

CRS Report for Congress

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Stem Cell Research

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Summary

Recent actions by the Department of Health and Human Services (HHS) and the National Institutes of Health (NIH) involving human embryonic stem cell research have rekindled debate over the difficult ethical and social issues surrounding embryo and fetal tissue research. Embryonic stem cells, which have the ability to develop into virtually any cell in the body, may have the potential to treat medical conditions such as diabetes, Parkinson's disease, and cancer. Following an HHS determination that the current ban on federal funding of human embryo research does not prohibit funding human embryonic stem cell research, NIH published guidelines for the support of such research in the *Federal Register* on August 25, 2000. However, some Members strongly disagree with the HHS decision and believe such research is banned by the rider that has been attached to each Labor, Health and Human Services and Education appropriations bill since 1995. This report, which will be updated as needed, discusses the status of research and key issues associated with human embryonic stem cells.

Embryonic Stem Cell Research and Potential Applications

Although most cells within an animal or human being are committed to fulfilling a single function in an organ like the skin or heart, a unique and important set of cells exists which is not so specialized. These *stem cells* – cells which retain the ability to become many or all of the different cell types in the body – play a critical role in repairing organs and body tissues throughout life. Although the term “stem cells” usually refers to these repair cells within an adult organism, a more fundamental variety of stem cells is found in the early stage embryo. These embryonic stem cells have a greater ability to become different types of body cells than adult stem cells. The earliest embryonic stem cells are referred to as *totipotent*, indicating that they can develop into an entire organism because they can produce both the embryo and the tissues required to support it in the uterus. Later in development, embryonic stem cells lose the ability to form these supporting tissues, but are still able to develop into almost any cell type found in the body. These *pluripotent* embryonic stem cells are the current focus of intense research interest.

Embryonic stem cells were first isolated from mice in 1981 and until recently, scientists have used only animal embryonic stem cells in research. In November 1998, two groups published the results of their work on human stem cells from embryos or fetuses.

For human development, the term embryo is used for the first 8 weeks after fertilization, and fetus for the 9th week through birth.¹ In both cases, the embryos and fetuses were donated for research purposes following a process of informed consent. University of Wisconsin researchers derived stem cells from 1 week old embryos produced via *in vitro* fertilization (IVF) for the treatment of infertility. Because the stem cells are located within the embryo, the process of removing the cells destroys the embryo. Johns Hopkins University investigators derived cells with very similar properties from 5 to 9 week old embryos or fetuses obtained through elective abortions.

Another potential source of embryonic stem cells is somatic² cell nuclear transfer, the cloning procedure used to produce Dolly, the sheep. Geron Corporation, a Menlo Park, California biotechnology company is currently funding work on stem cells created via this process.³ An alternate approach is the fusion of adult human cells with egg cells of other animals. In 1996, researchers at the University of Massachusetts fused a human cheek cell with a cow egg cell. The resulting hybrid cell had “embryo-like” characteristics and was generated for the purpose of making stem cells. This method is currently being pursued by Advanced Cell Technology Co. of Worcester, MA.⁴ Stem cells obtained from adult organisms are also the focus of research. However, some scientists believe adult stem cells should not be considered as an alternative to embryonic stem cells because of important scientific and technical limitations.⁵

Stem cell research was chosen by *Science* magazine in 1999 as its “breakthrough of the year.” Stem cells provide the opportunity to study the growth and differentiation of individual cells. Understanding these processes could provide insights into the causes of birth defects, genetic abnormalities, and other disease states. If normal development were better understood, it might be possible to prevent or correct some of these conditions. Stem cells could be used to produce large amounts of one cell type to test new drugs for effectiveness and chemicals for toxicity. Stem cells might be transplanted into the body to treat disease or injury (e.g., spinal cord). The damaging side effects of medical treatments might be repaired with stem cell treatment. For example, cancer chemotherapy destroys immune cells in patients making it difficult to fight off a broad range of diseases; correcting this adverse effect would be a major advance. Before stem cells can be applied to human medical problems, substantial advances in basic cell biology and clinical technique are required. The potential benefits mentioned previously are likely only after many more years of research. Technical hurdles include developing the ability to control the differentiation of stem cells into a desired cell type (like a heart or nerve cell), and, if stem cells are to be used for transplantation, the problem of immune rejection must also be overcome.

