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STEM CELLS

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By:

Joseph Hernandez

Kevin Locke

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APPROVED:

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

ABSTRACT

The purpose of this IQP is to show the current state and issues of stem cell research, and its impact on society. Its purpose is to persuade its readers to have a more open mind towards stem cell research, and to at least support some types of stem cell research that do not involve destruction of an embryo. It will explore the types and sources of stem cells, the uses of stem cells, and the ethics and laws pertaining to stem cell research.

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EXECUTIVE SUMMARY

Stem cells are long-lived cells in the body that have the ability to differentiate into specialized cells to create new tissues and are capable of self regeneration. A common misperception is that not all stem cells are equal, there are many different types. Some stem cells, such as embryonic stem cells have the potential to form many diverse tissues, while others that are more specialized can only form a few or even just one type of cell. Stem cells can be classified by potential or source. When classifying by potential (greatest potential first) the categories are: totipotent, pluripotent, mulitpotent, unipotent. Unlike any other human cell, a totipotent cell has the natural ability to form every cell in the human body, including the extra embryonic cells. Pluripotent stem cells are very similar to totipotent stem cells but can not make extra embryonic cells, ES cells are pleuripotent. Multipotent stem cells are stem cells that can produce a limited subset of cells, examples include neural stem cells and hematopoietic stem cells. Unipotent stem cells are similar to normal cells in the body, but unlike a regular cell, they are considered stem cells because they are self replicating. An example of unipotent stem cell is epithelial stem cells.

The second way to classify stem cells is by the type of tissue from which they are isolated. The two types are: adult stem cells and embryonic stem (ES) cells. ES cells are not specialized and have a greater natural potential. Adult stem cells are stem cells that are more specialized and are partially differentiated.

Considerable misinformation exists on exactly what has been achieved with stem cells to date. Since the fifties when bone marrow transplants with hematopoietic stem

cells were originally conducted, stem cell therapies have successfully evolved from one method of treating leukemia, into a more modern and technologically advanced approach to medicine in which stem cells and advanced harvesting techniques are used to combat all types serious medical conditions such as heart disease, diabetes, Multiple Sclerosis, and even in the repair of spinal cord injuries. Hematopoietic stem cells can be used to treat diseases of the blood such as leukemia, through treatments such as bone marrow transplants. Hematopoietic stem cells have also been used to treat immune system disorders, such as Crohn's disease, Behcet disease, and Krabbe disease. Pancreatic stem cells can be used to grow islet cells to combat diabetes. Stem cells, from the brain or nasal cavity of mice, have been used to trigger the regrowth of myelin in mice with multiple sclerosis. Adult stem cells (neural) have also been used to treat Parkinson's disease, through transplantation. An area of ongoing research is the treatment of spinal cord injuries with neural stem cells. There is also much research into the treatment of cancer and other diseases with stem cells.

As with most new technologies, stem cells are highly controversial. The moral dilemmas presented by stem cell research are as diverse as the research. These concerns take the form of both moral and religious objections. Catholics are against all ES and EG research, while Muslims and Jews feel that these areas of interest can be explored in a morally upright fashion, so long as the research saves human lives. The main issues with ES and EG research are: when does life begin, is the greater good a valid argument, and how does ES and EG research affect the donors. Those that believe life begins at conception tend to see ES research as morally wrong, while those who believe otherwise often can justify it for the "common good". The issue of parthenotes, embryos without

the ability to grow into a human, provides a possible alternative source for ES cells, but also has its opponents.

Laws are currently in place in most countries to regulate stem cell use. Whether the laws are strict or lenient depends on the country. Some countries like England and Sweden have liberal laws that allow most stem cell research. Other countries allow research as long as the ES cells are taken from a line derived from embryos from fertility clinics. The most strick countries do not allow any ES cell research.

PROJECT OBJECTIVES

The purpose of this project was to examine the highly controversial topic of stem cells, to discuss its impact on society, and to address many of the common misconceptions about stem cell research. This report is intended to serve as an introduction to the types of stem cells and their various sources, stem cell applications, the ethics concerning their research and use, as well as the laws that have been enacted to regulate and govern further research and developments. These issues were researched through the investigation of articles pertaining to both ongoing and previously conducted stem cell studies that were found in journals, newspapers, magazines, and on the internet.

CHAPTER-1: STEM CELL INTRODUCTION:

TYPES AND SOURCES

Stem cells are long-lived cells in the body that have the ability to differentiate into a specialized cell to create new tissues. Because of this tissue regenerative capacity, stem cells are of current medical interest. However, obtaining one type of stem cell, embryonic stem (ES) cells, destroys a living embryo, so many individuals are against their use. But ES cells are only one type of stem cell. The purpose of this chapter is to document the various kinds of stem cells, describing their potential and their sources.

Tests for Stem Cells

It is not easy to know when you have isolated a stem cell for use, but certain tests are commonly performed. The first test is to culture the cells for several months and make sure they remain undifferentiated. A cell that remains undifferentiated is a cell that has the same characteristics as its parent cell. Differentiated cells tend to be more specialized than their parent cell. This test assures that they have the potential for long term, self renewal. Another test is to identify certain surface markers that are only present on undifferentiated cells. For example, for Oct-4 is a transcription factor protein that turns genes on and off. This protein is present in many kinds of stem cells, and may help them differentiate (Stem Cell Basics- 2005). If scientists learn to control the action of this protein, and other proteins like it, someday it may be possible to grow replacement body parts, such as a kidney or heart.

Another test of stem cells is to make sure that they can differentiate into multiple types of cells. For example, for hematopoietic stem cells (HSCs) that form all the cellular components of blood, one such test is to inject them into a mouse that has been irradiated to kill off its own blood cells. If the mouse recovers and replenishes its blood supply, the injected HSCs are assumed to be stem cells. This test shows plasticity, the ability to form several types of cells, and self renewal.

Stem Cell Classification

Stem cells can be classified in several ways. The first way is by potential. Some stem cells have the potential to form many diverse cells, while others only can form a few or even just one type of cell. The divisions when classifying by potential (greatest potential first) are: totipotent, pluripotent, mulitpotent, unipotent. Each of these will be discussed in detail below. While the potential of each type is different, they all have potential medical applications. Recent research has shown that stem cell potential may partially be a result of environment. Cells from the brain, that normally produce neural cells, have been shown to grow blood cells when transplanted into bone marrow (Generalized Potential of Adult Neural Stem Cells- 2000). Thus, classifying by potential is done based on the cell's natural tendencies.

