ENDOCRINE SOCIETY
Hormone Science to Health

POSITION STATEMENT

STEM CELL RESEARCH

INTRODUCTION

Regenerative therapy using stem cells holds great promise for the treatment of millions of Americans with debilitating and possibly fatal diseases, including diabetes and other endocrine disorders. Although recent scientific advances have raised the profile of stem cell research and its contributions to regenerative medicine, major policy barriers remain that prevent progress in this promising area of biomedical research.

BACKGROUND

Stem cells have three important characteristics that distinguish them from other types of cells. First, they can self-renew for long periods through cell division. Second, they are unspecialized, meaning that they do not have the ability to perform tissue-specific functions. Finally, they can be induced to become cells with special functions, such as insulin-producing cells of the pancreas or the beating cells of the heart. Stem cells may be pluripotent, meaning that they are able to become any of the cell types that make up the body. Embryonic stem cells may also be totipotent, which means that they can form all cell types in a body including extraembryonic, or placental cells.

Naturally occurring stem cells are often defined by the developmental stage at which they are found. **Embryonic stem cells (ESCs)** come from a blastocyst (a ball of cells formed about 4 days after an egg is fertilized). These ESCs give rise to all of the cells of the developing body. Many years of detailed study of the biology of mouse ESCs led to the discovery, in 1998, of how to isolate stem cells from human embryos and grow human ESC lines in the laboratory. The embryos used in these studies were generated through in vitro fertilization for the treatment of infertile couples. Extra or non-viable embryos that were no longer needed for fertility purposes were then donated for research with the informed, written consent of the donors.

ESCs are not the only stem cells. **Adult or tissue stem cells** are present in individual organs of adults or children. These cells were discovered after extensive work on ESCs shed light on common characteristics of stem cells, allowing researchers to isolate stem cells from adult tissues where they serve to replenish dying cells of that organ throughout life.

To understand the significance of the embryonic versus adult stem cells, it is important to consider the cells in the context of what they can and cannot do. ESCs are totipotent, giving rise to any cell type present in the adult body. ESCs are easy to isolate because they are relatively abundant in the blastocyst. On the other hand, most naturally occurring adult stem cells are multipotent, giving rise to the multiple cells of the organ they reside in but not to cells of other organs. However, recent research has shown that some adult stem cells are more malleable than originally thought. Adult stem cells are more difficult to isolate because they are rare, comprising a very small percentage of cells in the adult tissue.

In the past decade, a Nobel Prize-winning discovery has enabled researchers to transform adult cells (e.g., from skin or blood) into cells with properties similar to those of ESCs. These induced pluripotent stem cells, or iPSCs, are now being used for potential applications in humans.

Another way to generate pluripotent ESCs is by injecting the nucleus (containing the cell's DNA and certain proteins of a non-stem cell into an unfertilized egg from which the nucleus has been removed. This process, called somatic cell nuclear transfer (SCNT), results in ESCs in which all the nuclear DNA are matched to those of the original non-stem cell. By introducing DNA from cells with disease-causing mutations, this technique allows for the generation of cells that scientists can study for disease progression and cures. SCNT is often referred to as therapeutic cloning because of the potential it has for fighting disease in patients. SCNT is a potentially powerful tool in research as well, for instance it is the only method by which scientists can tell if a developmental process depends on a nuclear component or non-nuclear feature.

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POLICY BACKGROUND

In the past 20 years, there have been several federal policies developed and implemented that have affected stem cell research. Under President George W. Bush, federally-funded human ESC research was limited to ESC lines derived no later than 9 p.m. EDT August 9, 2001; from embryos created for reproductive purposes; from embryos no longer needed for these purposes; with informed consent for the donation of the embryos; and without financial inducements provided for donation of the embryos. On March 9, 2009, President Obama signed Executive Order 13505 overturning the temporal restriction in the Bush policy, allowing for a greater number of cell lines derived from in vitro fertilization (IVF) embryos to be qualified for use in federally-funded research. A subsequent court challenge (Sherley V. Sebelius) to Executive Order 13505 was struck down by the District Court for the District of Columbia in 2011, and the US Supreme Court declined to hear the case, effectively leaving the DC Court's decision intact. Recognizing the promise of regenerative medicine, a field driven in part by the use of stem cell-based therapies, in 2016 the United States Congress created opportunities for a more flexible, accelerated approval pathway for certain regenerative therapies in the 21st Century Cures Act.

Although Executive Order 13505 and 21st Century Cures will help advance scientific progress on ESCs, they do not address policies related to funding for research on cell lines derived from sources other than IVF embryos, such as SCNT. The Dickey-Wicker Amendment, for example, prohibits the use of federal funds for the creation of human embryos for research purposes, or for research in which embryos are destroyed. This amendment prohibits not only federal funding of the derivation of human ESC lines, but also the funding of research utilizing parthenotes (unfertilized eggs that have been artificially activated with chemicals so that they divide). This restriction hinders US scientists from exploring the full potential of stem cells and applying related research findings to regenerative therapies, and also limits the ability of scientists to understand the human egg to zygote transition (the stages before and after fertilization or parthenogenic activation), hampering knowledge of a 12-hour period of biology essential to the development of offspring.

