



## The Regenerative Potential of Stem Cell Therapeutics in the Anti-Aging Setting

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### Introduction

Science now stands on the threshold of a new age in cellular therapy and tissue regeneration which will directly and beneficially impact how long, and how well, we will live in the coming decades. Stem cell therapeutics is the leading biomedical technology in the rapidly emerging field of regenerative medicine, a medical field in which science assists the human capacity to heal various tissues and organs. All of the most impressive demonstrations of regenerative medicine, since its inception in 2002, have used stem cells to trigger healing in the patient.

Stem cell therapy as a therapeutic intervention for aging is rooted in 30 years of research and clinical application. Stem cell therapeutics have been successfully utilized around the world to treat a wide range of aging-related disorders including heart disease, diabetes, stroke, cancer, obesity, arthritis, Parkinson's Disease, and other infirmities associated with aging metabolism.

As we age, our stem cell reserves with which we are born, decline. Our cells diminish in their ability to regenerate and repair tissue. Age-related changes occur in the skin, organs, sex glands, immune system, blood-forming system, muscles and other systems. These changes are all due to the decrease in the robustness of the cells and loss of stem cells. Because cells become progressively weaker over time and die, their replacement with new ones, can remediate aging. Evidence of an “anti-aging” effect of stem cells is reported in the medical literature. In one report, fetal liver cell and cord blood stem cell preparations improved immune function and hormonal balance in patients undergoing cosmetic procedures, and thereby enhanced the cosmetic outcome.

In this article, we will introduce the fascinating new science of stem cell therapeutics. Find out the basics about stem cell science, review some of the most recent milestones in stem cell therapeutics, and embrace the future potential for new medical treatments for aging-related disorders using stem cells.

### Basics About Stem Cells

Stem cells are different from other types of cells in three ways:

- ***Stem cells are unspecialized.*** One of the fundamental properties of a stem cell is that it does not have any tissue-specific structures that allow it to perform specialized functions. Unspecialized stem cells are important to the human body because they can become specialized cells, such as heart muscle cells, blood cells, or nerve cells.
- ***Stem cells are capable of dividing and renewing themselves for long periods.*** Unlike muscle cells, blood cells, or nerve cells—which do not normally replicate themselves—stem cells may replicate many times, a process known as proliferation. A starting population of stem cells that proliferates for many months in the laboratory can yield millions of cells. If the resulting cells continue to be unspecialized, like the parent stem cells, the cells are said to be capable of long-term self-renewal.
- ***Stem cells can give rise to specialized cells.*** In a process known as differentiation, unspecialized stem cells give rise to specialized cells. Inside stem cells, cellular genetic signals trigger differentiation. Outside the cell, chemicals secreted by other cells, physical contact with neighboring cells, and certain molecules in the microenvironment can cause stem cells to differentiate.

Stem cells are found in adult organs (bone marrow and brain tissue — adult stem cells), embryos (embryonic stem cells), and tissues that support the fetus (umbilical cord — cord blood stem cells, and placenta — placental stem cells).

Scientists have discovered that the more 'primitive' a stem cell is (that is, the less specialized it has become), the greater its capacity for regenerative medical use. Adult stem cells have been found to be limited in their utility, because they have already become specialized and thus their potential to regenerate damaged tissue is very limited. In addition, adult stem cells are difficult to grow in the lab and their potential to reproduce diminishes with age.

From a purely scientific standpoint, only stem cells from embryos, umbilical cords, and placentas, which have the capacity to become any kind of human tissue, have the potential to repair vital organs. Because bioethical issues negate the use of embryonic tissue, scientists are now focusing on the therapeutic potential of umbilical cord and placental stem cells, which can be readily and safely harvested from healthy, full-term, live births. In August 2005, University of Pittsburgh School of Medicine researchers suggested that placental tissue, "routinely discarded as medical waste, could feasibly provide an abundant source of cells with the same potential to treat diseases and regenerate tissues as their more controversial counterparts, embryonic stem cells." Dr. Stephen Strom and colleagues submit that cells from the outer membrane of the amniotic sac (known as amniotic epithelial cells) have strikingly similar characteristics to embryonic stem cells, including the ability to express two key genes that give embryonic stem cells their unique capability for developing into any kind of specialized. According to the results of their studies, amniotic epithelial cells could in fact be directed to form liver, pancreas, heart, and nerve cells under the right laboratory conditions.