¹ In contrast, HHS regulations define fetus as “the product of conception from the time of implantation.” (45 CFR 46.203)

² A somatic cell is a body cell, as opposed to a germ cell, which is an egg or sperm cell.

³ Weiss, Rick. Embryo Work Raises Specter of Human Harvesting. *The Washington Post*, June 14, 1999. p. A01.

⁴ Hall, Stephen S. The Recycled Generation. *The New York Times Magazine*, January 30, 2000. p. 30-35, 46, 74, 78-79.

⁵ Adult stem cells may not be as versatile in developing into various types of tissue as embryonic stem cells, and the location of the cells in the body might rule out safe and easy access.

Federal Funding of Research

To date, no federal funds have been used to support research on stem cells derived from either human embryos or fetal tissue obtained from abortions. The work at the University of Wisconsin and Johns Hopkins University was supported by private funding from Geron Corporation. Private funding for experiments involving embryos was required because Congress has attached a rider to the Labor, Health and Human Services and Education appropriations bill each year since FY1996 which prohibits HHS from using appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. This prohibition has been attached to subsequent appropriations bills through the current fiscal year.⁶ There is no similar federal prohibition on fetal tissue research; however, other restrictions do apply (see below).

Following the November 1998 announcement on the derivation of human embryonic stem cells, NIH requested a legal opinion from HHS on whether federal funds could be used to support research on human stem cells derived from embryos or fetal tissue. The January 15, 1999, response from HHS General Counsel Harriet Rabb found that current law prohibiting the use of HHS appropriations for human embryo research (the above mentioned rider) would not apply to research using human stem cells “because such cells are not a human embryo within the statutory definition.” The finding was based, in part, on HHS’s determination that the statutory ban on human embryo research defines an embryo as an *organism*. Human pluripotent stem cells are not and cannot develop into an organism; they lack the capacity to become organisms even if they are transferred to a uterus. As a result, HHS maintained that NIH could support research which uses stem cells but could not support research which derives stem cells from embryos.

Regarding research using stem cells derived from fetal tissue, HHS found that to the extent human stem cells are legally considered fetal tissue, they would be subject to certain other restrictions which safeguard against the inappropriate use of fetuses. For example, the statutory ban on sale for valuable consideration prohibits researchers with federal support from paying for the tissue, except reasonable payments associated with transportation, implantation, processing, preservation, quality control or storage of the tissue or cells. Other restrictions include the criminal prohibition on the directed donation of fetal tissue and the restrictions on fetal tissue transplantation research conducted or

⁶ The current rider, Section 510 of the FY2000 Labor, HHS and Education Appropriation in P.L. 106-113, prohibits HHS from using FY2000 appropriated funds for “(1) the creation of a human embryo or embryos for research purposes; or (2) 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 under 45 CFR 46.208(a)(2) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)).” The term “human embryo or embryos includes any organism, not protected as a human subject under 45 CFR 46 ... [the Human Subject Protection regulations] that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes [sperm or egg] or human diploid cells [cells that have two sets of chromosomes, such as somatic cells].”

funded by HHS.⁷ In addition, such research may be conducted only in accordance with applicable state or local law.⁸

Shortly after the opinion by the HHS General Counsel, NIH disclosed that the agency planned to fund research on pluripotent stem cells derived from human embryos and fetal tissue once appropriate guidelines were developed and an oversight committee established. NIH Director Harold Varmus appointed a working group which began drafting guidelines in April 1999. Draft guidelines were published in the *Federal Register* on December 2, 1999. About 50,000 comments were received during the public comment period which ended February 22, 2000. On August 23 NIH released final guidelines on the support of human embryonic and fetal stem cell research; *Federal Register* publication occurred on August 25, 2000. NIH began accepting grant applications for research projects utilizing human stem cells immediately. All such applications will be reviewed by the new NIH Human Pluripotent Stem Cell Review Group which was established to ensure compliance with the guidelines. Applications will also undergo the normal NIH peer-review process. The first grants are expected to be awarded in mid 2001.

