IQP-43-DSA-2303
IQP-43-DSA-0213

STEM CELLS

An Interactive Qualifying Project Report

Submitted to the Faculty of

WORCESTER POLYTECHNIC INSTITUTE

In partial fulfillment of the requirements for the

Degree of Bachelor of Science

By:

Patrick Hussey

Robyn Panciocco

August 24, 2005

APPROVED:

Prof. David S. Adams, Ph.D.
WPI Project Advisor

ABSTRACT

Stem cell research is revolutionizing the way we look at medicine. The potential for stem cells is bound only by our ability to understand their functions. Stem cells could be used for the treatment of many diseases and disabilities, which do not currently have treatments. Unfortunately, research within the United States has been stifled due to controversy over the derivation of embryonic stem cell lines and embryonic germ lines. If stem cell research is to fulfill its potential our legislative policies need to change.

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Stem cell research seeks to revolutionize the way the world understands human development, and to develop a new means for regenerating diseased tissues. Diseases and disabilities, for which there may be no current treatment, will have hope. This project examined the sources, applications, ethics, and laws pertaining to stem cells.

Chapter 1 discusses the types of stem cells and their sources. Embryonic stem (ES) cells are the inner cell mass of a blastocyst (a day 5 human embryo). In order to harvest these cells it is usually necessary to destroy an embryo, which is why ES cell research has been the focus of the ethical debate on stem cells. ES cells hold the most medical potential since they can differentiate into a variety of tissues, allowing us to manipulate or replace diseased cells. Embryonic germ (EG) cells are derived from the tissue of aborted fetuses, a stage well after blastocyst formation, thus ethicists oppose their use even stronger than ES cells. The opposition to abortion in general has lead EG cell research into overwhelming controversy. The cells the public is most unaware of are adult stem cells. These cells come from adult tissues, so for example neuronal stem cells might be used to cure a brain neurodegenerative disease. Because they come from adults, and do not require the destruction of an embryo, they are less prone to ethical opposition. Such cells include hematopoietic stem cells found in the bone marrow, mesenchymal stem cells that can potentially differentiate into a number of connective tissue types, intestinal stem cells, stem cells found for the skin, liver and neuronal stem cells. A newer method of obtaining embryonic stem cells is through the use of parthenotes. A parthenote is a term used to describe an egg, embryo, or organism produced without

fertilization. Such embryos can be used to provide ES cell lines, so in the future might serve as an alternative source for ES cells. Mammalian parthenotes cannot divide beyond the blastocyst stage, so they have less moral status than blastocysts derived from fertilized eggs (which can grow to adults).

Chapter 2 discusses research applications for the different types of stem cells. Many diseases result from the death or dysfunction of one or more types of cells. Replacing dying cells by utilizing stem cells' ability to differentiate into a variety of cells could offer more effective treatments or even cures.   Most ES and EG research has been performed on animals, human clinical trials with ES cells are only recently underway. However adult stem cells have already been used to save thousands of lives. Adult stem cells have been used for over thirty years in bone marrow transplants. Adult stem cells offer an alternative with less of an ethical debate surrounding their application. Recent studies show some success using adult stem cells in the treatment of Parkinson's, diabetes, and heart conditions. New research on ES and EG cells could aid in the identification of events that occur during normal human development, which might lead to a better understanding of birth defects and other conditions due to abnormal cell specialization and cell division. But the ethical debate surrounding the clinical applications of ES and EG cells has severely hindered progress.

Chapter 3 discusses the ongoing ethical debate over stem cells. As with any new technology there is a cloud of questions surrounding how we conduct research and how we use this new technology. Embryonic stem (ES) cell and embryonic germ (EG) cell research have been the main focus of the ethical debates surrounding stem cell research, most religions already support the use of adult stem cells. The source of ES and EG cells have been a particularly hot topic on the debates. Because there is a necessity to derive these types of cells from embryos or from aborted fetuses there is great concern as to whether it is ethical to use this type of research. This project closely examined the ethics of stem cell research from multiple religious and social points of view.

Chapter 4 covers the legislation enforced on stem cell research in the United States and the rest of the world. In August of 2001 President Bush made the decision to ban all federal funding for embryonic research using any ES cell lines derived after August 2001. This decision would prove to cripple the United States in its research on stem cells. Other countries such as Sweden, Israel, South Korea, and others have all ruled for the use of embryos in stem cell research, setting them ahead of the United States.

In conclusion, our project has taken a close look at everything involved with stem cell research. From our research we have concluded that stem cell research will eventually revolutionize health care and will create hope for otherwise hopeless victims of debilitating diseases. With this we have also concluded that if the United States does not change its policy regarding federal funding of ES and EG cell research, we will not be able to really participate or contribute in this world changing research.

PROJECT OBJECTIVE

The purpose of our project was to become educated in the technical aspects, applications, ethics, and legalities of stem cell research to understand the various kinds of stem cells, where we get them, and their impact on society. The outcome of the project is a paper reporting our findings, and the authors conclusions on key topics formulated by the research performed.

CHAPTER 1: STEM CELL TYPES AND SOURCES

Stem cells may be one of the most controversial and misunderstood topics today. The public often denounces the use of stem cells yet does not realize the many types and current applications of stem cells. Obtaining adult stem cells does not involve the destruction of an embryo. The public often associates stem cell research only with futuristic promises but in the past thirty years, thousands of lives have been saved by bone marrow transplants in which the live-saving component is adult hematopoietic stem cells. This chapter will explain what stem cells are, the types of stem cells and how we obtain them.

WHAT IS A STEM CELL?

A stem cell is a cell that is able to divide for indefinite periods of time in culture. Upon division, the cell can replicate creating more stem cells (Figure-1, path A), or can produce a variety of specialized cells found in the body (Figure-1, path B). A unique characteristic, stem cells divide indefinitely, either renewing themselves and/or producing differentiated progeny (NIH, May 2000). The defective cells in the body can be replaced using stem cells since they have the potential to make a variety of tissues. For example, stem cells could be used to replace the faulty brain cells in a patient suffering from Huntington's disease or the heart cells following a heart attack.

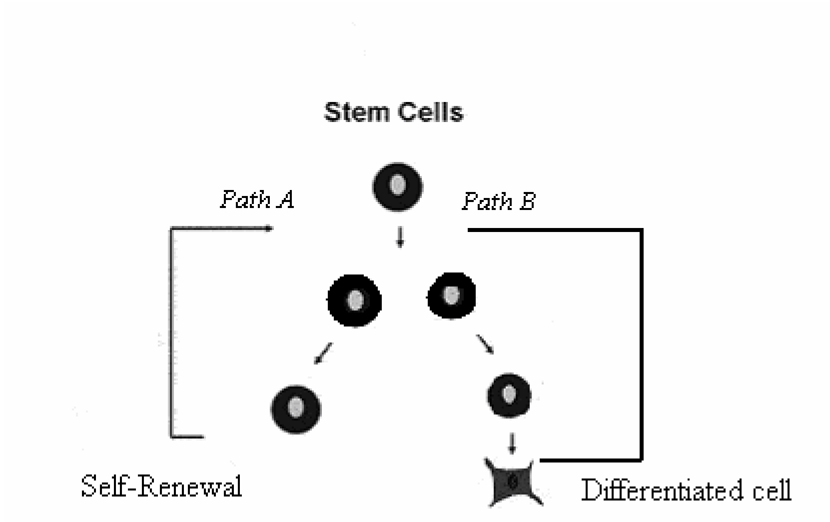


Figure 1. The Basic Maturation Path of Stem Cells (Harvard Stem Cell Institute, 2005).

STEM CELL CLASSIFICATION

One way to categorize stem cells is on the basis of their potential to form other cells. Newly fertilized eggs are totipotent, meaning they can differentiate into any cell found within the body. The blastocyst, a hollow ball of cells, is formed by day five or six as the fertilized egg divides. The inner cell mass of this blastocyst contains embryonic stem (ES) cells. These cells are pluripotent, meaning they can make a variety of tissues, but are not totipotent. ES cells have more medical applications than other types of stem cells because of their unique ability to make a variety of tissues. Unfortunately, to obtain ES cells, we must usually destroy an embryo. Two other types of stem cells are multipotent and unipotent stem cells. Multipotent stem cells have the ability to make several other kinds of one type of tissue; for example, hematopoietic (blood forming) stem cells (HSCs) have the ability to make several kinds of white and red blood cells, and platelets. Unipotent stem cells have the ability to make only one kind of cell, usually the same as the tissue they were isolated from. For example neuronal stem cells have the ability to make other neuronal cells.

Stem cells are also classified by whether they are isolated from embryos or adults. ES cells are usually obtained from aborted embryos. Adult stem cells are found within children and adults. They can produce cells to maintain our bodies, such as hematopoietic stem cells, neuronal (found in brain tissue) stem cells, and epithelial stem cells.

Embryonic Stem Cells and Embryonic Germ Cells

Embryonic stem (ES) cells are best described in the context of human development. Human development begins when a sperm from a male fertilizes an egg from a female. The resulting cell has the potential to form an entire organism. Within hours of fertilization, the single totipotent cell divides into two totipotent cells. If either can attach to the woman's uterus, a fetus could develop. Approximately four days later, after numerous cell divisions, the cells begin to specialize forming a blastocyst. A blastocyst is a small hollow sphere. The inner cell mass, composed of pluripotent ES cells, goes on to develop all of the tissues of the human body.

