

## Scientific Experts Agree: Embryonic Stem Cells Are Unnecessary for Medical Progress

"Had a major heart attack? In the not-too-distant future, doctors may be able to use stem cells to regenerate damaged heart muscle. And here's the exciting part: They can do it using stem cells that aren't extracted from human embryos.

"[G]iven the controversy over harvesting cells from embryos, doctors have been exploring other possibilities. The payoff: A team from the University of Texas M.D. Anderson Cancer Center in Houston recently repaired heart muscles in animals by injecting them with stem cells extracted from human blood. It's the stem-cell equivalent of Columbus reaching America: Not only would cells harvested from one's own body eliminate the risk that they would be rejected, but obtaining them would be a simple, painless proposition.

"This work gives us a way to get the cells that's as easy as giving a blood sample,' says Edward Yeh, M.D., lead author of the study. The real mind boggler is what the stem cells might mean to the 1.2 million Americans who suffer heart attacks each year."

— Special Report, "Good news about bad things that happen to your parents," USA Weekend magazine, March 5-7, 2004, p. 6, www.usaweekend.com/04\_issues/040307/040307aging.html#heart

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"A group of researchers from The Scripps Research Institute has identified a small synthetic molecule that can induce a cell to undergo dedifferentiation—to move backwards developmentally from its current state to form its own precursor cell.

"This compound, named reversine, causes cells which are normally programmed to form muscles to undergo reverse differentiation—retreat along their differentiation

pathway and turn into precursor cells. These precursor cells are multipotent; that is, they have the potential to become different cell types. Thus, reversine represents a potentially useful tool for generating unlimited supply of such precursors, which subsequently can be converted to other cell types, such as bone or cartilage.

"This [type of approach] has the potential to make stem cell research more practical,' says Sheng Ding, Ph.D. 'This will allow you to derive stem-like cells from your own mature cells, avoiding the technical and ethical issues associated with embryonic stem cells."

- Press Release, "Regenerative Chemical Turns Muscle Cells into Stem Cells, Say Scientists at The Scripps Research Institute," December 22, 2003, www.scripps.edu/news/press/122203.html

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"Scientists in Canada have turned adult skin cells into the building blocks of brain cells --opening the way for their use in new therapies for such incurable diseases. The discovery, by a team at the University of Toronto, is particularly exciting as it promises to provide a readily accessible and ethically neutral source of neural stem cells -- the precursors of nerve and brain tissue.

"While other groups have managed to create these cells before, they have generally required the use of adult stem cells from bone marrow, which are difficult and painful to extract, or embryonic stem cells, which require the destruction of a human embryo.

"If the Toronto technique is perfected for clinical use it would allow neural stem cells to be made from a patient's skin, ensuring a perfect genetic match that would not be rejected by the body. The cells would then be transplanted into the brains of people with neurological disorders, to replace, for example, the specialized dopamine neurons that are lost in Parkinson's disease."

- Oliver Wright, "Patients' Own Skin Cells Turned into Potential Alzheimer's Treatment," *The Times* (London), December 10, 2003, Home News, p. 8.

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"Massachusetts General Hospital researchers have harnessed newly discovered cells from an unexpected source, the spleen, to cure juvenile diabetes in mice, a surprising breakthrough that could soon be tested in local patients and open a new chapter in diabetes research...

"This shows there might be a whole new type of therapy that we haven't tapped into,' said Dr. Denise Faustman, MGH immunology lab director and lead author of the new study, which appears today in the journal Science. 'We've figured out how to regrow an adult organ'."

- R. Mishra, "Juvenile diabetes cured in lab mice," *The Boston Globe*, November 14, 2003, p. A2.

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"There is now an emerging recognition that the adult mammalian brain, including that of primates and humans, harbours stem cell populations suggesting the existence of a previously unrecognised neural plasticity to the mature CNS [central nervous system], and thereby raising the possibility of promoting endogenous neural reconstruction... Since large numbers of stem cells can be generated efficiently in culture, they may obviate some of the technical and ethical limitations associated with the use of fresh (primary) embryonic neural tissue in current transplantation strategies."

- T. Ostenfeld and C. Svendsen, "Recent advances in stem cell neurobiology," *Advances and Technical Standards in Neurosurgery*, vol. 28 (2003), p. 3.