The second way to classify stem cells is by the type of tissue from which they are isolated. The two types are: adult stem cells and embryonic stem (ES) cells. ES cells are stem cells isolated from embryonic stages of development. These cells are not specialized and have a greater natural potential. Adult stem cells are stem cells that are

more specialized and are partially differentiated. These cells are found in humans, even before birth. There are more types of adult stem cells than ES cells.

The basis for the formation of all cells in the human body is totipotent stem cells. These cells are represented by the single cell zygote, which is formed when a sperm cell fertilizes an egg. Unlike any other human cell, a totipotent stem cell has the natural potential to form every cell in the human body including the extra embryonic cells. The extraembryonic cells include the trophoblast, amniotic sac, and umbilical cord. Without the trophoblast, the embryo cannot be implanted to continue its development. Every human starts as a single totipotent stem cell. This single cell divides into more totipotent stem cells (this point is debatable, some scientists believe cells through the 4-8 cell stage are totipotent), which in turn differentiate into more specialized cells. A single totipotent stem cell, for this reason, is capable of forming an entire human being. This is one aspect of stem cell research that sets off moral triggers. People feel that doing scientific research with what could potentially develop into a human being, is unethical. Totipotent cells are self replicating, such that an entire line of stem cells can be created from just a few. By not needing to constantly have a fresh source of cells, the moral issues with the harvesting the cells are reduced in the eyes of some.

Pluripotent stem cells are very similar to totipotent stem cells. After around 4 days post-fertilization, the embryo exists as a blastocyst, which is a hollow shell of cells containing an inner cell mass. The inner cell mass is of much interest to researchers, as it consists of pluripotent ES cells. The only cells that pluripotent ES cells cannot form are the extra-embryonic cells. Other than these cells, needed for implantation, pluripotent

cells can form any cell in the human body. This subtle but important difference is what separates the pluripotent from totipotent. Like totipotent and all other stem cells, pluripotent stem cells are self replicating and are capable of producing a line of ES cells. Because these cells cannot naturally form the cells needed for implantation alone, these cells do not have the ability to form a human being. This is an important distinction, as doing research with these cells is not doing research with a human life. However, the problem is that to harvest the pluripotent ES cells, the blastocysts must be destroyed (Figure-1). As of now, the technology does not exist to allow the harvesting of part of the inner cell mass, while leaving the rest of the embryo intact. If researchers were able to remove only part of the inner cell mass and not harm the blastocyst, the remaining cells would theoretically be able to still be implanted and grow to term. Such an advance would remove some of the moral issue with ES stem cell research, especially the reservations to creating new ES cell lines.

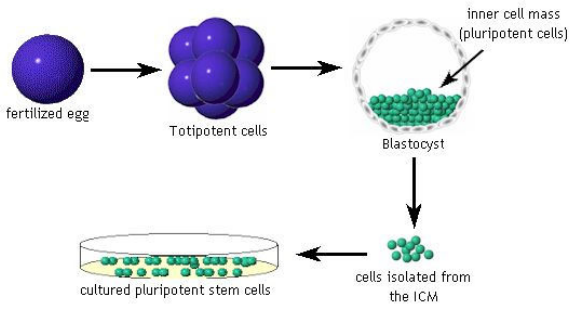

Figure-1: Isolation of ES cells from a Blastocyst
(Pinceton.edu Blastocyst Tutorial)

Multipotent stem cells are stem cells that can produce a limited subset of cells. Multipotent stem cells are adult stem cells. While self replicating, and able to produce a variety of cells, mulitpotent cells naturally only produce cells of a similar type. For

example, hematopoietic stem cells (HSCs) can produce red and white blood cells, but do not normally produce muscle or nerve cells. HSCs can produce a variety of blood and immune system cells, including red and white blood cells, lymphocytes, natural killer cells, and platelets, and reside in bone marrow (Green- 2001) (Figure-2). HSCs are also called 'blood stem cells'. These cells have shown great potential and play a large role in bone marrow transplants. Hematopoietic stem cells could be used to produce a reliable, sufficient blood supply.

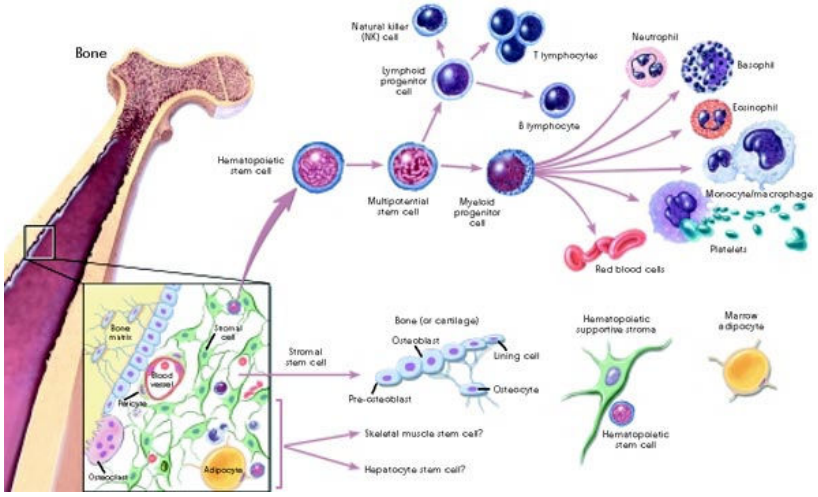

Figure-2: Differentiation of Bone Marrow Hematopoietic Stem Cells (Stem Cell Basics, 2005).

Another type of mulitpotent stem cell is neural stem cells. These cells can form neurons, astrocytes, and oligodendrocytes (Joshi and Behari, 2003). Neural stem cells exist in adults in the liver, pancreas, and brain. Mesenchymal stem cells are also multipotent, and can produce new bone cartilage and connective tissue.

Unipotent stem cells are also adult stem cells. They are similar to normal cells in the body, but unlike a regular cell, they are considered stem cells because they are self

replicating. They can self replicate but unlike any other type of stem cell, they cannot form another type of cell. An example of unipotent stem cells is skin cells. These unipotent stem cells can produce more skin cells, but cannot differentiate and create other tissue. Though useful in a specific application, such as new skin cells for burn patients, the unipotent stem cell does not have the widespread potential that other stem cells have. Unipotent stem cells are also found in the brain. These cells have great medical potential, especially in cases of brain damage, where new neurons could be grown to replace damaged neurons. These stem cells have only recently been found in adults. The earliest indication that neuronal stem cells exist came in 1992 and 1993 (Reynolds and Weiss, 1992; Lois and Alvarez-Buylla, 1993; Morshead et al, 1993). In 1998, Eriksson, showed that adult neural cells are generated in the hippocampus. These cells then migrate to their final positions in the brain.

