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# STEM CELLS AND SOCIETY

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# ABSTRACT

The purpose of this project is to build an in-depth compilation of information related to the topic of stem cells, and to make conclusions regarding the impact of this technology on society. This project is divided into four distinct chapters: 1. Stem Cell Types and Sources, 2. Stem Cell Applications, 3. Stem Cell Ethics, 4. Stem Cell Legalities. The first two chapters investigate the different types of stem cells while explaining their applications, both existing and potential. The latter two chapters explain the effects of the technology on society, and how society shapes the laws that can freeze or expand stem cell usage. Based on the research, a conclusion was reached that stem cells are and will be very beneficial to society, and the recent legislations in the US are helping expand the technology.

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# PROJECT OBJECTIVES

The objectives of this IQP were to examine stem cell technology, and determine its effects on society. Chapter 1 describes the classification of stem cells and the different sources from which they are isolated. This chapter also describes various abilities of each type. Chapter 2 focuses on various uses and applications that have been successful in the scientific field, as well as those that may be successful in the near future. These experiments encompass a wide range, from pre-clinical animal experiments to human trials, and include future possible uses of this technology. Chapter 3 describes the ethics regarding stem cells that make this technology a very controversial subject. This chapter introduces the main arguments in favor of and against stem cell research. The fourth chapter compares the laws of the United States to various international laws that govern the use of stem cells. Finally, the authors of this project put together a conclusion based on their thoughts on the use of certain stem cells, and their thoughts on the laws that affect stem cell use.

# CHAPTER-1: STEM CELL TYPES AND SOURCES

Since the beginning of time, human beings have been fascinated with the use of new technologies for the advancement of the human race. Many advances in science have provided new health care opportunities, such as new medicines to cure illnesses. As new technological advancements and discoveries are made, it can take society time to adapt to the new technology. One very good example of this is the topic of stem cells. Although these cells have the potential to save thousands of human lives, one type (embryonic stem cells) are highly ethically controversial, and society is still adapting to their use. But not all stem cells are equal, and some are far less controversial than others. The purpose of this chapter is to document the various kinds of stem cells, as a basis of subsequent chapters on their uses, ethics, and legalities.

**What Are Stem Cells?**

Stem cells are cells that have a long life (the ability to continuously divide) and an ability to differentiate (develop) into various other kind(s) of cells/tissues (GodandScience.org, 2009). These abilities allow them to replace cells that have died, so they have been used to replace defective cells/tissues in patients with diseases or defects. Thus, these cells are the basis of the new field of "regenerative medicine".

Stem cells are the foundation for every organ and tissue in the body. They are like a blank microchip that can be programmed to perform particular tasks. Stem cells are undifferentiated or "blank" cells that have not yet fully specialized, and distinguish themselves from other cell types because of two characteristics that are rare to any other type of cell. First, they can self renew, that is they can divide and create identical copies of themselves, sometimes

after long periods of inactivity. Second, under proper and correct physiologic or experimental conditions, stem cells can begin to develop into specialized tissues and organs that possess the tissue/organ's specific functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.

Stem cells are important for living organisms for many reasons. In the 3- to 5-day-old embryo, called a blastocyst, the inner cells (that contain embryonic stem cells) give rise to the entire body of the organism, including all of the many specialized cell types, such as the heart, lung, skin, sperm, eggs and other tissues. In some adult tissues, such as bone marrow, muscle, and brain, discrete populations of adult stem cells generate replacements for cells that are lost through normal wear and tear, injury, or disease. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes, and heart disease. However, much work remains to be done in the laboratory and the clinic to understand how to use these cells for cell-based therapies to treat disease.

**Stem Cell Classification**

Although the public often classifies "stem cells" into one large category, there are actually many different types of stem cells, which are not alike. And because each has different ethical concerns, it is important to understand the difference between the various types. The two main types are embryonic stem (ES) cells and adult stem cells (ASCs). Embryonic stem cells exist only at the earliest stages of embryonic development, while adult stem cells occur in the adult organism. The ASC category also loosely includes umbilical cord blood stem cells. Stem cells can also be categorized by their potentials, or their ability to form other tissues. *Totipotent*

cells (newly fertilized eggs) can form an entire organism. *Pluripotent* cells (ES cells) can form any type of cell except the placenta. *Multipotent* cells (i.e. hematopoietic stem cells), can form several types of related cells (in this example, several types of blood cells). *Unipotent* cells can usually form only one type of tissue, that from which they are isolated.

**Embryonic Stem Cells**

Embryotic stem (ES) cells are grown from the cells that make up the inner cell mass of a mammalian blastocyst. These highly controversial cells are derived from *in vitro* fertilization (IVF) embryos. Currently in the U.S., only excess eggs from IVF clinics, originally created for reproductive purposes but not needed by the parent donors, are used to derive ES cell lines (Kirschstein and Skirboll, 2001). Researchers can not use eggs fertilized in a woman's body. The IVF eggs are cultured about 5 days to the blastocyst stage. The blastocyst includes a the blastocoel (a hollow cavity inside the blastocyst), the trophoblast (the layer of cells that surrounds the blastocoel), and the inner cell mass (a group of cells at one end of the blastocoel that develop into the embryo proper). The inner cell mass cells are obtained by micropipettes, and the ES cells are grown (to make an ES cell line) in media containing growth factors to maintain their de-differentiation. These ES cells can proliferate indefinitely in culture, and can produce an unlimited source of cells that can differentiate into specific important adult cells such as bone, muscle, liver, or blood cells. ES cells are the most ethically controversial type, since the embryo used to obtain the inner cell mass is usually destroyed, thus some believe the isolation process ends the "life" of the embryo.

Mouse ES cells are the most highly studied, and have taught us about how pluripotent cells grow and specialize, and how mammalian embryonic development works. Indeed, mouse

ES cells have been a critical research tool for studying the function of individual genes and for modeling specific human diseases; mouse ES cells can be manipulated to contain specific genetic changes, and then used to generate transgenic mice containing this change to observe its effect.

In 1981, embryonic stem cells (ES cells) were first derived from mouse embryos by Martin Evans and Matthew Kaufman, and independently by Gail R. Martin (Evans and Kauffman, 1981; Martin, 1981). Martin is credited with coining the term "Embryonic Stem Cell". In 1998, a breakthrough occurred when researchers, led by James Thomson at the University of Wisconsin-Madison, and Shamblott at the NIH, first developed a technique to isolate and grow in cell culture human ES cells (Thompson et al., 1998; Shamblott, et al., 1999). ES cells are isolated by transferring the inner cell mass into a plastic culture dish that contains a nutrient broth known as culture medium. The cells divide and spread over the surface of the dish. The inner surface of the culture dish is typically coated with mouse embryonic skin fibroblast cells that have been treated with irradiation so they will not divide. This coating layer of cells is called a *feeder layer,* whose purpose is to provide a sticky surface to which the ES cells can attach, and that release specific nutrients into the culture medium. (Kirschstein and Skirboll, 2001). A problem with using mouse feeder cells for growing human ES cells is the uptake of "animal" proteins or viruses into the human cells, which some scientists believe negates their use for human clinical experiments. So researchers have recently devised ways to grow human ES cells without mouse feeder cells, by plating ES cells onto extracellular-matrix-coated plates that can be easily sterilized (Klimanskaya et al., 2005). This is a significant scientific advance because of the risk that viruses or other macromolecules in the mouse cells may be transmitted to the human cells.

The process of generating an ES cell line is somewhat inefficient, so lines are not produced each time an inner cell mass is placed into a culture dish. This inefficiency requires the destruction of many embryos to generate one ES line, and is often cited by ethicists as a strong reason for not working with ES cells. However, if the plated inner cell mass cells survive, and divide enough to crowd the dish, they are removed gently and plated into several fresh culture dishes. The process of re-plating or subculturing the cells is repeated many times and for many months. Each cycle of subculturing the cells is referred to as a passage. Once the cell line is established, the original cells can yield millions of ES cells for subsequent experiments or for therapy (Kirschstein and Skirboll, 2001). ES stem cells that have proliferated in culture for six or more months without differentiating, can be induced to differentiate into a variety of tissues, and appear genetically normal, are referred to as an ES cell line. At any stage in the culture process, batches of ES cells can be frozen and shipped to other laboratories for further culture and experimentation.