In 1998 at the University of Wisconsin, Dr. James Thompson developed a technique to isolate and grow the human embryonic stem cells (hESC) (Thompson, 1998). This research was conducted without federal funding because of the ban that prevented public funding of human embryo research Congress imposed in 1995. The technique involved using embryos from in vitro fertilization clinics, which were in excess of the clinical need. These extra embryos were created for the purpose of reproduction, not research. Couples with extra embryos were informed of the research and consented. Dr. Thompson isolated the inner cell mass of human embryos at the blastocyst stage, and fed it growth factors secreted from a "feeder layer" of mouse cells. Putting the mass in culture eventually resulted in a pluripotent ES cell line. Similar ES cells from mice could be used to create dopamine-secreting cells for Parkinson's patients (Figure-2, path A) or insulin-secreting cells for diabetic patients (Figure-2, path B).

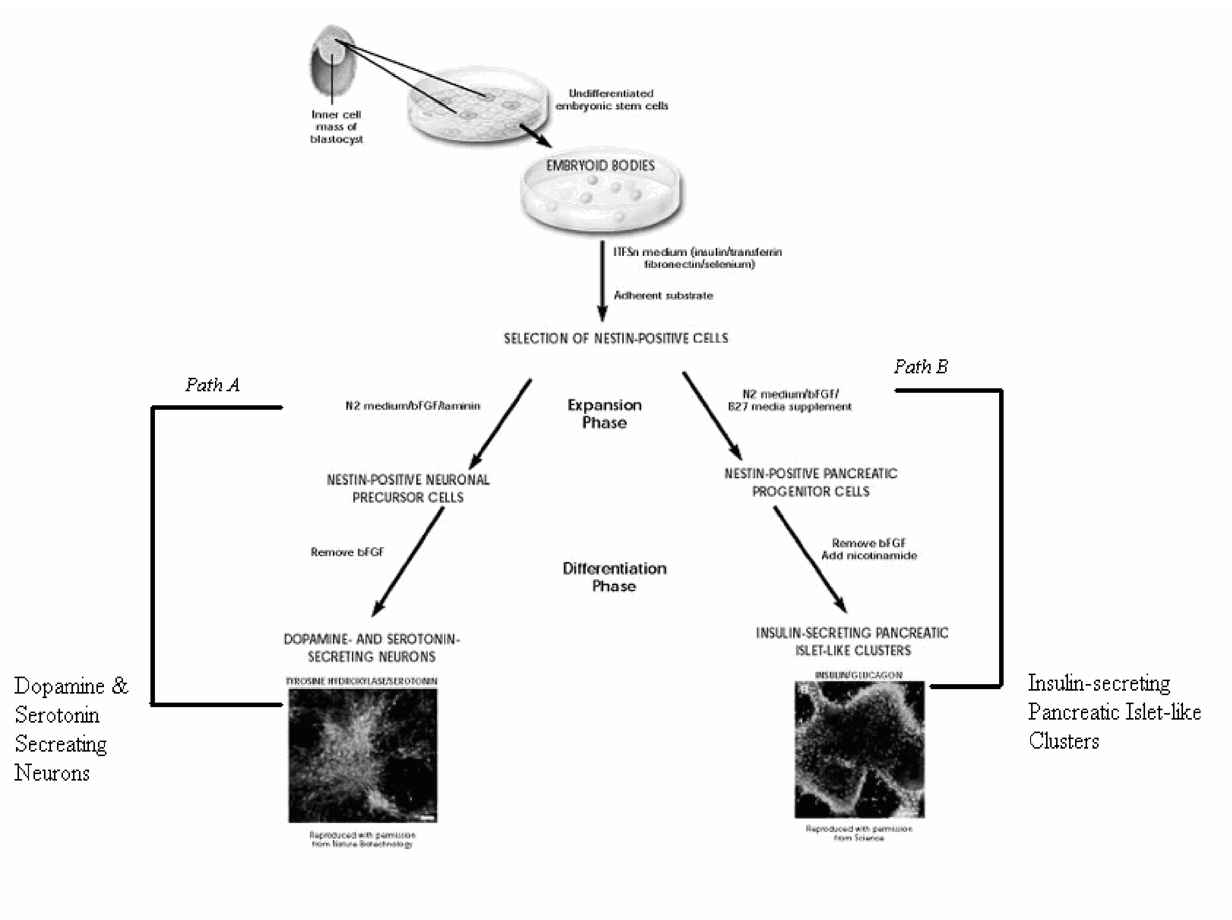


Figure 2. Directed Differentiation of Mouse Embryonic Stem Cells (NIH Stem Cell Basics-3, 2005).

Embryonic germ (EG) cells are cells found in early fetal tissue in an area called the gonadal ridge, the region of the fetus destined for testes or ovaries. EG cells are approximately five to nine weeks further along in development compared to only five days with ES cells, thus EG cells are obtained from a more mature fetus, and have strong ethical constraints in their use. The isolation and successful culture of EG cells was first reported in 1998 by Dr. Gearhart. Using aborted fetuses, Dr. Gearhart took cells from the gonadal ridge, and cultured them to produce a pluripotent EG stem cell line. Figure-3 contrasts ES and EG cells.

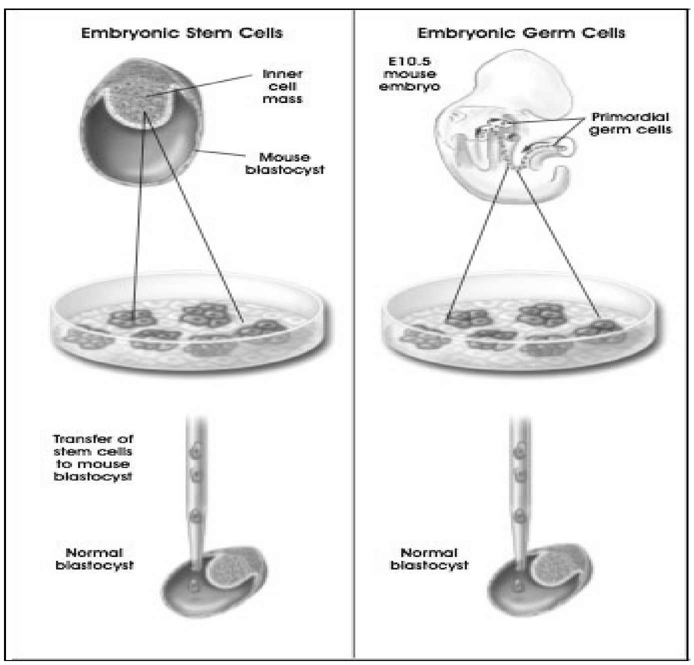


Figure 3. ES Cells versus EG Cells (NIH SCI Report, 2005).

Adult Stem Cells

Adult stem cells are obtained from adult organisms, not from embryos or fetuses, so they hold much promise for future research as replacements for ES cells. Adult stem cells have been isolated in a number of organs including bone marrow, umbilical cord, brain, and skin, in rodents, nonhuman primates, and humans. Recent studies suggest that a variety of tissues in adult animals and humans may harbor adult stem cells. This means that in our bodies, there are cells that can produce cells we need to maintain our bodies. Most adult stem cells are unipotent and, therefore, only able to make the same type of cell as the tissue they were derived from. Hematopoietic stem cells (HSCs) are multipotent and able to make the various cellular components of blood (Figure-4). For over thirty years, HSCs have been used in bone marrow transplants to save thousands of lives. Chemotherapy and radiation therapy destroys blood forming cells as well as cancer cells. HSCs are used to reconstitute blood following theses therapies so new cells can produce healthy blood forming cells.

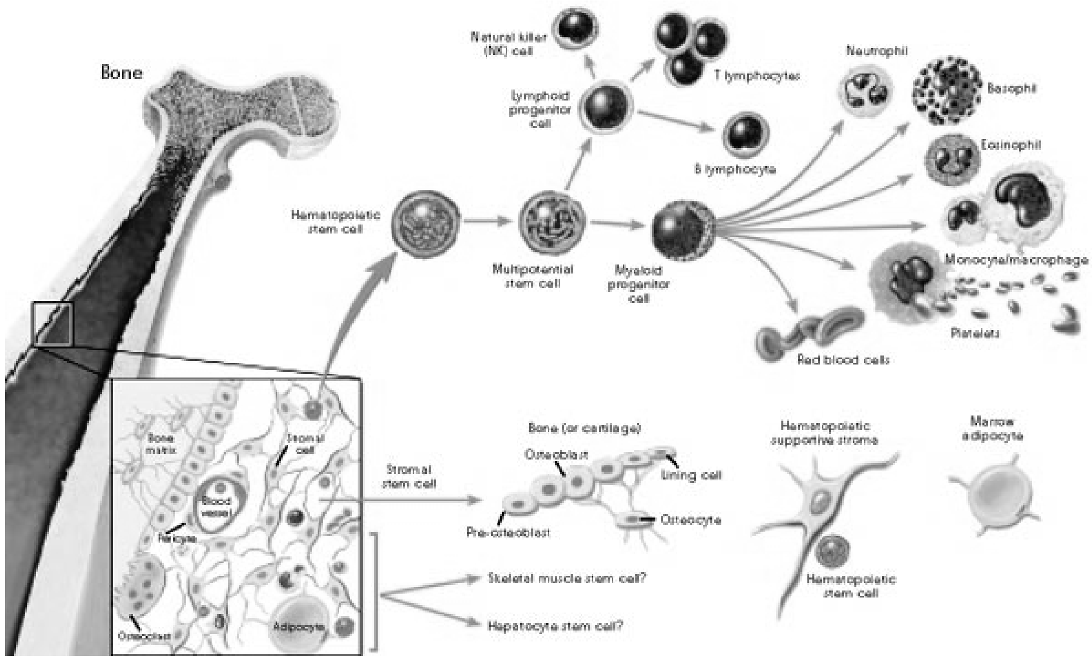


Figure 4. Hematopoietic and Stromal Stem Cell Differentiatio (NIH Stem Cell Basics-4, 2005).

