The Joint Subcommittee to Study the Medical, Ethical, and Scientific Issues Relating to Stem Cell Research Conducted in the Commonwealth

2006 Update

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The Rise and Fall of South Korea's Leading Stem Cell Researcher, Dr. Hwang Woo Suk

- Dr. Hwang's claims, as reported in the May 2004 and June 2005 issues of Science:
  - Successfully cloned first human embryo
  - Created 11 new patient-specific stem cell lines, using only 185 eggs
  - Reduced the average requirement of 242 eggs per cell line (2004) to 17 per cell line
  - Dr. Hwang denied knowledge of any ethical violations in the gathering of research eggs

“One of the biggest scientific frauds of all time” - BBC News (Newsnight)

- Investigators later learned:
  - Dr. Hwang fabricated his research results and doctored photographs to make his research appear legitimate
  - There was no evidence that Dr. Hwang created even a single patient-specific stem cell line, nor that they had the technology to do so
  - Between November 2002 and December 2005, Dr. Hwang’s lab received over 2,000 eggs
  - Dr. Hwang knowingly accepted donated eggs from female researchers in his lab, in violation of the Declaration of Helsinki

- As a result:
  - Dr. Hwang tried to resign from his position with Seoul National University, but they would not accept his resignation
  - He was later dismissed by the University
  - In May 2006, Dr. Hwang and several members of his lab were indicted on charges of fraud, embezzlement, and violation of the country's bioethics laws
  - Dr. Hwang is accused of embezzling $3 million for personal use and the illegal purchase of research eggs
  - If convicted, he could face prison time
  - The scientific community has responded by creating new ethical guidelines dealing with both the research process and the publication of research results

NIH 2006 Highlights of Stem Cell Research

- January 2006: University of Wisconsin scientists grow human embryonic stem cells without animal products.
  - Derived two new human embryonic stem cell (hESC) lines using only human products, in a completely defined medium
  - Animal products are frequently used to nurture cells in a lab dish, but scientists worry that these products may contaminate the new cells lines, making them unsuitable for therapeutic use

- January 2006: Australian scientists identify mouse stem cell capable of producing a complete, functioning breast.
  - Scientists may now look for similar cells in human breasts
  - Identification of such cells may aide in breast cancer research
  - May also allow scientists to grow human breast tissue for reconstructive surgery

- January 2006: NIH study finds in vitro fertilization (IVF) and somatic cell nuclear transfer (SCNT) derived mouse embryonic stem cells equal in their potential
  - SCNT - cloning (Dolly the sheep). Enucleated egg + somatic cell nucleus
  - SCNT created animals (Dolly) have physical abnormalities and die early
  - Would SCNT derived embryonic stem cells also be abnormal?
  - If this can be reproduced with human cells, it would prove that embryonic stem cells produced by IVF and SCNT have equal potential for therapeutic use

- February 2006: NIH-funded scientists expand mouse blood-forming (hematopoietic) stem cells
  - Hematopoietic cells are found in bone marrow and umbilical cord blood
  - These cells are destroyed by the treatment for blood cancer (and other serious blood disorders)
  - Scientists have previously had a hard time getting these cells to multiply in the laboratory
  - Here, scientists were able to increase the number of mouse hematopoietic cells by 24- to 30-fold.

- March 2006: NIH-funded scientists identified cell surface receptors vital to the survival of human embryonic stem cells (hESCs)
  - These receptors bind to proteins called neurotrophins, which prevents the cell from dying
  - This discovery could help scientists to grow large batches of hESCs to study

- April 2006: German scientists made adult mouse stem cells which normally produce sperm (spermatogonial stem cells, or SSCs) behave like embryonic stem cells (ESCs)
  - They grew the SSCs in the lab under standard ESC culture conditions
  - The cells then made several proteins characteristic of ESCs
  - When the scientists tested these cells for pluripotency, their results suggested that they could become any cell in the body
  - Scientists named the cells multipotent adult germline stem cells (maGSCs)
  - Similar cells in humans could provide a new source of patient specific stem cells, as well as more cell lines for research

- April - May 2006: Scientists increase knowledge of key characteristics of "stemness"
  - Scientists have identified portions of embryonic stem cells that must be studied to determine how these cells remain undifferentiated, yet are pluripotent