**Adult Stem Cells**

Sometimes referred to as tissue-specific stem cells, adult stem cells (ASCs) are found in adult tissues that have already been developed. Tissue-specific stem cells can be isolated from many tissues, including brain, heart, skin, intestine, mesenchyme, and bone marrow. Compared to embryonic stem cells, which can make replacement cells for any tissue, adult stem cells are normally dedicated to making primarily one particular tissue. Because the isolation of ASCs does not destroy an embryo, their use is far less controversial than ES cells. Under the Bush administration's 2001 ban on the use of federal funding to derive new ES cell lines, a strong push was made to develop the use of ASCs for therapy whenever possible as an alternative for ES

therapy. However the main debate with these cells is whether they are as medically useful as ES cells, since it is hard to obtain sufficient quantities (they are not easy to grow), and they can usually differentiate only into one cell type.

The history of research on adult stem cells began about 50 years ago. In the 1950s, researchers discovered that the bone marrow contains at least two kinds of stem cells. One population, called hematopoietic stem cells, forms all the types of blood cells in the body. A second population, called bone marrow stromal stem cells (also called mesenchymal stem cells (MSCs), or skeletal stem cells by some), were discovered a few years later. MSCs make up a small proportion of the stromal cell population in the bone marrow, and can generate bone, cartilage, fat, cells that support the formation of blood, and fibrous connective tissue (Stem Cell Basics, *2009).*

*Hematopoietic Stem Cells*

HSCs are the most researched of all types of stem cells. They have been used since 1957 in bone marrow transplants to aid patients recovering from cancer chemotherapy (Thomas et al., 1957). HSCs are multipotent stem cells that give rise to all the blood cell types, including myeloid (monocytes and macrophages, neutrophils, basophils, eosinophils, erythrocytes, megakaryocytes/platelets, dendritic cells), and lymphoid lineages (T-cells, B-cells, NK-cells). Compared to adult stem cells from other tissues, HSCs are easy to obtain. HSCs are found in the bone marrow of adults, which includes femurs, hip, ribs, sternum, and other bones. Traditionally, HSCs were obtained directly by removal from the hip using a needle and syringe, or from the blood following pre-treatment with cytokines, such as G-CSF (granulocyte colony-stimulating factors), that induce cells to be released from the bone marrow compartment (Hematopoietic Stem Cells, 2005). However, other sources for include umbilical cord blood

and placenta (Viacord, 2007). For experimental purposes, fetal liver, fetal spleen, and AGM (aorta-gonad-mesonephros) of animals are also useful sources of HSCs, but these fetal sources remain controversial for human use.

*Mesenchymal Stem Cells*

Mesenchymal stem cells (MSCs) are another well-characterized population of adult stem cells. These cells, also found in the bone marrow, can form a variety of cells in the laboratory, including fat cells, cartilage, bone, tendon and ligaments, muscles cells, skin cells, and even nerve cells (Jackson et al., 2007). Because of their ability to differentiate into a variety of cells (although not as many as ES cells), and their relative ease of isolation, MSCs are the subject of intense current research. MSCs have been studied in great detail, and scientists have extensive knowledge about how to grow these cells in culture.

Unlike most other human adult stem cells, MSCs can easily be obtained in quantities appropriate for clinical applications, making them good candidates for use in tissue repair (Jackson et al., 2007). Techniques for their isolation and propagation for long periods of time without loosing their capacity to form all the above cell types have been established.

*Neural Stem Cells*

In the 1960s, scientists studying rats discovered two regions of the brain that contained dividing cells that ultimately become nerve cells. Despite these reports, most scientists believed that the adult brain could not generate new nerve cells. It was not until the 1990s that scientists demonstrated that the adult brain contains stem cells that are able to generate the brain's three

major cell types — neurons, astrocytes, and oligodendrocytes (Rebuilding the Nervous System, 2005).

Today, scientists believe that stem cells in the fetal and adult brain divide and give rise to more stem cells or to several types of precursor cells. Neuronal precursors (also called neuroblasts) divide and give rise to nerve cells (neurons), of which there are many types. Glial precursors give rise to astrocytes or oligodendrocytes. Astrocytes are a kind of glial cell, which lend both mechanical and metabolic support for neurons; they make up 70 to 80 percent of the cells of the adult brain. Oligodendrocytes make myelin, the fatty material that ensheathes nerve cell axons and functions to speed nerve transmission. Under normal *in vivo* conditions, neuronal precursors do not give rise to glial cells, and glial precursors do not give rise to neurons. In contrast, a fetal or adult central nervous system NSC may give rise to neurons, astrocytes, or oligodendrocytes, depending on the signals it receives and its three-dimensional environment within the brain tissue (Rebuilding the Nervous System, 2005). Although there is now widespread consensus that the adult mammalian brain contains stem cells, there is no consensus about how many populations of CNS stem cells exist, how they may be related, and how they function *in vivo*. Because there are no markers currently available to identify NSCs *in vivo*, the only method for testing whether a given population of CNS cells contains stem cells is to isolate the cells and manipulate them *in vitro*, a process that may change their intrinsic properties.

*Cardiac Stem Cells*

The characterization of human cardiac stem cells (hCSCs) would have important clinical implications for the management of a failing heart. Scientists have established the conditions for the isolation and expansion of c-*kit*-positive hCSCs from small samples of myocardium

(Laugwitz et al., 2005). Additionally, these cells have been tested for their ability to form functionally competent human myocardium after infarction in immunocompromised animals. The hCSCs are self-renewing, clonogenic, and multipotent. hCSCs differentiate predominantly into cardiomyocytes and, to a lesser extent, into smooth muscle cells and endothelial cells. When locally injected in the infarcted myocardium of immunodeficient mice and immunosuppressed rats, hCSCs generate a chimeric heart, which contains human myocardium composed of myocytes, coronary resistance arterioles, and capillaries (Laugwitz et al., 2005).

In studies in which human CSCs are perfused into mouse hearts, the human myocardial cells are structurally and functionally integrated with the rodent myocardium, and contribute to the performance of the infarcted heart. Thus, hCSCs can be isolated and expanded *in vitro* for subsequent autologous regeneration of dead myocardium in patients affected by heart failure (Roell et al., 2007).

Researchers have isolated cardiac stem cells from rats and showed that when these cells were injected into rat hearts that had been damaged, they reconstituted the injured tissue. The same group has also detected similar cells in human hearts. The research, done at New York Medical College in Valhalla, could lead to new ways of treating heart disease. For example, the stem cells could be injected into diseased or damaged tissue so that new tissue could grow. The researchers are planning to submit a protocol to the U.S. Food and Drug Administration for a phase I clinical trial to test the safety of injecting cardiac stem cells in humans.

Piero Anversa and his colleagues identified pockets of stem cells in the interstices, or spaces, between muscle cells in the hearts of rats. When the stem cells were cultured and injected into rats with damaged heart tissue, 70 percent of the damaged myocardium was reconstituted

within 20 days. The researchers also found similar cells in humans by examining tissue from patients with heart disease who underwent cardiac surgery. It appeared that the accumulated stem cells had been attempting to repair heart damage *(Touchette, 2004).*

*Epithelial Stem Cells*

Most epithelial tissues self-renew throughout adult life due to the presence of multipotent stem cells and/or unipotent progenitor cells. Epithelial stem cells in the lining of the digestive tract occur in deep crypts and give rise to several cell types: absorptive cells, goblet cells, paneth cells, and enteroendocrine cells. Epithelial stem cells are specified during development, and are controlled by epithelial-mesenchymal interactions. Despite morphological and functional differences among epithelia, common signaling pathways appear to control epithelial stem cell maintenance, activation, lineage determination, and differentiation. Although we need to obtain a deeper understainding of these regulatory pathways, as their deregulation can lead to human disorders including cancer. Understanding epithelial stem cell biology has major clinical implications for the diagnosis, prevention, and treatment of human diseases, as well as for regenerative medicine (Kotton et al., 2001; Okamoto et al., 2002; Ortiz et al., 2003).

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# Chapter-2: Stem Cell Applications

*David Kulis*

## Introduction

Stem cells have the potential to cure many diseases that affect millions worldwide, because they have the ability to renew themselves and differentiate into different cells. Various types of diseases might be cured by treating with stem cells to grow new tissues and organs from undifferentiated cells that have the potential to develop into fully mature or differentiated cells. Whether the stem cells are embryonic or adult, there is great potential in the field of regenerative medicine. The purpose of this chapter is to document some of the uses for stem cells, as a prelude for subsequent discussions of their ethics and legalities, paying special attention to distinguish animal studies from human trials, and to distinguish completed experiments from future applications.

