinic. The process begins with one or more injections of hormones that cause ovaries to "superovulate"—to produce 12-20 eggs per menstrual cycle rather than the usual single egg. The eggs are then gathered from the ovary by follicular aspiration, in which a long needle is passed through the vagina into each ovary and eggs removed from the follicles by a suction device connected to the needle. All women who undergo follicular aspiration are given pain killers during the procedure and will feel cramping for up to a day afterward. The hormone injections can cause ovarian hyperstimulation syndrome (OHSS), and in the USA some 10% of women undergoing follicular aspiration for in vitro fertilization treatments experienced OHSS afterward. The risk is greater for women who are under 35 years old, have high estrogen levels, or have polycystic ovarian syndrome (cysts blocking follicles in the ovaries). The risk is also increased for women receiving injections of human chorionic gonadotropin (hCG) to help trigger ovulation, particularly if they receive more than one dose of hCG after ovulation. Risk is much lower among women given fertility drugs taken by mouth. Mild cases of OHSS produce abdominal bloat and discomfort, and water retention weight gain of about 5 pounds; these symptoms correct themselves in a few days with rest, ample fluids, and avoidance of stressful activity. Severe cases of OHSS produce weight gain of more than 10 pounds, severe abdominal pain and swelling, decreased urination, and shortness of breath. Such cases are usually treated in hospital where the woman's condition can be monitored as excess are removed from abdominal and chest areas and intravenous provision of nutritional fluids restores electrolyte balance. Severe OHSS can lead to life-

[9]O.J. Kim, B.J. Park, D.R. Sohn, S.M. Lee, and S.G. Shin, "Current status of the institutional review boards in Korea," *Journal of Korean Medical Science* 18 (1): 3-10 (2003).

threatening complications: blood clots, kidney failure, electrolyte imbalance, or massive fluid buildup in chest and abdomen.[10] It can also cause infertility.

The ethical standards for human subjects research most relevant to donors are the requirements for voluntary informed consent to the medical procedures involved, high standards of researcher competence, and provision of needed treatment for subjects experiencing ill effects.

Both the Nuremberg Code and the Helsinki Declaration gave detailed definitions of the required consent to participate. Article 1 of the Nuremberg Code specified that:

> … the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The Helsinki Declaration adopts similar standards. Paragraph 22 of the 2000 version read:

> In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely- given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

Paragraph 23 added:

> When obtaining informed consent for the research project, the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.[11]

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[10] Information on OHHS from the US National Institutes of Health MedlinePlus Medical Encyclopedia at http://www.nlm.nih.gov/medlineplus/ency/article/007294.htm (accessed 21 July 2009). The 10% incidence figure was calculated in 2007.

[11] Declaration of Helsinki, 2000, available at http://www.mch.org.tw/top_2/IRBWORD/Declaration%20of%20Helsinki.pdf (The World Medical Association's site at www.wmanet.org/e/policy now carries only the 2008 version).

Another statement of similar principles widely followed in Korea appears in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guidelines for Good Clinical Practice (ICH-GCP) adopted in 1997. The conference is a body consisting of drug regulatory agencies in the EU, Japan, and the USA plus pharmaceutical industry representatives; the GCP are jointly-established standards for clinical trials. Following the guidelines means the results data will be accepted by EU, Japanese, and US authorities. As pharmaceutical firms began pursuing trials in more countries, cooperating investigators elsewhere were brought within the guidelines, and they diffused through researcher communities in other parts of the world.

When the South Korean stem cell research projects began in 2002, scientists around the world generally agreed that undergraduate and graduate students, junior members of research teams, and other employees over whom researchers have supervisory authority should not be used as donors. Art Calpan, Head of the University of Pennsylvania Center for Bioethics, commented as the scandal broke in May 2004 that using students or junior members of research teams is bad because "it could certainly look like coercion was involved"[12] and other scientists expressed similar views. There was no global consensus on whether egg donors could be paid. Some countries prohibited payment; others allowed small payments as compensation for time or travel expenses; others allowed direct payment.

