

Stem Cell Research

**Stem Cell
Brief History**

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1878: The first attempts were made to fertilize mammalian eggs outside the body

1954: Scientist John Enders receives the Nobel Prize in Medicine for cultivating polio virus in human embryonic kidney cells.

1958: At the Jackson Laboratory in Maine, scientist Leroy Stevens discovers a tumor inside the scrotum of a mouse, and traces the origin of the tumor to a stem cell. He publishes his work on mouse teratocarcinomas (a type of cancer), becoming the first person to identify pluripotent tendencies of these cells.

1959: First animals made by in-vitro fertilization (IVF)

1960: Teratocarcinomas determined to originate from embryonic germ cells in mice. Embryonal carcinoma cells (EC) identified as a kind of stem cell.

1961: Till & McCulloch establish the foundation for stem cell science. Toronto scientists Drs. James Till, a biophysicist, and Ernest McCulloch, a haematologist, published accidental findings in “Radiation Research” that proved the existence of stem cells – cells that can self-renew repeatedly for various uses. Both worked for the Ontario Cancer Institute (OCI) at the time.

1964: Researchers note that a single cell in teratocarcinomas could be isolated and remain undifferentiated in culture. These types of stem cells became known as embryonic carcinoma cells (EC cells)

1968: The first bone marrow transplant (adult stem cells) is successfully used in treatment of SCID (Severe Combined Immunodeficiency).

1974: Congress Bans All Federally Funded Fetal Tissue Research The 93rd Congress implements a ban on nearly all federally funded fetal tissue research until the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research devises guidelines for it.

1974: **National** Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research within the Department of Health, Education, and Welfare to define policy for protection of human subjects during medical and/or scientific experiments.

1975: Ethics Advisory Board Established. Guidelines establish an Ethics Advisory Board for fetal and fetal tissue research that originate from abortions.

1980: President Reagan Kills Ethics Advisory Board. President Ronald Reagan decides not to renew the Ethics Advisory Board’s charter. The EAB had recommended federally funded investigations into the safety of in vitro fertilization using human embryos developed in vitro for no more than 14 days, but a de facto moratorium halts federal funding of human embryo research due to the EAB’s disbanding.



1981: The first isolation of embryonic stem cells in mice is performed by both researcher Gail Martin at the University of California in San Francisco and researchers Martin Evans and M.H. Kaufman at the University of Cambridge, England.

1988: Federal Panel Approves Funding of Embryo Research. Human Fetal Tissue Transplantation Research Panel reopens the question and votes 18-3 to approve the federal funding of embryo research. Despite this level of support for the research, the Department of Health and Human Services accepts the testimony of three conservative dissenters who argue that embryonic research would lead to an increase in abortions, and in response, extends the moratorium on this research.

1988: Biologist James Thomson of the University of Wisconsin-Madison reports in the journal Science the first successful isolation and culturing of human The first successful cord blood stem cell transplant is completed on a young boy with Fanconi's anaemia (a rare genetic disease). Since the boy's relatives are not a positive match for a bone marrow transplant, he receives cord blood from his healthy sister.

1990: President George H.W. Bush Vetos Bill Lifting Moratorium. Congress attempts to override the moratorium through legislation but President George H.W. Bush vetoes the measure.

1991: Natalie Curry, a young girl suffering from a rare blood disorder, has cord blood successfully transplanted to her from the umbilical cord containing stem cells of her infant sister Emily

1993: President Clinton Executive Order Lifts Moratorium. HHS Secretary Donna Shalala lifts the moratorium on federal funding of human embryonic research in accordance with President Bill Clinton's executive order.

1994: President Clinton Reverses Order. A National Institutes of Health human embryonic researcher panel supports the research but thousands of letters urge President Clinton to reverse his earlier decision. He agrees and federal funding of embryonic research is halted.