## Treating Diabetes with Stem Cells

Diabetes affects tens of millions of people in the United States. Those suffering from diabetes cannot produce or properly use insulin in their bodies. Insulin is a hormone required to convert sugar, starches, and other foods into energy (MAYO). Diabetics have too much glucose in their blood stream because their cells do not internalize it. There are several types of diabetes, but the most common are Type 1 and Type 2. Only about 10 percent of patients are diagnosed with Type 1, the body's failure to produce insulin, while most other cases have Type 2, the body's failure to use insulin (ADA). Both types have similar symptoms that include frequent urination, extreme thirst and hunger, fatigue, weight loss, and blurred vision (MAYO). Diabetes

can also lead to more serious problems if not treated properly, such as cardiovascular disease, nerve damage, kidney damage, eye damage, or osteoporosis.

Since there currently is no cure for diabetes, the disease can only be managed throughout the patient's life. Eating healthy and regular activity can subside the symptoms of diabetes. Patients with Type 1 and Type 2 have to monitor their glucose levels regularly. Those with Type 1 and some with Type 2 require insulin therapy which involves injecting or pumping insulin into the body. In severe cases, a pancreas transplant may be necessary but it is a risky option since the body generally rejects the new organ, and organ donors are always in short supply.

A number of successful advances in treating diabetes using stem cells have been tested in recent years, in both animals and humans, using both embryonic stem (ES) cells and adult stem cells (ASCs). In 2007 in England, 15 young patients diagnosed with Type 1 diabetes were injected with hematopoietic stem cells (HSCs) from their own blood (Pollack). The results showed that their bodies began producing insulin naturally again (Pollack). The patients in the study did not need insulin injections for up to 3 years. The team conducting the study hopes that they can rebuild the body's insulin producing cells by using stem cells.

In a 2009 report similar to the 2007 report mentioned above, patients with Type 1 diabetes were treated with adult HSCs from their own blood and showed major improvements in their insulin producing cells (Boyles). The treatment first focused on killing the patient's immune cells originally responsible for killing the insulin producing cells, and then replacing those cells with HSCs that would both replace the immune system and differentiate into insulin producing cells (Boyles). The treatment, called autologous nonmyeloablative hematopoietic stem cell transplantation, resulted in the patients being independent from insulin for up 2 years.

In another study reported in 2002, scientists used human embryonic stem cells to produce cells that produce insulin and control blood sugar in diabetic mice (Soria et al., 2002). This study provides solid evidence that human ES cells might be able to cure diabetes in humans. The findings in these studies provide favorable evidence for continued treatment of patients with stem cells, either HSCs or ES cells. Although the news is good, there is still a lot of work to do.

**Treating Spinal Cord Injuries with Stem Cells**

Injuries to the spinal cord are very serious and can disable a person. Most spinal cord injuries occur as a result of motor vehicle accidents, violence, falls, and sports related injuries. These injuries are caused by a blow that fractures or dislocates one or several of the vertebrae that protect the spinal cord. When the vertebrae fractures or slides, the spinal cord tissue may be torn or have pressure added to it resulting in disruption of the signals that nerves carry. In the result of a complete tear of the spinal cord, the nerve messages cannot be relayed to the other nerves below the injury, thus making the person paralyzed from that point down. Paralysis is the loss of muscle function which disables the person. An incomplete cord injury does not stop the nerve signals but the patient continues to have limited movement and feeling below the injury. A person with paralysis in the half of the body is classified as a paraplegic, while a person paralyzed in both the arms and legs is a quadriplegic. Nearly 85 percent of spinal cord injury patients who survive the first 24 hours are still alive 10 years later. The location of the tear in the spinal cord generally determines the severity of the injury. A break at the C-3 vertebrae and above generally results in death since the respiratory system cannot function properly. Breaks below the C-3 vertebrae generally result in paralysis or partial paralysis.

There is limited treatment for those with spinal cord injuries today. Since spinal cord injuries cannot be reversed, treatment focuses on preventing further injury, and allowing the patient to live a productive life with their disability. Immediate treatments include medications, immobilization, or surgery. Doctors provide patients with methlyprednisolone (Medrol) which minimizes the damage to the nerve cells and lessens the inflammation around the point of injury. This drug can cause some minor recovery, as long as it is given within the first 8 hours of the injury. The spine may need to be immobilized so that it can be put back in proper alignment. This is made possible through traction by which the patient has metal braces implanted or put in a body harness. Depending on the severity of the injury, emergency surgery is required to remove the bones or herniated disks that have torn or compressed the spine. After the patient is stabilized from the injury, the person must undergo ongoing care and treatment. This includes strenuous rehabilitation and a number of medicines that aid in functioning properly.

Applying regenerative cell therapy to spinal cord injuries has seen varied results in recent years. This approach has been tested on lab rodents for many years now, but not much on humans because of ethical concerns with ES cells. The extensive research and testing in rodents has yielded promising results for future human research. In 2005, mice with severe spinal cord injuries were injected with tissue from the brains of human fetuses and regained much of their ability to move normally (Weiss). A microscopic analysis of the injected cells determined that the fetal cells turned into oligodendrocytes, cells that wrap themselves around the injured nerve cells in order to help transmit electrical signals, while the other turned into neurons (Weiss). These findings provided more support that fetal tissues (presumably containing stem cells) have the ability to regenerate nerve cells and help heal spinal cord injuries. In another 2005 study, researchers found that cells harvested from human embryos and cultivated in special lab

conditions then injected into the injured spinal cords of rats allowed the rats to recover almost completely (Weiss). This recovery only occurred in rats that had been treated within 10 months. After the 10 month period, the results were minimal. The results from experiments in rodents have sparked the science community's interest in pursing clinical studies in humans.

In January 2009, the U.S. Food and Drug Administration (FDA) allowed, for the first time ever, clinical trials of therapy derived from human embryonic stem cells. This was a major break through for those in the regenerative medicine world. A small number of patients suffering from acute spinal cord injuries were eligible for injections of nerve cells designed to enable electrical signals to travel from the brain to the rest of the body (Kaplan). A 2009 publication based upon an Ecuador study 2 years ago by DaVinci Biosciences, showed evidence that injecting spinal cord injury patients with adult autologous bone marrow derived stem cells improved the quality of life for both acute and chronic spinal cord injury patients (DaVinci). The patients showed restored significant movement, sensation, and bladder function (DaVinci). This study also provided hope that adult HSCs can be used to treat other patients by injecting them directly into the spinal column, the spinal cavity, or intravenously. Since embryonic stem cell therapy for humans has only been recently moved into clinical trials (NY Times, 2009), there is hope in regards to reversing the damage done by spinal cord injuries using stem cells.

**Treating Parkinson's With Stem Cells**

Parkinson's disease is one of the most common neurodegenerative disorders. It is caused by the gradual loss of dopamine producing brain cells. Dopamine is responsible for normal muscle movement and functioning. A lack of dopamine in the human body cannot support normal movement. The primary symptoms of Parkinson's include tremors, or shaking of the

hands, arms, legs, jaw, and face, stiffness of the limbs and torso, slowed movement, and impaired balance and coordination. In time, these symptoms worsen, and patients have difficulty walking, talking, and completing the simplest tasks. Parkinson's generally affects people over the age of 50. In America, 50,000 new patients are diagnosed with Parkinson's disease every year.

Presently, there is no cure for Parkinson's disease. Though, in recent years, there have been significant advances in to treating the disease. A number of medications have been developed to stifle the symptoms of Parkinson's. Patients are generally given a drug called levodopa which can be combined with carbidopa (NINDS PD info). The body's nerve cells use the levodopa to make dopamine to restock the brain's supply. There are also a number of other drugs such as bromocriptine, pramipexole, and ropinirole that mimic the effects of dopamine (NINDS PD info). This in turn suppresses the symptoms of the disease, but over time the body gets accustomed to the dopamine levels, and the doses need to be increased from time to time. In a sense, the patient is fighting a losing battle as time progresses. In severe cases, surgery may be required to control symptoms. Ablation is a procedure that targets and destroys the area of the brain plagued with Parkinson's. The tissue eliminated is supposed to eliminate the electrical impulses that produce involuntary movements. In deep brain stimulation, the area affected is not destroyed but rather inactivated (MAYO). Pallidotomy is a surgery focused on the precise area that controls certain symptoms. A probe measures abnormal electrical activity and then the surgeon burns a tiny hole in to the cells resulting in immediate results (MAYO).

Parkinson's disease may possibly be the best candidate for total treatment using stem cells, because scientists already know which type of nerve cell is needed to alleviate the symptoms, and several animal studies have already shown strong success. In a 2002 study,

embryonic stem cells were implanted into rats with brain damage similar to Parkinson's disease and as a result, the brain cells began producing dopamine and the symptoms from the disease gradually diminished (Schoenstadt). This was the first study to prove that unspecialized embryonic stem cells could develop into dopamine-producing cells without any pretreatment (Schoenstadt). A variety of studies have also shown that Parkinson's patients can be treated with fetal tissue transplants (presumably containing neural stem cells) with strong success (Madrazo et al., 1988; Lindvall et al., 1989; Freed et al., 2001, Mendez et al., 2002).