As mentioned above, when classifying stem cells by source there are adult stem cells and embryonic stem cells (ES). Although each is a valid source of useable stem cells, their usefulness varies greatly. ES cells are the most useful as they are the least differentiated. On the other hand, adult stem cells are more specialized, and therefore have less potential. Adult stem cells have many different types and can be harvested in a nonfatal manner. The ability to harvest adult stem cells, without the destruction of a potential human life, is one reason why adult stem cell research should be strongly supported. Though these cells are more specialized than ES cells, they still are quite useful and are being found to have much greater potential than once was thought.

Umbilical Cord Stem Cells

Umbilical cords are a great source of multipotent adult stem cells. Umbilical cord stem cells should not be considered a moral threat. They are isolated from a recently born baby's umbilical cord blood. These cells are harvested without harming the baby, and are cells that would normally be discarded and die. A recent trend is to save and freeze these cells as to provide a source of stem cells in case the child should need them later in life. The umbilical blood cells are used in marrow replacement treatments. These cells are useful not just for the child, but can also be used in marrow replacement for related and unrelated patients. The umbilical cord contains large amounts of hematopoietic stem cells, much larger concentrations than the marrow of an adult (Viacell, 2006). The umbilical cord also contains high concentrations of high level progenitor cells. Progenitor cells are parent cells that produce a line of cells that are more specialized than the parent cells. Marrow replacement is commonly used to treat leukemia, certain other cancers, and some blood disorders. The marrow is typically taken from a healthy related marrow donor. The injected stem cells colonize the patient's marrow, and differentiate to form new blood components. Patients with marrow replacement that uses umbilical cord blood cells, rather than adult marrow, have a higher recovery rate, due to the higher concentrations of progenitor cells and hematopoietic stem cells.

The umbilical cord blood also has a greater expansion potential than the adult marrow, due to the presence of less specialized stem cells. Transplantation from umbilical cord blood is also less likely to result in tissue rejection. This is thought to be due to the unspecialized stem cells in umbilical cord blood. They have not yet developed

all of the surface markers that are present on most adult cells. The lack of these markers makes the patient's immune system more likely to ignore the graft. The umbilical cord blood also has less immune cells than adult blood. This helps minimize the rare cases of graft verse host disease, where the immune system cells in the graft attack the host's body. The advantages of umbilical cord stem cells over marrow cells clearly illustrate some of the reasons that scientists prefer to work with less specialized stem cells, such as ES cells. Some umbilical cord stem cells have the same surface markers as ES cells, giving hope that someday umbilical cord stem cells could be used in place of ES cells in research. Umbilical cord stem cells have been convinced to create liver and pancreatic cells *in vitro*. Though these cells have not been used yet to treat non-blood disorders, there is hope that someday they could be used to treat diseases such as diabetes. Mesenchymal stem cells are also found, in low concentrations, in umbilical cord blood and, in larger concentrations in the Wharton's jelly in the cord.

Bone Marrow Stem Cells

Bone marrow contains several types of adult stem cells. The main type of stem cell found in bone marrow is hematopoietic stem cells. These stem cells also are found in the peripheral blood but in much lower concentrations. In the blood, HSC are found at a rate of about 1 in 100,000 cells, while in marrow the rate is 1 in 10,000 (Stem Cell Basics- 2005). The higher concentration of stem cells allows for a marrow transplant to be more effective than a blood transfusion in treating blood disorders or aiding the recovery of the hematopoietic system.

These hematopoietic stem cells are hard to identify in culture because they act and appear like many other blood and marrow cells. For example, some HSC have the same appearance as ordinary white blood cells. The only way of telling these cells apart is the HSC's ability to self replicate and to differentiate into other cells. This can be a time consuming and frustrating test, as the cells cannot be isolated on an individual level and therefore it is impossible to be certain that all of the cultured cells are HSCs.

Another type of stem cell found in bone marrow is the mesenchymal stem cell (MSC). These cells are also known as marrow stromal cells. MSC are commonly isolated from the marrow aspirates taken from the iliac crest. MSC can form osteoblasts, chondrocytes, myocytes, adipocytes, and neuronal cells. Osteoblast cells secrete osteoid, a substance with high concentrations of collagen, which mineralizes and forms bone. These cells play an important role in maintaining bone strength. Chondrocytes are the cells that build and maintain cartilage. Myoctes are commonly referred to as muscle fiber. Cardiac (smooth) muscle cannot repair after an injury, unlike skeletal muscle. Because of this limitation, MSC hold vast medical promise for the treatment of cardiac problems. Scientists hope to use MSC to grow new cardiac cells, to repair a damaged heart. Adipocytes are the main adipose tissue (fat) cells.

Brain and Spinal Cord Stem Cells

The brain and spinal cord are another location containing stem cells. They contain Neural Stem Cells (NSC) (Figure-3) that differentiate into cells such as neurons, astrocytes, and oligodendrocytes.

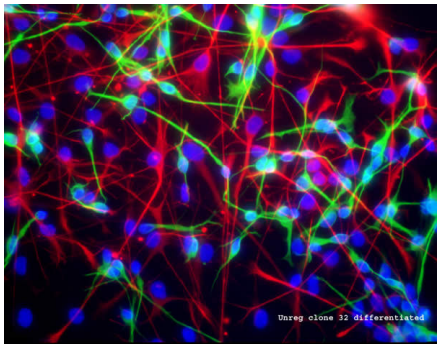

Figure-3: Neural Stem Cells.
Reneuron reneuron.com.

Research has shown that NSC exposed to retinoic acid differentiate into neurons (Huettner, 2006). Astrocytes are glial cells that provide physical support, nourishment, and maintain the environment for neurons. Oligodendrocytes perform a similar role for axons- they nourish and provide support for the axons. Oligodendrocytes also produce the myelin sheath that protects axons. The ability to produce oligodendrocytes makes NSC useful in multiple sclerosis and leukodystrophy research, diseases that attack the myelin sheaths. NSC have been proven to form hematopoietic cells when grafted into the bone marrow of mice. This plasticity, outside of what has been observed in nature, suggests that part of the limitation on stem cell plasticity comes from the stem cell's environment (Generalized Potential of Adult Neural Stem Cells- 2000). Recently, two more types of stem cells have been found in the brain. These are ependymal cells and subventricular zone astrocytes. These cells were found to form neurospheres, just like NSC.