1995: Dickey-Wicker Amendment. Congress bans the federal funding for research on embryos through the Dickey-Wicker Amendment, named after its sponsors Jay Dickey (R-AR) and Roger Wicker (R-MI). The amendment prohibits the use of federal funds for "the creation of human embryo or embryos for research purposes; or research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero.

1995: For the first time, University of Wisconsin scientists successfully isolate embryonic stem cells in a primate--rhesus monkeys.

1998: James Thomson Isolates Human Embryonic Stem Cells. University of Wisconsin scientist James Thomson isolates human embryonic stem cells and shows their potential to rejuvenate and to specialize into tissues. This discovery also initiates the ethical debate on human embryonic stem cell research because his team derives the stem cells through a process that destroys human embryos.

1999: HHS Legal Opinion OKs Research on hESC Lines. NIH Director Harold Varmus receives a legal opinion from DHHS general council Harriet Rabb. Rabb finds that the Dickey-Wicker amendment does not apply to federal funding for research on embryonic stem cells because the cells do not meet the statutory definition of an embryo. The cells, however, would have to be derived with private funding.



1999: Harold Varmus Appoints Oversight Committee. Harold Varmus appoints an oversight committee to draft guidelines for federally funding embryonic stem cells. The committee includes scientists, clinicians, ethicists, lawyers, patients, and patent advocates.

1999 to 2000: NIH Guidelines and Bush Disapproval. The NIH develops guidelines for funding human embryonic stem cell research, but presidential candidate George W. Bush declares his opposition to the research in a campaign speech, so the NIH remains cautious about entertaining funding proposals until after the presidential election.

2000: Influx of Responses on Proposed Guidelines. Over 50,000 responses had been received on the committee's proposed guidelines.

2000: NIH Guidelines for Research Go Into Effect. NIH Guidelines for Research Using Human Pluripotent Stem Cells are published in the Federal Register over the summer and go into effect. They stipulate: human embryonic stem cells must be derived with private funds from frozen embryos from fertility clinics; they must have been created for fertility treatment purposes; be in excess of the donor's clinical need; and obtained with the consent of the donor. These guidelines also outlawed the federal funding of stem cells derived from embryos created by SCNT, even if the derivation took place with private funds.

2001: Grant Application Review Postponed for Bush Administration. NIH postpones reviewing grant applications for human embryonic stem cell research in order to give the Bush administration time to review HHS policies.

2001: President Bush Prohibits Federal Funding of Human Embryonic Stem Cell Research. President Bush prohibits the federal funding of any research using stem cell lines derived after August 9, 2001, but his policy does not affect research in the private sector or research conducted with state funding. The president claims that more than 60 stem cell lines are available for funding.

2003: April: The International Human Genome Sequencing Consortium announces the completion of the Human Genome Project--the sequencing of the human genome.

2004: February: South Korean scientists Stem Cells: Body's Starting Point Woo Suk Hwang and Shin Yong Moon of Seoul National University announce their creation of embryonic stem cells from cloned human embryos. Their research is published the following month in the prestigious peer-reviewed Science journal.

2004: May: Britain opens up the world's first government-financed stem cell bank containing embryonic and stem cell lines.

2004: President's Council on Bioethic: "Monitoring Stem Cell Research". The President's Council on Bioethics, chaired by Leon Kass, publishes Monitoring Stem Cell Research, a report that contains "no proposed guidelines and regulations, nor indeed any specific recommendations for public policy." But according to Kass, the overarching goal of the report is "to convey the moral and social importance of the issue at hand and to demonstrate how people of different backgrounds, ethical beliefs, and policy preferences can reason together about it."

2005: National Academies Releases "Guidelines for Human Embryonic Stem Cell Research". The National Academies releases its "Guidelines for Human Embryonic Stem Cell Research." In the news release, committee co-chair Richard O. Hynes explains, "A standard set of requirements for deriving, storing, distributing, and using



embryonic stem cell lines – one to which the entire U.S. scientific community adheres- is the best way for this research to move forward.”

2005: May: South Korean scientists led by Woo Suk Hwang of South Korea report their creation of 11 new stem cell lines.

