POSITION STATEMENT REGARDING
THE USE OF EMBRYONIC AND
ADULT HUMAN STEM CELLS IN
BIOMEDICAL RESEARCH

October 2004

PREAMBLE

The American Academy of Neurology (AAN) and the American Neurological Association (ANA), organizations representing over 18,000 neurologists and neuroscience professionals, support government funding of basic, clinical, and translational research that will ultimately benefit patients with neurological diseases. The AAN and ANA believe that the use of human pluripotent stem cells (also known as human embryonic stem cells) in biomedical research may have enormous potential to benefit people affected by neurological disease throughout the world. In particular, the research involving such cells could improve the lives of many Americans suffering from neurological diseases, examples of which are ALS (Lou Gehrig’s disease), Alzheimer’s disease, epilepsy, Huntington’s disease, multiple sclerosis, Parkinson’s disease, spinal cord injury, and stroke.

While the potential of embryonic stem cell research to result in breakthrough therapies is real, it is important to recognize that the translation of research into therapy will take many years, and it is also possible that such therapies may not ever be realized. Similarly, while the use of adult stem cells for research is recognized as an alternative to the use of embryonic stem cells, the potential for translating adult stem cell research into therapy is far more uncertain. Nonetheless, the only way to know whether either embryonic or adult stem cell research can result in new therapies is to pursue such research under rigorous scrutiny. To quote the preliminary conclusions of the President’s Council on Bioethics January 2004 report, Monitoring Stem Cell Research, “This research is expensive and technically challenging, and requires scientists willing to take a long perspective in order to discover, through painstaking research, which combinations of techniques could turn out to be successful. Strong financial support, public and private, will be indispensable to achieving success.”

All research, including stem cell research, must meet the standards of scientific and ethical oversight by external peer review. The AAN and ANA promote the highest standards for oversight, which many consider to be that attached to federally funded research. In 2000, the NIH issued Guidelines for Research Involving Human Pluripotent Stem Cells, enabling scientists to conduct federally funded embryonic stem cell research (ESCR) within the constraints of federal oversight and standards. Those guidelines were altered by Presidential order on August 9, 2001, limiting ESCR to stem cell lines that had already been derived at that time. Practical experience since August 2001 demonstrates the scientific restraints that these limits have placed on ESCR in the United States. In fact, as of September 1, 2003, there were only 12 human embryonic stem cell lines that federally supported researchers could purchase. While private stem cell researchers in the United States are free to study the other embryonic stem cell lines, keeping pace with researchers in other countries, they are not subject to federal scientific and ethical scrutiny. Thus, a potential adverse consequence of federal restrictions on funding of ESCR is that the NIH standards for ethical and scientific oversight cannot be enforced on research the federal government does not fund.
Some believe that the process of stem cell research involving somatic cell nuclear transfer (i.e., cloning) cannot be limited to populations of cells to be used for therapeutic purposes, but rather, will lead to reproduction, meaning the cloning or reproduction of a human being. While this outcome is far removed from current scientific knowledge and technical capabilities—it is known that there are serious health problems in animals cloned with these techniques, and all major scientific and professional associations support a ban on reproductive cloning—it remains imperative that research in this field is conducted under the highest scientific standards and ethical safeguards, similar to those applied to ESCR. (A report on the subject of somatic cell nuclear transfer is attached as an appendix.)

The AAN and the ANA recognize and respect the concerns of many of their members and the public regarding important ethical principles and values that pertain to research using human embryonic stem cells. On the one hand is respect for human life and concern about the moral status of the blastocyst (which is simultaneously the earliest form of a human embryo and the source of embryonic stem cells for research) and the fact that the process of obtaining stem cells results in the destruction of the blastocyst. While on the other hand is a strong moral obligation of physicians and scientists to pursue research that may result in beneficial treatments for diseases that affect many persons. In consideration of taking a specific position on the use of human embryonic stem cells for research, the AAN and the ANA recognize that strongly held and disparate views exist, and it is thus unlikely they can satisfy the concerns of all their members or the public.