Applying stem cells to humans suffering from Parkinson's disease is the next step. Knowing which cells are the root of the disease's symptoms allows scientists to more easily implant stem cells in a specific location to eliminate the disease. One issue is identifying which type of stem cells function safely and efficiently for this application. Scientists agree that neural stem cells are favored over embryonic stem cells because they can only develop into nerve cells (European). This approach has been tested on animals and has seen much better results in comparison to previous stem cell therapies aimed at Parkinson's (European).

**Treating Cardiovascular Disease with Stem Cells**

Cardiovascular disease or heart disease is the number one killer worldwide. The term cardiovascular disease includes a range of diseases that affect the heart and blood vessels. Some of these diseases are coronary heart disease, high blood pressure, congestive heart failure, angina, and stroke. In the United States alone, there are over 80 million people with one of more forms of cardiovascular disease (CVD Stats). The symptoms for each condition vary. The most common symptoms are chest pain, shortness of breath, and pain or numbness in the extremities. This pain or numbness is caused by constricting blood vessels in that part of the body which

causes poor blood flow.  Other symptoms include either a racing or slow heartbeat. Heart disease is generally caused by buildup of fatty plaques in the arteries which is a result of an unhealthy diet or poor lifestyle decisions such of lack of exercise, high stress, or smoking (MAYO). Family history is also a key factor in whether or not someone develops cardiovascular disease. The best way to prevent heart disease is to live a healthy lifestyle and avoiding activities that increase the risk of developing the disease.

Traditional treatments for the various conditions for cardiovascular disease include lifestyle changes, medications, and a variety of medical procedures or surgery. Regardless of how severe a patient's heart condition is, doctors recommend changes in lifestyle such as eating a low-fat, low-sodium diet, regular exercise, quitting smoking, and limiting alcohol intake. These simple changes can reduce high blood pressure and lower cholesterol. There are also a number of medications that can help lower high blood pressure, reduce cholesterol levels, and thin the blood. Some of these drugs are diuretics, aspirin, statins or fibrates (MAYO). More severe conditions such as heart attacks and strokes may require surgery. The most common procedure is coronary angioplasty, which is performed by inserting a catheter into an artery in the arm or leg, and then threading a balloon to the constricted artery and inflating the balloon so that the artery can function properly again (MAYO). Another surgery, coronary artery bypass, requires removing the blocked portion of the artery and replacing it with a vein from another part of the body (MAYO). Irregular heartbeats can be treated with medications that regulate the heartbeat or a pacemaker may have to be implanted to ensure a regular heartbeat. Traditional procedures and medications have come a long way and there is still room for improvement for treating heart disease conditions.

Though traditional treatment can sometimes be successful in stabilizing heart conditions, the heart lacks the ability to regenerate itself for a large wound. Regenerative medicine using stem cells can make this possible. There are three types of cells in the heart: myocytes, vascular endothelial cells, and muscle cells (Semsarian). Studies in labs have been able to develop new cardiomyocytes and vascular endothelial cells. Most of the work regarding stem cells and heart disease has been done on rodents where heart failure is induced, then stem cell therapy is introduced by injecting stem cells directing into heart muscle, coronary arteries, or through bone marrow transplantation (Semsarian). In a study focused on heart muscle damage caused by heart attack in mice, implanted stems cells multiplied and transformed into new heart muscle cells that healed 70 percent of the damaged area (Semsarian). Another experiment involving rodents suffering from heart disease were injected with adult human stem cells and differentiated into new blood vessels resulting in improved cardiac function (Semsarian). Other experiments on rodents have yielded similar results. The success in studies in rodents has sparked great enthusiasm for applying stem cell therapies in humans suffering from cardiovascular disease symptoms.

Though the potential for stem cell therapy for treating heart disease in humans is great based on the animal model successes, there has been limited work done due to regulations. In 2008, a clinical study done by a U.S. cardiologist reported successful observations of regenerating damaged heart tissue using adult stem cells extracted from a patient's blood ( US Cardio). The adult stem cells were taken through a standard blood draw, the stem cell population was sent to a lab and developed into millions of cells, and then the cells were injected into the patient and migrated to the area needing repair (US Cardio). From there, the stem cells

developed into new heart tissue, blood vessels, and dramatically improved the patient's heart function.

*In vitro*, human ES cells (Kehat et al., 2001) and human adult cardiac stem cells (CSCs) (Beltrami et al., 2003) have already been shown to be capable of differentiating into mature cardiac lineages. The medical literature also reports that human heart attack patients have successfully been treated with adult cardiac stem cells (Britten et al., 2003; Siminiak et al., 2004) and with bone marrow stem cells (Lunde et al., 2006; Schächinger et al., 2006).

## Chapter-2 Conclusion

After delving into various diseases that can potentially benefit from stem cell treatments, there still remain many questions in the regenerative medicine field as to how efficient these treatments will be, and which types of stem cells function best for a given application. With regulations recently lifted for federal support of ES cell research, and more funds provided, the potential for stem cell applications is endless.

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# CHAPTER-3: STEM CELL ETHICS

The discovery and cultivation of both embryonic and adult stem cells have led to fascinating and beneficial developments for society. However, the use of embryonic stem (ES) cells has sparked heated debates for and against their use, becoming one of the world's most controversial ethical dilemmas. In polls conducted by ABC News and the Washington Post from April 2004 to January 2007, about 60% of Americans at that time supported ES cell research, 40% opposed, and the remaining were unsure how they felt (ABC News, 2007). At the center of the debate is the destruction of an embryo when new ES cell lines are prepared. Those opposed to ES cell research view the tiny embryos (the size of a period at the end of this sentence) as the start of life, and compare destroying these embryos to abortion (Nisbet, 2004), an opinion formed the beliefs of some conservative religions. Those that support ES cell cultivation emphasize the fact that the human embryos are still in their very early stages of development (day-5 post fertilization) and are only *potential* life that have not yet become individualized. Whose word does one trust when the question centers on the beginning of life? And if one believes that the embryos represent the start of life, will he look past that and realize the life-saving potential of the stem cells for already living individuals? The answers to these questions form the main arguments in stem cell debates, and are the subject of this chapter.

## Scientific Dilemmas

### *Scientific Support for Stem Cell Research*

Within the scientific community there are those who wholeheartedly support ES cell research, while others believe we may be overstepping boundaries in the name of science.

Similarly, among the world's religions there are those who see the destruction of human embryos as murder, while other religions argue life begins much later than day-5 and ES cell research should be encouraged. Some religious leaders support the scientific communities efforts in making advancements in medicine, but feel that they could achieve the same goals using stem cells taken from adults. The ethics of each group's reasoning must examined to fully understand the stem cell dilemma.

The central issue behind the stem cell research debate boils down to how the opposing sides classify the human embryos necessary to create the stem cells. Clearly, those in support of the research do not view these early human embryos as life and so do not find it morally wrong to destroy them in favor of creating ES cells. These supporters see human embryos as a group of day-5 human cells that *may* one day become a human life (if implanted), but are not yet considered alive (O'Mathuna, 1999). Those who argue against stem cell research view these embryos as the earliest stages of human life and consider them as individuals who have the full right to a life, even in their microscopic stage. It is interesting to note that although supporters of ES cell research view human embryos as a group of cells, they still treat them with much more respect than other growing cells, being sure not waste or destroy anymore than is necessary. This special treatment for "a bunch of cells" suggests that the scientists realize they are walking an ethical tightrope, but have decided that the stem cells' potential to cure diabetes or Alzheimer's is too great of an opportunity to pass up.

The main debate focuses on the classification of the inner cell mass (ICM), which is necessary for extracting ES cell lines. While the ICM is referred to as the "essence" or vital part of embryonic development, in its isolated form the ICM no longer has the potential to develop into a fetus because it lacks the trophoblast cells necessary for full embryonic development.

Thus, fertilized embryos without reimplantation into the uterus are not fully viable embryos, nor are extracted ICM cells. Theoretically, ICM cells could become viable once more only if injected back into a blastocyst, which is then implanted into a uterus (deWert and Mummery, 2003).