In 2002-03, South Korean law about medical research had several gaps. The Korean Food and Drug Administration oversaw the use of human subjects in commercial research projects, including clinical trials, but its authority did not extend to scientific research. Supervision of scientific research was left to the Institutional Review Boards of individual universities or hospitals. The typical IRB did require human subjects to give voluntary, written consent to participate. Korean regulations banned donations from junior members of research teams,[13] but did not specifically ban paying donors. Korean participants in a UNESCO-sponsored workshop on bioethics held in Seoul in mid-November 2004 noted that "There are currently no special guidelines or regulations on human research other than within the medical field, and this deficiency needs to be addressed. For international research, Korean medical scientists are required to observe ICH-GCP."[14]

II. The Controversy

In 2002 when his team began their effort to develop patient-specific stem cell lines by extracting stem cells from cloned embryos, Dr. Hwang Woo-suk was one of South Korea's leading stem cell researchers. He already had a record of considerable research accomplishment, was skilled at organizing teams for large projects, and had sufficient international reputation to recruit foreign collaborators. He was a veterinarian, on the Veterinary Faculty at Seoul National University, and therefore not qualified to perform medical procedures on humans. Acquisition of human oocytes for his research was accomplished by various

[12] David Cyranoski, "Korea's stem-cell stars dogged by suspicion of ethical breach." *Nature* 429 p. 3 (6 May 2004).

[13] Noted in Kristen Philipkoski, "Jabs, honors for stem-cell expert," *Wired Magazine* 16 Nov. 2005. Available from http://www.wired.com/medtech/health/news/2005/11/69596 (accessed 20 July 2009).

[14] Quoted from the summary of proceedings of the UNESCO-Korean National Commission for UNESCO workshop on "Ethics around the World – Seoul: Towards a Declaration on Universal Norms on Bioethics" 16 November 2006 available at http://unesdoc.unesco.org/images/0014/001495/149562e.pdf (accessed 16 July 2009).

physician collaborators at Hanyang University Hospital, MizMedi Women's Hospital, Hanna Women's Clinic and Chiel General Hospital in Seoul.

Collaborators at Hanyang University Hospital submitted plans for the experiments and for procurement of oocytes to its Institutional review Board, which approved them. Enough oocytes were acquired to begin the cloning and stem cell extraction in late 2002- early 2003. Meanwhile, Hwang and his collaborators also worked on other projects, including efforts to clone animals. Results of the experiments were published in leading scientific journals. *Science* published his team's claim to have cloned human embryos in August 2004[15] and to have derived patient-specific stem cells in May 2005.[16] *Nature* published his team's claim to have cloned a dog in August 2005.[17]

Though online supplementary material published with the 2004 paper in *Science* indicated that volunteers were not paid and had provided informed consent on forms detailing how the eggs would be used, rumors that two female members of Hwang's research team had donated eggs and that other donors had been paid began to circulate in late 2003. Science journalists on *Nature's* staff made some inquiries and published a short comment about the allegations in May 2004.[18] Hwang denied the allegations and was supported in his denial by members of the Hanyang University Hospital IRB. However, the controversy did not go away. In late May, Members of the South Korean Bioethics Association called on Hwang to answer continuing questions about the egg donors and the sources of his research funding. *Nature* printed another report about the controversy in its June 3rd issue.[19]

Public support for Hwang's research remained high. Publication of the patient-specific stem cell paper in *Science* had triggered a threefold rise in prices of South Korean biotech stocks. In late June, the South Korean Ministry of Science and Technology honored Hwang with the new title of Supreme Scientist and awarded him the equivalent of US$15 million in research support. An internet "I love Hwang Woo-suk" fan club also appeared. Excitement continued as MgenBio, a Seoul National University-affiliated venture firm set up by Hwang and others, announced successful cloning of transgenic pigs expressing human leukocyte antigen (HLA)-G, which is thought to improve immune tolerance of humans to transplanted pig tissues. If the antigen had the expected effects, this would permit using pig organs, cells, or tissues in a range of disease treatments.[20] Korean media reports that the government planned to establish a World Stem Cell Hub to be a repository of stem cells were confirmed in October when South Korean President Roh Moo-hyun authorized allocation of government funds for its establishment at Seoul National University and appointed Hwang as its President. In mid-November, the government indicated that it would provide 11.5

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[15] Hwang, W.-S. *et al*. "Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst". *Science* 303 (#5664), 1669–1674 (2004).

[16] Hwang, W.-S. *et al*. "Patient-specific embryonic stem cells derived from human SCNT blastocysts" *Science* 308 (#), 1777–1783 (2005).