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"Stem cells in our bone marrow usually develop into blood cells, replenishing our blood system. However, in states of emergency, the destiny of some of these stem cells may change: They can become virtually any type of cell – liver cells, muscle cells, nerve cells – responding to the body's needs. Prof. Tsvee Lapidot and Dr. Orit Kollet of the Weizmann Institute's Immunology Department have found how the liver, when damaged, sends a cry for help to these stem cells. 'When the liver becomes damaged, it signals to stem cells in the bone marrow, which rush to it and help in its repair – as liver cells,' says Lapidot...

"The findings could lead to new insights into organ repair and transplants, especially liver-related ones. They may also uncover a whole new stock of stem cells that can under certain conditions become liver cells. Until a few years ago only embryonic stem cells were thought to possess such capabilities. Understanding how stem cells in the bone marrow turn into liver cells could one day be a great boon to liver repair as well as an alternative to the use of embryonic stem cells."

- "Weizmann Institute scientists find that stem cells in the bone marrow become liver cells," EurakAlert, August 11, 2003, www.eurekalert.org/pub\_releases/2003-08/wi-wis\_1081103.php

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"Recently, adult stem cells originating from bone marrow or peripheral blood have been suggested to contribute to repair and genesis of cells specific for liver, cardiac and skeletal muscle, gut, and brain tissue... Using adult stem cells to generate or repair solid organ tissue obviates the immunologic, ethical, and teratogenic issues that accompany embryonic stem cells."

- M. Korbling, Z. Estrov and R. Champlin, "Adult stem cells and tissue repair," *Bone Marrow Transplantation*, August 2003 (Supplement 1), p. S23, www.nature.com/cgi-taf/DynaPage.taf?file=/bmt/journal/v32/n1s/full/1703939a.html&filetype=pdf

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I.S. Abuljadayel, Chief Scientific Officer of Tri-Stem Inc., talking about his study in the July 2003 *Current Medical Research and Opinion* on producing pluripotent stem cells from adult blood cells:

"This new technology offers a viable option for the generation of large numbers of

pluripotent stem cells. These are likely to have many clinical and research applications. The source material is blood, the most accessible tissue in our body which can be extracted by simple venipuncture or aphaeresis. The procedure raises no ethical concerns and removes the need to resort to embryos or aborted fetuses. The technology is also cost-effective, donor-friendly producing relatively large quantities of stem cells within a short time, which could eventually save patient lives and shorten patient waiting lists."

- "Stem cell-like plasticity induced in mature mononuclear cells," *Reuters Health*, July 7, 2003

"This is an example of promising experimental therapies involving stem cells from bone marrow. Until just a few years ago, conventional wisdom held that only embryonic stem cells could turn into any cell in the body. But that thinking began to change as studies showed that stem cells from bone marrow could become heart, muscle, nerve, or liver cells. Now, the results of clinical trials conducted in Britain, Germany and Brazil show that heart patients injected with their own bone marrow cells benefit from the treatment."

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- N. Touchette, "Bone Marrow Stem Cells Heal the Heart," Genome News Network, May 2, 2003, www.genomenewsnetwork.org/articles/05\_03/sc\_heart.shtml

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"Stem cells from bone marrow can transform into insulin-producing cells, scientists have shown, suggesting a future cure for diabetes...

"Transplants of pancreatic cells have been tried between people, but the supplies are restricted and recipients have to take strong anti-rejection medication. Embryonic stem cells have also been converted into insulin-producing cells, but also produce immune-rejection, in addition to ethical concerns. But taking bone marrow cells from a patient, developing them into beta cells and then reimplanting them would have none of these difficulties. Also, much of the technology for bone marrow transplantation is already well developed, says study leader Mehboob Hussain, at the New York University School of Medicine.

"I am absolutely excited by the potential applications of our findings,' he said. 'In our body, there is an additional, easily available source of cells that are capable of becoming insulin-producing cells.""