The AAN and ANA conclude that the potential benefits of research involving human embryonic stem cells are sufficient to continue such research, that it should be conducted with strict oversight, and that the ethical safeguards developed by the NIH respect both the moral status of the embryo and public sensitivity to this issue, while ensuring that progress in critical medical research continues.

---

1 www.bioethics.gov/reports/stemcell/index.html
2 65 FR 51976 and 65 FR 69951; stemcells.nih.gov/news/newsArchives/stemcellguidelines.asp
4 stemcells.nih.gov/info/faqs.asp#registry
AAN AND ANA’S POSITION

The AAN and ANA have adopted the following principles relating to the use of embryonic human pluripotent stem cells:

1. We support federal and state use of the 2000 NIH Guidelines as the ethical and scientific standard for research involving human pluripotent stem cells, with certain exceptions made to address advances in somatic cell nuclear transfer (addressed in part 4). These guidelines respect both the moral status of the embryo and public sensitivity to this issue, while ensuring that progress in critical medical research will continue. The guidelines also deal appropriately with informing and obtaining consent of potential donors of material, with prohibitions on improper inducements to such donors, and with the protection of donor privacy;

2. We support expansion of federal and state funding for human pluripotent stem cell research projects to include all embryonic stem cell lines developed under appropriate ethical and scientific guidelines, not just those permitted by the 2001 presidential order. Time is valuable: although private companies are currently conducting research on pluripotent stem cells, these firms are limited in number and their research is not subject to NIH oversight, which limits scientific and ethical scrutiny and the pace of discovery. Changing federal funding policy is critical to permit the full capacity of the biomedical research workforce in the United States to discover and develop the full potential of human pluripotent stem cells under appropriate scientific and ethical guidance;

3. We support continuing research on both embryonic and adult stem cell lines. Prevailing scientific opinion is that it is far too early to know if adult stem cells have the same potential as do embryonic stem cells. For diseases that prove not to be treatable with adult stem cells, impeding human pluripotent stem cell research risks unnecessary delay for patients who may die or endure needless suffering while the effectiveness of adult stem cells is evaluated;

4. We support somatic cell nuclear transfer for purposes of creating stem cells to be used in biomedical research and treatment (therapeutic cloning), and oppose somatic cell nuclear transfer for purposes of producing a human child (reproductive cloning).

5. The AAN and ANA acknowledge differing ethical opinions on the status of embryos that cannot be resolved to the satisfaction of all through medical science alone. Consequently, the AAN and ANA recommend that ESCR and somatic cell nuclear transfer research proceed under federal oversight, ensuring that the highest quality and most promising research is conducted with utmost regard for ethical standards.

6. Because scientific knowledge regarding stem cell research is evolving, the AAN and ANA will periodically review this position and revise it as indicated.

Approved October 2004
American Academy of Neurology (AAN)
American Neurological Association (ANA)
Somatic Cell Nuclear Transfer (SCNT) is a technique to produce stem cells that genetically resemble the cells of a living person. SCNT is often referred to as “therapeutic cloning” because the stem cells so produced may have applications to treat degenerative or acquired structural disease in the person from whose genetic material the stem cells were created.

**The promise of stem cells**

Because of their extraordinary potential, stem cells have received close scrutiny since first being isolated in 1998. Stem cells: (1) can reproduce themselves for long periods of time in culture and (2) have the potential to differentiate into specialized cell types (brain cells, heart muscle cells, liver cells, etc) in the proper environment. Stem cell research can increase our understanding of disease mechanisms and holds promise for treating patients with devastating neurological conditions.