[17] Hwang, W.-S. et al., "Dogs cloned from adult somatic cells". *Nature* 436 (#7051): 641

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[18]Comment, "Ethics of therapeutic cloning," *Nature* 429 (# 6987): 1 (6 May 2004).

[19]David Cryanoski, "Korean bioethicists call for inquiry into stem cell work" *Nature* 429 (#6991): 490 (3 June 2004).

[20] The state of knowledge at the time is summarized in Jeffrey L. Platt, *Xenotransplantation: Basic Research and Clinical Applications*. Totawa, NJ Humana Press, 2002.

billion won ($11 million) for the Hub and make it independent from Seoul National University. Plans also called for establishment of regional affiliates in cooperation with universities in other countries, and representatives of the Hub began visiting potential collaborators abroad.

Doubts about the propriety of the oocyte donations continued to swirl, and at about the same time two of Hwang's US-based collaborators, Dr.Gerald Schatten of the University of Pittsburgh (USA) and the Pacific Fertility Clinic in San Francisco California, announced they were suspending their collaborations with Hwang. Schatten released a statement saying that the decision was based on concerns about the oocyte donations:

> Yesterday information came to my attention suggesting that misrepresentations might have occurred relating to those oocyte donations. The nature of this information mandates confidentiality. I have contacted appropriate academic and regulatory agencies regarding this new information and accordingly have suspended my collaborations with Dr. Hwang.[21]

This was an issue on which he was very sensitive because earlier in his career he had unknowingly worked with illegally procured oocytes.[22] Commentators soon noted that he was in a good position to know the details of the Korean situation because one of the junior researchers later revealed as a donor was working in his lab at the time.[23]

Comments about the situation from European and US scientists in mid-November concentrated on two charges: securing egg donations from female researchers within Hwang's laboratory group and incomplete information about the risks of follicular aspiration. Researcher donation was not allowed in mainstream laboratories in the United States and elsewhere in the world because of the potential for coercion. US-based commentators also recalled that in California, where *in vitro* fertilization was widely practiced and human embryonic stem cell research being advanced under a $3 billion public bond issue, some egg donors had died after egg extraction procedures.

Plans to establish the regional affiliates ("sub hubs") soon ran into problems. Efforts to establish a sub hub In San Francisco were stymied when both the University of California San Francisco (UCSF) and the California Institute for Regenerative Medicine (the central coordinator of the State-funded stem cell research effort) declined to participate. Arnold Kriegstein, Head of UCSF's Institute of Tissue and Stem Cell Biology told journalists he had met with Hwang's representatives but decided not to participate owing to concerns about the vagueness of guidelines regarding egg donor recruitment and tracking of research materials transferred between labs. British scientists expressed similar concerns as efforts to establish a sub hub at the University of Edinburgh also came to nothing.[24]

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[21] Quoted in David Glenn, "In South Korea, ethics questions prompt a stem-cell pioneer to resign a top post." *The Chronicle of Higher Education* 52 .16 (Dec 9, 2005)

[22]Lila Guterman, "A Silent Scientist under Fire" *Chronicle of Higher Education*, 52.22 (3 Feb 2006), pp. A15-A19

[23][note missing at this time]

[24] C. Holden "Stem-cell research: Korean cloner admits lying" *Science* 310 (#5753): 1402-1403 (2 December 2005).

The controversy intensified in South Korea and elsewhere on November 21st when Dr. Roh Sung-il, Head of the fertility clinic at MizMedi Women's Hospital where many of the oocytes used by Hwang's team were donated, held a news conference and told the assembled journalists that in 2002 he had paid some 20 women the equivalent of US$1,400 each for donating the eggs used in the research for Hwang's 2004 embryo cloning paper. Roh added that payment had become unnecessary later because women were willing to donate eggs without compensation after Hwang's work became well-known. He also insisted that Hwang did not know about the early payments. Roh's claim that payments were unneeded later appeared to be confirmed by news that the non-profit foundation established by Hwang's supporters the same day to secure egg donations had been contacted by 800 women volunteering to become donors before the end of the week.

