BIOETHICS AND THE STEM CELL RESEARCH DEBATE

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Since its birth in the 1970s, bioethics—the study of ethical issues in science and medicine—has grown to become a significant academic and service-oriented discipline with its own research centers, conferences, journals, and degree programs. As these issues have moved to the center of public debate, the law has assumed an increasingly important place in the discipline of bioethics.

The growing importance of the law as a forum for the debate and mediation of bioethical issues is apparent on several fronts. In the United States Supreme Court, bioethical issues have been central to key reproductive privacy cases, from the Court's 1973 decision in Roe v. Wade, 410 U.S. 113, to its 2000 decision in Stenberg v. Carkart, 530 U.S. 914, which struck down a controversial Nebraska partial-birth abortion law. In state courts, bioethical considerations inform judges' balancing of patient health care confidentiality with a "duty to warn" of potentially dangerous patient behavior (see, for example, the California Supreme Court's landmark 1976 decision, Tarasoff v. Regents of the University of California, 17 Cal. 3d 425). At both the state and federal levels, bioethical debates help shape end-of-life statutes and

court cases, including Cruzan v. Missouri Dept. of Health, 497 U.S. 261 (1990), in which the U.S. Supreme Court upheld the State of Missouri's requirement for clear and convincing evidence that a person in a persistent vegetative state had expressed a wish not to be kept alive by life-sustaining equipment.

Today, embryonic stem cell research stands out as a critically important issue about which we have neither ethical consensus nor clear, comprehensive regulation. The ethical debate centers on the fact that stem cell research involves the destruction of very early human embryos. On the federal level, funding for stem cell research has been limited to research using stem cells derived from a limited number of stem cell "lines." On the state level, approaches range from legislative restrictions on stem cell research to the State of California's plan to provide $3 billion in stem cell research funding through the voter-approved California Institute for Regenerative Medicine.

4 In order for potentially revolutionary stem cell research to progress, scientists' long-term needs must be effectively coordinated with appropriate and effective ethical and legal guidance. This article provides brief scientific background and then discussion of key ethical and legal/regulatory issues that surround embryonic stem cell research.

Background

Embryonic stem cells are precursor cells that have the capacity to divide for indefinite periods of time in culture and to give rise to virtually any type of specialized cells in the body. They are derived from the inner cell mass of a 100-cell blastocyst—a very early embryo, usually only 3–4 days old—long before the cells have started to specialize to create a nervous system, spine and other features that, with further development, would transform the embryo into a fetus. Typically, these cells are derived from embryos that originally were created for infertility treatment purposes through in vitro fertilization, but that are no longer desired or needed by the infertile couple for treatment. The extraction of the stem cells from the blastocyst necessarily requires the destruction of that blastocyst.

Because embryonic stem cells are capable of self-renewal and can differentiate into a wide variety of cell types, potential applications of embryonic stem cell research are far-reaching. For example, embryonic stem cell research holds out great promise to those suffering from Type I diabetes. Type I diabetes is an autoimmune disease characterized by destruction of insulin-producing cells in the pancreas. Some of the current efforts to treat these patients use donated human pancreases for transplantation of islets—clusters of cells on the pancreas that produce insulin—in an effort to restore the insulin-secreting function. Islet transplantation efforts are limited by the small numbers of available donated pancreases, as well as the toxicity of immunosuppressive drug treatments that are required to prevent graft rejection. Use of embryonic stem cells that are instructed to differentiate into pancreatic islet cells has the potential to overcome the shortage of effective material to transplant.

Similarly, embryonic stem cell research offers tremendous potential to those suffering from nervous system diseases that result from loss of nerve cells. Since mature cells cannot divide to replace cells that are lost, therapeutic possibilities do not exist in the absence of a new source of functioning nerve tissue. Conceivably, however, with embryonic stem cell research, nerve cells that make the chemical dopamine

could be created for individuals with Parkinson's disease, cells responsible for the production of certain neuro-transmitters could be reconstituted for individuals with Alzheimer's, the motor cells that activate muscles could be replaced for ALS patients, and glia (cells that perform numerous functions within the human nervous system) could be formed for individuals with multiple sclerosis.

In addition to these promising therapeutic applications of embryonic stem cell research, such research also could provide new insights into how human beings, organs and tissues develop. It also has the potential to substantially change the development and testing of pharmaceutical products. New medications could be tested initially on cells or tissues developed from embryonic stem cells, and only those drugs initially found to be safe and effective would be tested further on animals and humans.

Ethical Issues

Notwithstanding the promise of embryonic stem cells, several ethical issues have made stem cell research controversial. The most vexing ethical issues surrounding embryonic stem cell research, which focus on the moral status of the very early embryo, arise from the fact that isolating embryonic stem cells requires destruction of the embryo.

Some who condemn embryonic stem cell research believe that the embryo is a full person or human subject, with full rights and interests from the moment of conception. Others take a developmental view of personhood, believing that the embryo only gradually becomes a full human being and that the very early embryo is not entitled to the same moral protections to which it would be entitled at a later developmental stage. Still others hold that while the embryo represents human life, such life is not a "person" at any time prior to birth.

The role of science in deciding the difficult ethical question of the moral status of the very early embryo is unresolved. Key issues in deciding this question include the following:

- How significant is it that at less than 14 days a blastocyst has no neural tissue? Some contend that this fact makes derivation of stem cells from a blastocyst prior to this developmental stage no different than allowing organ donation at the point of brain death.
- Is it ethically significant that until formation of the primitive streak at 14 days, a blastocyst can undergo complete fission to form an identical twin? One commentator contends that since "individuality is a sine qua non for personhood, it seems safe to consider 14 days of normal embryonic development to be the minimum requirement for a human being to emerge."
- Is the argument for the protection of the "potential" for human life affected by scientific assertions that an embryo does not have such potential unless it is implanted in a uterus?
- Is it ethically significant that a blastocyst created by somatic cell nuclear transfer, if implanted, would be extremely unlikely to develop into a human being? As one commentator notes, "cytoplasmic factors would have to act on an adult nucleus to produce the same patterns of gene activation that are critical for early embryonic development."