CLINICAL OPPORTUNITY

Breakthroughs in stem cell research have the potential to realize immense benefits to patients. Therapeutic cloning utilizing a patient's own cells or genetic material could be used in treating injury and disease without creating a need for patients to commit to a lifetime of immunosuppressive therapy associated with conventional organ donation. Because SCNT, like iPSCs, would generate stem cells containing a patient's precise genetic make-up, the patient's body would not recognize them as foreign and would not reject them. SCNT-derived ESCs could therefore be used for replacement of diseased or damaged tissue or for research into the origin of disease. However, it is important to delineate the differences between SCNT for the purposes of therapeutic cloning, as opposed to reproductive cloning. When SCNT-derived blastocysts are created for research applications and therapeutic cloning, they are not implanted and are thus not allowed to develop beyond the blastocyst stage. In contrast, reproductive cloning, which is largely restricted to livestock, takes the additional step of implanting the SCNT-derived blastocyst in the attempt to generate a new living organism identical in nuclear makeup to the parent organism. Human reproductive cloning is widely viewed as unethical and irresponsible, with significant safety concerns.

In recent years, scientists have explored research opportunities to study developing human tissue and organs in animals through the introduction of human pluripotent stem cells into early stage embryos of non-human vertebrate animals, termed human-animal chimera research. Given the ethical issues associated with such research, the NIH issued a moratorium on the funding of such research in 2015, in order to more fully explore the state of the science and issues associated with this research. In 2016, the NIH proposed revised guidelines on the use of stem cells clarifying that human pluripotent stem cells may only be introduced into non-human primate embryos after the blastocyst stage. The proposed revisions also prohibit "research involving the breeding of animals where the introduction of hESCs or human induced pluripotent stem cells may contribute to the germ line to include any human cells that may result in the formation of human gametes."

POSITIONS

The Endocrine Society supports: 1) NIH funding for regenerative medicine and research using stem cells, inclusive of ESCs, iPSCs, SCNT, and parthenotes, and 2) overturning temporal restrictions in the original Bush (2001) policy.

The Endocrine Society asserts that for the full potential of stem cell research to be reached, the number of stem cell lines readily available to scientists must increase. Transplantation of human tissues such as the pancreas, kidneys, hearts, and bone marrow cells has given years of quality life to many patients. But transplantation requires a lifetime of immunosuppressive therapy, reducing the quality of life for transplant patients. For many specialized cells that may become dysfunctional, such as brain cells, which are lost in patients with Parkinson's disease, stem cells represent the only potential source of tissue for transplant. Furthermore, cell-based therapies using stem cells have shown promise towards generating a functional cure for diabetes. Funding of stem cell research is vital to ensure the progression of medical technology and the health of US citizens.

POSITION STATEMENT

The Endocrine Society recognizes that there are complicated and significant ethical issues surrounding the use of ESCs in research and medical practice. Federal oversight is therefore necessary to ensure adherence to the highest ethical and scientific research standards. For instance, clear boundaries should be developed between therapeutic cloning and reproductive cloning. Additionally, careful oversight should be exercised for research programs that involve human-animal chimera research. We support the guidelines established by NIH to ensure the ethical derivation of human ESCs from donated IVF embryos, and the proposed revisions clarifying the allowable uses of non-human primate embryos. However, the Society encourages the agency to broaden its stance to allow federal funding for research on cells from other sources such as SCNT.

Endocrine Society members recognize the enormous potential of stem cell research in understanding the processes whereby cells differentiate to form new tissues and organs and the potential such work has for improving human health and well-being. At the same time, the Society acknowledges that all research, but especially research involving human ESCs and for cells derived through SCNT, must adhere to the highest ethical and scientific standards. We are also concerned about the potential misuse of unproven and unregulated stem cell therapies. The Endocrine Society therefore supports appropriate public oversight of stem cell research and therapeutic use to assure that such standards are always met.

In summary, the Endocrine Society supports the following positions for research involving human stem cells:

- An increase in NIH funding for stem cell research, consistent with overall increases in the NIH appropriation;
- An increase in the number of human embryonic stem cell lines for NIH-funded research;
- A broadening of the scope and availability of federally-funded research to include parthenotes and stem cells generated through somatic cell nuclear transfer, and from unused IVF embryos;
- The proposed revisions (as of August 4, 2016) to the NIH Guidelines for Human Stem Cell Research involving human-animal chimera research;
- Federal oversight of embryonic stem cell research to ensure that ethical standards are always met.

While the Endocrine Society's positions on this issue represent a majority opinion, we recognize that different views may exist among individual members regarding the ethics and morality of the use of stem cells, particularly those of human embryo origin, in research.