So strong was the support for Hwang that after Munhwa Broadcasting Company showed a segment of its news program *PD Su-Cheop* (*Producer's Notebook*) discussing the egg donation controversy it was accused of being unpatriotic, several advertisers dropped their ads, demonstrators picketed company headquarters in Seoul, and the program's producers of the program were threatened in posts to Internet chat boards. Many Koreans agreed there had been ethical lapses, but felt the controversy and the pressure on Hwang reflected efforts to impose Western standards on Korean scientists. Supporters were also quick to point out that payments to donors were not banned in South Korea in 2002-03. The Bioethics and Biosafety Act adopted in late 2003 but not scheduled to take effect until January 2005 closed the door indirectly by providing in Article 13, paragraph 1 that embryos can be produced from sperm and oocytes only for the purpose of pregnancy and in Article 13, paragraph 3 that "No one shall induce or assist in providing or utilizing sperm or oocytes for the purpose of receiving financial reward, property, or any other personal benefits."[25] However, the new law also permitted the practice already adopted in many other countries of allowing research to be performed with "spare" embryos.

On November 24th Hwang called a press conference to announce his intention to resign as President of the World Stem Cell Hub. He claimed he had rejected proposals that team members donate eggs while acknowledged that two members of his team had done so. He said they had gone ahead and donated under false names, he had found out about the donations later, and lied about the source of eggs to protect their privacy. To critics pointing out that he should have been aware that having members of the research team act as donors contravened the Helsinki Declaration, Hwang replied that he was unaware of that Declaration.

Hwang's defenders in the government and among the public still felt the charges reflected an unfair imposition of foreign standards on Korean researchers. Health Ministry official Choi Hee-joo was quoted on November 24th as saying the women providing eggs for Hwang's research were motivated by a desire to serve science, their actions accorded with Asian ethical conceptions, and neither they nor Hwang's team should be judged by Western standards.

On November 29th, controversy about the propriety of oocyte donations was swamped by claims that Hwang's team had fabricated data in their May 2005 paper claiming to have created patient-specific stem cell lines. Tipped off, Munhwa Broadcasting raised the charges in another segment of *PD Su-Cheop.*

[25] South Korean Biosafety and Bioethics Act 2005 (Act No. 7150), unofficial English translation by Koo Young-mo and John McGuire Nov. 2004, available at ruhr-uni-bochum.de/kbe/Bioethics&BiosafetyAct-SouthKorea-vl.0.pdf (accessed 16 July 2009).

Though this intensified ire against Munhwa, the charges were quickly elaborated by scientists and became the subject of worldwide discussion in early December.

In mid-December Seoul National University convened a 9-scientist internal review panel to look into all of the charges against Hwang. Its reports in December and January confirmed the charges that he had faked data in the stem cell papers. They also confirmed irregularities in procurement of oocyte donations. First, the review panel concluded that Hwang's team had used at least 273 eggs to produce embryos, rather than the 185 they reported in the May 2005 *Science* paper. It also rejected Hwang's claim that he was unaware of egg donations by female researchers on his own team after being informed that he had distributed egg donation consent forms to his researchers and even gave one of them a ride to MizMedi Hospital for the egg extraction procedure.

In its 2008 report on the controversy, South Korea's National Bioethics Committee summarized the egg donations secured by Hwang's collaborators as follows:

Location	type	women	donations	eggs acquired
MizMedi Hospital	paid	63	75	1336
Hanna Women's Clinic	in-kind benefit	23	25	313
MizMedi Hospital	volunteer	14	14	182
Hanna Women's Clinic	volunteer	11	12	230
Hanyang Univ. Hospital	volunteer	8	9	121
Cheil General Hospital	volunteer	1	1	8
MizMedi Hospital	researcher	2	2	31
Hanyang Univ. Hospital	ovary removal 1	114	114	more than 537
Hanyang Univ. Hospital	ovary removal 2	72	113	not reported

[ovary removal 1 = data in Ryu Young-june 2004 MA Thesis]
[ovary removal 2 = data from Seoul Prosecutor's Office for 2002-2003]

The Committee also noted information about side effects. 17.9% of the donors treated at MizMedi Hospital suffered OHSS afterward; one paid donor who donated twice needed hospitalization for OHSS both times. 2 of the 11 volunteer donors at Hanna Women's Clinic suffered ascites afterward. No cases of side effects were reported from Hanyang University Hospital or Cheil General Hospital.[26]

