**Testimony**
**Before the Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, and the Committee on Health, Education, Labor, and Pensions**
**United States Senate**

# The Promise and the Challenge of Stem Cell Research


*Statement of*

## Story C. Landis, Ph.D.

***Director***
***National Institute of Neurological Disorders and Stroke***
***National Institutes of Health***
***U.S. Department of Health and Human Services***


**For Release on Delivery**
**Expected at 9:30 a.m.**
**Friday, January 19, 2007**

Opening Remarks

I am pleased to appear before you today to testify about the science of stem cell research. I look forward to discussing ongoing federal support of both embryonic and non-embryonic stem cell research and scientific progress, including the recently published findings on amniotic fluid stem cells and other studies raising the possibility that non-embryonic stem cells have similar properties allowing them to differentiate into many different cell types.

The Need for Research to Explore the Potential of Human Stem Cells

Stem cells are cells that can multiply without changing, that is, self-renew, or can differentiate to produce specialized cell types. Stem cells have been derived from both embryonic and non-embryonic tissues, and these cells have different characteristics. Both embryonic and non-embryonic stem cells show potential for developing treatments for human diseases and injuries. Because of this, this Administration in 2001 became the first to fund research on human embryonic as well as adult stem cells. There are many ways in which human stem cells might be used in basic and clinical research. However, only further research will overcome the technical hurdles between the potential of stem cells and the realization of these uses.

The most obvious potential application of human stem cells would be the generation of cells and tissues for cell-based therapies. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat a number of common diseases and disorders, including Parkinson's disease, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.

To realize the potential of stem cell-based therapies for pervasive and debilitating diseases, scientists must learn to reliably manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation, and engraftment. Although scientists are making progress, we cannot yet control the differentiation of stem cells adequately. To be useful for transplant purposes, stem cells must:

*Proliferate extensively and generate sufficient quantities of specialized cells.

*Differentiate into the desired cell type(s).

*Survive in the recipient after transplant.

*Integrate into the surrounding tissue after transplant.

*Function appropriately for extended periods of time.

*Avoid harming the recipient in any way.

Stem cells have many other potential uses. Studies of human embryonic stem cells, for example, yield information about the complex events that occur during the initial stages of human development. A primary goal of this research is to identify the molecular mechanisms that allow undifferentiated stem cells to differentiate into one of the several hundred different cell types that make up the human body. Scientists know that turning genes on and off is central to this process. A significant challenge for stem cell research is that scientists do not yet fully understand the signals that turn specific genes on and off to influence the differentiation of the

stem cell into a specialized cell with a specific function, like a nerve cell. This knowledge not only offers the opportunity to learn how to control stem cells from both embryonic and non-embryonic sources, but also to better understand the cause of a number of serious diseases, including those that affect infants and children, which in turn could lead to new and more effective intervention strategies and treatments.

Among other applications, human stem cells could also be used to speed the development of new drugs. Initially testing thousands of potential drugs on cells in cell culture is potentially far more efficient than testing drugs in live animals. *In vitro* systems are useful in predicting *in vivo* responses and provide the benefits of requiring fewer animals, requiring less test material, and enabling higher throughput. New medications could be tested for safety on the specific types of human cells that are affected in disease by deriving these cells from human stem cell lines. Other kinds of cell lines are already used in this way. Cancer cell lines, for example, are used to screen potential anti-tumor drugs. The availability of useful stem cell lines could allow drug testing in a wider range of cell types. However, scientists must learn to control the differentiation of stem cells into the specific cell type on which drugs will be tested.

Federal Funding of Stem Cell Research

NIH has acted quickly and aggressively to provide support for this research in accordance with the President's 2001 stem cell policy. Since 2001, NIH has invested nearly $3 billion on all forms of stem cell research. Within this total, NIH has contributed more than $130 million in research studying human embryonic stem cells, more than $1.1 billion on research using human

non-embryonic stem cells, nearly $509 million on nonhuman embryonic, and more than $1.2 billion on nonhuman non-embryonic stem cells.

Additionally, in FY 2007, it is projected that NIH will spend more than $30 million on human embryonic stem cell research and about $200 million on human non-embryonic stem cell research, while also investing nearly $100 million on nonhuman embryonic stem cell research and more than $270 million on nonhuman non-embryonic stem cell research.

In addition to this ample support, NIH has encouraged stem cell research through the establishment of an NIH Stem Cell Task Force, a Stem Cell Information Web Site, an Embryonic Stem Cell Characterization Unit, training courses in the culturing of human embryonic stem cells, support for multidisciplinary teams of stem cell investigators, and a National Stem Cell Bank and Centers of Excellence in Translational Human Stem Cell Research, as well as through extensive investigator initiated research. NIH determined that access to hESC lines listed on the NIH Stem Cell Registry and the lack of trained scientists with the ability to culture hESCs were obstacles to moving this field of research forward. To remove these potential barriers, the National Stem Cell Bank and the providers on the NIH Stem Cell Registry together have currently made over 700 shipments of the hESC cell lines that are eligible for federal funding, as posted on the NIH Stem Cell Registry web site. In addition, the NIH-supported hESC training courses have taught over 200 scientists the techniques necessary to culture these cells. We plan to continue to aggressively fund this exciting area of science.