Since no embryo is destroyed to obtain adult stem cells, there is less of an ethical debate surrounding that research. In fact as discussed in Chapter 3, all four major religions support the use of adult stem cells. But although adult stem cells and EG cells offer medical promise, they have some disadvantages. Adult stem cells have not been isolated for all of the tissues in the body. No cardiac or pancreatic islet stem cells have been found yet. Adult stem cells are often present in small quantities, quantities may decrease with age, and are they are difficult to isolate and purify. EG cells are also present in small quantities, so the feasibility of large scale sourcing and manufacturing is limited. Also, research on EG cells has been halted because of the ethical issues concerning abortion and the destruction of human tissue while obtaining EG cells.

Because of these negatives for adult and EG cells, pubic debate on the use of ES cells must still continue.

Parthenotes

A parthenote is a term used to describe an egg, embryo, or organism produced without fertilization. In nature, only some insects, reptiles, aphids, and turkeys are capable of this process. For example, bees and ants produce their "workers" via parthenogenesis. Female reptiles, including some other animals, are able to produce offspring without fertilization from a male sperm. During this process, called parthenogenesis, female eggs divide, developing into embryos and eventually offspring.

In the lab, parthenotes can be created from monkeys and humans using chemically treated eggs that begin dividing without fusing with a sperm. Using chemicals that mimic the sperms arrival, scientists have been able to obtain parthenote blastocysts from monkey (Cibelli et al, 2002) and man (Cibelli et al, 2001), although ES cell lines have only been derived from monkey parthenotes so far (Cibelli et al, 2002; Kiessling, 2005). The mammalian parthenotes created in a lab cannot make entire organisms because they cannot grow beyond the blastocyst stage. This is because producing a normally developing embryo requires an egg from a female that is fertilized by a sperm from a male in mammals. When a sole egg is stimulated to divide on its own, the resulting parthenote can only survive early stages of development before it is naturally terminated.

Mammalian embryo blastocyst parthenotes may have the potential to produce ES cells. Because mammalian parthenotes cannot divide beyond the blastocyst stage, they have less moral status than blastocysts derived from fertilized eggs (which can grow to adults). So the recent excitement about parthenotes is focused on their potential as an alternative source of ES cells without using fertilized eggs, the latter of which some characterize as murder. Monkey parthenotes have successfully produced stem cells which have developed into intestine, skeletal muscles, retina, hair follicles, cartilage, bone, nerve cells and heart cells that beat in unison (Weiss, 2001).

There are some major technical problems surrounding parthenogenesis in humans. First, scientists do not know whether these cells are dangerously inbred. Normal development requires both male and female chromosomes, found in the sperm and the egg. Due to the use of only one set of chromosomes, stem cells from this process may uncontrollably divide, like tumor cells. Second, viable eggs are very difficult to obtain from postmenopausal women. Unfortunately, these are the women who most likely will suffer from a degenerative disease and need the stem cell treatment. Third, parthenogenesis does not produce a normally developing embryo. Although the parthenote will naturally terminate itself, federal law still considers it an embryo (Weiss, 2001).

CHAPTER 2: STEM CELL APPLICATIONS

The cost and psychological tolls of chronic, degenerative and acute disease in the United States are enormous. For example, in the United States alone, the total cost of treating diabetes is approaching $100 billion (http://www.diabetes.org/ada/c20f.asp). The public may have some confusion over stem cells chances for success in the treatment of degenerative conditions, which afflict 128 million people in the United States (Chapman, A. 1999). Actual human lives have been saved by stem cells. The progress scientists have made using animals supports the use of stem cells as a treatment for a variety of diseases. In this chapter we will present the work that has been performed with stem cells as well as some future applications.

POTENTIAL APPLICATIONS OF PLURIPOTENT STEM CELLS

USES FOR RESEARCH

There are many reasons that the isolation of human pluripotent stem cells is important. The complex events that occur during normal human development could be further understood. Cancer, birth defects and other conditions are due to abnormal cell specialization and cell division. Understanding the mechanisms behind these serious medical conditions requires the identification of factors involved in the cellular decision making process that result in cell specialization. Many diseases result from the death or dysfunction of one or more types of cells. Replacing dying cells by utilizing stem cells ability to differentiate into a variety of cells could offer more effective treatments or even cures. The most promising research involves diseases of the nervous system. For example, Alzheimer's disease is associated with the dysfunction of the cells that make acetylcholine, a neurotransmitter particularly important in muscle stimulation. Huntington's disease is connected with cells that make gamma aminobutyric acid, also a neurotransmitter that blocks nerve impulses. Possibly the most well known examples are amyotrophic lateral sclerosis (ALS) and Parkinson's disease. ALS is linked to motor nerve cells that activate muscles and Parkinson's is related to the cells that produce dopamine.

The most far-reaching potential application of human pluripotent stem cells is the generation of cells and tissues for cell therapies. Currently, donated organs and tissues are the most commonly used way to replace ailing or destroyed tissues. Unfortunately, donations are limited. There simply is not enough to go around. Stimulating pluripotent stem cells to develop into specialized tissues offers possible treatment to suffering patients. This method could be used to treat a myriad of diseases and conditions including Parkinson's disease, Alzheimer's disease, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis. Treating a diseased heart with healthy heart muscle cells, grown from pluripotent stem cells, has shown promise in mice. After transplanting the healthy cells into a diseased heart, the new cells repopulated the heart with healthy cells and beat in unison with the host cells.

A major problem with organ transplantation is rejection. Somatic cell nuclear transfer (SCNT) offers the possibility of developing cells from the patient. This process involves replacing the nucleus of an unfertilized egg cell with the nucleus from a somatic cell (for example a skin, heart or nerve cell) (www.aamc.org). The unfertilized egg cell with replaced nucleus is then stimulated to divide. Once the cell begins dividing, stem cells can be extracted five to six days later. These new stem cells can go on to develop into a variety of replaceable organs and tissues. The patient need not fear the possibility of rejecting the transplant because it came from the patient's own cells. Another method being testing to produce immunologically compatible cells involve the major histocompatibility complex (MHC). The MHC is a large cluster of genes essential to the human immune system. The MHC genes encode human leukocyte antigens (HLA). HLAs are proteins displayed on the cell surface, which define a person's tissue type. If foreign HLAs are detected, then the cells or tissue displaying them are destroyed. This is why the body rejects grafts and transplants from donors without a matched tissue type. Using stem cell technology would give doctors a method of ensuring the transplant is not rejected.

Drug development could also be improved using pluripotent stem cells. Instead of testing new drugs entirely on animals, the drugs could be tested on human cell lines, resulting in more accurate and effective medicines. The benefits and toxic effects of biologicals, chemicals, and drugs could be tested on human pluripotent stem cell lines. For example, cancer cell lines can be used to screen potential anti-tumor drugs. If pluripotent stem cells were more accessible, many more drugs could be tested on a wider variety of cell types. The current problem lies in the required testing conditions. To be effective, scientists must create identical testing conditions when comparing different drugs. Currently, scientists have limited knowledge and ability to control the differentiation of stem cells into the particular cell type needed for testing. Since the biological signals controlling differentiation are not completely known or understood, it would be extremely difficult to mimic conditions precisely and consistently for each drug tested.

THE TREATMENT OF DISEASES USING EMBRYONIC STEM CELLS

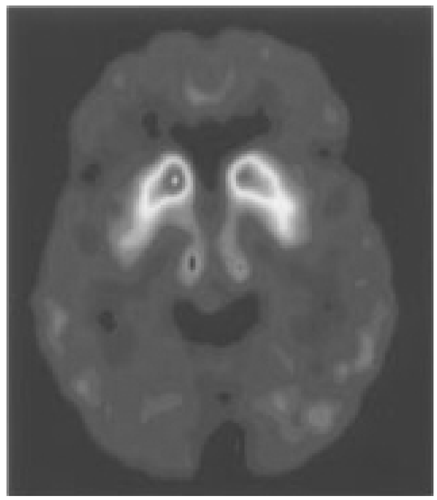
Neural Stem Cells: ALS and Parkinson's Disease.

ALS, also known as Lou Gehrig's disease, is a neurodegenerative disease, attacking the upper and lower motor neurons and deteriorating the brain and spinal cord. The upper motor neuron symptoms include spasms, rigidity and abnormal reflexes while the lower motor neuron symptoms include weakness and atrophy. A very common symptom is weakness in a hand, foot, or leg. Sufferers generally die from this disease within two to six years of diagnosis. Unfortunately the biological mechanisms that cause ALS are only partially understood. The only known cause is a mutation in a specific gene (SOD1 gene), which contributes to the number of inherited cases (www.als.org). This mutation results in the production of a defective protein that kills motor nerve cells. Only 5 to 10 percent of all reported ALS cases are familial cases. All other cases usually arise suddenly in normally healthy people.