*Surplus IVF Embryo Debate*

The debate over the use of surplus IVF embryos is not new, and has occurred since the application of animal IVF techniques to humans in the late 1960's. The debate is rooted in three main principles: the principle of proportionality, the slipper slope argument, and the principle of subsidiarity. The *principle of proportionality* is a guideline that tries to ensure unnecessary steps are not taken to achieve a goal. In the case of stem cell research, the scientists involved make it clear that they are working towards an important goal of saving lives, and that stem cell research is necessary to achieve that goal. The question of proportionality comes in when the discussion of research restrictions takes place. Those in support of stem cell research do not understand why there is a distinction made between the use of embryos for reproduction and their use for cell therapy. A number of countries have actually limited ES cell research to only embryos made in IVF clinics for reproduction purposes. With the vast medical potential of embryo cultivation, should governments really justify limiting their use to the single cause of infertility? Supporters of stem cell research argue that cell therapy has the potential to cure debilitating diseases that affect far more humans than infertility does, so as a result the authors of this report argue that stem cell research satisfies the principle of proportionality.

The *slippery slope principle* states that thedevelopment of one technology subsequently leads to the research and development of an undesirable second technology. This is the empirical

variation of the principle. A classic example of this is the discovery and development of nuclear power leading to the creation of weapons of mass destruction. The logical variation of the principle states that the moral acceptance or justification of one practice leads to the justification of the second undesirable practice. For example, the recent development of face transplant surgery can help those born with deformities or those who have suffered an accident live a more normal life, however this development could also lead to people getting face transplant surgery simply to alter their appearance, even if they do not need it. The slippery slope may apply to stem cell research because while the stem cells are developed in hopes of curing serious diseases, some argue they could also be used for cosmetic rejuvenation (Nuffield Council on Bioethics, 2000). This fear leads to even more opposition against ES cell research. The other concern is that therapeutic cloning (to make ES cell lines genetically identical to a patient) may eventually lead to human reproductive cloning (to make another human being genetically identical to another). The authors of this report believe that neither argument is strong enough to discontinue the progress made in ES cell research, especially considering the life saving potential of the technology.

The *principle of subsidiarity* justifies the development of a technology when no suitable alternatives exist to accomplish the specified goals. Extensive research must be done on these alternatives before they can be considered. If they are worthy of further study, then there are more questions to consider such as whether to halt research on the original and focus on the alternatives, or to develop them concurrently. More research means more costs. Scientists must also consider how alternative methods will affect the patients involved. These factors tie into the most important question: will the findings be worth the research? Embryonic stem cell research has been conducted for years and scientists are optimistic about accomplishing the goals of

research. They may find that the alternatives (adult stem cells) have no potential to achieve the same goals as ES cells, resulting in a waste of effort in researching these alternatives. It may not be wise to halt or slow down ES cell research in favor of these new, less controversial, or unproven methods.

From the evidence presented, it is clear that supporters of embryonic stem cell research have strong arguments, justified by scientific facts and classifications. Thorough analysis explains why the embryos used to cultivate stem cells should not be treated as, nor held in the same regard as, live embryos. In fact, the embryos can only become viable through manipulation, reimplantation into a uterus. Although it is true that throughout history there have been groups of people who have used advancements in technology for their own personal gains, but despite the misuse, we would find it difficult to live without these developments. In our eyes, speculation of misuse is not a strong enough reason to halt the development of a technology that has the potential to save lives.

*Scientific Objections*

Although scientific analysis and definition can provide evidence to support embryonic stem cell research, some groups within the scientific community oppose this research. For example, it can be argued that ES cell research has a negative effective on the lives of the women who donate their eggs necessary for the research (Check, 2006). The majority of eggs are taken from women already undergoing fertility treatment, but the supply from these women is not considered sufficient. In the past, some scientists have turned to asking healthy women to give up their eggs, receiving compensation in return for their donations, but this practice is now outlawed in the US. There is worry that compensating women for their donations will lead to

women in need of money donating their eggs despite the possible complications and risks. Despite the fact that scientists have used egg collection techniques for about 40 years now, little is known about the health risks of donating eggs (Pearson, 2006). Though evidence is scarce, some scientists suggest that the drugs used to stimulate ovulation can lead to the development of certain cancers, as for the case of a woman who died from cancer in 1994. The controversy comes from the fact that healthy women are being asked to undergo a possibly dangerous procedure in the name of research, not to achieve a family. One example of a danger is ovarian hyperstimulation syndrome, a condition that causes too many eggs to develop at once causing fluid to leak out of blood vessels and collect in a woman's abdomen. The syndrome causes nausea, bloating and, rarely, kidney failure and death. However, this syndrome only effects about 6% of women who receive fertility drugs. Additionally, in a study conducted by Radboud University Medical Centre in Nijmegen (the Netherlands) records of women who underwent the procedure from 1984 to 2006 show that only 6 women died from the drugs. Although skeptics may wonder why there is such concern over such a relatively low number of deaths, the scientific community is more concerned with the possible long-term effects of the fertility drugs.

One of the long-term effects of fertility drugs may be cancer, according to a 1994 study, specifically ovarian and breast cancer. According to the same study, women who took the fertilty drug clomiphene citrate were 11 times more likely to develop ovarian tumors. But there is some controversy surrounding these studies, as pregnancy can protect against ovarian cancer. Some believe that it is the condition of infertilty, not the fertility drugs themselves, that causes the cancer.

Though there is a slight link to these deadly diseases and fertilty drugs, the true concern is of the unkown. Scientists neither been able to prove nor disprove the possible negative effects

of fertility drugs. This lack of confirmation either way should deter healthy, fertile women from undergoing the procedure, but in the past they were drawn by the financial compensation and perhaps the feeling that their eggs may lead to the cure for a deadly or crippling disease. This opposition to embryonic stem cell research is similar to debate regarding when to consider an embryo as a human life. In this case though, there is no question that the main concern is the lives of the living. Though the risks are either rare or unknown, the remote possibilty that stem cell research can lead to the deaths of people may produce much more opposition than before.

Another scientific opposition to stem cell research is that recent research inducing adult cells to dedifferentiate into ES-like cells, may negate the use of ES cells derived from embryos (Sample, 2009). A variety of labs have succesfully found a way to take adult skin cells and manipulate them to behave like embryonic stem cells. Although the initial 2007 study involved four genes to perform the induction, including potentially cancer causing c-Myc, later studies leave out this gene. This is clearly a huge accomplishment as the use of induced pluripotent (iPS) cells would potentially end the use of embryonic stem cells and the controversy that comes from them. But scientists are far from proving these new cells are truly as medically potent as embryo derived ES cells.

**Religion's Role in the Stem Cell Argument**

An additional source of information on the stem cell ethics debate is derived from the world's major religions, and whey they argue life begins. The religions with the highest number of adherents include Christianity, Buddhism, and Judaism (Major Religions…2005). An examination of their values and beliefs will offer insight into why their adherents do or do not support ES cell research.

*Christianity and Stem Cells*

Christianity and its followers have had much to say about the stem cell research debate, particularly the leaders of the Catholic Church. In 2001, the U.S. Catholic Conference of Bishops was quick to express their displeasure with former President Bush's decision to allow federal funding (although limited) for stem cell research (US Bishops…2006). Bishop Joseph A. Fiorenza called the decision "morally unacceptable." The bishops feared that the government's willingness to support research that "relies on the destruction of some defenseless human beings" would create an atmosphere of very little respect for the value of a human life. They did not see how Bush could justify treating what they considered to be human lives as mere objects of research. Fiorenza does acknowledge that there could be medical potential in stem cell research, but he does not believe that the potential justifies the sacrifice of human lives. Chicago's Archbishop Francis E. George compared the embryonic destruction to history's tendency to subject the "disposed" and "easily overlooked" to the worst scientific research abuse. The statements of these two bishops clearly reflect the Catholic Church's belief that the tiny embryos used for ES cell research must be treated as human beings and not simply as a cluster of cells. Bishop Donald Wuerl adds that a stem cell "contains the elements out of which comes the fully developed person." Former leader of the Catholic Church, Pope John Paul II likened stem cell research to abortion, euthanasia, and other forms of death because they all involve the deaths of innocent lives that have no way of protesting and defending themselves from the act (Filteau, 2007). From these statements, it is clear to see that the Catholic Church does not support embryonic stem cell research. Its leaders view the tiny embryos as innocent human lives, and consider it morally wrong to take those lives away in the name of science. It is worth noting that

not all Christian denominations denounce ES cell research. Episcopalian and some Luthern denominations support both ES and adult stem cell research.