Legal Issues

12 Federal and state legislatures have begun to grapple with the ethical questions involved in stem cell research, but to date, there is no comprehensive or consistent regulation of stem cell research in the United States. Since 1996, riders to federal appropriations language (known as the "Dickey Amendment") have prohibited use of federal funds for "the creation of a human embryo or embryos for research purposes," as well as "research in which a human embryo or embryos are destroyed, disabled or knowingly subjected to a risk of injury or death greater than allowed for research on fetuses in utero . . ." In January 1999, however, the General Counsel of the Department of Health and Human Services (HHS) determined that federal law does not prohibit public funding of embryonic stem cell research as long as the research to be funded does not include derivation of the stem cells from the embryo (and, therefore, destruction of the embryo). In other words, cells could be derived from embryos destroyed in private labs with private money, and then shipped to federally funded scientists for study.

Following this legal clearance from HHS, the director of the National Institutes of Health (NIH) convened a 13-member working group to draw up guidelines for research using embryonic stem cells. This group's guidelines, which became effective August 2000, state that research involving embryonic stem cells is acceptable as long as

- the stem cells come from spare embryos that were originally created through in vitro fertilization for infertility treatment purposes,
- the embryos have not reached the developmental state at which the mesoderm is formed,
- the researcher is not involved in the infertility treatment for which the embryos were created and has not played any role in the donors' decision to donate the embryos for research,
- there is no directed donation of embryos for the derivation of stem cells for eventual use in transplantation, and
- the stem cells are not added to human or animal eggs or embryos via somatic cell nuclear transfer.

On August 9, 2001, however, President Bush effectively suspended the NIH 2000 guidelines. He announced that federal funding for embryonic stem cell research would be available only under the following conditions:

- the stem cells are derived from stem cell lines existing as of August 9, 2001,
- the lines were derived with proper informed consent of the embryo donors,
- the embryos used were originally created through in vitro fertilization for infertility treatment purposes, and
- there were no financial inducements made to the embryo donors.
- No federal funds may be used for derivation or use of stem cells derived from newly destroyed embryos, creation of human embryos for research purposes, or cloning of human embryos for any purpose.

Many contend that the president's restrictions on federal funding of embryonic stem cell research are inhibiting the ability to unlock the potential of embryonic stem cells. One concern relates to recently discovered chromosomal rearrangements in embryonic stem cells over time, which suggest that the federally approved lines may have limited therapeutic potential. Additional concerns relate to the limited number and the narrow racial diversity of the federally approved stem cell lines.

16 Moreover, in addition to the federal funding restrictions, embryonic stem cell research is also subject to some restrictive state laws. While California is providing government funding for stem cell research through the California Institute for Regenerative Medicine, and New Jersey, Massachusetts, Illinois, Wisconsin, and Texas are considering funding measures, other states—including Iowa, Louisiana, Michigan, Arkansas, Nebraska, North Dakota, South Dakota, and Virginia—have laws that limit embryonic stem cell research.

On the other hand, stem cells, as well as their derivation and their uses, are eligible for federal patent protections. In fact, a number of patents relating to human embryonic stem cells have been filed—the most fundamental of which are the "Thomson" patents, named after the University of Wisconsin researcher who led a group that developed the technique for isolating and growing human embryonic stem cells. Thomson patents relate to the methods of deriving and maintaining human embryonic stem cells in vitro, and the products of those methods. These patents were assigned by the inventors to the Wisconsin Alumni Research Foundation, which exclusively licensed their commercial applications within certain fields of use to Geron Corporation, and made licenses to practice under the patent rights for research purposes available through a non-profit corporation.

Some have questioned the ethical acceptability of patenting embryonic stem cells. For example, one commentator has questioned whether the federal government's opposition to direct federal funding of post-August 2001 stem cell lines is consistent with its sanction of exclusive property rights in such lines, since these patent-protected rights can create "indirect research funding" through rewarding market investments. However, such qualms collide with the United States Supreme Court's declaration that "everything under the sun" isolated or manipulated by humanity may be patented and that patent law is not intended to displace the police powers of the states with respect to safety, health and morality. Ironically, then, the current federal position is to allow sensitive ethical questions on stem cell research to be decided by the marketplace, with private money developing products that receive patent protection without the regulatory oversight that would apply to federally funded research.

Conclusion

Stem cell research has emerged as a potential political issue that could play a role in the 2006 mid-term elections and beyond. In his 2006 State of the Union speech, President Bush called upon Congress "to pass legislation to prohibit the most

egregious abuses of medical research," including "human cloning in all its forms." Some commentators have criticized this statement for failing to distinguish between human reproductive cloning, which most experts oppose, and therapeutic cloning, in which cloning techniques are used to produce blastocysts for stem cell extraction, not embryos for implantation. In Congress, there are signs of division in the Republican majority on the question of stem cell research. A bill easing current federal restrictions on stem cell research passed the Republican-controlled House of Representatives in 2005 but stalled in the Senate, which is scheduled to take up the bill sometime in 2006. Several key senators, including Senate Majority Leader Bill Frist (R-Tenn.), have spoken in support of the bill.

20 In the meantime, there is no consensus concerning ethical questions surrounding embryonic stem cell research. Continued careful attention to ethical review of the issues that surround this promising research, and consistent incorporation of such analysis into evolving laws and regulations, will assure the appropriate and effective use of this emerging knowledge.