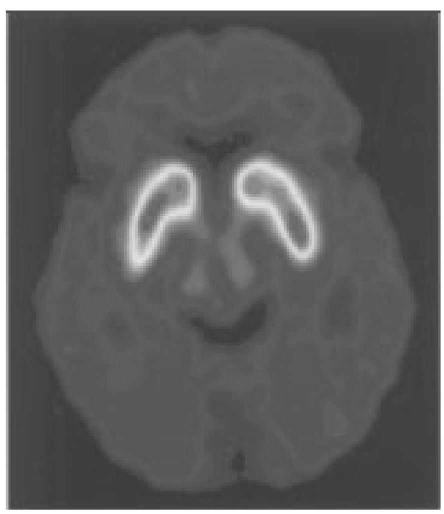
In July of 2001, researchers from John Hopkins University released a tape that proves that stem cells hold much promise. The tape shows 120 mice and rats paralyzed by a motor neuron disease similar to ALS. Once the mice showed signs of motor neuron degeneration similar to that seen in patients with ALS, fluid containing human embryonic stem cells was infused into the rodent's spinal cord. All 120 showed signs of improvement and some ability to move. Some even regained movement of their extremities, were able to bear their own weight and move around after being treated with embryonic stem cells (Kay, 2001).

Parkinson's disease affects the cells that produce dopamine in the brain. Dopamine, a hormone-like substance, is an essential neurotransmitter. Imbalanced amounts of dopamine can cause brain diseases and dysfunctions. It is critical to how our brains control our movements. Parkinson's disease is caused by the death of a group of dopamine-producing neurons in the substantia nigra. This causes low levels of dopamine to be secreted, resulting in the characteristic jerky, uncontrolled movements. Parkinson's disease affects about two-percent of the population over age seventy. Symptoms include slow and stiff movements, problems with balance and walking, and tremors. Stooped posture, a short shuffling pace, falling, and incontinence can be seen in advanced cases of Parkinson's. The current treatment for Parkinson's disease is a drug called Levodopa (L-dopa), which is converted to dopamine in the brain. This can alleviate the associated symptoms for some. However, as the neurons continue to die, the drug's effectiveness decreases.

Parkinson's disease is a logical candidate for cell replacement therapy because conventional treatments have had limited success. Researchers have had some success treating patients by grafting immature neurons from aborted human fetuses into the affected region. Many patients who undergo this experimental procedure have up to a fifty- percent reduction in symptoms and continue to benefit years after the grafts were implanted. The success of this surgery depends on the survivability of the implanted neurons and making functional connections at the appropriate locations within the brain (Dunnett, 2001). Clearly the mechanism that killed the patient's original cells is not killing the new cells. Researchers can now measure the amount of dopamine being produced using Positron Emission Tomography (PET) images. Figure 5 compares the production of dopamine (bright white in the diagram) before (top) transplantation of the grafts and after (bottom).



Before Surgery



After Surgery

Figure 5. PET Images of Dopamine Levels Following Dopamine-Neuron Transplantation. Dopamine appears as bright white (NIH SCI Report, 2001).

In 1990, the National Institutes of Health funded two double-blind clinical trials of fetal tissue implantation. Neither the patient nor the researcher knew who would receive the experimental treatment. Half of the patients underwent a sham surgery and the other half had fetal tissue implanted into their brain. Patients who received the implants showed no significant improvement (Freed, 2001). However, PET scans and autopsies of patients who received the implants proved that some of the dopamine neurons survived and grew.

The problem with treating Parkinson's patients with embryonic stem cells lies in quantity. It takes approximately six fetuses to provide the stem cells needed to treat one Parkinson's patient. There will always be more patients suffering than there will be replacement tissue. For this reason, and many others, growing ES cell lines, or adult stem cell treatments may be a more feasible approach.

ADULT STEM CELL APPLICATIONS

Embryos are not the only source of stem cells. The public is often unaware that some adult tissues contain stem cells. These adult stem cells are able to regenerate the tissue they were isolated from but are not able to generate multiple kinds of tissues like ES cells. They have fewer ethical concerns because their use does not destroy an embryo. In fact, all four major religions support the use of adult stem cells. The use of adult hematopoietic stem cells in bone marrow transplants has paved the way for the transplantation of pancreas, skin and brain cells. Many organs have tissue-specific stem cell populations. Although only hematopoietic and neural stem cells can currently be isolated, it is clear that the isolation of tissue-specific stem cells will enable cell replacement therapy.

THE TREATMENT OF DISEASES USING STEM CELLS

Hematopoietic Stem Cells: Autoimmune Diseases

Hematopoietic Stem Cells (HSCs) primary purpose is to replenish the blood. HSCs can be cultured to produce stromal stem cells, which differentiate into cartilage and bone. These cells will help create bone after a bone fractures. For other thirty years, hundreds of thousands of lives have been saved through the use of adult hematopoietic stem cells in bone marrow transplants. Hematopoietic stem cells (HSCs) are the "active" component of bone marrow treatments, and these cells create new cellular components of blood (white cells, red cells, platelets) in cancer patients following radiation or chemotherapy.

A new topic in HSCs therapy is the isolation of HSCs from umbilical cord samples instead of bone marrow. Mothers can donate the cord at birth, which can then be used for research purposes, or for treating family members in the future. Cord blood registries are companies that store umbilical cord blood for a fee. After the child is born, the umbilical cord is specially packaged and then shipped to their holding facility. There, the stem cells in the umbilical cord are frozen in a cryogenic tank at –400 degrees Fahrenheit. Currently, these facilities house over 30,000 samples from families. The initial cost is $1,300 followed by a storage fee of $95 per year. Another option is public blood banks, which are free and found in major cities, but the abundance of HSCs in whole blood is far less than in cord blood. Cord blood has treated a wide range of cancers, genetic diseases, immune system deficiencies and blood disorders (Marin, CBS 2002).

HSCs are more abundant in umbilical cord blood than bone marrow, and the cells are more primitive so there is less chance of immunorejection (Viacell, 2002). Blood disorders, such as sickle cell anemia have been successfully treated using stem cells found in umbilical cords (Marin, 2002). HSCs are injected intravenously and then migrate to the bone marrow. If successful, the HSCs will rebuild a new immune system by producing healthy cells to replace diseased blood. HSCs from cord blood are less likely to cause a transplantation complication called graft-versus-host disease, in which white blood cells from a donor attack tissues of the recipient. In a recent review of umbilical cord blood transplantation, Laughlin cites evidence that cord blood causes less graft-versus-host disease Laughlin writes that it is yet to be determined whether umbilical cord blood HSCs are, in fact, longer lived in a transplant recipient. Researcheres found that cells from human cord blood had a greater proliferation capacity than cells dervived from adult bone marrow. White blood cells from cord blood engrafted better in a mouse model, which was genetically altered to tolerate the human cells, than did their adult counterparts.

Hematopoietic stem cells could also be a promising treatment for autoimmune diseases. Autoimmune diesases occur when the immune system is unable to recognize our own cells from foreign cells in the body. Our cells begin to attack other necessary cells in our body. This results in tissue destruction and tissue inflammation. The inflammation leads to the development of swollen blood vessels in vasculitis, destruction of the joints in rheumatoid arthritis, the destruction of the insulin producing beta cells of the pancreas in type 1-diabetes, or damage to the kidneys in lupus. Autoimmune diseases can be organ specific or non-organ-specific. Type 1 diabetes is an example of an organ-specific autoimmune disease because pancreatic beta cells are destroyed, which contribute to the production of insulin. The reasons for the failure of the immune system are not completely known. Similarly, multiple sclerosis is caused by the breakdown of the protective myelin sheath that covers the nerves. However, diseases such as lupus are characterized by vast injury due to reactions against many organs and tissues. Genetic factors, environmental and hormonal influences, and some infections may contribute to tolerance and the development of autoimmune disease (Cooper, 1998). Current treatments for autoimmune diseases include the systemic use of anti-inflammatory drugs and potent immunosuppressive agents. But these treatments have a variety of side effects ranging from upset stomach, indigestion, and stomach ulcers.

Lupus afflicts mostly African-American and Hispanic women. This disease affects the entire body including muscles, skin, joints, the brain and nerves as well as all major organs. The major problem with treating lupus is the lack of a specific target for therapy. Using hematopoietic stem cells to treat lupus is currently being testing in early clinical trials. The stem cells would destroy the long-lived and auto-reactive immune cells and create a properly functioning immune system. To do this, researchers inject a growth factor into the patient. This growth factor intices large amounts of hematopoietic stem cells to be released from the bone marrow. These cells are harvested from the blood and purified. The healthy stem cells are stored until a sufficient quantity of them are obtained. The patient is then exposed to chemotherapy or radiation therapy to kill the defective cells. The purified, healthy hematopoietic stem cells are returned to the patient via a blood transfusion and then migrate to the bone marrow and begin producing new, mature immune cells (Stem Cells: Scientific Progress and Future Research, 2001). The immune system is essentially restored. However, the long recovery period can put the patient at risk for bacterial, fungal and viral infection.

Recent studies suggest that this therapy is an effective and long-term treatment for lupus. A follow-up study of seven patients who underwent the treatment conducted one to three years later found that they remained free from active lupus. The patients continuously improved after treatment. Since the adult stem cells came from their own body, immunosuppressive drugs were not required (Burt, 2000).

Epidermal Stem Cell Treatments: Skin Substitutes

The skin is the largest organ in the body. It is also the first line of defense against dehydration, injury and infection. For these reasons, the skin has evolved an elaborate differentiation process. Mammalian skin consists of a dermal and epidermal component. The epidermal components contain stem cells and are located outside the base of the hair follicle.

