Human Embryonic Stem Cell Research

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INTRODUCTION

The American Thoracic Society (ATS) is an organization dedicated to serving patients with lung disease through research, advocacy, training, and patient care. As such, it supports making federal funding available for research using human embryonic stem cells with appropriate guidelines and federal and institutional oversight. Research on stem cells is increasing our understanding about how organs develop normally from single cells and also about how healthy cells can replace those that are damaged by disease. This very new area of scientific investigation is particularly exciting because of the possibility that it may lead to the use of cell-regenerative therapies to treat human diseases (1, 2), including several forms of lung disease. Use of stem cells in research may benefit patients with lung diseases in several ways. These potential benefits include improving our understanding of developmental and genetic lung diseases as well as of a wide range of adult lung diseases, including asthma, emphysema, lung cancer, fibrotic lung disorders, and adult respiratory distress syndrome (ARDS) (3). This greater understanding, in turn, could offer one of the most hopeful and exciting new avenues for treatment of these disorders. At the same time, it is important to recognize that there are many scientific and ethical barriers that must be overcome before this technology can be translated into clinically useful treatments for patients.

Embryonic stem cells are unique in their ability to renew themselves indefinitely by producing identical cells. In addition, under certain physiologic or experimental conditions, they can be induced to give rise to many different types of cells, each with specialized functions (1, 2). In 1998, Thomson and colleagues discovered how to isolate such pluripotent embryonic stem cells from human embryos in culture (4). The embryos used in these experiments were created originally for use in *in vitro* fertilization (IVF). They existed only in the culture dish and each contained about 20–100 cells. When they were no longer needed for IVF, they were donated for research with the informed consent of the donors. Cells isolated from these embryos, when grown in culture, become pluripotent embryonic stem cells that reproduce indefinitely and are capable of forming many of the specialized cell types of the body. These cells have the potential for use in the treatment of life-threatening lung diseases, such as emphysema, interstitial lung diseases, asthma, lung cancer, and ARDS, as well as Parkinson's and Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis, through their ability to generate replacement tissue for damaged cells or organs.

In addition to embryonic stem cells, there are populations of cells in adult tissues, often referred to as "adult stem cells," that appear important for normal tissue maintenance as well as for repair after injury. In the lung, current evidence suggests that such cells may participate in repair and re-growth after injury and may originate from within the lung itself or from distant sites such as the bone marrow (5). While it is possible that such cells ultimately will be useful as alternatives to embryonic stem cells to prevent or treat lung disease, the therapeutic potential of adult stem cells for use in patients with lung diseases is not known (5). Furthermore, as compared with adult stem cells, pluripotent embryonic stem cells have a higher growth potential, can differentiate into many different types of specialized cells of adult tissues, and thus are an especially promising potential source of reparative cells for patients with lung diseases. Strong encouragement should be given to further investigations aimed at identifying adult stem cells in the lung and at understanding the role of nonlung stem cells in lung repair. However, these approaches should neither distract from nor preempt research for which the goal is to assess the use of pluripotent embryonic stem cells for the treatment of lung diseases.

An important new source of embryonic stem cells is through use of a technique called somatic cell nuclear transfer, also referred to a therapeutic cloning (6). In this technique, nuclei from the cells of living patients with specific diseases are isolated and used for the generation of embryonic stem cells. This is achieved by placing one such nucleus into a donated unfertilized egg from which the genetic material has been removed and then stimulating the egg to divide to the stage when stem cells can be derived in culture. These cells can then be induced to develop in the laboratory into specialized cells such as nerve cells that are affected by the disease in question. In the future, by watching what happens to these cells, and how they differ from normal cells over time, scientists can learn about the pathogenesis of the disease and about interventions that may be used to treat it. In addition, embryonic stem cells derived by this technique ultimately may be useful for cell-based replacement therapy for the original patients from whom they were derived. This is because they are genetically identical to the patient and are not rejected by the immune system. While an important step toward realizing the promise of stem cell research, this approach raises new ethical and regulatory issues that must be addressed carefully (7).