- S. Bhattacharya, "Bone marrow experiments suggest diabetes cure," *NewScientist.com News Service*, March 17, 2003, www.newscientist.com/news/news.jsp?id=ns99993508

A professor at the University of Auckland School of Medicine in New Zealand, on brain repair:

"The announcement that stem cells can be obtained from aborted human foetuses or

from spare embryos from *in vitro* fertilisation procedures has been met with both enthusiasm and opposition. Less controversial, and probably more notable, is the recent demonstration that stem cells can be obtained from adult brain tissue, raising the exciting possibility that these 'neural stem cells' can be utilized to generate cells for autologous brain cell transplants....

"The use of adult stem cells in cell transplantation therapy could obviate the need to use stem cells derived from human embryos or human fetal tissue. At present, there are no legal or ethical concerns regarding research with adult stem cells. Furthermore, adult stem cells derived directly from the patient would reduce the likelihood that the transplanted cells would be rejected... Our studies are most advanced in Huntington's disease and our very recent results are very exciting."

- R. Faull, "Research in New Zealand on Huntington's Disease and Stem Cells," *Huntington's News: The Quarterly Newsletter of the Huntington's Disease Associations of New Zealand*, December 2002, www.geocities.com/graham\_tay/ResearchStem1202.htm

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"The use of human embryonic stem cells has been confronted with major obstacles because of bio-ethical and political issues involved obtaining them, as well as the suggestion that embryonic stem cells may lack appropriate developmental instructions, making them potentially less feasible for engrafting into adult tissue...

"As compared to embryonic stem cells, adult derived stem cells are endowed with additional developmental instructions and may be better suited for therapeutic purposes. According to [Dr. Shahin Rafii of Cornell University Medical College], 'We are approaching a day when a patient's own stem cells can be induced to divide and develop into tissue that can replace that which is diseased or destroyed, making overcrowded organ transplant lists and rejection of foreign tissues a thing of the past'."

- "Mechanism For Regulation Of Adult Stem Cells Found," *UniSci - Daily University Science News*, May 31, 2002, http://unisci.com/stories/20022/0531021.htm

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On the versatility of adult hematopoietic (blood-producing) stem cells, HSCs:

"[R]ecent studies have suggested that a subpopulation of HSCs may have the ability to contribute to diverse cell types such as hepatocytes, myocytes, and neuronal cells, especially following induced tissue damage... These surprising findings contradict the dogma that adult stem cells are developmentally restricted."

- K. Bunting and R. Hawley, "The tao of hematopoietic stem cells: toward a unified theory of tissue regeneration," *Scientific World Journal*, April 10, 2002, p. 983.

Commenting on a study by researchers at New York University, Yale and Johns Hopkins:

"There is a cell in the bone marrow that can serve as the stem cell for most, if not all, of the organs in the body,' says Neil Theise, M.D., Associate Professor of Pathology at NYU School of Medicine... '(t)his study provides the strongest evidence yet that the adult body harbors stem cells that are as flexible as embryonic stem cells'."

- "Researchers Discover the Ultimate Adult Stem Cell," *ScienceDaily Magazine*, May 4, 2001, www.sciencedaily.com/releases/2001/05/010504082859.htm

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"Umbilical cords discarded after birth may offer a vast new source of repair material for fixing brains damaged by strokes and other ills, free of the ethical concerns surrounding the use of fetal tissue, researchers said Sunday."

- "Umbilical cords could repair brains," Associated Press, February 19, 2001, available at www.intelihealth.com/IH/ihtIH/WSIHW000/333/7228/311894.html

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"[O]rgan-specific adult stem cells appear to display much more plasticity than originally thought. Stem cells isolated from one tissue can differentiate into a variety of unrelated cell types and tissues... These findings raise the exciting possibility of using bone marrow transplantation to treat a wide variety of disorders, such as muscular dystrophies, Parkinson disease, stroke, and hepatic failure."

- E. Kaji and J. Leiden, "Gene and Stem Cell Therapies," *Journal of the American Medical Association*, February 7, 2001, p. 547

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"[S]ince adult bone marrow has recently been found to contain stem cells of previously unrecognized 'plasticity' that are able to form a variety of types of cell -muscle, liver, neural, bone, cartilage, endothelial, and perhaps others -- it may be possible to use marrow stem cells in cytotherapeutic approaches to a wide spectrum of diseases, such as cardiac disorders, muscular dystrophy, liver disease, neurodegenerative conditions, and joint diseases."