- May 2006: Somatic cell nuclear transfer (SCNT) works better if donor nucleus is less mature
  - Using SCNT to create new embryonic stem cell lines is inefficient process
  - One reason may be the use of mature, differentiated donor nuclei
  - These mature cells are likely to have already switched off important developmental genes, and made modifications to their DNA through methylation
  - Scientists here used non-embryonic stem cells, whose nuclei are less likely to have undergone these changes
  - Data show this process to be 3 times more efficient than with mature cells

- June 2006: Nanog reprograms mouse brain stem cells
  - Human embryonic stem cells can “reprogram” adult cells to make them behave like ESCs
  - Privately funded UK scientists found a 200-fold increase in this reprogramming when they engineer the stem cells to overexpress the gene Nanog
  - Nanog in important in maintaining stem cells’ self-renewing properties
  - Process has not been perfected; the reprogrammed cells have 4 copies of cellular DNA, instead of the normal 2
  - If this could be replicated in humans, it would be the first step in getting adult cells to behave like stem cells for use in treating human beings

- July 2006: Neurons grown from embryonic stem cells restore function in paralyzed rats
  - NIH supported scientists used mouse embryonic stem cells to make functional motor neurons
  - Motor neurons are nerve cells in the spinal cord that send fibers called axons to the muscles of the muscles used to move the body
  - Previously paralyzed rats treated with these motor neurons were able to move their legs again, although they could not walk or grip their feet as well as uninjured rats
  - Scientists had previously been able to coax human embryonic stem cells into becoming a type of cell that repairs damaged spinal cord insulation, called myelin
  - Scientists have also used human non-embryonic neural stem cells to help replace damaged rat spinal cord nerve cells

- August 2006: Signaling molecules may help adult brain repair itself following a stroke
  - Cell signaling proteins are used by neighboring cells to communicate, in order to organize themselves
  - Cell signaling is critical in the development of the nervous system
  - Scientists hypothesized that these cell signaling proteins might also be important in preserving the nervous systems stem cells later in life
  - When injected into normal adult rat brains, these proteins helped maintain the adult neural stem cells
  - When injected into the brains of rats that had suffered a stroke, scientists observed an increase in the number of dividing neural stem cells
  - The rats' gradual improvement in motor skills, not seen in rats injected with a control substance, is attributed to the increase in dividing neural stem cells
  - Scientists hope to optimize the use of signaling proteins to treat brain injuries such as stroke

- August 2006: Scientists reprogram adult mouse skin cells by adding defined factors
  - Japanese government funded scientists reprogrammed adult mouse skin cells to behave like embryonic stem cells by engineering the cells to express 4 defined factors, and growing them in ESC culture conditions
  - These four factors are known to be important for maintaining “stemness” in ESCs
  - Scientists call these reprogrammed adult cells “iPS” for “induced pluripotent stem” cells
  - They will next try to determine if human adult stem cells can also be reprogrammed using this method

- August 2006: Scientists create “ethical” stem cells
  - Advanced Cell Technology, a biotechnology company in California, has developed a new method of producing new embryonic stem cell lines which leaves the embryos intact
  - This method uses a single cell, or blastomere, from 2-3 day old human embryos
  - It was derived from a process used in in vitro fertilization to detect for serious genetic defects, called preimplantation genetic diagnosis, or PGD
  - In PGD, if the removed cell is found to be healthy, the embryo can be implanted into a woman’s uterus and regenerate the lost cell and continue developing
  - In this study, 91 blastomeres from 16 embryos were used, 53 of which divided
  - Of those 53, 19 stem cell outgrowths were formed, making them unsuitable for research
  - Two full stem cell lines were formed

- Criticism for this new process
  - Opponents of stem cell research point out that none of the embryos used were actually allowed to continue development, so it is unclear whether they would actually be able to develop normally
  - In fact, in this study, all 16 embryos were actually destroyed
  - Critics also say that if the single cell taken is capable of growing into a new embryo, scientists will be facing the same issue of destroying human life, even if the original embryo remains intact
  - Former President Bush advisor Jay Lefkowitz, who helped formulate the President's 2001 policy, said that if this new technique is eventually shown to work without destroying embryos, it would probably satisfy the President's ethical concerns

Federal and State Stem Cell Activities in 2006

- ***FEDERAL ACTIVITY***
  - In August of 2001 President Bush issued an executive order announcing that his administration would allow federal funding only for research on the embryonic stem-cell lines that existed at that time and researchers have since found that many of those lines are contaminated and unusable for research