Parthenotes

One exciting new development in ES research is parthenotes. In nature, certain species, such as turkeys, aphids, and especially insects like bees and ants, are capable of reproducing in an unusual manner. The female is able to produce offspring without the

male. Their eggs divide on their own, and grow into adulthood. These offspring are referred to as parthenotes. Scientists are conducting research into achieving this with mammalian eggs. The eggs are chemically treated to replicate the arrival of sperm. The eggs then divide and form blastocyst embryos, but these embryos can not develop past an early fetal stage. Initial human parthenotes were found to be peculiar, as they did not contain stem cells (at the 100 cell developmental level) (Cibelli et al., 2001). Research has since shown that it is possible to derive ES cell lines from monkey parthenotes (Cibelli et al., 2002). Very recently, claims exist for the development of ES cell lines from human parthenotes (Marchant, 2006). These impotent synthetic embryos may provide moral relief for ES research. Because they cannot result in an adult, some scientists consider parthenotes as morrally separated from traditional embryos. Parthenotes have great medical promise as a source of genetically identical tissue transplants that the body would not reject.

Male parthenotes have also been shown to be feasible. The genetic coding is removed from an egg and two sperm, from the same donor, are added. The egg is then chemically treated to divide. This has the potential to be useful for male patients, who might need replacement tissue.

Embryonic Germ (EG) Cells

EG cells are taken from the tissue of aborted fetuses. The cells are set aside by the body for future reproduction. The fetuses are typically aborted around 7 to 9 weeks after conception, and thus are a highly controversial source of stem cells. These EG cells

are isolated from human fetal gonads (Figure-4). The germ cells are pluripotent and can differentiate into three germ lines: ectoderm, mesoderm, and endoderm. Because these cells have similar potential to the ES cells, some researchers feel these are an alternative to ES cells. These cells have great application potential, as they are seem to be less likely to form tumors when transplanted, as compared to ES cells. Because the body only begins with 50 of these cells, they are difficult to isolate.

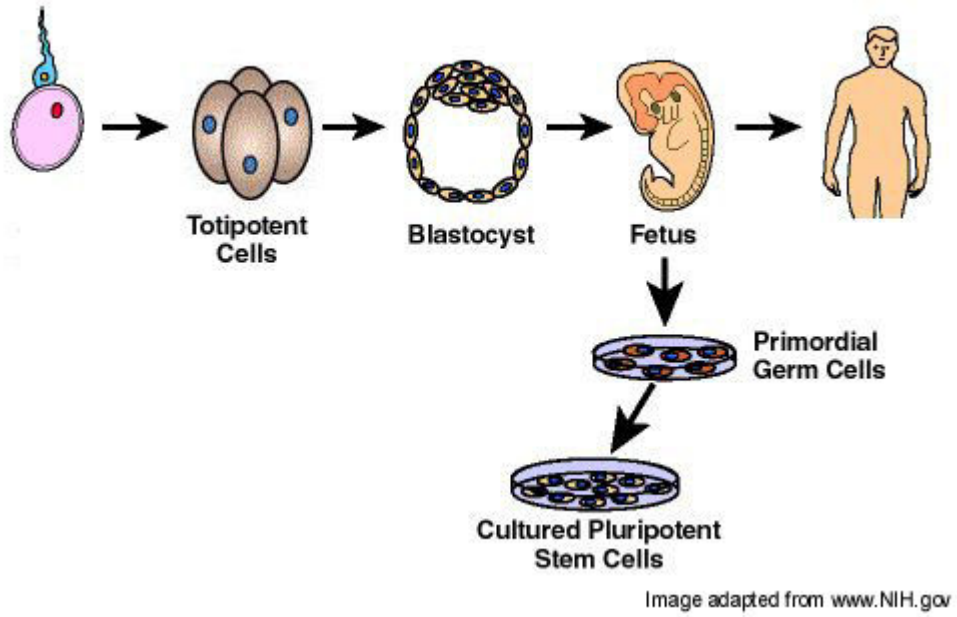

Figure-4: Derivation of Embryonic Germ (EG) Cells
(Fetal Tissue Diagram, 2006)

CHAPTER-2: STEM CELL APPLICATIONS

While the debate about embryonic stem cell harvesting and use by doctors and scientists remains at the forefront of the stem cell debate being conducted by politicians and world leaders, doctors and other members of the medical community have been developing new ways for stem cells to be utilized in the treatment of a variety of medical conditions and diseases for many years. While the technology and applications of stem cell therapies may be constantly advancing, the idea of using stem cells as a treatment method is far from a novel idea, as there have already been more than seventy medical conditions successfully treated by the use of stem cells in documented studies (Earll, 2005). Many people who are ethically against the use of "stem cells" do not realize that different types of stem cells have been used by doctors to treat of many different medical ailments for more than fifty years. Another common misconception believed by the public is that all stem cell research and therapies used by doctors rely upon the controversial embryonic stem cells (ES). The stem cells primarily used in these early therapies are not ES cells whose harvesting require the termination of a living organism, but instead are adult stem cells that can be non-fatally harvested from tissues such as umbilical cords, pancreases, eyes, skin, and brains (Earll, 2005). Since the fifties when bone marrow transplants with hematopoietic stem cells were originally conducted, stem cell therapies have successfully evolved from one method of treating leukemia into a more modern and technologically advanced approach to medicine in which stem cells and advanced harvesting techniques are used to combat all types serious medical conditions such as heart disease, diabetes, Multiple Sclerosis, and even in the repair of spinal cord

injuries (Earll, 2005). Stem cell therapy aims to replace the "master cells" that differentiate into the cells that have become damaged or destroyed by diseases or trauma with therapeutic cells that trigger the body into naturally repairing the damage and hopefully reversing the effects of the condition that the patient suffers from (Escolar et al., 2005). Due to a great deal of misinformation on the web concerning what has currently been achieved with stem cells versus what is hype, the purpose of this chapter is to document some of the real studies that have been done with stem cells.

