

## **Practical Problems with Embryonic Stem Cells**

**While some researchers still claim that embryonic stem cells (ESCs) offer the best hope for treating many debilitating diseases, there is now a great deal of evidence contrary to that theory. Use of stem cells obtained by destroying human embryos is not only unethical but presents many practical obstacles as well.**

“Although embryonic stem cells have the broadest differentiation potential, their use for cellular therapeutics is excluded for several reasons: the uncontrollable development of teratomas in a syngeneic transplantation model, imprinting-related developmental abnormalities, and ethical issues.”

-Gesine Kögler et al., “A New Human Somatic Stem Cell from Placental Cord Blood with Intrinsic Pluripotent Differentiation Potential,” *Journal of Experimental Medicine*, Vol. 200, No. 2 (July 19, 2004), p. 123.

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From a major foundation promoting research in pancreatic islet cells and other avenues for curing juvenile diabetes:

“Is the use of embryonic stem cells close to being used to provide a supply of islet cells for transplantation into humans?”

“No. The field of embryonic stem cells faces enormous hurdles to overcome before these cells can be used in humans. The two key challenges to overcome are making the stem cells differentiate into specific viable cells consistently, and controlling against unchecked cell division once transplanted. Solid data of stable, functioning islet cells from embryonic stem cells in animals has not been seen.”

-“Q & A,” Autoimmune Disease Research Foundation,  
[www.cureautoimmunity.org/Q%20&%20A.htm](http://www.cureautoimmunity.org/Q%20&%20A.htm), accessed July 2004.

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“‘I think the chance of doing repairs to Alzheimer’s brains by putting in stem cells is small,’ said stem cell researcher Michael Shelanski, co-director of the Taub Institute for Research on Alzheimer’s Disease and the Aging Brain at the Columbia University Medical Center in New York, echoing many other experts. ‘I personally think we’re going to get other therapies for Alzheimer’s a lot sooner.’ ...”

“[G]iven the lack of any serious suggestion that stem cells themselves have practical potential to treat Alzheimer’s, the Reagan-inspired tidal wave of enthusiasm stands as an example of how easily a modest line of scientific inquiry can grow in the public mind to mythological

proportions.

“It is a distortion that some admit is not being aggressively corrected by scientists.

“‘To start with, people need a fairy tale,’ said Ronald D.G. McKay, a stem cell researcher at the National Institute of Neurological Disorders and Stroke. ‘Maybe that’s unfair, but they need a story line that’s relatively simple to understand.’”

-Rick Weiss, “Stem Cells an Unlikely Therapy for Alzheimer’s,” *Washington Post*, June 10, 2004, p. A3.

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“ES [embryonic stem] cells and their derivatives carry the same likelihood of immune rejection as a transplanted organ because, like all cells, they carry the surface proteins, or antigens, by which the immune system recognizes invaders. Hundreds of combinations of different types of antigens are possible, meaning that hundreds of thousands of ES cell lines might be needed to establish a bank of cells with immune matches for most potential patients. Creating that many lines could require millions of discarded embryos from IVF clinics.”

-R. Lanza and N. Rosenthal, “The Stem Cell Challenge,” *Scientific American*, June 2004, pp. 92-99 at p. 94. [Editor’s note: A recent study found that only 11,000 frozen embryos are available for research use from all the fertility clinics in the U.S., and that destroying all these embryos for their stem cells might produce a total of 275 cell lines. See *Fertility and Sterility*, May 2003, pp. 1063-9 at p. 1068.]

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“Embryonic stem cells have too many limitations, including immune rejection and the potential to form tumors, to ever achieve acceptance in our lifetime. By that time, umbilical cord blood stem cells will have been shown to be a true ‘gift from the gods.’”

-Dr. Roger Markwald, Professor and Chair of Cell Biology and Anatomy at the Medical University of South Carolina, quoted in “CureSource Issues Statement on Umbilical Cord Blood Stem Cells vs. Embryonic Stem Cells,” *BusinessWire*, May 12, 2004, also at <http://curesource.net/why.html>.

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“‘We’re not against stem-cell research of any kind,’ said [Tulane University research professor Brian] Butcher. ‘But we think there are advantages to using adult stem cells. For example, with embryonic stem cells, a significant number become cancer cells, so the cure could be worse than the disease. And they can be very difficult to grow, while adult stem cells are easy to grow.’”

-Heather Heilman, “Great Transformations,” *The Tulanian* (Spring 2004 issue), at [http://www2.tulane.edu/article\\_news\\_details.cfm?ArticleID=5155](http://www2.tulane.edu/article_news_details.cfm?ArticleID=5155).