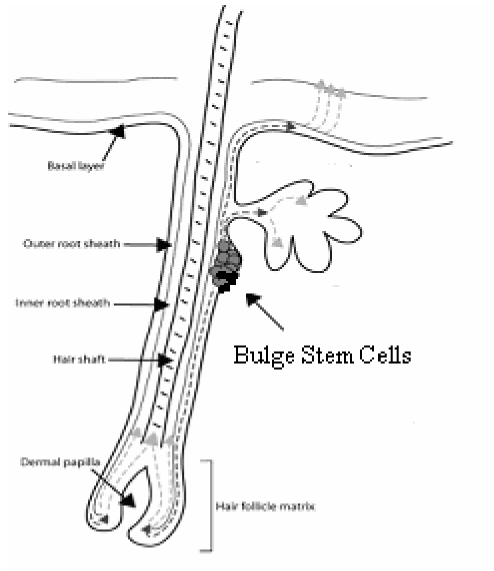


Figure 6. The location of epithelial stem cells (Alonso, 2003).

Tissue, or epithelial, stem cells form the cellular base for the development and repair of tissues and organs. These cells are pursued because they have the potential of therapeutic reprogramming to grow human tissue in vitro for human disease treatment, although they are difficult to identify and characterize. Mammalian skin epithelium has is quickly produced, which becomes more rapid after injury due to burn or wounding. In recent years a significant body of work has begun to characterize the skin epithelial stem cells, both in tissue culture and in mouse and human skin (Alonso, 2003).

Skin grafting has already been proved useful in clinical applications because of their accessibility and ability to be cultured. Cultured epithelial stem cells are most prominently used to replace skin that has been burned, has chronic open wounds or ulcers (Alonso, 2003). Using the patient’s own cells allows for long-term repopulation of skin. Currently, affected areas of skin are replaced with portions of healthy skin. This method id effective but is limited by the surface area of unaffected skin. Culturing stem cells allows for more of the affected area to be treated however, it takes time, leaving the patient with open wounds making them susceptible to infection. There are other potential applications of cultured epithelial stem cells besides replacing damaged skin. Researchers are also considering them as delivery instruments for gene therapy (Alonso, 2003).

There are four current skin constructs that are commercially available. Genzyme Tissue Repair is offers a product called Epicel that takes a small sample of the patient's skin and then grows sheets of the same skin in about sixteen days (www.genzymebiosurgery.com). Integra LifeSciences Corporation engineered a wound dressing using synthetic collagen and silicon layers. Organogenesis Corporation's Apligraft is similar to Integra LifeSciences' skin substitute, however it incorporates human fibroblasts (dermal cells), which forces the epidermal cells to multiply causing the replication of the human epidermis (www.apligraft.com). The final skin grafting product is Advance Tissue Science's Transcyte. This graft uses cultured fibroblasts and nylon layers to reproduce the dermis.

Scientists are now trying to create skin substitutes that are readily available and do not cause rejection of the transplant (autologous transplant). The best method to obtain cultured epithelial autografts is through taking a small biopsy and putting it in culture. The biopsy is done in hairy sites because adult pluripotent stem cells are located at the base of the hair follicle (Coulomb, 2002). Cells are then cultured and placed on the patient's wound to promote healing.

Neural Stem Cell Treatments: Parkinson's Disease

Neural stem cell transplantation occurs when there is a loss of brain function. Researchers have had some success treating Parkinson's patients by grafting neurons from aborted fetuses into the affected region of the brain. Many patients who undergo this experimental procedure have up to a fifty- percent reduction in symptoms and continue to benefit years after the grafts were implanted. However, there neuronal grafts are not the only option. Wesley Smith from the National Review points to a study conducted using adult stem cells. A 49-year-old man was diagnosed with a progressive case of Parkinson's disease. Drug therapy did not help, so he tried an experimental procedure. Adult stem cells were harvested from the patient's brain using a standard brain biopsy method. The cells were cultured to several million cells, with twenty-percent maturing into dopamine producing neurons. In March 1999, the cells were injected into the man's brain. Three months later, the man's motor skills had improved by thirty-nine- percent and the dopamine production was up fifty-five- percent (Smith, 2002).

Pancreatic Stem Cell Treatments: Diabetes

Currently, there are 16 million people suffering from diabetes. It causes almost 200,000 each year, more than breast cancer and AIDS combined (www.diabetes.org). Diabetes is a group of diseases that are described by abnormally high levels of the sugar glucose in the bloodstream. The excess glucose causes the complications of diabetes, including blindness, kidney failure, stroke, and heart disease. There are two main types of diabetes; type 1 diabetes, known as juvenile-onset diabetes, affects mostly children, and young adults and type 2 diabetes, called adult-onset diabetes, affects mostly adults. Diabetes develops when the body's own immune system does not recognize its own islet cells and therefore regards them as foreign invaders. The immune system attacks the islet cells of the pancreas, which normally produce insulin. The absence of insulin prevents glucose from entering the cell and glucose accumulates in the blood (www.diabetes.org).

There is currently no cure for diabetes. People with type 1 diabetes must rely on blood glucose concentration monitoring and take insulin shots. People with type 2 diabetes can often control their blood glucose concentration with diet, exercise and oral medications. Each year 1,300 people with type 1 diabetes receive whole-organ pancreas transplants and 83 percent will have no symptoms of diabetes. To prevent the body from rejecting the transplant, patients must take powerful immunosuppressive drugs for life. These drugs mute their immune system, making the patient highly susceptible to infections. Some physicans oppose the transplantions because the infections may be more life-threatening than diabetes itself.

In 2000, researchers announced that ductal cells isolated from adult human pancreatic tissue could be induced to produce insulin when exposed to glucose (Bonner-Weir, 2000). The hope is that a biopsy may be done to remove duct cells from a patient, culture them and give the healthy islets back to the patient. Both type 1 and type 2 diabetes could be treated with this therapy. These results have been confirmed by another group of researchers who also cultured cells from pacreatic ducts in humans and

mice. Implanting the cultured cells reversed diabetes in mice (Stem Cells: Scientific Progress and Future Research, 2001). More recent studies suggest that only embryonic stem cells are the only cells capable of differentiating in beta cells (Dor, 2004).
Using adult stem cells to treat diabetes is still in its infancy and studies using embryonic stem cells have had more success. ES cells are able to generate cell lines that are free of contaminants and can self renew, although until a theraputically useful source is developed all avenues must be explored.

Cardiac Treatments

In the United States, it has been estimated that congestive heart failure afflicts 4.8 million people and there are 400,000 new cases each year (Stem Cells: Scientific Progress and Future Research, 2001). This disease is caused by the destruction of cardiomyocytes, the heart's muscle cells. Hypertension, cornonary artery disease or a heart attack can kill these cells. Although there have been advances in surgical procedures, drug therapy, and organ transplantation the heart remains weak and the patient often dies within five years of diagnosis. Stem cells could offer a cure if damaged cardiomytes can be replaced.

The cardiomyte is the heart muscle cell that contracts to force the blood out of the heart's pumping chamber, known as the ventricle. Two additonal specialized cells are the vascular endothelial cell and the smooth mucle cell. The vascular endothelial cell forms the lining of new blood vessels and the smooth muscle cell forms the blood vessel walls (Stem Cells: Scientific Progress and Future Research, 2001). These two cells contribute to the network of arteries responsible for transporting nutrients and oxygen.

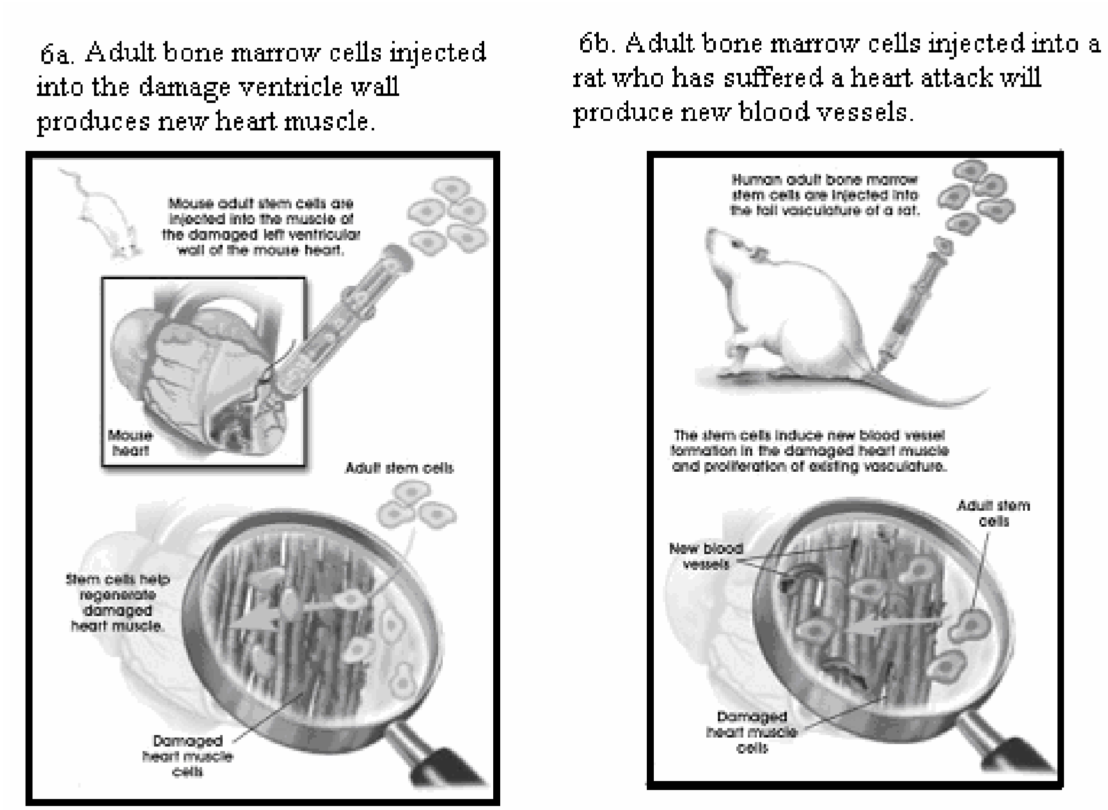


Figure 7. Heart Muscle Repair with Adult Stem Cells. (© 2001 Terese Winslow, Lydia Kibiuk)

To test the theory that heart muscles can regenerate if given healthy cells, researchers induced heart attacks in a group of mice. Heart attacks damage the cardiomyocytes, vascular endothelium and muscle cells in the heart resulting in severely damaged blood vessels. This damage reduces blood, oxygen and nutrients going into and out of the heart. Following the heart attack, researchers isolated a group of adult bone marrow cells in the mice. These bone marrow cells had the ability to develop into many cell types. These cells formed new cardiomyocytes, vascular endothelium and smooth muscle cells when injected into damaged ventricle walls within the heart (Figure 6a). New coronary arteries, arterioles, and capillaries were formed, and within nine days occupied 68 percent of the damaged portion. Essentially, the dead myocardium was replaced with functioning tissue. The mice that received the transplant were more likely to survive than the mice that did not receive the transplant. Follow-up experiments are now being conducted to extend the posttransplantation analysis time to determine the longer-range effects of such therapy (Stem Cells: Scientific Progress and Future Research, 2001).