Adult Stem Cell Applications

Hematopoietic Stem Cells

One of the earliest and most commonly used stem cell applications over the past half century was the transplantation of healthy bone marrow into a patient who was suffering from a disease that destroys the body's immune system such as leukemia. Leukemia and other diseases like it result in an immunodeficiency disorder caused by improperly functioning bone marrow. Leukemia is actually a type of cancer that is commonly associated with children and young adults that destroys bone marrow, which is the tissue that contains hematopoietic stem cells (HSCs) which are responsible for making all the cellular components of blood such as white blood cells, red blood cells, and platelets. Leukemia results in the body having a high level of immature white blood cells, which in turn can lead to the likelihood of the patient becoming increasingly susceptible to infections and weakness as the illness progresses. There are two common leukemia treatment procedures used by doctors. In the first treatment option, doctors

harvest healthy bone marrow from a location in the same patient where the marrow is deemed 'healthy' and transplant it into the area affected by the cancer, in what is called an autograft procedure. Another option the doctors can choose is to remove healthy bone marrow from a separate matching donor patient which can then be transplanted into the sick patient in what is termed an allograft procedure. Using an allograft is advantageous if a good matching donor is available for the transplant because in most cases the patient himself has a severely weakened immune system, and does not have enough healthy bone marrow that can be harvested and transplanted. The transplanted bone marrow contains the hematopoietic stem cells that recolonize the patient's bone marrow, and differentiate into the necessary cell types that allow the body to naturally produce healthy bone marrow and blood, hopefully producing healthy mature white blood cells, and ultimately increasing the ability of the patient's immune system to function normally.

The first successful bone marrow transplant that resulted in long term survival of a patient suffering from leukemia was performed by Dr. Donnall Thomas in 1956 (Piccolo, 2006). Dr. Thomas removed bone marrow from a healthy twin sibling which was then transplanted into the sick patient. This procedure caused the leukemia symptoms to recede over time, eventually putting the cancer into remission. The next advance in leukemia treatment came when doctors were able to successfully match and transplant bone marrow from a donor which was not related to the sick patient. When an unrelated donor must be used, a healthy matching source is found, and the bone marrow is removed from the donor's hip in a minimally invasive procedure. The first successful bone marrow transplant involving the use of marrow from an unrelated donor was conducted on a five year old boy in 1973 at the Sloan-Kettering Cancer Center in New

York. A matching donor was found in Denmark, and the child required seven different marrow transplants to allow his body's immune system to function normally (Piccolo, 2006).

Treatment of Diabetes with Adult Pancreatic Stem Cells

Diabetes is a serious condition caused by the improper function of the pancreas. In a healthy human, the pancreas produces insulin, which is a chemical needed by cells to use the glucose in the body that comes from food, the liver, and muscles. A Type-I diabetic is someone whose pancreas does not properly function, meaning that little or no insulin is produced by their pancreas. There are two types of diabetes, Type I and Type II. Type I diabetes is also known as "Juvenile Diabetes" and is a condition where the pancreas does not produce any insulin at all, while Type II diabetes results in the pancreas producing insufficient insulin levels later in life (or the body quits being sensitive to the insulin that is made), hence its other name, "Adult Onset Diabetes." Over time, the excess glucose levels in the blood can result in both temporary and permanent health problems ranging from a minor problem like fatigue, to a major one like blindness or even death (What is Diabetes?, 2005). Diabetes stem cell therapy requires the harvesting and implementation of pancreatic stem cells which are used to grow new islet cells which are destroyed by diabetes. This type of therapy has been shown to have the potential to decrease the need for pancreas (or kidney following pancreatic failure) transplantation in patients suffering from diabetes, as it helps the pancreas to function properly and naturally supply the body with insulin. One study shows that one year after islet cell transplantation, many diabetics' pancreases are functioning at normal levels,

meaning the patient no longer requires the frequent insulin injections (Hughes, 2005). Researchers at Harvard recently conducted a trial on mice where mice suffering from Juvenile Diabetes were injected with adult stem cells. This therapy resulted in the complete disappearance of all symptoms of diabetes in the mice, and is awaiting clinical trials in human patients (Kodama et al., 2003). Another study conducted first with ES cells from mice, then with human ES cells, has shown that embryonic stem cells could also be used in therapies to treat diabetes. The ES cells differentiated into islet cells that produce insulin. This study is discussed in more detail below in the subsection on ES cells. However as this treatment method would require the use of the ethically controversial ES cells, it is not a viable treatment method in human patients at the present time (Assady et al., 2005). Future use of stem cells to efficiently treat diabetes without requiring an organ transplant or long term dialysis use would be ideal, as the supply of matching, healthy organs, and the high costs and risks associated with dialysis are severe problems for doctors, insurance companies, and patients to overcome (Earll, 2005).

Treatment of Multiple Sclerosis with Adult Stem Cells

Multiple Sclerosis (MS) is a disease that affects the Central Nervous System (CNS) which can create a variety of degenerative health problems for people suffering from it. Normal, healthy people have a layer of myelin that acts as a sheath and surrounds the nerves in the body. This myelin tissue sheath protects the nerves and also helps the body conduct nerve impulses which control all of the body's functions. MS patients experience a gradual breakdown of the myelin layer surrounding their nerves, resulting in the formation of sclerosis, also known as scar tissue regions, around the

nerves. The scar tissue prevents natural regeneration of the myelin sheath, ultimately leaving the nerves unprotected and incapable of proper nerve impulse conduction. MS eventually results in nerve damage that can cause painful long term health problems such as bladder and bowel dysfunction, feelings of vertigo, and problems walking, and even seizures (About MS, 2005).

Over the years, a variety of therapies have been used to combat MS, ranging from drug treatments to physical therapy regimens. Now many doctors are conducting studies on the use of stem cells to help treat MS. Adult stem cells are harvested from the brain or nasal cavity of mice, and implanted in the areas afflicted by sclerosis in a mouse MS model to trigger natural myelin growth, and help the body repair the lesions formed by the disease. It has been shown in some studies to successfully stabilize or even reverse many of the symptoms (Earll, 2005).

Treatment of Parkinson's disease Using Adult Neural Stem Cells

Parkinson's disease is another condition that like MS affects the central nervous system. It is caused by the destruction of dopamine producing brain cells. Dopamine is a chemical needed by the body for normal motor skills and movement. Parkinson's is a degenerative disease that results in the gradual deterioration of patient's bodily control, leading to symptoms such as uncontrolled muscle spasms and a decline in coordination. For years the primary method of treating Parkinson's disease has been very long-term drug treatment programs, which have yielded mixed results. The drugs have been successful in temporarily alleviating some of the symptoms and delaying the progress of the disease, but over extended periods of time the patients almost always experience a

worsening of symptoms as the disease overwhelms the drugs (Stem Cells, 2001). However in the late 1990's neurologists began to experiment with the use of adult stem cells as a possible treatment for Parkinson's disease. One such trial was conducted on a man named Dennis Turner who had suffered from the effects of Parkinson's for more than fourteen years. Prescribed medication had become ineffective at controlling the symptoms, and by that stage Mr. Turner had almost completely lost control of the right side of his body, primarily experiencing extreme difficulty controlling the use of his arms. Turner's neurologist approved him for the stem cell trial, and neural stem cells were harvested from his brain and transplanted into the left side of his brain. The cells were placed in the left half of his brain because the left lobe of the brain controls the function of the right side of the body where his paralysis was the worst (Levesque, 2002). The operation was a success, as Mr. Turner experienced almost complete remission of his condition, experiencing no new symptoms of Parkinson's disease for more than four years, and he is considering undergoing another procedure to transplant more stem cells into the right half of his brain, hoping the further improve his condition. Mr. Turner was able to return to a normal, active life after the procedure, something that would have been highly unlikely had he continued only on a drug therapy regimen (United States – Turner, 2004).

