BENG 090
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Federal Funding for Embryonic Stem Cell Research

Executive Summary
by Jurist Tan

On October 15, 2005, scientists from University of Minnesota reported how their human embryonic stem cells (hESCs) had developed the ability to kill tumor blood cells, the cause of leukemia.[1] On November 20, 2005, Imperial College London reported the successful conversion of human embryonic stem cells into cartilage cells, a possible therapy for sports injuries and hip replacements.[2] On November 28, 2005, Thomas Jefferson University, Philadelphia, successfully used chemicals of human origin in producing dopamine, the protein lacking in people with Parkinson's disease, from human embryonic stem cells, marking the safest technological advancement for the disease so far.[3] On December 5, 2005, *Asia Times* reported the claim of Dr. Geeta Shroff of Bombay, India, that her embryonic stem cell-based therapy produced significant recovery in her patient's bone-marrow damage.[4] Right at this moment, the University of

[1] Woll, Petter S, et al. *Human Embryonic Stem Cell-Derived NK Cells Acquire Functional Receptors and Cytolytic Activity*. 2005. J. Immunol. 175: 5095 - 5103.
[2] *Scientists use stem cells to grow cartilage*. 2005. Faculty of Medicine, Imperial College London.
[3] *Coaxing human embryonic stem cells to make dopamine.* 2005. Medical Research News (www.news-medical.net).
[4] Batsu, Indrajit. *India embraces stem cell research*. 2005. Asia Times Online (www.atimes.com).

Edinburgh, UK, is approaching a cure for Alzheimer's with embryonic-developed neuron cells,[5-6] while scientists in Jerusalem[7], Germany[8], and Spain[9] are working on islet cells for diabetes.[10]

Embryonic stem cell research is progressing, and it is progressing fast. Possessing the unique ability to transform into any type of cell such as those of the eyes, skin, heart, and even brain,[11] embryonic stem cells hold tremendous potential to replace defective cells in human bodies. The world's embryonic stem cell industry is bringing that potential closer to reality each and every day. Such, unfortunately, is not the case for United States.

In 2001, pressured by the ongoing debate, President George W. Bush limited federal funding to the existing 60 cell lines.[12] Of those, 16 are contaminated and 38 are kept inaccessible by their holders, leaving researchers with a mere 22.[13] With $30 billion of government funding per year, the problem is not the lack of money –it is, rather, the ineffective distribution. Under this policy, government funding is directed toward *only* these 22 lines, despite the fact that they may be as contaminated as their counterparts. Moreover, since many of the cell lines come from private sources with commercial interests,[14] they are difficult to obtain.[15] Still, not one cent is to be spent on embryonic stem cell research using new lines in any way, forcing scientists who manage to produce purer cell lines to find, if possible, private funding and move, with

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[5] *Scientists make nerve stem cells.* 2005. BBC News.
[6] Conti L, et al. *Niche-Independent Symmetrical Self-Renewal of a Mammalian Tissue Stem Cell*. 2005. PLoS Biol. Aug 16;3(9):e283.
[7] Schuldiner, M., et al. 2000. *Effects of eight growth factors on the differentiation of cells derived from human embryonic stem cells*. Proc. Natl. Acad. Sci. U. S. A. *97,* 11307–11312.
[8] Ruediger, M., NIH personal communication (http://stemcells.nih.gov/info/scireport/chapter7.asp#Ruediger).
[9] Soria, B, et al. 2000. *Insulin-secreting cells derived from embryonic stem cells normalize glycemia in streptozotocininduced diabetic mice*. Diabetes. *49,* 157–162.
[10] *Stem Cells and Diabetes*. 2002. National Institute of Health.
[11] *Stem Cell Basics.* 2005. National Institute of Health (http://stemcells.nih.gov/info/basics).
[12] Bush, George W. *Remarks by the President on Stem Cell Research*. 2001. The White House.
[13] *Information on Eligibility Criteria for Federal Funding of Research on Human Embryonic Stem Cells*. 2005. National Institute of Health.
[14] *Embryonic Stem Cells Ethical Debate.* Wikipedia (http://en.wikipedia.org/wiki/Stem_cell#Private_funding)
[15] Gupta, Sanjay. 2002. *Access may complicate stem cell study*. CNN Medical Unit (July 17, 2002).

significantly high costs, to new laboratories.[16] With one person dying from Parkinson's disease every hour and about a million of others waiting for help,[17] we cannot afford this delay—we must channel our federal funding to more effective embryonic stem cell lines, regardless of when they are created.