CHAPTER 3: STEM CELL ETHICS

Figure 1 Cartoon by Gary Marsten

Stem cells have been a controversial topic in ethics ever since they were discovered. The major ethical concern plaguing stem cells has been their derivation. Embryonic stem (ES) cells are derived from embryos early in their development. Embryonic germ (EG) cells are derived from the tissue of aborted fetuses, even later in development than ES cells. These two types of stem cells have triggered one of the largest ethical debates in the past century. Many varied social, religious, political and ethical viewpoints have fueled this debate. Another factor contributing to the amount of controversy over stem cells is ignorance. People are forming opinions, and making ethical and moral judgments without knowing anything about what they are judging. Ignorance and misunderstanding have plagued stem cells from the start, with most people assuming all stem cells are alike. We must be educated about where, how and when stem cells can be derived in order to make any opinion on the topic.

Religion is the starting place for the ethical opposition to stem cell research because of its tremendous influence on the general public and, unfortunately, politics. The sources of turmoil in the religious part of the debate are the two moral obligations instilled upon people by the majority of religions. The first being that we, as humans, have the moral obligation to help other people in need. Promises held in stem cells seek to revolutionize worldwide medical care, and start healing people that have no hope at the moment. The other moral obligation is that we must not assume the role of creator. In the scope of this ideology we do not have the authority to choose life or death for another human being. This is where abortion, EG cells, ES cells and stem cell research in general collide with religious belief.

The initial question that rises from this debate is whether it is ethical to destroy an embryo or a fetus. Separate from stem cell research, there is currently a large ethical battle over the question of whether abortion should be legal. A question, coupled to the last, is when does a fertilized egg become human. At one end of the spectrum of views on the human status of the embryo is the view that, from conception, the embryo is fully a person with all the rights any person has, most notably the right to life. At the other end of the spectrum stands the view that the early embryo is little more than cellular material the size of the dot at the end of this sentence, which demands little, if anything, of us morally. Reductionist views of the fetus are often found, for example, in the writings of those whose moral views are shaped by the law. Consider the work of the well-known and influential legal scholar John Robertson. Although Robertson would probably dispute the characterization of his view as the extreme, one that embryos are merely biological material, the way he frames his discussion of embryo research and the uses of the embryos indicates that his view is extreme. For Robertson, the real question in the debate about embryo research is whether the reproductive freedom that justifies assisted reproduction also justifies embryo research. In his book, *Children of Choice,* Robertson tells us that the fundamental question is this: "Does procreative liberty entitle people to use their reproductive capacity to produce products or material to serve nonreproductive ends?" (Robertson 1994) Once the question is framed in this way, the only real reason to oppose embryo research is that it may involve a kind of symbolic harm to embryos, and this harm will almost always be outweighed by the potential benefits of embryo research.

VIEWS OF THE FOUR MAJOR RELIGIONS

The four major religions in the United States certainly disagree on many issues of the embryonic research debate. One question of religious concern is whether it is even ethical to use something that has the potential to be human in research. Should we take something that could become a human and use it for the preservation of our society. Ethicists say the right and wrong of destroying even unwanted embryos in order to do promising medical research depends on what you think those embryos are. If they have the moral status of persons, many argue, then they cannot be treated as a means to even the most humanitarian end. If they are other than future persons, then doing the research may seem to help the greater good.

CATHOLIC

Catholic view on the status of an embryo is that, from conception, there is human life. We see this, for example, in the Instruction Donum Vitae, issued by the Vatican's Congregation for the Doctrine of the Faith (CDF) in 1987 (http://www.cin.org/vatcong/donumvit.html), where it is written: "The human being is to be respected and treated as a person from the moment of conception; and therefore from the same moment his rights as a person must be recognized, among which in the first place is the inviolable right of every innocent being to life." The implication of this view of the fetus for Catholic teaching on abortion has long been clear: abortion is an abominable crime. In Donum Vitae, however, the CDF draws out the implications of this view of the fetus for embryo research as well. "No objective," the CDF writes, "can in any way justify experimentation on living human embryos or fetuses, whether viable or not, either inside or outside the mother's womb." Indeed, this has been the consistent response of the Catholic Church to every new scientific development in reproductive technology that involves manipulating early embryos. Whether the issue is IVF or embryo freezing, preimplantation genetic diagnosis or ES cell research, all are wrong—indeed, the suggestion is that all are murderous, because all typically involve the destruction of a living person in the eyes of the Catholic Church. The U.S. Roman Catholic Bishops oppose the research as "immoral, illegal, and unnecessary." They say life is sacred from the moment of conception.

Although the Catholic Church condemns embryonic stem cell research, they do support some forms of research. Adult stem cell and parthenote research are both accepted by the majority of Christian religions with the exception of a few radical factions, who view all stem cell research as “playing” God.

JEWISH

There is an emerging consensus of Reform Jewish authorities that tissue obtained from either therapeutic or spontaneous abortions may be used for purposes of life-saving or life-enhancing research and treatment. Jewish requirements that we use our God-given knowledge to heal people, together with the concept of pikuach nefesh (Scheib, 2005) (the primary responsibility to save human life, which overrides almost all other laws) has been used by Jewish legal authorities to justify a broad range of organ transplants and medical experimentation. These requirements likewise justify the use of fetal tissue transplants. The Religious Action Center of Reform Judaism also approves, saying what would be "immoral and unethical" is cutting off funds for promising medical research. The Union of Orthodox Jewish Congregations agreed, saying, "an isolated fertilized egg does not enjoy the full status of personhood" (www.pbs.org). Judaism also condones the use of adult stem cells and parthenotes in stem cell research.

MUSLIM

Embryonic stem cell research is not opposed by the Muslim religion, although there is still some debate as to when ensoulment occurs. Some Islamic scholars hold favorable views toward embryonic stem-cell research from the perspective of sharia (Islamic law). Most of these scholars believe ensoulment of the embryo occurs on the 120th day of the pregnancy (well past the 5 day old blastocyst from which ES cells are isolated), and that is the point when it gains its moral status or rights as a legal person. Other Islamic scholars, however, say ensoulment occurs on the 40th day (also well past 5 days). According to another view of sharia, there is a distinction between potential life and actual life. Although life begins at conception in the womb, an embryo formed by artificial fertilization is not in its natural environment. If it is not placed in the womb it will not survive and it will not become a human being. Iranian scientists developed human embryonic stem-cell lines in 2003 with the approval of Ayatollah Seyed Ali Khamenei, Iran's supreme religious leader. Singapore, where Muslims have a slight majority, has also produced embryonic stem-cell lines. And nonembryonic stem-cell research, using adult and umbilical stem cells is conducted in Iran, Saudi Arabia, and Malaysia. In 2003, a scholar in Cairo issued a fatwa (Islamic religious ruling) stating that therapeutic cloning of embryos would be considered lawful and could be compared to the accepted practice of donating cells, tissues, or organs for transplants.

HINDU

Many Hindus see the soul - the true Self (or atman) - as the spiritual and imperishable component of human personality. After death destroys the body, the soul soon finds a new temporal home. Thus, for Hindus as much as for Catholics, life begins at conception. The ancient system of Indian medicine known as Ayurveda assumes that fetuses are alive and conscious when it prescribes a particular mental and spiritual regimen to pregnant women.

American scientists and businessmen note enviously that religious and moral considerations do not seem to inhibit Indian biotechnologists. But this indifference to ethical issues would have certainly appalled Gandhi, father of the Indian nation. Gandhi accused Western medicine, along with much of modern science and technology, of inflicting violence upon human nature. His vegetarianism and belief in nonviolence were derived from Indian traditions, mainly Hinduism, which is also the faith, though loosely defined, of most Indian scientists and businessmen.

WHY WE NEED ES AND EG CELLS FOR RESEARCH

The reason that researchers need ES and EG cells is because of our lack of knowledge about human genetics and development. We are only beginning to understand the very basics of embryonic development, and such research needs to be done to understand how to repair developed humans. The issue socially is whether we should be able to use an aborted fetus for EG cell research, separate from the issue of abortion. The other issue is whether it is ethical to use human embryos from fertility clinics for research. Unused embryos from couples using IVF or other infertility procedures can be donated for research, donated for infertile couples, destroyed, or permanently frozen. All will eventually be destroyed. These “extra” embryos could be used for research that would benefit society as a whole, and are going to be destroyed, essentially wasted. Using these for research would be the logical decision, seeing that they will be used to benefit all humans, and are going to be destroyed. But many people oppose the use of these ES cells for research. Getting these ES cells from spontaneous abortion has proven to be unreliable because of the specific time frame in which it must occur and the chances of it happening outside the hospital environment. The spontaneously aborted embryos also usually have genetic anomalies that prevent them from being used for research.