Other studies are also being conducted in the battle against Parkinson's disease that do not require the harvesting and transplant of stem cells. The patients are injected with a neurotrophic factor protein found in the body that induces the production of stem cells found in their own brain. One year after the study, patients have experienced favorable results with their Parkinson's symptoms, with more than sixty percent of the

patient's who have had this protein injection showing increased mobility and reduction in symptoms of Parkinson's (Gill, 2003).

Use of Adult Hematopoietic Stem Cells to Treat Non-Blood Disorders

Adult HSC transplants have also been successful in the clinical treatment of other autoimmune disorders such as lupus, Crohn's disease, Behcet disease, and a degenerative genetic disorder that is similar to MS called Krabbe disease. All of these disorders result in a breakdown of the afflicted person's immune system, leading to the onset of health problems like pneumonia, intestinal and oral sores, skin lesions, blood deficiency, and abdominal discomfort. The studies conducted show that many patients suffering from diseases resulting in insufficient immune system function that received hematopoietic stem cell transplants showed an improvement in their condition, or complete remission of their conditions. Krabbe disease is a rare condition that arises in newborn children. It is caused by a genetic abnormality that results in the body not producing an enzyme needed to form the myelin sheath needed to protect the nervous system. If the disease is not caught soon after birth, the infant's brain will not develop correctly and the newborn will begin to rapidly lose motor functions, and likely will die by the age of two. Research teams in North Carolina have shown that if the newborn receives an immediate transplant of HSCs harvested from their own umbilical cord blood it can allow the infant's body to naturally produce the myelin needed so that natural brain development can be restored (Stem Cell Research Foundation, 2005).

Treatment of Spinal Cord Injuries With Adult Neuronal Stem Cells

Spinal cord injuries often result in paralysis that affects the patient's use of their limbs, whether it is just the lower half of their body in the case of paraplegia, or both the legs and arms when the patient suffers quadriplegia. These injuries typically occur when a person suffers a trauma which severely injures the spinal column, resulting in damage to the nervous system. In years past, many doctors had offered a very grim prognosis to the people suffering these injuries as there were not any reliable therapies capable of reducing or completely reversing the paralysis. Patients afflicted with paralysis usually faced a best case scenario where after many years of grueling physical therapy regimens they might regain some muscle and bladder control, and maybe some feeling in their limbs.

However new studies that use adult neuronal stem cell transplants as part of a paralysis treatment program have had very positive results. Neural stem cells are typically the stem cells that have been studied in connection with damaged nervous system therapies. These neural stem cells are shown to be able to produce neurons, which are the cells mainly responsible for the transmission of most of the body's electrical impulse. Neural stem cells can be found in both fetal and adult brains, and can differentiate to form cells found both in the brain and spinal column (Stem Cells: Scientific Progress, 2001). These stem cells are harvested from the patient and transplanted to the injured area. Alternate sources for these stem cells used to induce regeneration of the nervous system include the nasal cavity and umbilical cord blood due to the cells from both sources contain neural stem cells, although these studies remain controversial. Neuronal stem cells include cells that are used by the body to repair the

scar tissue that has formed along the spinal column and lead to myelin growth, as well as the formation of new nerves, ultimately allowing normal electrical impulses to be conducted by the nervous system (Hughes, 2005). There are over sixty documented cases where patients have received these neuronal stem cell transplants and regained muscle control lost after the injury, and in some cases the patients are even able to walk again with the use of crutches or braces (Stem Cell Treatment, 2004). One such case dealt with an 18 year old female from Colorado whose spinal cord was completely severed in an automobile accident, leaving her a quadriplegic. Immediately after the accident it was determined by her doctors that not only she would never walk again, but it was unlikely that she would regain use of her arms either. However, with the help of friends and family she researched alternate treatments in hope of a miracle (United States – Peduzzi, 2004). They found the Proneuron Biotechnologies Ltd. Company located in Israel that offered a stem cell and macrophage transplant therapy to help treat paralysis by allowing the body to naturally regenerate the spinal cord tissues that were destroyed by the trauma. The procedure was a success, and has since returned muscle control and feeling to all four limbs (United States – Dominguez, 2004). The success of these recent studies have given new hope to doctors and people suffering from paralysis worldwide, and are leading to more research into the use of stem cells as a means of combating paralysis.

Treatment of Cardiovascular Disease with Adult Stem Cells

Cardiovascular disease is the leading cause of death in the United States. Worldwide heart disease and heart trauma injuries are among the leading causes of death

in every country across the globe (Viacord, 2002). There are over twenty million people worldwide who are at a high risk for suffering heart failure, and every year thousands of people are emitted to emergency rooms as a result of suffering severe heart trauma, so naturally the medical community is always searching for new methods for the prevention and treatment of the conditions that lead to heart disease and to save patients who suffer cardiac injuries (Aronow, 2005). Many current conventional treatment methods used to combat heart conditions, such as drug therapies, the implantation of heart defibrillators and cardioverters, recommended exercise regimens, and dietary restrictions can be successful for short term results, but in the long term as the person ages it is common for the patient to experience another heart attack or cardiac episode.

Doctors are now conducting studies on the use of HSCs or skeletal muscle stem cells to help restore normal heart function after patients suffer a heart attack, heart failure episode, or degenerative heart diseases. HSCs or skeletal muscle stem cells are harvested from the patient's body and transplanted into their arteries after they are stabilized. It has been shown that this procedure can significantly increase the heart's pumping ability, oxygen capacity, and cardiac tissue regeneration; all of which greatly increase the patient's chances for long term survival after suffering a severe cardiac episode (Hughes, 2005).