LIMITATIONS OF GEORGE W. BUSH ADMINISTRATION'S POLICY ON HUMAN EMBRYONIC STEM CELL RESEARCH

On August 9, 2001, President Bush announced his decision to restrict the use of federal funds for research on human embryonic stem cells to those cells that had been removed from embryos on or before that date (8). Other criteria established by the policy for federal funding were that:

- the stem cells must have been derived from an embryo that was created for reproductive purposes only;

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- the embryo was no longer needed for these purposes;
- informed consent must have been obtained for the donation of the embryo;
- no financial inducements were provided for donation of the embryo.

This policy has placed extremely serious limitations on embryonic stem cell research in this country. Although it was estimated that 60–80 cell lines would be available, in fact only 22 cell lines produced before the policy announcement are actually useable. All these have been maintained in culture in contact with mouse cells, rendering them inferior to newer cell lines that have been maintained under more pristine conditions (9). It has been estimated that more than 120 new embryonic stem cell lines have been created worldwide since the policy announcement (9). However, U.S. scientists studying these cell lines cannot obtain grant support for their work from the National Institutes of Health (NIH). They must find funding from nonfederal sources that may provide research support that is less predictable than the NIH. Some nonfederal organizations that support lung research are reluctant to fund research involving human embryonic stem cells because of concerns about alienating potential donors. In addition, scientists who do obtain nonfederal funding for human stem cell research must keep all their resources (equipment, technical support, reagents, etc.) completely separate from NIH-funded resources, something that usually requires completely separate laboratories. The study of human embryonic stem cells is in its infancy, and the current policies threaten to starve the field of new trainees entering the field.

Considerable dissatisfaction with the limitations imposed in 2001 has been expressed by the scientific community, including at the National Institutes of Health (10). Senator William Frist has announced his support for expanding the numbers of embryonic stem cell lines available for research using federal funds. Measures to loosen the restrictions have been proposed, and H. R. 810, the Stem Cell Research Enhancement Act, was passed in the House of Representatives with bipartisan support.

ATS STATEMENTS

ATS supports the following principles regarding human embryonic stem cell research to ensure that this field receives adequate federal funding for its growth while still making certain that the research is conducted in a legal and ethical manner:

I. Human embryonic stem cell research is a relatively new technology that offers great potential for providing new insights into the causes of disease and for the development of novel and effective therapies.

II. Though significant scientific advances in the area of human embryonic stem cell research may be possible through use of private and state support, federal funding for human embryonic stem cell research is necessary to continue the very highest quality research in this area, to foster the growth of this important new field of investigation, and to encourage young scientists to enter the field.

III. The ban on the use of federal funds for research using human embryonic stem cells generated after August 9, 2001, should be removed.

IV. Scientists working in this field should be permitted to derive stem cells from embryos that are stored at *in vitro* fertilization (IVF) clinics. In all cases, informed consent must be obtained for the donation of the embryos, financial inducements must not be permitted for donation of the embryos, and there must be a clear separation between the process of informed consent and the scientists doing the research.

V. Federal funds also should be permitted for the creation and use of embryonic stem cell lines by somatic cell nuclear transfer. Again, informed consent must be obtained from the patients from whom the somatic cell nuclei are obtained and from the women donating the eggs, and all other guidelines should be followed. This technology holds promise as a tool for providing increased understanding of many diseases as well as for creating therapeutic cells immunologically compatible with the patients being treated.

VI. The ATS acknowledges and respects the ethical debate surrounding the use of human embryos for research purposes and stands firmly opposed to the use of somatic cell nuclear transfer for the purpose of creating a fetus or for other reproductive purposes.

VII. The ATS supports ongoing efforts to establish guidelines and responsible practice of embryonic stem cell research, such as those being developed by the National Research Council and the Institute of Medicine of the National Academies (11).

This statement was prepared by the ATS Research Advocacy Committee.

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