The current policy was essentially based on good reasons. For instance, opponents of this research are accurate when they claim that the cells, replicating in an undifferentiated state, have the risk to develop into tumors.[18] In a series of early experiments, collection of uncontrolled, developing cells occurred, raising doubts on whether embryonic stem cells could ever become a reliable human treatment.[19-20] The latest advances, however, have found ways to prevent this from happening. By giving the right signals, cells can be developed into a mature state in a dish before transplantation, preventing them from developing into unwanted cell types.[21] In addition, instead of using mouse-feeder cells to induce development, which, as many suspected correctly, causes contamination,[22] scientists in Roslin Institute, UK, managed to keep their cell population pure by using only human protein and neonatal foreskin;[23] scientists at Advanced Cell Technology in Massachusetts, US, have even produced embryonic stem cells without using any animal feeder

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[16] Dunn, Kyla. 2005. *The Politics of Stem Cells.* Nova, Science Now.
[17] *Statistics about Parkinson's Disease.* Wrong Diagnosis (http://wrongdiagnosis.com/p/parkinsons_disease/stats.htm).
[18] Tzukerman M, et al. 2003. *An experimental platform for studying growth and invasiveness of tumor cells within teratomas derived from human embryonic stem cells*. National Academy of Sciences, USA 100 (23): 13507-13512.
[19] Wakitani S, et al. 2003. *Embryonic stem cells injected into the mouse knee joint form teratomas and subsequently destroy the joint.* Rheumatology 42 (1): 162-165.
[20] Scharnhorst V, et al. *Differential regulation of the Wilms' tumor gene, WT1, during differentiation of embryonal carcinoma and embryonic stem cells*. Cell Growth & Differentiation 8 (2): 133-143.
[21] Zhang SC, et al. 2001. *In vitro differentiation of transplantable neural precursors from human embryonic stem cells*. Nature Biotechnology 19 (12): 1129-1133.
[22] Holden C. 2005. *Human embryonic stem cells - Getting the mice out of ES cell cultures*. Science 307 (5714): 1393-1393.
[23] Coghlan, Andy. 2005. *Human embryonic stem cells grown animal-free*. New Scientist.

cells.[24] Thus, the risk of tumor is now, at the very least, greatly reduced under careful maintenance and preservation.

But the mere fact that they may not cause tumors is not enough. By stopping embryos' development and, thus, their life potential, derivation of embryonic stem cells brings up strong ethical objections from religious groups and ethicists alike.[25-26] Some justifiably claim that the government should not be using more money from taxpayers who do not believe in using embryos for research.[27] It is noteworthy, however, to look at the science of embryonic stem cell derivation before deciding the morality of such action.

Contrary to common belief, embryonic stem cells are not taken from "fetuses with tiny, waving hands and feet."[28] On the fourth or fifth day of its development, an embryo reaches a state called blastocyst, a collection of approximately 100 cells. Consisting of trophoblast, a layer of cells that surrounds the blastocyst; the blastocoel, a hollow cavity inside the blastocyst; and inner cell mass, a group of approximately 30 cells, including stem cells, at one end of the blastocoel;[29] a blastocyst is "far from possessing a nervous system (or any other organs) and, biologically speaking, does not have feelings."[30] Removing stem cells from blastocysts is, thus, just removing a group of cells from another group of cells.

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[24] Klimanskaya I, et al. 2005. *Human embryonic stem cells derived without feeder cells*. Lancet 365 (9471): 1636-1641.
[25] *Stem Cell Research and Catholic Church.* 2005. American Catholic (http://www.americancatholic.org/News/StemCell).
[26] Guenin, Louis. 2005. *The Ethics of Human Embryonic Stem Cell Research*. International Society for Stem Cell Research (http://www.isscr.org/public/ethics.htm).
[27] *Fact Sheet: Valuing Life Through Embryo Adoption and Ethical Stem Cell Research*. 2005. The White House (http://www.whitehouse.gov/news/releases/2005/05/20050524-10.html).
[28] Kinsley, Michael. *If You Believe Embryos Are Humans…* 2001. TIME Magazine (Vol. 157 No. 25).
[29] *Stem Cells Information.* 2002. National Institute of Health.
[30] *Embryonic Stem Cells Ethical Debate.* 2005. Wikipedia (http://en.wikipedia.org/wiki/Stem_cell#Embryonic_stem_cell_ethical_debate)

Aside from that, it should not be forgotten that people who need this research do not have much time, and within this time span, most of them do not even enjoy a good quality of life. Throughout the history of science, there have always been ethical objections towards new alternatives to save lives –removing one's organ and donating it to another, for example, was strongly opposed years ago for being "unnatural". Laws, however, have always provided mechanisms to ensure that every scientific progress urgently needed is implemented in the most ethical way possible. In organ donation, such mechanisms include personal and family's consent, in addition to the doctor's permission.[31] In embryonic stem cell research, blastocysts are taken from in-vitro fertilization clinics as spares from IVF treatments; they are tagged with specific instructions *not* to be implanted in any woman's womb and to be donated for research.[32] Before donation was made possible, these spares were either destroyed or frozen in thousands.[33] Thus, considering the urgent need for embryonic stem cell research, opposing attempts to save lives with these blastocysts while supporting their destruction is hardly justifiable.