A procedure conducted in 2003 illustrates the potential for stem cell therapies to help heal even the most severe cardiac problems. A 16 year old Michigan boy suffered major cardiac trauma after being shot directly in the heart by a nail gun which lead to the boy eventually going into cardiac arrest. His doctors initially determined that he would need to receive a heart transplant and undergo long term medication therapies to stabilize

his condition. However, his doctors did offer an alternate treatment method and discussed with his family the use of an experimental stem cell procedure to help repair his heart. This novel procedure had never been conducted on a human patient, and involved the transplantation of stem cells extracted from his body into his injured heart. Before the operation, doctors put the boy on a drug to stimulate the body into producing the stem cells needed for the procedure. After a four day drug regimen doctors harvested the stem cells from the patient's body, which were then transplanted into the arteries surrounding the heart using a heart catheter. A team of doctors lead by Dr. William O'Neill completed the surgical stem cell transplant on February 21st, 2003, and within one week of the operation the teenager was able to be discharged as it was shown that the heart's performance was steadily improving, with cardiac output increasing from twenty five percent before the procedure, to thirty five percent of normal output volumes after the transplant. The stem cell transplant conducted by Dr. O'Neill's team was truly the first of its kind and allowed the body to repair the tissues surrounding the heart that had been destroyed by the trauma on its own, instead of requiring multiple corrective surgeries. The success of this operation will definitely lead to future research in the use of stem cells as a method of rapidly repairing damaged cardiac tissues without the use of highly invasive open heart surgery or heart transplant (Philipkoski, 2003).

Studies are also being conducted on regenerating tissues other than those found in the nervous system, pancreas, and heart. These studies have focused on tissues found in organs like the eyes, liver, and kidneys. The cornea is a very delicate and crucial layer of tissue on the surface of the eye that acts as the eye's primary means for focusing light. If the cornea gets destroyed by disease or injury, it is likely the patient will suffer

significant loss of eyesight (Eye Bank Association of America, 2001). Until recently there was little that could be done to help repair any damage to the cornea. Corneal transplants, where healthy cornea tissue is harvested and transplanted onto the diseased or injured cornea, combined with limbal stem cell transplants are becoming a popular corneal blindness treatment method used by ophthalmologists. Limbal stem cells are harvested from a healthy source and transplanted to the injured eye, in the hopes that they will differentiate into new corneal epithelial cells, improving the ability of the cornea to function normally (Schwab, 2000). This combination treatment procedure has yielded very good results, with eyesight being successfully restored to patients that in some cases have been blind for more than forty years (Hughes, 2005). Tissue regeneration through the use of stem cells as a treatment method for conditions causing failure in organs like the liver and kidneys are also being widely studied by the medical community. Renal failure (kidney failure) is a very problematic condition, as it often leads to multiple organ failure if the condition is not quickly corrected. Clinical trials have been conducted where patients suffering from kidney and multiple organ failure have received stem cells to help at least stabilize the tissues and increase the ability of these organs function until a complete organ transplant operation can be conducted.

Treatment of Cancer Using Adult Stem Cells

Cancer is a highly researched health problem, like heart disease, it is another one of the leading causes of death worldwide. With many types of cancer, current treatment methods are not significantly effective in increasing the afflicted patient's lifespan. In the United States alone it was determined that over ten million people had died between the

years of 1950 and 1974 from various forms of cancer, and those numbers will rise dramatically over the next twenty five years as the population continues to grow exponentially, resulting in an increase of people at risk to develop terminal forms of cancer (Devesa et al., 1999). Cancer is a condition where cell growth cannot be controlled by the body, resulting in the uncontrolled rapid production of cells. The massive amounts of new cells produced by cancer can form into tumors that continue to grow and eventually overwhelm the body, and cause the death of cells needed for the body to function normally. Cancer can be caused by the patient's repeated exposure to outside factors like carcinogens, such as cigarette smoke or asbestos, that cause cell mutations, or cancer can also be caused genetically inherited traits that result in unnecessary cell differentiation (National Cancer Institute, 2005). Many popular cancer treatments involve techniques such as chemotherapy and radiation therapy. These methods have shown to be effective in at least slowing down the cancer or putting it into remission for some time, but both treatment options have negative side effects as radiation and chemotherapy do not exclusively target and kill the cancerous cells, but can cause cell death in healthy cells as well (Viacord, 2002).

The medical community is now researching and developing the ability to use stem cells in the battle against many types of cancer. It has been shown that the transplant of stem cells into cancerous regions of the body results in the formation of cells that target and attach themselves to the cancerous cells and can trigger cell death, eventually reducing the number of cancer cells and size of the tumor as the process repeats many times. Aside from the formerly mentioned leukemia, stem cells have been successfully used in the treatment of cancers such as: liposarcoma, Non-Hodgkins and Hodgkins

lymphoma, and neuroblastoma to name a few (Viacord, 2002). After the positive results doctors have seen so far from these successful treatments, there is no doubt that as stem cell technology advances there will be more research into stem cell applications in the fight against all different types of cancer that effect millions of people annually.

ES Cell Therapies

Embryonic stem (ES) cell therapies are among the most sought after medical advances as scientists conducting laboratory studies are just beginning to be able to harness a fraction of their power. However, with as much support that the ES cell research movement has from the medical community and liberals around the world, there are just as many people who are concerned with the moral and ethical concerns that their use creates. Because of these ethical concerns, ES cell studies have yet to be approved for human clinical studies, so as of now scientists have been relegated only to conducting ES cell tests in animal studies. This is not abnormal though, as all new clinical procedures and treatments must first be shown to have positive results in pre-clinical studies conducted on animals before human trials are given approval. ES cell animal studies have yielded positive results in tests conducted so far on the treatment of animals with diabetes or cardiac problems, giving researchers hope that soon they will be able to unleash ES cells as superior treatment methods for a variety of human medical conditions. As scientists continue to make advances and conduct studies that are successful in showing the medical advantages to ES cell use it is likely that many people that oppose their use will see the benefits of ES cell therapies, resulting in the alleviation of some of the regulations which restrict researchers from openly pursuing human ES cell

applications.

As was briefly discussed earlier in this paper, an Israeli research team headed by Suheir Assady was successful in showing that it is possible to induce the differentiations of human ES cells into insulin islet cells. This *in vitro* study was conducted on human ES cells that were allowed to differentiate. The resulting cell cultures were examined using an immunohistochemical staining technique that showed the successful production of insulin in the medium, meaning that there were islet cells produced (Assady et al., 2005). The results from this study are encouraging, but this technique's application is still not ready for human *in vivo* studies.

However, the Assady study was based on an earlier *in vivo* study conducted by a team based in Spain on the treatment of diabetic mice using harvested rodent ES cells. Researchers from the Institute of Bioengineering at Miguel Hernandez University in Alicante, Spain were able to use ES cells to produce rodent insulin producing cells *in vitro*. Clusters of these cells were then transplanted into the pancreas of live diabetic mice. It was shown that within one week all symptoms of hyperglycemia had subsided and the mice were now able to naturally normalize their blood glucose levels after eating a meal (Soria et al., 2000).