- A. Eaves, Book Review of *Hematopoietic Stem Cell Therapy* by E. Ball et al., *New England Journal of Medicine*, February 8, 2001, p. 463

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"Early results suggest that ductal tissue taken from human cadavers can be grown in culture to form functioning [pancreatic] islet cells. Such a source of tissue... could prove better than relying on fetal tissue, and may even lead eventually to autologous pancreatic transplants."

- A. Berger, "Transplanted pancreatic stem cells can reverse diabetes in mice," *British Medical Journal*, 18 March 2000, p. 736

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Using stem cells from the bone marrow of adults and children, researchers have found that they can "become brain cells and liver cell precursors, plus all three kinds of muscle -- heart, skeletal and smooth... Besides skirting the ethical dilemmas surrounding research on embryonic and fetal stem cells, adult cells ... might have another advantage: They may be easier to manage."

- G. Vogel, "Can Old Cells learn New Tricks?", *Science*, February 25, 2000, pp.1418-1419

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"[T]he adult central nervous system, long thought not to contain cells capable of dividing, in fact harbors stem cells. Such cells may help treat Alzheimer's and Parkinson's disease. In addition, ...hematopoietic stem cells from bone marrow may one day provide transplants to replace blood and immune cells."

- P. Hines, B. Purnell, J. Marx, "Stem Cells Branch Out," *Science*, February 25, 2000, p. 1417

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"While Geron (Corp.) has nabbed the early lead in exploiting embryonic and primordial fetal stem cells, almost a dozen other biotech firms are elbowing their way into a crowded field to develop therapies using so-called 'adult' stem cells. Once thought to be less versatile than primordial stem cells because they have already made a commitment to become particular cell types, these cells are now turning out to have greater than expected capabilities. What's more, they pose fewer ethical problems because they can be obtained from sources other than embryos or aborted fetuses. And the companies using them argue that it may require less work to transform them into specialized cells for transplantation."

-E. Marshall, "The Business of Stem Cells," *Science*, February 25, 2000, pp.1418-1419

Commenting on new ways to "regenerate" and transplant patients' own brain cells to treat Parkinson's and other diseases: "What we have is a protocol in which we don't have to harvest 12 or 15 fetuses, we don't have to give immunosuppressant therapy, and we don't have to worry about viral disease transmission."

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- Michel Levesque, director of neurofunctional surgery at Cedars-Sinai Medical Center in Los Angeles, quoted in M. Moran, "For cell transplants, is one brain better than two?", *American Medical News*, May 3, 1999, p. 29

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Adult "precursor" or stem cells "may prove much more useful to medical science" than embryonic cells. "Scientists used to think that such potential for cellular regeneration was present only in embryos -- that, for example, humans had made their lifetime supply of brain cells by age 17. But that canon is steadily eroding... 'I

think we will find these stem cells in any organ that we look,' says Harvard Medical School researcher Evan Y. Snyder."

- L. Johannes, "Adult Stem Cells Have Advantage Battling Disease," *Wall Street Journal*, April 13, 1999, p. B1

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Recent research shows that mesenchymal stem cells in adult bone marrow "can in principle be used to repair bone, cartilage, tendon and many other injured or aged tissues... The cells would be derived in many cases from the patient's own bone marrow and thus present no problem of immune rejection."

- N. Wade, "Discovery Bolsters a Hope for Regeneration," *New York Times*, April 2, 1999, p. A17

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New research suggesting that nerve stem cells "can de-differentiate and reinvent themselves" as blood-producing stem cells "means that the need for fetal cells as a source of stem cells for medical research may soon be eclipsed by the more readily available and less controversial adult stem cells."

- D. Josefson, "Adult stem cells may be redefinable," *British Medical Journal*, 30 Jan. 1999, p. 282

Due to advances in the use of the anti-aging enzyme telomerase, "the ability to rejuvenate specific cells in the body opens up a dazzling array of possibilities. Doctors could grow skin grafts for burn victims using their own skin, insulin-producing cells for diabetics, or muscle tissue for sufferers of muscular dystrophy."

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- R. Larson, "Scientists find new life for old cells," *Washington Times*, Dec. 29, 1998, p. A1

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