*Buddhism and Stem Cells*

Although Buddhism differs greatly from Christianity in several ways, Buddhists have a similar stance to Catholics in the stem cell research debate (Keown, 2001). The idea of rebirth or reincarnation is central to the religion's opposition to embryonic stem cell research. They believe that life begins at conception, and that the new life contains the karmic essence of a recently deceased person. Therefore, this new life should be entitled to the same rights as an adult, and Buddhists view ES cell research in the same light as abortion or IVF treatment where spare embryos are destroyed. Despite these strong beliefs, there is some dissention among Buddhists in regards to stem cells that are taken from aborted fetuses. Some believe it does not go against Buddhism's teaching because in this case, no life is destroyed because of the stem cell cultivation, as the fetus was already dead. This is comparable to organ donation, where it is necessary to obtain legal permission from the next of kin to harvest the organs. On the other hand, some Buddhists are opposed to this because the stem cells result from another immoral act (abortion). Also, the mother giving permission for the cultivation of the stem cells is also directly responsible for the abortion, raising the concern of women getting pregnant just to abort. Thus, while Buddhists generally oppose embryonic stem cell research, there is some disagreement on the subject.

*Judaism and Stem Cells*

Finally, Judaism is much more accepting of embryonic stem cell research than Christianity and Buddhism. Although traditional Jewish law states than an unborn child has the potential for human life, Yoel Jakobovits, a staff member at John Hopkins University has a slightly different interpretation of Jewish law. He states that, according to Jewish law, an early fetus is only water for the first 40 days after conception. It only becomes considered a potential human life if it is *implanted* into the uterine wall. Once this happens, it is considered a potential human life and cannot be aborted for stem cell cultivation even if it is to "save another life." If the embryo has *not* been implanted into the uterine wall and is simply in a petri dish or part of a group of embryos left over from IVF treatment, Jewish law does not consider it unjust to perform research on them, or use them in the cultivation of stem cells. This examination of Jewish law reveals that Judaism's followers would support embryonic stem cell research as long as the embryo has not reached the stage that Judaism considers "potential human life."

*Religious Support of Adult Stem Cell Research*

All major world religions agree on one stem cell point, that research with *adult* stem cells should continue. Pope Benedict XVI has urged the Catholic Church's scientific institutions to develop closer relationships with those in the scientific community working with adult stem cells (Catholic Online, 2008). His belief is that a breakthrough in adult stem cell research would "relieve needless human suffering." While showing support for adult stem cell research, he stressed that he still does not support embryonic stem cell research because it does not respect human life, which, according to Catholic law, begins at conception. Pope Benedict believes adult stem cell research has the same potential to save human lives as embryonic stem cell

research, without sacrificing embryos (despite scientific evidence showing that adult stem cells are much harder to isolate and grow, and lack the same pluripotency as ES cells). This show of support for adult stem cell research, combined with the recent breakthroughs made in the field, could have a large impact on the stem cell debate.

**Another Form of Questionable Ethics**

One caution in the stem cell debate focuses on the recent exposure of errors made in the formation of polls meant to represent the opinions of the American public. Showing that the numbers of those in support has been downplayed, or the numbers of those opposed, are exaggerated can have an affect on those who are undecided. Citizens who were unsure of how to answer in polls are pushed into going with the increasingly popular argument. Our everyday interactions and experiences have shown us that if someone is unsure about something or does not have full knowledge of the subject, they will not be quick to support nor oppose it.

We have also seen the effects of a *survey bias* on poll results. Results can be affected by the way questions are formed, or the connotation of words used in the question. Evidence of this has been found in several polls concerning embryonic stem cell research (Nisbet, 2004). Matthew Nisbet found that a poll conducted by the Juvenile Diabetes Research Foundation, which emphasized that the cells were "donated for research" and could cure several diseases, showed that 65% showed support for the research. On the other end of the spectrum, a poll conducted by National Council of Catholic Bishops described the cells as "live", said cells were "destroyed," and made it a point to say the research would be paid with "tax dollars." The results of this poll showed that 70% were opposed to the research. This survey bias calls into question the ethics of both parties. Without giving the public a clear, universal definition and

classification of embryonic stem cells, and their cultivation process, it is difficult for people to give accurate opinions. Both sides are using the power of word connotation and misinformation to gain support for their respective causes. It is difficult to express one's true opinion on something so important when the two sides really cannot agree on what they are arguing about.

**Chapter-3 Conclusions**

The stem cell research ethical debate centers around how an individual or group identifies an embryo. Major religions have taken opposition against ES cell research because they consider early embryos as human beings. Both Buddhism and Christianity (especially the Catholic denomination) teach its followers that life begins at conception, likening the destruction of human embryos to abortion and euthanasia. In each of these acts, the victims are unable to defend themselves. Judaism shows stronger support, as Jewish law does not consider an embryo in a petri dish, or left over from IVF treatment, as a potential human life unless it is implanted into a uterus. Therefore, they see no problem in using these embryos for stem cell research. Generally, though, these religions do not support any type of stem cell research that results in the destruction of potential human lives. What one considers a potential human life differs for each religion and how its followers interpret the teachings of that religion.

On the scientific side of the debate, other points to consider are the vast medical potential of ES cells, whether donating eggs (and the accompanying hormone treatment) can harm the woman donor, and whether iPS cells truly have the same medical potential as embryo derived ES cells. While some argue the ES cell research debate is generally a battle between science and religion, recent breakthroughs with iPS cells may be able to bring the opposing sides together if the iPS cells truly are pluripotent. Initial test indicate they are, but only continued research will

answer this important question. If this is proven true, it may finally end the stem cell debate, allowing both sides to focus on what some call a coming medical miracle.

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# Chapter 4: Stem Cell Legalities, and Political Policies in the U.S and World

*Jordan Belliveau*

Undoubtedly, stem cell research, and more specifically the use of embryonic stem (ES) cells, is a highly contested and controversial subject. The destruction of an *in vitro* fertilized (IVF) blastocyst embryo to isolate ES cells has spawned numerous debates from various factions on the ethical issues versus the potential advantages to society and scientific advancement. This topic is widely considered one of the most controversial topics in the world, and especially in the U.S. where public opinion has forced its way into the political arena. Politicians realize that many votes can be swayed based on this important topic, as we have seen in the past several elections. As is true for any controversial technology, world leaders have established stem cell policies to ensure the views of their country are clear. With the recent presidential elections in the U.S., this country has experienced a roller coaster ride in its views as the Bush 2001 policies were replaced by the 2009 Obama policies. The purpose of this chapter is to document some of the U.S. and international stem cell policies used to regulate this controversial new technology.

## Stem Cell Policies in the U.S.

### *In Vitro Fertilization*

The controversy over stem cell research could be said to have started in the late 1960's with the advent of *in vitro* fertilization (IVF). During IVF, egg and sperm are donated by parents having trouble with conception. The egg and sperm are united in a test tube, and grown about 5 days to the blastocyst stage to give vigor to the new embryo. At this time the embryo is implanted into the mother's uterus to hopefully produce a child. When the family has enough

children, the excess IVF embryos are usually discarded by the clinic. The embryo discard process polarized society; some argued that destroying an embryo is murder, as the embryo has the *potential* to become a child. As science advanced, other uses became available for the usually discarded IVF embryos, including using them to produce new ES cell lines. So with donor consent, embryos were sometimes used for this purpose, but this process only further polarized society as it increased the use of embryos for research instead of reproduction.

The subsequent 1973 decision by the U.S. Supreme Court on *Roe vs. Wade* (Vestal, 2008) also contributed to the bioethical debate. This case legalized some types of abortion in the U.S. As aborted fetal tissue became available for research purposes, scientists experimented with using fetal tissue implants to treat neurological conditions, such as using fetal brain tissue to treat Parkinson's disease (Lindvall et al., 1989). Many bioethicists believe that the early debates over the use of IVF embryos and aborted fetal tissue laid the ground work for subsequent debates on the destruction of IVF embryos to derive ES cells.

*President Clinton's Stem Cell Policies*

With the election of President Bill Clinton, the public knew that he favored stem cell research and consequently would pursue legislation to allow the federal funding of human embryo stem cell research in the U.S. Despite disapproval from conservatives, President Clinton persisted, and in 1993, President Clinton and Congress passed the *National Institutes of Health Revitalizations Act* (Dunn, 2005). This act gave the National Institute of Health (NIH) direct authority to fund human embryo research. After a year of appointing scientists and ethicists to its advisory committees and subsequent debates, the NIH finally came to a decision to allow the destruction of spare IVF embryos for research funding.

Clinton had an agenda with regards to stem cell research. He had had a childhood friend whose children suffered from diabetes, and he believed that stem cell research, especially ES cell research, would lead to breakthrough developments in many diseases. In a statement addressing his stand on stem cell research, Clinton revealed his personal attachment to the research:

> Diabetes afflicts two children of my friend and former Chief of Staff, Erkines Bowles, as well as millions of other Americans, with a disproportionate impact on our minority population. When I became President, I learned that diabetes and its complications account for a staggering twenty-five percent of all Medicaid costs. That's a big reason why, as President, I supported stem cell research. (Clinton, 2004)

However, for this reason, Clinton's decisions on stem cell research were viewed by some conservatives as prejudicial and emotion-based, not scientifically influenced (ES cells have not yet been used to treat diabetes in human patients). Many people believe that Clinton did not possess adequate scientific working knowledge of stem cell research to make such bold statements supporting this controversial procedure.