On the other hand, adult stem cells and gene therapy are also rapidly advancing to cure some genetic diseases. With the controversy surrounding embryonic stem cells, some believe that funds should, instead, be channeled to these alternatives. We must not forget, however, that one option cannot simply replace another. For instance, many of the prospective therapies for Alzheimer's and Parkinson's cannot rely on adult stem cells alone, because one pure population of brain cells is, in its nature, very difficult to isolate.[34] In cases of genetic diseases, adult stem cells cannot be used for auto-transplantation nor donated to someone else, as risk of

[31] *U.S. Department of Health and Human Services Advisory Committee on Organ Transplantation (ACOT) Recommendations 36-4*. 2004. Health Resources and Services Administration (HRSA).
[32] *Stem Cell Basics.* 2005. National Institute of Health (http://stemcells.nih.gov/info/basics).
[33] Kinsley, Michael. *The False Controversy of Stem Cells*. 2004. TIME Magazine (Vol. 163 No. 22).
[34] Pecorino, Lauren. 2001. *Stem Cells for Cell-Based Therapies*. Action Bioscience (http://www.actionbioscience.org/biotech/pecorino2.html).

immunological rejection is high.[35] Greatly influenced by their environment, adult stem cells also possess much less differentiation capability, e.g. stem cells in the brain can only transform into neurons, and bone marrow-derived stem cells can only transform into blood cells or mesenchymal stem cells, producing fat, cartilage, bone, and muscle.[36] Therefore, unlike embryonic stem cells, it is difficult to develop adult stem cells into the cell types that we need. Over the years, scientists have tried to transdifferentiate, as in developing stem cells from one body part to another,[37-38] but the results are either dysfunctional or turn out to be hybrid, genetically inapplicable cells.[39-40] Even now, studies on transdifferentiation are still heavily based on embryonic stem cells and their pluripotent nature.

Meanwhile, gene therapy poses completely different problems. Using virus as its most effective vector to deliver therapeutic genes,[41] there is high risk of complications which may result in severe repercussions.[42] Up until now, the FDA has not approved any gene therapy method for sale, and the current therapies are still experimental with no significant success in clinical trials.[43] Even with the latest advancements, most of its treatments are only slowing down the progress of diseases, such as the case in Batten disease.[44] The diseases which need embryonic

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[35] *Frequently Asked Questions.* 2005. National Institute of Health (http://stemcells.nih.gov/info/faqs.asp).
[36] *The Latest Research on Bone Marrow Stem Cells*. 2003. Stem Cells Information Center.
[37] Bjornson, Christopher R.R., et al. *Turning Brain into Blood: A Hematopoietic Fate Adopted by Adult Neural Stem Cells in Vivo*. Science Vol. 283, p534-537.
[38] Mezey, Eva, et al. *Turning Blood into Brain: Cells Bearing Neuronal Antigens Generated in Vivo from Bone Marrow*. 2000. Science Vol. 290, p1799-1782.
[39] Ying, Qi-Long, et al. *Changing Potency by Spontaneous Fusion.* 2002. Nature Vol. 416 p545-548.
[40] Wurmser, Andrew E, Fred H. Gage. *Cell Fusion Causes Confusion.* 2002. Nature Vol. 416 p485-487.
[41] Naldini L, Blomer U, Gallay P, et al. 1996. In vivo gene delivery and stable transduction of nondividing cells by a lentiviral vector. Science 272 (5259): 263-267.
[42] Philipkoski, Kristen. 2003. *Perils of Gene Experimentation.* Wired News (http://www.wired.com/news/business/0,1367,57752,00.html).
[43] *Gene Therapy.* 2005. Human Genome Project Information (http://ornl.gov/sci/techresources/Human_Genome/medicine/genetherapy.shtml).
[44] Sleat DE, et al. 1997. *Associations of mutations in a lysosomal protein with classical late infantile neuronal ceroid lipofuscinosis*. Science, Vol. 277, No. 5333, pp. 1802-1805.

stem cells most are diseases currently treated, but not cured, by gene therapy, such as cancer[45] and sickle cell disease.[46]

Embryonic stem cells will never be a cure for all, and they may or may not lead to a feasible therapy anytime soon; but with the unique abilities that they possess, even the knowledge we gain from the research will be crucial for other fields, other research, and other possible therapies, such as adult stem cells and gene therapy. Funding embryonic stem cells does not mean that funding for adult cells or gene therapy should be cut—it only means that the current funds should not be limited to inaccessible, contaminated cells. Right now, the remaining 22 cell lines are not enough; we need the right mutations, combinations of genes, and broad diversity of cells to study several types of cancer, let alone other diseases.[47] Considering the variety of population we aim to cure, we need to allocate our budget to purer, more effective cell lines. Support the federal funding for expansion on embryonic stem cell research now –those lives may be in your hands.

[45] Chengwen Li, et al. 2005. *Adeno-associated virus vectors: potential applications for cancer gene therapy*. Nature 12**,** 913–925.
[46] Wilson, Jennifer Fisher. 2002. *Murine Cell Therapy Corrects Symptoms of Sickle Cell Disease.* The Scientist Vol. 16, Issue 6, p36.
[47] Weissman, Irving L. *Stem Cells–Scientific, Medical, and Political Issues*. 2002. N Engl J Med, Vol.346, No.20, p1577.