**Types of stem cells**

Stem cells are defined by their potential for differentiation as **totipotent**, **pluripotent**, and **unipotent**, and, by their source, as **embryonic** or **adult** (see Glossary). The fertilized egg is a **totipotent** stem cell because from it develops all cell types of the human organism, including the structural elements that support the pregnancy. **Embryonic** **stem cells** form the inner cell layer of the 5-day embryo, the blastocyst. Every human cell type arises from this collection of 30 or so stem cells in the blastocyst. **Embryonic stem cells** removed from the blastocyst can reproduce in culture and differentiate into any cell type and thus are **pluripotent stem cells**. Adult stem cells are undifferentiated cells that reside in differentiated tissues or organs and are considered **unipotent stem cells**. When removed from the organism they have limited potential to reproduce themselves in culture and differentiate into cell types besides...
those from which they were isolated. Although all types of stem cells are currently undergoing detailed study, most scientists agree that embryonic stem cells offer the greatest potential for the study and treatment of human disease.

**Sources of embryonic stem cells**

Embryonic stem cells are isolated from the inner cell layer of the blastocyst. Figure 1 depicts the isolation of stem cells from embryos created by the in vitro fertilization technique of assisted reproduction. The egg is fertilized with sperm in the laboratory and the fertilized egg is then allowed to divide for approximately 5 days to the blastocyst stage. Cells in the blastocyst form an inner cell layer surrounded by an outer cell layer. The outer cell layer gives rise to most of the supporting cells of pregnancy. Cells in the inner layer are pluripotent stem cells—they can develop into any type of human cell, but not into the supporting structures of pregnancy. Each blastocyst has about 30 cells in the inner layer. Once isolated from the inner cell layer, these cells are called embryonic stem cells. Embryonic stem cells are usually derived from donated frozen embryos. These embryos have been created by in vitro fertilization of an egg by a sperm for the treatment of infertility. Couples who decide not to implant these embryos donate them for stem cell research. Federal funding of embryonic stem cell research is currently restricted to those stem cell lines that were isolated prior to August 9, 2001. SCNT is a novel technique to isolate embryonic stem cells. (see figure 2) In SCNT, the nucleus is removed from an egg derived from a donor through hormonal stimulation of the ovaries. A blood, skin or other cell is removed from an adult donor. The donor nucleus is inserted into the enucleated donor egg, and the egg is stimulated to divide. After 5 days, the blastocyst has formed. Stem cells from the inner cell layer are then removed from the blastocyst.

**The potential of SCNT for neurological diseases**

Neurological diseases are an important cause of premature death and disability. Because neural tissues have an extremely limited ability to regenerate and repair damage, there is a compelling need for novel approaches to neurodegenerative and acquired structural neurological diseases. Stem cell research offers the potential to produce transplantable cells to replace cells lost due to degenerative and acquired structural damage in neurological conditions such as Parkinson’s disease, Huntington’s disease, spinal cord injury and stroke. Preclinical studies show that immature cells (human fetal cells or embryonic stem cells) can survive, make functional connections with host tissues and improve the signs of these and other neurological illness.
A drawback of donor embryonic stem cells in transplantation is that they may be identified as foreign by the recipient tissue and incite an immune rejection of the transplant material. A source of stem cells that is genetically like the transplant recipient obviates the need for anti-rejection therapies. Through SCNT, customized stem cells can be cultured in the laboratory, and induced to differentiate into any needed cell type.

SCNT-derived stem cells will likely contribute to several research areas besides neurotransplantation. In particular, SCNT-derived stem cells can be used to study: (1) polygenic disorders (due to aberrant interplay of more than one gene) because the entire abnormal genome can be used to create the stem cells under study and (2) trophic factors and other signaling compounds that might offer treatment strategies for rescue or repair of damaged nervous system tissue. Moreover, stem cells might be used to carry gene therapy to targeted tissues.

In summary, stem cell research is in its infancy and it is unknown which sources of stem cells will ultimately prove most useful and cost effective for the study and treatment of neurological diseases. Consequently, the American Neurological Association and the American Academy of Neurology recommend that stem cell research, including SCNT, should proceed under federal oversight, ensuring the highest quality research with utmost regard for ethical standards.

March 25, 2003
Kathleen M. Shannon, MD
Matthew Rizzo, MD