In 1995, a short time after Clinton's initial approval of the research, Congress overrode his decision on certain types of stem cell research "enacting an appropriations rider, that remained on the books through the Bush administration, that prevents NIH from funding any research that harms or destroys human embryos" (Vestal, 2008). Congress disapproved the funding of any research that proved harmful to or destroyed human embryos. As a response, Clinton was quoted as saying, "I believe the American people believe it's a pro-life decision to use an embryo that's frozen and never going to be fertilized for embryonic stem cell research...." (Dickson, 2009). This could be interpreted as President Clinton wanting the country to head in a different direction than Congress was steering it. It was these beliefs of the unequivocal benefits of stem cell research that caused President Clinton to be one of the most controversial on this

topic. President Clinton, in a sense, was the lightning rod for a topic which would prove to be a burning matter for the two Presidents to follow Clinton.

*President Bush's Stem Cell Policies*

After an historic (and highly contested) 2001 election, George W. Bush was sworn in as the 43rd President of the United States. Raised in various locations in Texas, President Bush brought a very strong Christian background to his stand on stem cell research. Bush believed that:

> "Human life is a sacred gift from our creator. I worry about a culture that de-values life, and believe as your president, I have an important obligation to foster and encourage respect for life in America and throughout the world." (George W. Bush, radio address, 2001).

Although religion was not his primary argument against the advancement of stem cell research, it proved to be a driving force during his presidency. On August 9, 2001, Bush declared he would not allow federal funding to derive new ES cell lines after that date (Babington, 2006). This left ES cell researchers extremely limited in which ES cell lines could be used. Having access to a variety of ES cell lines is significantly important because some of the earlier derived lines did not grow well. New ES lines needed to be established to help cure diseases such as Parkinson's, diabetes, and Alzheimer's. Unlike adult stem cells, ES cells have the ability to grow to unlimited quantities, and they can be used to create many different types of human tissue.

Bush's 2001 stem cell policy was highly controversial. Some scientists argued that the number of available ES cell lines was grossly insufficient to support ES research. Eventually members of the U.S. Senate voted 63-37 in 2006 to overturn the 2001 law to loosen restrictions on ES cell research (Bash and Walsh, 2006). This Senate bill was never enacted. President Bush

had to issue his first veto in office. "The bill, which the Senate passed Tuesday, 63-37, would have loosened the restrictions on federal funding for stem-cell research" (Bash and Walsh, 2006). The bill was vetoed by President Bush even with the House of Representative trying to override the veto, but they could not obtain enough votes. Bush specifically targeted ES cell research because he believed the bill "would support the taking of innocent human life in the hope of finding medical benefits for others" (Babington, 2006). Two years later, Bush again vetoed a bill from the Senate that pushed for stem cell research enhancement. This second veto, as explained by Bush, was determined by his belief that stem cell research is not moral because of the destruction of human embryos.

Although Bush did not support these two Senate bills, he did sign a "human fetus bill" that banned the creation of human fetuses that would be used only for the production of organs. To follow this bill, Bush hoped to pass another bill to allow stem cell research only if the research did not destroy human embryos (Babington, 2006). But this latter bill was quickly dismissed by the House as a political move by Bush to try to ease the opinions of stem cell research supporters.

Although Bush and Congress did not always vote in agreement, Congress did play an important role in stem cell research progress. Congress voted in 2001 to make human cloning illegal, a process that would yield patient-specific stem cell lines for research. Here, Bush was in agreement with Congress, "I strongly oppose human cloning, as do most Americans. We recoil at the idea of growing human beings for spare body parts or creating life for our convenience" (George W. Bush, radio address, 2001). An expansive anti-cloning bill was eventually passed in July 2001.

After Bush passed his legislation banning federal funding of ES cell research, public disagreement grew dramatically. Opposition included high ranking officials in which Bush publically acknowledged, “I have friends whose children suffer from juvenile diabetes. Nancy Reagan has written me about President Reagan's struggle with Alzheimer's. My own family has confronted the tragedy of childhood leukemia. And like all Americans, I have great hope for cures.” (George W. Bush, radio address, 2001). Not only was Bush sent numerous letters trying to persuade him to accept stem cell research, but he was publically criticized by numerous senators. Senator Richard Durbin disputed Bush’s ban with his conviction that, "Those families who wake up every morning to face another day with a deadly disease or a disability will not forget this decision by the President to stand in the way of sound science and medical research" (Babington, 2006). "I am pro-life, but I disagree with the President's decision," said Senate Majority Leader Bill Frist (Tenn.), "Given the potential of this research and the limitations of the existing [human embryonic stem cell] lines eligible for federally funded research, I think additional lines should be made available" (Babington, 2006). Another Senator, Tom Harkin of Iowa, questioned the ban on embryo destruction saying "If that's murder, how come the President allows that to continue [in IVF clinics for excess embryos]? Where is his outrage? …a shameful display of cruelty, hypocrisy and ignorance" (Babington, 2006).

As a push to keep his public persona in a positive standing, Bush rebutted these disparities by making it publically known that he was in favor of the advancement of science and technology. Also, Bush addressing the nation, saying:

> I also believe that great scientific progress can be made through aggressive federal funding of research on umbilical cord, placenta, adult and animal stem cells, which do not involve the same moral dilemma. This year your government will spent $250 million on this important research. (George W. Bush, radio address, 2001)

Even though Bush was in favor of science and technology, the fact still remained that he would not support ES cell research because he deeply vowed that it was wrong to destroy embryos for research.

When Bush vetoed the 2001 bill for stem cell research, he did not know that it would have such an adverse affect. At first, it seemed like stem cell research had been nationally diminished by the efforts of President Bush. Soon after, the researchers and the general public began to protest more and more on the subject, eventually leading to a break through. A majority of the vocal populous now favored stem cell research with its possibly of curing some life threatening diseases.

Eventually, individual states and their representatives took action against the federal funding ban, and began pouring millions of millions of dollars into their own specific states' research. The Bush veto led many states to be innovators of stem cell research, including major contributors: California, Wisconsin, New Jersey, and Massachusetts. In Massachusetts, many advances are being made with stem cell research. Governor Mitt Romney was the first governor of Massachusetts to deal with the stem cell research proposal. Although Romney was against ES cell research, "the Massachusetts Legislature …..overrode Gov. Mitt Romney's (R) veto of a measure aimed at supporting human embryonic stem cell research in the state" (Massachusetts Stem-Cell Bill Becomes Law Despite Veto, 2005). Eventually, in 2007, "Governor Deval L. Patrick '78 announced a $1.25 billion funding initiative earlier this week for life science research in Massachusetts that will focus in part on embryonic stem cells" (Marks, 2007). Massachusetts is now one of the leaders in stem cell research among the United States.

Along with the financial push from the states, another silver lining was found in the federal ban of embryonic stem cell research funds. James Battey, who serves as head of the

National Institutes of Health's Stem Cell Task Force, proclaimed that the ban might actually turn out to be beneficial, as it forced researchers back to basics. "There's an enormous amount of basic research that can be done and needs to be done before anybody anticipates any [ES] clinical trials…All of these basic studies can be done right now, with human embryonic stem cell lines that you can order today on the NIH registry" (Agnew, 2003). Dr. Battey also raised awareness that researchers were shunning away from entering the field, and there are not enough researchers in the ES field. In order for the field to advance, more trained scientists must be available in the United States. The individual state's funding led to more scientists being trained in stem cell research, to effectively dismiss the goals proposed by President Bush and his veto.

*President Obama's Stem Cell Policies*

When newly elected President Barack Obama took office in January of 2009, researchers around the United States excitedly waited for him to lift the 2001 Bush federal ban for ES cell research. On March 9th, 2009, the handcuffs that stem cell researchers had been detained with for eight and a half years were released. President Obama granted federal funding to develop new ES cell lines, with the restriction that the embryos used are derived from excess IVF embryos, with no paid donors. At the signing of the executive order, President Obama proclaimed:

> "At this moment, the full promise of stem cell research remains unknown, and it should not be overstated. But scientists believe these tiny cells may have the potential to help us understand, and possibly cure, some of our most devastating diseases and conditions." (Childs, 2009)

President Obama wants the United States to thrive as one of the world's leading nations in the realm of medical discoveries. A key slogan for President Obama's campaign was "Hope".