The NIH guidelines prohibit funding for the derivation of human stem cells from embryos remaining after infertility treatment; this is currently prohibited by the previously mentioned appropriation rider. In this respect, the NIH is more restrictive than other groups such as the National Bioethics Advisory Commission (NBAC)⁹ and an expert British panel¹⁰ which both recommended support for the derivation of stem cells from such embryos. The NIH guidelines allow funding of research to derive stem cells from fetal tissue, as well as research utilizing such stem cells; this is in agreement with NBAC recommendations and current law. Other areas of research ineligible for NIH funding under the guidelines include: (1) research in which human stem cells are utilized to create

⁷ The NIH Revitalization Act of 1993 (P.L. 103-43) allows federal support of human fetal tissue transplantation research using tissue from induced abortions under certain conditions only if the transplantation is for *therapeutic purposes*. The Act contains several provisions intended to decouple the decision to have the abortion from the choice to donate the tissue for transplantation and to insulate the decision from financial considerations.

⁸ See 45 CFR 46.210. Nine states ban embryo research entirely; the bans apply even to researchers receiving federal funds who used embryos as a source of stem cells. Sixteen states ban the sale of parts of embryos or fetuses, which might prevent the commercial use of stem cells from embryos. From: Andrews, Lori B. Legal, Ethical and Social Concerns in the Debate over Stem Cell Research. *Chronicle of Higher Education*, v. 45, January 29, 1999. p. B4-B5.

⁹ The September 1999 NBAC report, Ethical Issues in Human Stem Cell Research, can be found at [<http://www.bioethics.gov>]. NBAC was established by Executive Order 12975 on October 3, 1995; a September 16, 1999 executive order extended the NBAC charter until October 2001. NBAC makes recommendations to the National Science and Technology Council on bioethical issues arising from research on human biology and behavior. The commission has already completed reports on human cloning, the use of human biological materials, and treating persons with mental disorders. On November 14, 1998, President Clinton requested NBAC to conduct a review of the issues associated with stem cell research.

¹⁰ The British report "Stem Cell Research: Medical Progress With Responsibility," was released along with nine recommendations on August 16, 2000. Full text of the report can be found at: [<http://www.doh.gov.uk/cegc/stemcellreport.htm>]. On December 19, 2000, the House of Commons voted (366-174) to allow stem cell research using embryos up to 14 days old.

or contribute to a human embryo; (2) research in which human stem cells are combined with an animal embryo; (3) research in which human stem cells are used for reproductive cloning of a human; (4) research in which human stem cells are *derived* using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg; (5) research *utilizing* human stem cells that were derived using somatic cell nuclear transfer; and (6) research utilizing stem cells that were derived from human embryos created for research purposes, rather than for infertility treatment. The NBAC report is silent on areas 1-3 and in agreement with the guidelines on areas 4-6.

Congressional Actions

The January 15, 1999 opinion by HHS General Counsel Harriet Rabb and the decision by NIH to fund human embryonic stem cell research in the near future was strongly opposed by many Members of Congress. In a February 11, 1999 letter from 70 Members to HHS Secretary Donna Shalala, they stated that “any NIH action to initiate funding of such research would violate both the letter and the spirit of the federal law banning federal support for research in which human embryos are harmed or destroyed.” The authors of the letter also objected to HHS General Counsel Rabb’s definition of human embryo: “an entity is an embryo only if one can show that it is capable, if implanted in the womb, of becoming a born human being.” The letter stated that “this narrow definition has no support whatsoever in federal law.” In a February 23, 1999 letter, Secretary of HHS Donna Shalala responded that the definition of embryo used in the HHS opinion “relies on the definition provided in the statute itself.” Secretary Shalala’s letter stated that the federal ban only applies to research in which human embryos are discarded or destroyed but “not to research preceding or following on such projects [in which human embryos are discarded or destroyed]. Moreover, ... there is nothing in the legislative history to suggest that the provision was intended to prohibit funding for research in which embryos – organisms – are not involved.”