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“There are still many hurdles to clear before embryonic stem cells can be used therapeutically. For example, because undifferentiated embryonic stem cells can form tumors after transplantation in histocompatible animals, it is important to determine an appropriate state of differentiation before transplantation. Differentiation protocols for many cell types have yet to be established. Targeting the differentiated cells to the appropriate organ and the appropriate part of the organ is also a challenge.”

-E. Phimister and J. Drazen, “Two Fillips for Human Embryonic Stem Cells,” *New England Journal of Medicine*, Vol. 350 (March 25, 2004), pp. 1351-2 at 1351.

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Harvard researchers, trying to create human embryonic stem cell lines that are more clinically useful than those now available, find that their new cell lines are already genetically abnormal:

“After prolonged culture, we observed karyotypic changes involving trisomy of chromosome 12..., as well as other changes... These karyotypic abnormalities are accompanied by a proliferative advantage and a noticeable shortening in the population doubling time. Chromosomal abnormalities are commonplace in human embryonal carcinoma cell lines and in mouse embryonic stem-cell lines and have recently been reported in human embryonic stem-cell lines.”

-C. Cowan et al., “Derivation of Embryonic Stem-Cell Lines from Human Blastocysts,” *New England Journal of Medicine*, Vol. 350 (March 25, 2004), pp. 1353-6 at 1355.

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“[Johns Hopkins University] biologist Michael Shambloott said...major scientific hurdles await anybody wishing to offer a treatment, let alone a cure, based on cells culled from embryos.

“Among the major obstacles is the difficulty of getting embryonic stem cells – master cells that generate every tissue in the human body – to become exactly the type of cell one wants... Scientists...haven’t been able to guarantee purity – cells, for instance, that are destined to become muscle cells and nothing else...”

“Transplanting a mixed population of cells could cause the growth of unwanted tissues. The worst case could see stem cells morphing into teratomas, particularly gruesome tumors that can contain hair, teeth and other body parts.

“Another issue is timing... Stem cells pass through many intermediate stages before they become intermediate cells such as motor neurons or pancreatic or heart cells. Deciding when to transplant remains an open question, and the answer might differ from disease to disease.

“...In tackling Lou Gehrig’s disease, [Johns Hopkins neurologist Dr. Jeffrey] Rothstein figured that cells that haven’t committed themselves to becoming motor neurons would stand the best

chance, once implanted, of reaching out and connecting with the cells that surround them. What he found, however, is that these immature cells didn't develop much once transplanted into lab animals."

-Jonathan Bor, "Stem Cells: A long road ahead," *Baltimore Sun*, March 8, 2004, p. 12A.

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"Tony Blau, a stem-cell researcher at the University of Washington, said it is 'extremely laborious' to keep embryonic cells growing, well-nourished and stable in the lab so they don't die or turn into a cell type with less potential. Researchers need to know how to channel the stem cells to create a specific kind of cell, how to test whether they're pure, and how to develop drugs that could serve as a sort of antidote in case infused stem cells started creating something dangerous, such as cancer.

"Big companies, Blau said, want to know that their drugs will be almost completely stable, standard, pure and consistent, because they can behave differently if they aren't. Stem cells never will achieve that kind of standardization, Blau said, because living cells are more complex than chemically synthesized drugs."

-Luke Timmerman, "Stem-cell research still an embryonic business," *Seattle Times*, Business & Technology section, February 22, 2004, at [http://seattletimes.nwsourc.com/html/business/technology/2001862747\\_stemcells22.html](http://seattletimes.nwsourc.com/html/business/technology/2001862747_stemcells22.html).

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"[W]ithin the ESC research community, realism has overtaken early euphoria as scientists realize the difficulty of harnessing ESCs safely and effectively for clinical applications. After earlier papers in 2000 and 2001 identified some possibilities, research continued to highlight the tasks that lie ahead in steering cell differentiation and avoiding side effects, such as immune rejection and tumorigenesis."

-Philip Hunter, "Differentiating Hope from Embryonic Stem Cells," *The Scientist*, Vol. 17, Issue 34 (December 15, 2003), at [www.the-scientist.com/yr2003/dec/hot\\_031215.html](http://www.the-scientist.com/yr2003/dec/hot_031215.html).

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"Long-term culture of mouse ES [embryonic stem] cells can lead to a decrease in pluripotency and the gain of distinct chromosomal abnormalities. Here we show that similar chromosomal changes, which resemble those observed in hEC [human embryonal carcinoma] cells from testicular cancer, can occur in hES [human embryonic stem] cells.... The occurrence and potential detrimental effects of such karyotypic changes will need to be considered in the development of hES cell-based transplantation therapies."