## **Basics About Stem Cell Therapeutics**

Pluripotent stem cells (in the forms of embryonic, umbilical cord, and placenta) represent hope for millions of people around the world who are afflicted with various aging-related disorders including Parkinson's, Alzheimer's, diabetes, heart disease, stroke, and spinal cord injuries.

Scientists have proceeded cautiously with pluripotent stem cell therapies because embryonic stem cells from a donor introduced into a patient have the potential to cause transplant rejection. This issue may soon be resolved, as in May 2005 South Korean researchers announced that they successfully created stem cells tailored to individuals. The South Koreans used cloning technology to take skin cells from nine different people — adults and children, males and females — and fuse the cells with donor eggs. Because the researchers had removed the eggs' nucleus prior to fusion, the new combined cells contained only the genetic material from the nine people's cells. In these combined cells, the researchers were able to grow batches (lines) of embryonic stems cells that perfectly matched each person. The process used was not new — in fact, it is how the famous cloned sheep Dolly was created. But instead of creating a new organism, the technology was used to produce perfectly matched cells that might one day be used to regenerate tissues specific to individuals and their injuries and diseases.

## **The Vast Potential of Stem Cell Therapeutics**

In the anti-aging setting, the most important potential application of human stem cells is the generation of cells and tissues that could be used for cell-based therapies. Today, donated organs and tissues are often used to replace ailing or destroyed tissue, but the need for transplantable tissues and organs far outweighs the available supply. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including Parkinson's and Alzheimer's diseases, spinal cord injury, stroke, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis. In addition, if scientists can harness stem cells' ability to become specialized into any type of cell, they may be able to use them to treat any number of diseases and conditions.

### ***Heart Disease***

It may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease. Preliminary research in mice and other animals indicates that bone marrow stem cells, transplanted into a damaged heart, can generate heart muscle cells and successfully repopulate the heart tissue. Other recent studies in cell culture systems indicate that it may be possible to direct the differentiation of embryonic stem cells or adult bone marrow cells into heart muscle cells.

In January 2005, researchers from University of South Florida reported that stem cells taken from human umbilical cord blood reduced heart attack damage in rats. The stem cells, injected into rat hearts just after they suffered

induced heart attacks, greatly reduced the amount of heart damage and restored heart pumping function to near normal. Drugs were not needed to prevent the rats' immune systems from rejecting the human stem cells. Dr. Robert Henning and colleagues speculate that umbilical cord stem cells could someday offer a new way to limit or repair heart attack damage in people.

In May 2005, a Pennsylvania woman underwent stem cell therapy in Thailand aimed at treating her heart condition, non-ischemic cardiomyopathy. She received minimally invasive, direct stem cell injections to the heart. Post-treatment, the woman was in less pain and her exercise tolerance had increased greatly. She reported that "within weeks [her] symptoms had greatly decreased while [her] energy level simultaneously increased." Testing in September 2005 at University of Pittsburgh Medical Center confirmed that her Ejection Fraction (EF) rose, from 25-30% pre-treatment, to stand at 41%; other cardiac markers, including stroke volume, also increased.

In early 2005, Tufts University researchers identified stem cells that could benefit people with myocardial infarction. The stem cells were able to induce generation of new heart cells and formation of new blood vessels – two key components of successful myocardial repair. The researchers are hopeful that their results will provide a foundation on which new approaches to repair the damaged heart can be based.

## ***Diabetes***

Stem cells may prove to be helpful in treating type 1 diabetes. With this disease, islet cells in the pancreas, which produce the crucial hormone insulin, are damaged by the person's immune system. Without daily insulin injections, Type-1 diabetics face decreased lifespan. Daily insulin injections are cumbersome and sometimes painful, and so they dramatically compromise quality of life.