NIH-supported scientists have developed efficient techniques to derive dopamine-producing nerve cells from human embryonic stem cells. The loss of dopamine-producing nerve cells is responsible for the movement problems of Parkinson's disease. When grafted into the brain of a rat model for Parkinson's disease, the stem cell-derived dopamine cells significantly improved the animals' movement. However, after three months of transplantation, the scientists found that treated rats' brains contained groups of undifferentiated cells that had become tumors. (*Nature Medicine* 12:1259–1268, laboratory of S. Goldman). This had not been observed in other studies that transplanted neural stem cells and emphasizes the need for scientists to learn to better regulate cell division in transplanted pluripotent stem cells, whatever the source, before they may serve as a renewable source of replacement dopamine-producing nerve cells to treat Parkinson's disease in humans. These results demonstrate both the potential and the challenge of stem cell research.

In recent years, NIH-supported scientists have demonstrated that even the adult human brain can generate new nerve cells. Studies focused on encouraging the innate potential of stem cells that are normally present in the adult brain are another avenue of research that has also shown potential for treating Parkinson's disease. In recent experiments, researchers used drugs to activate adult stem cells in the brains of adult rats with experimental Parkinson's disease, which increased the proliferation of replacement cells and improved movement (The Journal of Neuroscience 26:7272-7280, laboratory of C. Eckman).

Currently, scientists are also using stem cells from a variety of sources to help animals with spinal cord injuries regain movement. Human embryonic stem cells have been coaxed into

becoming a type of cell that repaired damaged nerve fiber insulation called myelin (*The Journal of Neuroscience* 25:4694–4705, laboratory of H.S. Keirstead). Human non-embryonic neural stem cells helped replace damaged rat spinal cord nerve cells and myelin (*Proceedings of the National Academy of Sciences of the USA* 102:14069–14074, laboratory of A.J. Anderson). NIH-supported scientists now report that they can use mouse embryonic stem cells to make functional motor neurons, which are the spinal cord cells that send long nerve fibers called axons (the threadlike extensions on a neuron, or nerve cell, which conducts nerve impulses) to connect with leg muscles and other muscles used to move the body. The scientists combined several methods to coax the mouse embryonic stem cells to become motor neurons, to overcome molecules that restrain axon growth in adults, and to attract the motor neuron axons to the correct muscles. Previously paralyzed rats treated with the motor neurons were able to move their legs again, although they could not walk or grip with their feet as well as uninjured rats. This research gives scientists insight on how they might one day replace human motor neurons damaged by spinal cord injuries and motor neuron diseases such as Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS) and spinal muscular atrophies. (*Annals of Neurology* 60(1)32–44, laboratory of D. Kerr)

Japanese and NIH-funded scientists used mouse embryonic stem cells to make liver-like cells to create an implantable bioartificial liver. Chronic liver diseases such as cirrhosis and hepatitis affect 25 million Americans and scientists hope to overcome the shortage of organs available for transplants by using liver cells derived from stem cells to replace lost liver function. This implanted device uses liver cells to replace some liver function. Ninety percent of mice with liver failure that were implanted with the bioartificial liver survived at least three times longer

than the untreated mice. If scientists can repeat these results with liver cells made from human stem cells, the technique offers potential both to individuals born with liver problems and to those who develop liver disease later in life. (*Nature Biotechnology* 24:1412–1419, laboratory of I. Fox).

Amniotic Fluid Derived Stem Cells

As you all know, there has been much interest in the recently published article in *Nature Biotechnology* by Dr. Anthony Atala and colleagues at Wake Forest University regarding stem cells isolated from the amniotic fluid that cushions the developing fetus in the uterus. Amniotic fluid is collected from pregnant women during amniocentesis to test for a variety of congenital and developmental diseases and disorders. Scientists have previously reported that some of these cells can differentiate into fat, muscle, bone, and nerve cells. Dr. Atala's work extends our knowledge of the properties of these amniotic fluid-derived stem cells (AFS).

Dr. Atala and colleagues showed that AFS could produce cells that originate from each of the three embryonic germ layers that give rise to all of the cells in the body. More specifically, the scientists were able to develop in-vitro conditions that produced nerve cells, liver cells, and bone-forming cells from AFS. The AFS-derived human nerve cells were able to make proteins typical of specialized nerve cells and were able to integrate into a mouse brain and survive for at least two months, although it is not yet clear whether these cells have all the properties of normal neurons. They also showed that AFS cells were also self-renewing and maintained the normal number of chromosomes after a long time in culture over many cell divisions. However, undifferentiated AFS did not make all of the proteins expected in embryonic stem cells, and they

were not shown to form a teratoma (a germ cell tumor), one of the essential characteristics of embryonic stem cells. Thus, given the characteristics of AFS, scientists conclude that these cells may be multipotent rather than pluripotent. Although scientists do not yet know how many different cell types AFS are capable of generating, banked AFS may one day enable the generation of tissue-matched cells for transplantation into humans.

Conclusion

Since 2001, NIH has aggressively pursued research using embryonic and non-embryonic stem cells that will be useful for basic, translational, and clinical studies. We are continuing to move this research forward through training programs, the establishment of the NIH stem cell characterization unit, and the many grants that have been made to scientists to explore stem cell research. With NIH support, scientists have already made remarkable progress in understanding human embryonic stem cells, and we will provide continued support for these research efforts, consistent with Administration policy.

I will be more than happy to answer any questions.