-J. Draper et al., "Recurrent gain of chromosomes 17q and 12 in cultured human embryonic stem cells," *Nature Biotechnology*, Vol. 22 (2003), pp. 53-4.

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“James A. Thompson of the University of Wisconsin, Madison, and his colleagues managed to isolate and culture the first human embryonic stem cells in 1997. Five years later, big scientific questions remain. [Harvard embryonic stem cell researcher Doug] Melton and his colleagues, for instance, don't yet know how to instruct the totipotent stem cells to become the specific cells missing in a diabetic person, the pancreatic beta cell.

“‘Normally, if you take an embryonic stem cell, it will make all kinds of things, sort of willy-nilly,’ says Melton.”

-J. Mitchell, “Stem Cells 101,” PBS Scientific American Frontiers, May 28, 2002, [www.pbs.org/saf/1209/features/stemcell.htm](http://www.pbs.org/saf/1209/features/stemcell.htm).

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“Unlike stem cells isolated from the embryo, [adult stem cells] do not carry the same risks of cancer or uncontrollable growth after transplant, and they can be isolated from patients requiring treatment, thus avoiding all problems of immune rejection and the need for immune suppressive drugs that carry their own risks.

“...Embryonic stem cells are promoted on grounds that they are developmentally more flexible than adult stem cells. But too much flexibility may not be desirable. Transplant of embryonic cells into the brains of Parkinson's patients turned into an irredeemable nightmare because the cells grew uncontrollably. Embryonic stem cells also show genetic instability and carry considerable risks of cancer... When injected under the skin of certain mice, they grow into teratomas, tumors consisting of a jumble of tissue types, from gut to skin to teeth, and the same happens when injected into the brain.”

-Dr. Mae-Wan Ho and Prof. Joe Cummins on behalf of the Institute of Science in Society (ISIS), “Hushing Up Adult Stem Cells,” ISIS report, February 11, 2002, at [www.isis.org.uk/HUASC.php](http://www.isis.org.uk/HUASC.php).

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“‘I even hear from patients whose fathers have lung cancer,’ said Dr. Hogan, a professor at Vanderbilt School of Medicine. ‘They have a whole slew of problems they think can be treated. They think stem cells are going to cure their loved ones of everything.’

“‘If it ever happens, it will not happen soon, scientists say. In fact, although they worked with mouse embryonic stem cells for 20 years and made some progress, researchers have not used these cells to cure a single mouse of a disease...

“‘Scientists say the theory behind stem cells is correct: the cells, in principle, can become any specialized cell of the body. But between theory and therapy lie a host of research obstacles...the obstacles are so serious that scientists say they foresee years, if not decades, of concerted work on basic science before they can even think of trying to treat a patient.’”

-Gina Kolata, "A Thick Line Between Theory and Therapy, as Shown with Mice," *New York Times*, December 18, 2001, p. F3.

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"Mice cloned from embryonic stem cells may look identical, but many of them actually differ from one another by harboring unique genetic abnormalities, scientists have learned..."

"The work also shows for the first time that embryonic stem cells...are surprisingly genetically unstable, at least in mice. If the same is true for human embryonic stem cells, researchers said, then scientists may face unexpected challenges as they try to turn the controversial cells into treatments for various degenerative conditions."

-Rick Weiss, "Clone Study Casts Doubt on Stem Cells," *Washington Post*, July 6, 2001, p. A1.

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"ES cells have plenty of limitations... For one, murine ES cells have a disturbing ability to form tumors, and researchers aren't yet sure how to counteract that. And so far reports of pure cell populations derived from either human or mouse ES cells are few and far between – fewer than those from adult stem cells."

-Gretchen Vogel, "Can Adult Stem Cells Suffice?," *Science*, Vol. 292 (June 8, 2001), pp. 1820-1822 at 1822.

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"Rarely have specific growth factors or culture conditions led to establishment of cultures containing a single cell type.... [T]he possibility arises that transplantation of differentiated human ES cell derivatives into human recipients may result in the formation of ES cell-derived tumors... Irrespective of the persistence of stem cells, the possibility for malignant transformation of the derivatives will also need to be addressed."

-J. S. Odorico et al, "Multilineage differentiation from human embryonic stem cell lines," *Stem Cells* Vol. 19 (2001), pp. 193-204 at 198 and 200, at <http://stemcells.alphamedpress.org/cgi/reprint/19/3/193.pdf>.