Unfortunately we are at a stage right now where we need ES cells to be able to advance our understanding of the human body on a genetic level, and to save lives via therapy.

CHAPTER 4: STEM CELL LEGALITIES

Figure 2 Cartoon by Vic Harville

Stem cell research in the U.S. has been delayed mostly due to politics. In 2001 President Bush declared that all government-funded research could only work with ES cell lines that were in existence before August 9, 2001. The decision has crippled the United States' ability to conduct stem cell research. The government declared that there were over 60 ES cell lines available for research, when in reality there were only about 19, as determined by subsequent genetic analysis. President Bush also proposed a ban on cloning technology. This proposal came after Advanced Cell Technology (Worcester, MA) announced it had successfully cloned a human embryo for research. This announcement magnified the misunderstanding revolving around human stem cell research and cloning. The words cloning and embryonic research triggered an immediate response from a more or less neutral uneducated government. People hear cloning and think about Dolly the cloned sheep, or about scientists creating clones of people. This is a misconception commonly made by a large part of society. The reality of the cloning was that Advanced Cell Technology had cloned a human embryo for ES cell research. The possibility of creating a developed cloned human without problems is a long way off, and people do not understand the difference between that kind of cloning and cloning to create new ES cell lines.

The thing that most of the people opposing stem cell research and cloning research are forgetting is that someone is going to do the research whether we think it is right or not. We, as a world power, should lead the scientific community into the unknown of stem cell technology. Instead, research is halted due to all of the ethical issues that arise from the idea of stem cells. Stem cell ethics and policy should be looked at carefully, but they should be looked at in an educated framework. Forming opinions about something that is unknown should be frowned upon, but popular figures in our society have come out condemning it without any understanding. In order for our society to make a conscious, educated decision about stem cell research we must strive to educate everyone involved in legislative decisions.

STEM CELL RESEARCH IN OTHER COUNTRIES

Although human ES cells were first isolated in the U.S., other countries have begun the race for stem cells, and we are having difficulty staying in the game due to our crippling stem cell research laws. On July 7, 2005 the Korean government gave permission for stem cell research. Seoul National University Professor Hwang Woo-suk, the world-renowned cloning pioneer, was already allowed to conduct his stem cell studies in January. Maria Biothec head Dr. Park Se-pill is one of the leaders in creating new stem cell lines from frozen embryos. He harvested 7 stem cell lines from 20 frozen embryos in 2004. This is an unprecedented success in harvesting stem cell lines from frozen human embryos. In the Czech Republic new stem cell lines were created last year at the Mendel University of Agriculture and Forestry. Sweden allows stem cells to be harvested from unused IVF embryos. Sweden also has more than 30 research teams and over 300 people doing the research, setting them far ahead in the stem cell manpower. Researchers in Sweden have been conducting stem cell research for over 15 years now and have the most funding for their research. "Professor Patrik Brundin, who heads the section for Neuronal Survival at the Wallenberg Neuroscience Centre at Lund University, has been transplanting neural tissue from aborted embryos six to eight weeks old into patients with Parkinson's disease for more than 15 years". (http://www.geocities.com/giantfideli/CellNEWS_Swedens_stem_cell_success.html) For this and other reasons, the Swedish have been granted a lot of private funding from Parkinson's charities and private donations. Michael J. Fox, the actor afflicted with Parkinson's disease, donated US$4.4 million to the Swedish for research developing a new line of cells to specifically do research on Parkinson's disease. The Czech Republic, Singapore, Israel, Sweden and Finland have all created new stem cell lines that use human feeder-cells rather than mouse. The advantage to this is that there is no chance of implanting stem cells that carry mouse born viruses. The US has one privately funded laboratory that has created stem cells using human feeder cells. Susan Fisher's California lab is the only lab in the US that has successfully created these cells under private funding from Geron Corp. But due to the lack of federal funding in the United States we have fallen behind from the stem cell frontier. The numbers below speak for themselves.

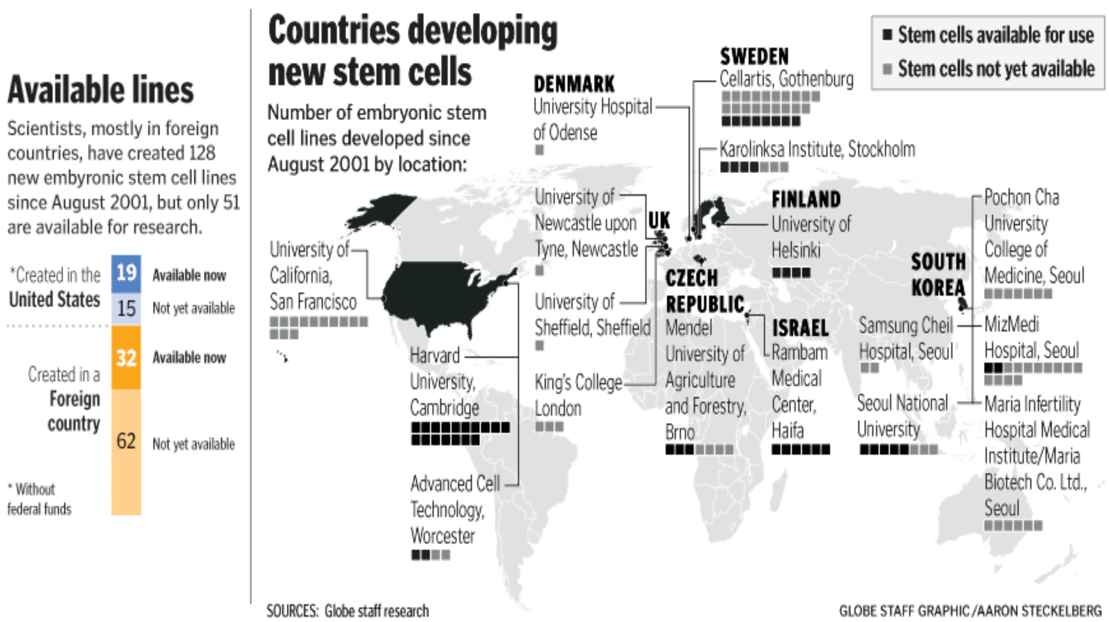


Figure 3. Countries Developing New Stem Cells. Boston Globe http://www.boston.com/news/science/articles/2004/06/02/stem3/

In the United States we currently have 19 ES cell lines to conduct research. The rest of the world has begun to pass the US in stem cell technology, and the number of ES cell lines available for research. Not only are we losing the stem cell race but we are also losing some of the best scientists in the world to other countries. The lack of federal funding and the restrictions on stem cell research has caused some of the best minds in our country to either choose not to work with stem cells, or to move abroad where stem cell research is less restricted to conduct their research.

PROGRESS WITHIN THE UNITED STATES

The United States has made some progress in the past 2 years. Although there was little congressional activity on stem cells after the President's decision on stem cell research, some Members of Congress and many patient advocacy groups continued to express concern that the President's policy hinders the progress of stem cell research. When the approximate number of currently available stem cell lines was revised to 20 from 60, several Members of Congress introduced bills during the spring of 2004 that would have required funding for human ES cell research using newer ES cell lines. On April 28, 2004, more than 200 Members of the House sent a letter to the President urging an expansion of the policy; a similar letter from the Senate followed. Former President Ronald Reagan's death from Alzheimer's disease on June 5, and former First Lady Nancy Reagan's subsequent pleas to expand the policy led to significant media coverage during the summer of 2004. The issue of stem cell research also played a large part in the 2004 presidential election.

When the 109th Congress convened, several Members of Congress reintroduced legislation that had been introduced during prior Congresses. Action by several States to authorize and fund human ES cell research created additional pressure on Congress to consider legislation in this area. In fact, in an effort to support State actions related to human ES cell research, Representative Nancy L. Johnson introduced H.R. 1650, the Stem Cell Research Investment Act of 2005. The bill would allow States to issue $30 billion worth of zero-interest bonds to fund stem cell research, giving bondholders federal tax credits in lieu of interest payments.

On May 24, 2005, the House passed H.R. 810, the Stem Cell Research Enhancement Act of 2005, by a vote of 238 to 194. The bill, strongly opposed by the White House, would effectively overturn the policy established by President Bush in August 2001. The vote was particularly significant because included 50 Republican Members who voted in favor of the bill, and who were the Chairs of 7 Committees and 13 Subcommittees.

The bill H.R. 810, which was passed by Congress, is the Stem Cell Research Enhancement Act of 2005. The bill if passed would effectively overturn the President's decision on stem cell research. It Requires the Secretary of Health and Human Services to conduct and support research using human ES cells, and requires the following criteria be met: 1) the stem cells must be derived from embryos that were created for fertility purposes, in excess of clinical need, and donated from in vitro fertilization clinics, 2) prior to consideration of embryo donation, it must be determined that the embryos would never be implanted in a woman and would otherwise be discarded, and 3) donation must be made with written informed consent and without any financial or other inducements.

PUBLIC OPINIONS IN THE UNITED STATES

Public outcry and celebrity endorsement have put stem cells on the move again. It is only a matter of time before the US has to change its policies on ES cell research.