In April 2005, Stanford University researchers were able to coax stem cells to develop into the insulin-producing cells that are lacking in diabetes. Dr. Seung Kim and colleagues found that when they added a cocktail of chemicals to fetal brain stem cells, the cells changed, and they were able to produce insulin in response to blood sugar levels. The research, conducted on mice, is expected to offer an avenue for scientists to explore in the search for ways to replace islet cells in type-1 diabetic men and women.

Ongoing research aims at finding a way for stem cells to form new, healthy islet cells which could then be injected into the liver of a person who has diabetes. This may eliminate the need for insulin injections. In addition, new studies indicate that it may be possible to direct the differentiation of human embryonic stem cells in cell culture to form insulin-producing cells that eventually could be used in transplantation therapy for diabetics.

## ***Parkinson's Disease***

Parkinson's Disease (PD) — a condition marked by tremors and loss of muscle control — is caused by the loss of certain brain cells that create the chemical dopamine. Stem cells could potentially be used to replace such cells. In fact, Parkinson's may be one of the first diseases to be treated with stem cells.

Experts have already prompted embryonic stem cells to specialize into cells similar to the dopamine-creating cells (DA neurons) needed to relieve the symptoms of the disease.

In a recent study, scientists directed mouse embryonic stem cells to differentiate into DA neurons by introducing the gene *Nurr1*. When transplanted into the brains of a rat model of PD, these stem cell-derived DA neurons reinnervated the brains of the rat Parkinson model, released dopamine and improved motor function.

Regarding human stem cell therapy, scientists are developing a number of strategies for producing dopamine neurons from human stem cells in the laboratory for transplantation into humans with Parkinson's disease. The successful generation of an unlimited supply of dopamine neurons could make neurotransplantation widely available for Parkinson's patients at some point in the very near future.

## **Neurodegenerative Diseases**

In January 2005, researchers from University of Wisconsin-Madison reported that they successfully coaxed human stem cells to become spinal motor neurons, critical nervous system pathways that relay messages from the brain to the rest of the body. The new development could one day help victims of spinal-cord injuries, or pave the way for novel treatments of degenerative diseases such as amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. With healthy cells grown in the lab, scientists could, in theory, replace dying motor neurons to restore function and alleviate the symptoms of disease or injury. In the immediate future, the finding is expected to allow researchers to create motor neuron modeling systems to screen new drugs and improve their efficacy for these disorders.

In September 2005, scientists from University of California-Irvine found that injections of human stem cells into partially paralyzed mice directly repaired some of the damage caused by spinal cord injury, thereby allowing the animals to walk again. While this study was not the first to show that stem cells offer hope for spinal cord injury, the study is the first to suggest that the connections the stem cells form to help bridge the damaged spinal cord are key to recovery. In this study, the stem cells did not merely form new nerve cells. They also formed myelin, the type of cells that create the biological insulation that nerve fibers need to communicate. Thus, this study is heralded as a key advancement in possible therapeutics for various neurological diseases that involve myelin loss, most notably including multiple sclerosis (MS).

Earlier in 2005, a separate team of researchers also from the University of California-Irvine reported that rats with disabling spinal injuries could walk nearly normally again after getting injections with human embryonic stem cells.

## **Concluding Remarks**

Seventy-two percent (72%) of American consumers favor stem cell research and therapy (survey conducted by KRC Research, July 2004). In addition, 78% of Americans think it is very important that the US participate as a global leader in medical and scientific research (survey conducted by *Parade* magazine, July 2005). Yet, the United States lags in the stem cell research arena. According to Princeton University, the nation's share of new publications in stem cell research is unexpectedly low and declining, with the U.S. political environment speculated as a major factor.

Stem cell therapies are among the world's greatest collective scientific breakthrough, possessing the clear potential to revolutionize the practice of medicine and improve the quality and length of life. Stem cell therapeutics is the leading biomedical technology with a promising future in the anti-aging setting, enabling immune restoration and stimulation, tissue engineering, cellular repair, and organ regeneration.

Given the enormous promise of stem cells to the development of new therapies for the most devastating diseases, it is important that Americans show their support for this line of research. Many states have approved, or are considering for approval, legislation that allocates multi-million dollar investments to encourage corporate- and university-level research into stem cell therapeutics. It is a medical science that deserves universal support.

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