2005: President’s Council on Bioethics: “Alternative Sources of Pluripotent Stem Cells”. The President’s Council on Bioethics releases a white paper titled “Alternative Sources of Pluripotent Stem Cells”

2006: January: Experts from Seoul National University announce that Woo Suk Hwang's 2004 and 2005 research results are fraudulent. The journal Science withdraws both of Hwang's papers. Hwang resigns from the university and faces criminal investigation.

2006: July: President Bush exercises his first presidential veto against legislation expanding federal funding for stem cell research. Bush explains his actions by stating, "If this bill would have 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."

2006: August: The Advanced Cell Technology Company reports successfully removing a cell from a human embryo and extracting stem cell lines, without harming the embryo. However, their assertion of not harming the embryo is later disproved.

2006: ISSCR Guidelines. The International Society for Stem Cell Research releases its “Guidelines for the Conduct of Human Embryonic Stem Cell Research.”

2007: New NAS Guidelines. The National Academies releases the 2007 amendments for its guidelines.

2007: President Bush Calls for Work on Alternate Sources. President Bush issues an executive order calling upon the HHS secretary to support and encourage research on alternative sources of pluripotent stem cells. He also requests that the Human Embryonic Stem Cell Registry be renamed the Human Pluripotent Stem Cell Registry.

2007: Yamanaka and Thomson Independently Derive iPS Cells. Shinya Yamanaka of Kyoto University and James Thomson of the University of Wisconsin-Madison both publish papers on their separate discoveries of induced pluripotent stem cells. These pluripotent cells were created from skin cells that had four genes inserted into them with viruses. This procedure resulted in the skin cells acquiring properties similar to embryonic stem cells. Researchers were able to coax these so-called iPS cells into becoming beating heart cells and nerve cells.

2008: Report: Only 16 of 21 Lines Eligible for Federally Funding Were Ethically Derived. Robert Streiffer, a bioethicist at the University of Wisconsin-Madison, publishes a paper detailing his investigation into the consent forms for the federally approved human embryonic stem cell lines. Although 21 lines were viable at the time, he discovers that no more than 16 are both viable and ethically derived.

2008: NAS Release New Guidelines. The National Academies releases the 2008 amendments for its guidelines.

2008: ISSCR Releases Guidelines for Clinical Translation. The International Society for Stem Cell Research releases its new Guidelines for the Clinical Translation of Stem Cells



2009: New Administration Begins. Barack Obama is sworn in as the 44th president of the United States, having promised to change the current restrictions on human embryonic stem cell research.

2009: President Obama Reverses George W. Bush's 2001 Executive Order. President Obama Issues Executive Order: Removing Barriers to Responsible Scientific Research Involving Human Stem Cells

2010: Geron Initiates Clinical Trial of Human Embryonic Stem Cell-Based Therapy. Geron Corporation announced the enrollment of the first patient in the company's clinical trial of human embryonic stem cell (hESC)-derived oligodendrocyte progenitor cells, GRNOPC1.

2010: Advanced Cell Technology Wins FDA Approval to Test Stem Cell Therapy For Degenerative Eye Disease. Regenerative medicine company, Advanced Cell Technology received federal approval from the US FDA to begin a multi-centre clinical trial that tests human embryonic stem cell treatment on patients with Stargardt's Macular Dystrophy, a disease that causes blindness.

2011: Stem cell pioneer Ernest McCulloch dies. Ernest McCulloch, who was part of the team that first proved the existence of stem cells, died at the age of 84 just days before a celebration to mark the 50th anniversary of the discovery. The cause of death is unknown. McCulloch was born in Toronto and worked as a lead researcher at the Ontario Cancer Institute and the Institute of Medical Science at the University of Toronto.

2011: Vatican hosts adult stem cell conference. An international conference opens in Rome Wednesday devoted to medical applications of adult stem cells. "We see tremendous potential in these cells," says Vatican spokesman Tomasz Trafny, in a phone interview.