H.R. 810 Stem Cell Research Enhancement Act

- In July, President Bush executed the first veto his presidency, on a bill that would have allowed couples who have had embryos frozen for fertility treatments to donate them to researchers rather than let them be destroyed;
- President Bush said that the bill "crossed a moral boundary " and that "if this bill were to become law, American taxpayers would, for the first time in our history, be compelled to fund the deliberate destruction of human embryos, and I'm not going to allow it"

- Other federal regulation of stem cell research
  - The president signed legislation to ban the commercial production of human fetal tissue, known as "fetal farming" -- S. 3504 the "Fetus Farming Prohibition Act of 2006“
  - Current federal policy does not place any restrictions on adult stem cell research beyond the requirements that apply to all scientific research involving human subjects
  - In FY 2005 the federal government spent $199 million on human non-embryonic research, which includes research on adult stem cells, cells from umbilical cord blood, and cells from aborted fetal tissue
  - Although the federal government limits the use of its funds for embryonic research, it does not restrict state or private sector funding of embryonic stem cell research

- ***STATE ACTIVITY***
  - According to NCSL, from 2004 to 2006, state legislatures considered approximately 400 bills that would affect some or all forms of stem cell research, and the rapid pace of legislative activity is not expected to slow in the near future

- **Maryland -** In 2006, Maryland became the one of five states to authorize tax dollars for embryonic stem cell research
  - $15 million dollars effective July 1, 2006
  - Legislation establishes a clear process for reviewing research projects and allows the money to be used for the most promising proposals for study involving embryonic or adult stem cells
  - Established a 15-member commission that reviews proposals, and will include two experts in biomedical ethics and religion
  - Authorizes the use only of embryos that would otherwise be discarded by fertility clinics

- **California -** California Institute for Regenerative Medicine (CIRM); governed by the Independent Citizens Oversight Committee (ICOC)
  - Established in 2004 with the passage of Proposition 71, the California Stem Cell Research and Cures Act
  - Provided $3 billion in funding for stem cell research
  - Called for the establishment of entity to make grants and provide loans for stem cell research, research facilities and other vital research opportunities
  - The program withstood a state constitutional challenge in 2006, the judge finding that the CIRM is firmly under the management and control of the state, accountable to the public, and has proceeded in that manner in carrying out its operations
  - That decision is currently on appeal
  - Awarded its first 16 grants ($12.1 million) in April to non-profit institutions to train 169 research fellows
  - On August 22 the institute solicited its first research grant proposals (made possible by a loan from the Governor, necessary because of the program being involved in legal proceedings)

- **Illinois** - Illinois Regenerative Medicine Institute was established in July 2005 by Governor Rod R. Blagojevich (executive order) to provide state support for stem cell research
  - Awarded first grants in April 2006 of $10 million; and in August 2006 awarded $5 million more
  - Proposed over $100 million dollars for stem cell research in the next 5 years for the FY2007 budget; the proposal is currently awaiting action
  - The Governor's Executive Order establishing the program mandated that no funding will be authorized for research involving human cloning, nor will funding be awarded to anyone who purchases or sells embryonic or fetal tissue for research purposes

- **New Jersey** - New Jersey Stem Cell Institute
  - The Institute was created by a memorandum of understanding between Rutgers University and the University of Medicine and Dentistry of New Jersey in response to the state's need and desire to make significant advancements in stem cell research
  - In December 2005 $5 million in grants were awarded to 17 institutions for research on stem cells from embryos and other sources
  - Stem Cell Research Grant Program (State program that supports the New Jersey Stem Cell Institute)-- The New Jersey Commission on Science and Technology reports $23 million in appropriations to the Institute for stem cell grants in FY 2005 and FY 2006

- **Connecticut - (SB 934 -2005)**
  - Beginning on June 30, 2006, and each year for 10 years, at least $10 million is available from the Stem Cell Research Fund for grants-in-aid to eligible institutions;
  - establishes a stem cell research advisory committee, stem cell research peer review committee, and Connecticut Innovations Inc., as the entities to conduct grant reviews; --
  - applications for the $20 million the state of Connecticut set aside this year for stem cell research grants were due in July; and 70 applications were received and made available for peer review on August 4

- **Missouri--**Constitutional Ballot Initiative; Amendment 2--
  - An Amendment to the Missouri Constitution will be on the November 7 ballot which would protect research involving somatic cell nuclear transfer, or therapeutic cloning
  - The Amendment would also protect the use of leftover human embryos from in vitro fertilization procedures, if the embryos' donors give permission
  - This was a citizen initiated proposal made possible by thousands of signatures