Many poles conducted in the US have shown public backing for ES cell research and funding. A recent pole conducted by Reasearch!America and PARADE sampled 1,000 people across the country. The sample was proportionate to the country's demographics, including geography, gender and ethnicity. The survey, fielded June 4–9, 2005, has a theoretical sampling error of ± 3.1%. The pole resulted in the following results (http://www.stemcellresearchfoundation.org/WhatsNew/July_2005.htm#8\):

Six in 10 Americans (58%) say they support using ES cells in medical research, according to a new national poll by Research!America and PARADE magazine. Three in 10 (29%) are opposed. The poll asked 1,000 adults their views on ES cell research and the importance of maintaining U.S. leadership in research. Results will be published in the July 10, 2005 issue of PARADE.

Other key findings include:

- Six in 10 Americans (63%) believe the U.S. should have a uniform national policy for medical research using ES cells.
- Almost as many (57%) favor federal funding of ES cell research.
- Many Americans (62%) say they are following the issue of stem cell research at least somewhat closely, but 37% say they are not.
- Of those who oppose ES cell research, 57% say their opposition is based on religious objections.
- Nearly half (49%) of those who identify themselves as Republicans, 71% of Democrats, and 53% of Independents say they support ES cell research.

With the rest of the world beginning new stem cell research and approving embryonic stem cell research it is only a matter of time before the US has to change its laws regarding the use of embryos in stem cell research. Public support for stem cell research in our country will eventually prevail. If we are to be the leaders of the free world then we must direct stem cell research in a positive direction and lead the scientific community in stem cell research. Given the promises and the worldwide support for the research the United States should proceed conducting safe, responsible, and ethical research in stem cells.

CONCLUSION

Most cells within an animal or human being are committed to fulfilling a single function within the body. In contrast, stem cells are a unique and important set of cells that are not specialized. Stem cells retain the ability to become some or all of the more than 200 different cell types in the body and thereby play a critical role in repairing organs and body tissues throughout life. Although the term stem cells is often used in reference to these repair cells within an adult organism, a more fundamental variety of stem cells is found in the early stage embryo. Embryonic stem cells may have a greater ability to become different types of body cells than adult stem cells.

Stem cell research has been the target of many recent ethical debates, mainly because of the controversy over how they are derived. In August 2001, President Bush announced that for the first time federal funds would be used to support research on human embryonic stem cells, but funding would be limited to "existing stem cell lines." The National Institutes of Health (NIH) has established the Human Embryonic Stem Cell Registry, which lists 78 stem cell lines that are eligible for use in federally funded research. However, only 19 embryonic stem cell lines are currently available. Scientists are concerned about the quality and longevity of these stem cell lines. For a variety of reasons, many believe research advancement requires new embryonic stem cell lines, and for certain applications, stem cells derived from cloned embryos may offer the best hope for progress in understanding and treating disease. A significant number of pro-life advocates support stem cell research arguing that saving the life of a real person takes precedence over a blastocyst that only has the potential to become a human. Those opposed are concerned that the isolation of stem cells requires the destruction of embryos.

Misconception and ignorance have restricted stem cell research in the United States. Our policy makers and our general population need to become educated in order to make the right decision about stem cell research. Religion and state should be separated once again, and our policy makers should start listening to the people. Without federal funding and public backing for stem cells, we are going to delay what is eventually going to be realized as a major medical revolution.

BIBLIOGRAPHY

Bonner-Weir, S., Taneja, M., Weir, G.C., Tatarkiewicz, K., Song, K.H., Sharma, A., and O'Neil, J.J. (2000). *In vitro* cultivation of human islets from expanded ductal tissue. *Proc. Natl. Acad. Sci.* U. S. A. *97,* 7999–8004.

CellNEWS, Sweden's Stem Cell Success (2002) http://www.geocities.com/giantfideli/CellNEWS_Swedens_stem_cell_success Accessed 8-03-05

Cibelli JB, Kiessling AA, Cunniff K, Richards C, Lanza RP, West MD (2001) Somatic Cell Nuclear Transfer in Humans: Pronuclear and Early Embryonic Development. *Journal of Regenerative Medicine* **2**: 25-31. Data includes human parthenotes.

Cibelli JB, Grant KA, Chapman KB, Cunniff K, Worst T, Green H, et al (2002) Parthenogenetic Stem Cells in Non-human Primates. *Science* **295**: 819.

Chapman, A., Frankel, M., Garfinkel, M. *"Stem Cell Research and Applications: Monitoring the Frontiers of Biomedical Research".* American Assoication for the Advancement of Science and Insitute for Civil Society. Novemeber, 1999.

Cooper, G., Hausman, R. Sinauer Associates, Incorporated. The Cell: A Molecular Approach (Third Edition). January, 2004.

Cooper, G.S., Dooley, M.A., Treadwell, E.L., St Clair, E.W., Parks, C.G., and Gilkeson, G.S. (1998). Hormonal, environmental, and infectious risk factors for developing systemic lupus erythematosus. *Arthritis Rheum*. *41,* 1714–1724.

Donum Vitae, Congregation for the Doctrine of the Faith http://www.cin.org/vatcong/donumvit.html Accessed 7-05-05

Dunnett, S.B., Bjorklund, A., and Lindvall, O. (2001). Cell therapy in Parkinson's disease—stop or go? *Nat. Rev. Neurosci*. 2, 365–369.

Farley, Margaret A. (1999) "Roman Catholic Views on Research Involving Human Embryonic Stem Cells". *Ethical Issues in Human Stem Cell Research*, Volume III: Religious Perspectives.

Freed, C.R., Greene, P.E., Breeze, R.E., Tsai, W.Y., DuMouchel, W., Kao, R., Dillon, S., Winfield, H., Culver, S., Trojanowski, J.Q., Eidelberg, D., and Fahn, S. (2001). Transplantation of embryonic dopamine neurons for severe Parkinson's disease.

N. Engl. J. Med. 344*,* 710–719.

Green, R. Human Embryo Research Debates: Bioethics in the Vortex of Controversy. Oxford University Press. July 2001.

Harvard Stem Cell Institute. http://stemcell.harvard.edu/public/stemcells.php Accessed 6-22-05.

Jewish Virtual Library, Ariel Scheib http://www.jewishvirtuallibrary.org/jsource/Judaism/pikuach_nefesh.html Accessed 7-13-05

Kay, K. & Henderson, M. "Paralyzed Mouse walks again as Scientists Fight Stem Cell Ban." *Times Newspapers Limited*. July 26, 2001.

Kim, D.K., Fujiki, Y., Fukushima, T., Ema, H., Shibuya, A., and Nakauchi, H. (1999) Comparison of hematopoietic activities of human bone marrow and umbilical cord blood CD34 positive and negative cells. *Stem Cells*. 17, 286–294.

MacKey, M.C. (2001). Cell kinetic status of haematopoietic stem cells. *Cell. Prolif. 34,* 71–83.

Marin, C. (2002) "*The Holy Grail"*. CBS Broadcast, 60 Minutes II.

NIH SCI Report. http://stemcells.nih.gov/info/scireport/appendixB.asp Accessed 7-28-05

NIH, Stem Cell Basics-3. http://stemcells.nih.gov/info/basics/basics3.asp Accessed 6-22-05.

NIH, Stem Cell Basics-4. http://stemcells.nih.gov/info/basics/basics4.asp Accessed 6-22-05.

NIH SCI Report. http://stemcells.nih.gov/info/scireport/chapter9.asp Accessed 7-29-05

Parson, A. The Proteus Effect: Stem Cells and Their Promise for Medicine. National Academy Press. September, 2004.

PBS, Religious views on stem cell research, episode 448, July 27, 2001 http://www.pbs.org/wnet/religionandethics/week448/perspectives.html Accessed 8-03-05

Robertson, John A. (1994), Children of Choice: Freedom and the New Reproductive Technologies, Princeton University Press.

Ruse, M., Baird, R., Pynes C., (et. al). Stem Cell Controversy: Debating the Issues. Prometheus Books. November, 2002.

Shannon, Thomas (2001) Human Embryonic Stem Cell Therapy. *Theological Studies* **62**: 811-824.

Smith, Wesley J (2002). "Spinning Stem Cells." National Review Online. http://www.nationalreview.com/comment/comment-smith042302.asp

Stem Cell Research Foundation http://www.stemcellresearchfoundation.org/WhatsNew/July_2005.htm#8\ Accessed 8-03-05

"Stem Cells: Scientific Progress and Future Research Directions" (2004) Department of Health and Human Services. Site updated June 10, 2004. http://stemcells.nih.gov/info/scireport

Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, Jones JM (1998) Embryonic Stem Cell Lines Derived From Human Blastocysts. *Science* **282**: 1145-1147.

Traynor, A.E., Schroeder, J., Rosa, R.M., Cheng, D., Stefka, J., Mujais, S., Baker, S., and Burt, R.K. (2000). Treatment of severe systemic lupus erythematosus with high-dose chemotherapy and haemopoietic stem-cell transplantation: a phase I study. *Lancet 356,* 701–707.

Vogel, G (2000) "Can Old Cells Learn New Tricks?" *Science Magazine* 287: 1418. American Association for the Advancement of Science.

Weiss, R. *"Parthenotes Expand the Debate on Stem Cells." The Washington Post.* December 9, 2001. http://www.washingtonpost.com/ac2/wp-dyn/A18046-2001Dec9?language=printer

Viacell (2002) www.viacellinc.com

Viacord (2002) www.viacord.com

White House Press Release (2001) http://www.whitehouse.gov/news/ Accessed 7-05-05