The stem cell research issue threatened to hold up passage of the FY2000 Labor, Health and Human Services and Education appropriations bill. In the House, Representative Jay Dickey proposed an amendment to restrict federally funded stem cell research to work on cells derived from fetal tissue. Representative Dickey, the author of the congressional funding ban on embryo research, withdrew his amendment at the request of House leadership who were concerned that controversial amendments might slow down passage of the appropriation bill. In the Senate, the issue held up passage of the FY2000 LHHHS appropriation bill until Senate leadership agreed to drop language endorsing the research and take it up as a separate bill in the second session.

S. 2015 (Specter), introduced on January 31, 2000, would have given NIH authority to fund the derivation of stem cells from surplus IVF embryos, an activity forbidden under the NIH guidelines and prohibited by the appropriation bill rider. In contrast, the bill broadly prohibits support of embryo research unrelated to stem cells. This provision represents a more permanent legislative prohibition than the appropriations rider (which must be renewed each year) banning support of research involving the destruction of human embryos. There was no further action on this bill. On February 2, 2000, **H.Res. 414** (Maloney) was introduced in the House “expressing the sense of the House of Representatives supporting federal funding directed toward human pluripotent stem cell research to further research into Parkinson’s disease and other medical conditions.” On February 4, 2000, a group of 20 Republican Senators reportedly sent a letter to DHHS in

opposition to the proposed NIH guidelines for support of human embryonic stem cell research asserting that such support is contrary to the requirements of the agency's appropriations language. The authors of the letter asked that NIH withdraw the proposed guidelines, and indicated that should the NIH adopt the draft guidelines, further steps might be taken to oppose them, including a possible lawsuit to enforce the federal ban.¹¹

Ethical Issues

The central controversy surrounding human stem cell research is the source of the cells. The debate primarily arises from differences in deeply held religious and philosophic views. For most who believe that the embryo is a human being from the moment of fertilization, the derivation of stem cells from either very early or pre-implantation embryos created by IVF or from the tissues of aborted fetuses is ethically unacceptable. From this viewpoint, even though the proposed guidelines do not support activities which *directly* destroy embryos, support of research on components of the embryo would tacitly endorse such destruction. Supporters of this view argue therefore that the guidelines would violate federal bans on human embryo research. From this perspective, the possible benefits of stem cell research cannot and should not justify the actions necessary to obtain the cells. Opponents of stem cell research propose that research on *adult* stem cells, which they claim could provide similar therapeutic benefits without the need for fetal cells, be supported instead. Not all scientists agree, however, that adult stem cells hold as much potential as embryonic stem cells.

Those who support embryonic stem cell research believe that pre-implantation embryos do not have the same moral and legal status as persons. They acknowledge that embryos are genetically human, but hold that they do not have the same moral relevance because they lack specific capacities, including consciousness, reasoning and sentience.¹² The NBAC received testimony from witnesses of many religious traditions that were open to the use of early embryos (remaining from infertility treatments) for stem cell research as well as many who were opposed. "Jewish and Islamic ethicists supported stem cell research while Protestant and Catholics were mixed. ...[W]hile the early human embryo is worthy of respect, it ought not to be given personal moral status until there has been sufficient development of the embryo."¹³ Supporters argue that the potential human health and scientific benefits the research holds should be an ethical argument for its support. Patient groups have also asserted that, because of the potential of human stem cells for the treatment of disease, it is immoral to discourage such research because it could save many lives. In addition, supporters believe that the oversight which would come with federal grant support would result in better and more ethically controlled research in the field than if funding was from private sources alone. Supporters also argue that the efforts of both federally supported and private researchers are necessary to keep the United States at the forefront of what they believe is a very important, cutting edge area of science.

¹¹ Brainard, Jeffrey. 20 GOP Senators Urge NIH Not to Finance Stem-Cell Research. *The Chronicle of Higher Education*, February 25, 2000. p. A40.

¹² Presentation by Steinbock, B., Department of Philosophy, SUNY, Albany, New York. NIH Human Embryo Research Panel Meeting. February 3, 1994.

¹³ Wildes, Kevin W. The Stem Cell Report. *America*, October 16, 1999. p. 12-14.