Christopher Hook, Director of Ethics Education at the Mayo Graduate School of Medicine, disagreed with Obama on stem cell research:

> There is a lot of political currency that comes with being seen as pro-progress, pro-health, pro-hope, and pro-science. Consequently, it is often difficult for politicians to question or oppose something that is constantly hyped as the cure for everything, even if such claims are vastly overblown, devoid of evidence, and may have a huge ethical price tag. Hope sells (Christian Today, 2004).

With respect to his statement about the claims having a "devoid of evidence" Chapter-2 in this IQP report shows various uses for ES cells, including several proven applications. In a recent 2009 interview with CNN's Sanjay Gupta, former President Clinton expressed his views on the potential reassessment of the value of stem cell research with President Obama:

> We want to solve -- we want to find out about whether Parkinson's and Alzheimer's can be reversed. We want a whole range of other things. And I think at some point, you know -- maybe it's -- decades down the way. If somebody severs an arm and you try to sew it back on, and you're missing some component things, if you can figure out how to fill in the blanks, I think people would like that. So I think we'll just have to debate it as we go along. I think -- I was anxious for the president to do this and get this research going again. (Balan, 2009)

In response to Obama reversing the ban, the National Institute of Health (NIH) was mandated to finalize an ethical guideline for research in 120 days, which after several drafts was eventually approved on July 7, 2009 (Holden, 2009). The importance of establishing federal funding for ES cell research was highlited in a televised *Nova Science* special:

> "Most basic biomedical science in this country—the early, exploratory research—is funded by federal dollars, with the National Institutes of Health taking the lead (to the tune of $20 billion in research-related funding a year). Scientists say that no field of research can flourish without access to this kind of government support" (Dunn, 2005).

Now that the NIH has proposed the new guidelines, the general opinion of the researchers is satisfied. The NIH estimates that up to 700 ES cell lines may eventually be approved by the new guidelines for research purposes (Holden and Kaiser, 2009).

Not all scientists are satisfied with the new NIH guidelines. In general, there are three major topics that are being questioned from the guidelines: grandfathering previous approved lines, informed consent, and the oversight of the research. The focal concern over grandfathering previous approved lines stems is the wording of the new guidelines. "Many stem cell lines derived according to earlier requirements may not conform to new ones, and may therefore be disqualified for use in federally funded research" (Cohen, 2009). This causes a problem because the aspect of grandfathering in cell lines is not specifically addressed and needs to be specified in more detail. Many scientists propose that the NIH should follow the NAS guidelines as to:

> Categorically "grandfather in" or permit continuation of research on cell lines previously approved by NIH; they also allow the use of other previously derived cell lines if investigators provide a local Embryonic Stem Cell Research Oversight (ESCRO) committee with documentation that establishes use of an informed consent process that this oversight body considers acceptable (Cohen, 2009).

The second issue of informed consent highlights the new guidelines as being too closely related to the old guidelines set forth by President Bush's administration. There are four process/statements that are lacking in the new NIH guidelines which researchers and the public believe should be added. With the 2009 NIH Guidelines, patients do not need to be presented with a description of the research data on their application, a description of the risks they are taking, or a commitment to adhere to the best practices with the donor's embryo. Also, informed consent is limited to frozen embryos, not to donors of the sperm and egg at time of donation.

The NIH needs to look more intensely into the new guidelines and examine, "States that have devoted substantial resources to addressing informed consent in regulations governing publicly funded hESC research, such as California, which offers useful models for national standards" (Cohen, 2009). Unfortunately, the oversight proposed by the NIH guidelines has been criticized as unstable:

> In authorizing the expansion of federal funding for hESC research,
> President Obama made an explicit commitment to strict oversight.
> Yet, in the draft NIH guidelines, it is difficult to find a trace of the strong
> local and national oversight provisions developed by the NAS (Cohen, 2009).

In the years before the guidelines, the NIH worked together with Institutional Review Boards to aid the local oversight of stem cell research. But now the NIH draft guidelines do not have any local oversight for the research. The critics proclaim that the NIH needs to form a committee that would serve as overseers of the research so it can operate as smoothly as possibly.

A major disappointment to some scientists is the fact that the NIH did not, "open the door to the use of embryos created for research purposes—including through somatic cell nuclear transfer (cloning) and parthenogenesis (from an unfertilized egg)" (Marvis, 2009). But NIH director Raynard Kington disputed these disappoints by acknowledging, "there's strong, broad support for allowing research on surplus embryos from fertility clinics…there's no similar broad support for using the other sources…cell lines created solely for research either by IVF or SCNT Holden and Kaiser, 2009). Although some of these concerns with the draft guidelines were allievated in the final July 7 guidelines, some scientists consider the guidelines to be a work in progress, and a majority of researchers are pleased that many of new stem cell lines will be available (Holden, 2009).

**International Stem Cell Policies**

Around the world, much stem cell research has occurred, especially in countries with progressive stem cell policies such as Sweden and South Korea. Some scientists consider Sweden to be the world leader in stem cell research. "The country's stem cell industry has all the right ingredients for future expansion and success: strong public support, a favorable bioethical climate, a tradition of science and research, and strong government funding" (Sweden's Stem Cell Success, 2002). The main distinction from many other countries, including the United States, is that Sweden does not have any difficulty deriving ES cell lines from excess IVF embryos. Perhaps the US will catch up with Obama's new policy in place. The Swedish government backs the funding of the research and knows that they need to continue it in order for the research to be fully effective.

In addition, with its very progressive stem cell policies that allow paid egg donors, South Korea has made many advances in the realm of stem cell research. Unfortunately, the initial claim by Hwang's lab of human embryo cloning (Park et al., 2005) was subseqently withdrawn due to fraud. But based on Korea's overall success, South Korea plans to institute a worldwide stem cell bank to help provide ES cell lines to other countries. Because of South Koreas acknowledgement of the importance of stem cell research, they have become one of the leaders in the field and are making their results available to the rest of the world.

Headed in the different direction from the United States is Germany. Germany virtually has a full ban on ES cell research and its imports into the country. In 2002, "340 of 618 parliamentarians voted to allow the import of ES stem cells for scientific research, but only under close government control" (Kim, 2002). This move was deemed by many as a move to look like

liberalization. Before there was no significant law about the restrictions of the imports, but, "Now we'll have a very restrictive law on the way the import is regulated, and that is more than we had before" says Regine Kolleck, Deputy Chair of the National Ethics Council and a specialist on health technology assessment at the University of Hamburg (Kim, 2002). But four years later, Germany publically announced its disapproval for ES cell research advocating for a European Union wide ban on the research saying, "The European Union science program should not be used to give financial incentives to kill embryos," German Research Minister Annette Schavan wrote in a letter to the Finish EU presidency, according to Reuters. "The current proposal from the European Commission and the European Parliament does not rule this out" (Deutsche, 2006). It is negative proposals like these that sent ES cell research in the United States into turmoil under the Bush administration. However, Obama's pro-stem cell research stand could transform the United States into a country which formulates important advances in this area to rival Sweden or South Korea.

**Chapter-4 Conclusion**

After researching the legalities of stem cell research, I believe that a country's government must fully believe in this type of research and mandate its funding. Sweden has shown that you must be fully invested in the project and maintain the funding necessary for the program's growth. The United States has a unique dilemma in regards to sentiments for the governmental funding of ES cell research—it is dependent upon the beliefs of the current president who may only be in office for potentially four years. As the president is a dynamic speaker, he may sway public opinion, but opposition will always follow this controversial subject. The United States has the potential to be a pioneer in the research with the availability

of top research facilities along with some of the most gifted minds in the world. What it lacks is a united front for the advancement of this research so that the government would be persuaded to support this important endeavor on an ongoing basis.

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# PROJECT CONCLUSIONS

Based on the research performed in this IQP, we authors have formulated our own opinions about some key questions on stem cells. We believe that since embryonic stem (ES) cells can be isolated, cultivated, and differentiated to allow new tissue formation for almost any type of cell in the body, these cells should be used in research to continue to improve the technology as best it can. Although we feel strongly about expanding the use of ES cells, our research documents that many other individuals do not, so we agree that adult stem cells should be used whenever possible, although our research indicates these cells are quite difficult to grow in culture. iPS technology may eventually replace ES cell usage, but only if the cells are truly pluripotent. With respect to the embryos to obtain ES cells, we believe the embryos should be taken from excess IVF embryos originally created for reproductive purposes and slated for discard, because these embryos already have donor consent. These embryos are already slated for destruction, and if they can be used to save lives, why not. With respect to stem cell laws, we feel that Sweden's philosophy and legislations on stem cells are the ones we support the most. Sweden strongly supports stem cell technology, and that country is one of the forerunners of stem cell research.