III. Implications

The controversy over methods of recruiting egg donors reflected the combination of global consensus on some points and continuing disagreement about others. Though there is a long history of self-experimentation – including use of family members and associates – in medical research, today there is consensus that students and junior members of research teams should not be used as donors to avoid even the suggestion of compulsion. There is still no agreement on whether donors may be paid. Article 12(1) of the European Union's 2004 Tissue and Cells Directive specifies that Member States should establish systems of voluntary and unpaid tissue and cell donation but may allow "compensation which is strictly limited to making good the expenses and inconveniences related to the donation" and must define

[26] Republic of Korea, National Bioethics Committee, 2008. English-language summary available in Appendix 2.

the conditions under which compensation will be paid in national law or regulations. The US National Institutes of Health guidelines also recommend against payments to egg donors, though advertisements soliciting egg donations to help infertile couples conceive offer significant payments. In June 2009, the New York State (USA) Stem Cell Board, which oversees the state government's 11 year, $600 million dollar program, approved payments of up to $10,000 per donation to overcome the scant supply of suitable eggs. Even proponents of the measure worried that some women would try to donate multiple times for the money, and proposed maintaining a general donor register to keep this from happening.[27]

Hwang's foreign collaborators were nervous about the egg donor recruitment scandal even before the data fabrication charges became public or Hwang confessed he was aware at the time that younger female members of his research team had donated eggs. Hwang's team could have continued work without the foreign collaborators, but their concerns certainly contributed to the World Stem Cell Hub's difficulty finding foreign institutions willing to host regional affiliates in fall 2005.

The data fabrication scandal was a more significant setback to South Korean aspirations than the egg donation scandal because the ethical questions involved provoked no disagreement. While a few commentators felt that data fabrication contributed to discrediting science generally, most agreed that the scientific requirements for repeatability of results make detection of data fabrication more likely in scientific work than in business, journalism, or politics. As Rob Carlson put it, "There is no other human institution so ruthless in chopping out the dead wood. After all, if you are lying or pulling a fast one, the very last thing you want to do is get a bunch of really smart people trying to catch you out, all of whose professional standing improves if they do." This protective mechanism is very strong in areas of well-established science. In the more rapidly changing, and more exciting, areas of frontier science, where results have not yet been tested by others, competition is sharper and there is more room for cheating. Yet, even there, as the Hwang case shows, others' inability to replicate results will inspire doubts.

Though some observers feared that revelations of Hwang's data fabrication would discredit science generally, the effects were confined mainly to stem cell research, and even there they were relatively short lived because of the multiple methods available for acquiring stem cells. Embryo cloning is very inefficient; the first successful animal cloning, of Dolly the sheep, occurred after 276 unsuccessful attempts. Hwang's data fabrication confirmed other scientists in the view that there were no shortcuts on the horizon, and promoted efforts to develop other methods of acquiring stem cells. While the World Stem Cell Hub folded, the Korean Research Institute of Bioscience and Biotechnology (KRIBB) still exists. Its researchers are active in stem cell and other biotechnology research, and KRIBB maintains collaborations with research institutions and biotechnology companies around the world. Korean scientists remain active in the field, and the egg donor controversy led to significant improvement in supervision of human subjects research by the South Korean Ministry of Health and Institutional Review Boards.

South Korean Legislation, Regulations, and Guidelines in force, 2009

from International Compilation of Human Research Protections 2009 Edition, p. 67.
Compiled by the Office for Human Research Protections, U.S. Department of Health and Human Services available at http://www.hhs.gov/ohrp/international/HSPCompilation.pdf (accessed 31 July 2009)

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Drugs

Supervising Agency: Korea Food and Drug Administration (Korean): www.kfda.go.kr/

Legislation: Pharmaceutical Affairs Act (No. 91235) Articles 10 and 31-34 (2008)

Regulations: Enforcement Rule of Pharmaceutical Affairs Act Articles 22, 31-34

Guidelines: 1.) Korean Good Clinical Practice Public Notification of Food and Drug Administration, No. 2007-4 (2007)

2.) Guideline for Investigational New Drug Application: Public Notification No. 2004-51 (2004)

Privacy/Data Protection

Supervising Agency: Ministry of Public Administration and Security: http://www.mopas.go.kr

Legislation: Act on the Protection of Personal Information Maintained by Public Agencies No. 8871 (2008)

Genetic Research

Supervising Agency: Ministry of Health, Welfare, and Family Affairs: http://english.mw.go.kr/

Legislation: Bioethics and Safety Act, Chapters 2, 6, 9, 24, 31, 38, and 41 (2005 and 2008 amendments)

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