Other successful ES cell studies have been conducted on animal subjects, mainly rodents. ES cells have been used in the treatment of rats with severe spinal cord damage, as well as in the treatment of mice who suffer from hemophilia or cardiac problems. In the spinal cord study, ES cells harvested from a mouse were transplanted into the damaged spinal cord of a rat after it suffered severe spinal trauma. The rats were examined two to five weeks after ES cell injection, and it was shown that the transplanted

cells had survived and differentiated into cells that had begun to repair the damage from the initial trauma. As a result of the production of new cells found in their nervous system, the rats showed improvement in their condition, as there was a noticeable improvement in coordination, and the rats were able to bear more weight on their hind limbs (McDonald et al., 1999). In another study conducted at the University of North Carolina, hemophilic murine livers were injected with a compound made up of murine ES cells and natural growth factors. The injected mice were then able to manufacture hepatocytes, which are the liver cells that produce the factor IX protein that leads to blood clotting. The study also showed positive long term results, as the injected mice were continuing to naturally produce factor IX more than one hundred days after the initial injection procedure, showing that the mice experienced a complete remission of the hemophilia (Sciencedaily.com, 2005).

While embryonic stem cell research is undoubtedly the cutting edge of newly developing medical treatments, the ES cell studies conducted so far have been done exclusively on animals because there have not been any studies approved for human testing. However, since the animal studies have shown a lot of positive results, it is likely only a matter of time until researchers receive approval to begin the ES cell research in human test subjects.

Chapter Conclusion

Stem cell research, clinical trials, and successful applications that have been conducted or are being currently conducted are most likely only beginning to scratch the surface of what science will be able to use these "master cells" for as human technology

and understanding of the body increases in the future (Earll, 2005). A White House report from 2001 discusses how even five years ago when many of these studies were in their early stages it was still believed that stem cell research could lead to the development of therapies that could be used to combat diseases that more than one hundred and twenty million American citizens suffer from (Viacord, 2002). Future advancements could include, but are certainly not only limited to, the use of stem cells in the tissue engineering and production of new organs, skin, cartilage, ligaments, and tendons for transplant, as well as the ability to help reverse the effects of diseases that arise as people age such as Alzheimer's disease, osteoporosis, and perhaps even being able to be used against the aging process itself (Stem Cells: Scientific Progress, 2001).

CHAPTER-3: STEM CELL ETHICS

The moral dilemmas presented by stem cell research are as diverse as the research. These concerns take the form of both moral and religious objections. This is not to say that all religious groups see the issue in the same light. There is dissent even among the Christian community as to the morality of the issues. This section will first explore the main moral issues with stem cell research. The second section will provide insight to the views of various religions on the contested issues of ES and EG research. This section will present little detail on adult stem cell research as there is little objection to this research among the religious communities.

Adult Stem Cell Ethics

The average person needs to consider adult stem cell research before they decide to be against all stem cell research. Much of the adult stem cell research is already accepted in mainstream society. Few people would pause to consider the morality of receiving a bone marrow transplant if they were suffering from leukemia or lymphoma, even though they might not be aware this is a direct application of stem cell research. The hematopoietic stem cells, located in the marrow, are the cells which restore the hematopoietic system of the patient. Without any stem cell research, bone marrow transplants would not exist and thousands of people's lives would not have been saved. Continuing research with adult stem cells has resulted in other potential treatments, including the ability to repair damaged heart muscle, repair damaged nerves in the spinal

cord, and to create antibodies that attack tumors. Current research has pushed the bounds of what adult stem cells are capable of. There are few, if any, moral objections to research to find the capabilities of adult stem cells since no embryos are destroyed to obtain them. With research showing that stem cells, once thought to produce only cells from their native system, are capable of producing cells of a different tissue, the uses of adult stem cells are increasing rapidly. Unlike ES or EG cells, adult stem cells are collected without any lasting harm to the donor. The ability to collect these cells without destroying a life (or even a potential life) allows the research to be conducted in good conscious.

Some religious groups have pushed for increased adult stem cell research, and the cancellation of ES and EG research due to these factors. They also feel that the stability of the adult cells makes them have a greater advantage over ES and EG cells. ES and EG cells have been shown to differentiate quickly, after transplant, and have formed tumors. For these reasons, adult stem cell research should be fully supported both by public and private funding. One of the few objections to adult stem cell research deals not with allowing adult stem cell research, but rather with the particular applications. For example, some object to using mouse feeder cells to grow human ES cells, as they feel that cross species mixing might occur, and that would be morally hazardous.

EG Cell Ethics

EG research is a deeply emotional issue for many people. Because aborted fetuses are used to obtain EG cells, people have very passionate feelings about it. Some people see the great potential of the cells and see these stem cells as their only hope.

Others feel that the abortion of the fetus makes the research impossible to justify. There are also those whose opinions fall in between the two extremes. They feel it is acceptable to use fetal tissue, which would be normally thrown away, but would be firmly against a medical abortion that would be solely performed to obtain the tissue. To the authors of this IQP, this stance is the most reasonable and should be encouraged. To discard useful stem cells that might be used for the good of mankind just because they are obtained from an already aborted fetus is unreasonable. This is not to say that abortion should be encouraged to provide a ready source of EG cells, but rather to say that abortion happens, and it is more wrong to discard the tissue than it is to put it to good use.

Some are against EG research because they feel that the use of aborted tissue might encourage women to have abortions. If the woman was unsure whether to keep the baby or to have an abortion, the usefulness of the tissue might push the woman towards abortion. But to disallow all EG research because of this potential is foolhardy. Assuming one feels abortion is wrong, a person who decides to abort based on this flimsy excuse, would not be a person of moral standing. They could be also expected to make immoral choices in other aspects of their life. If society bans all EG research just to discourage the immoral individual, it would be ridiculous. Society might was well ban medicine as it might be abused by immoral people. All society can do is conduct morally upright research and hope that individuals will act in a moral and acceptable manner. If one does not feel abortion is morally hazardous, then they would probably not object to EG research and thus need no convincing. EG research has shown great potential and has resulted in the regeneration and repair of spinal cord nerves in mice. Such advances could provide a great service to the human race, so continued research is quite merited.

ES Cell Ethics

ES research is one of the most controversial areas of scientific research today. The expectations are only matched by the dissent to the research. The main moral dilemma is the destruction of the embryo, thus each person needs to make their own informed decision as to when life truly begins. If the person determines that life begins at conception, ES research is harder, if not impossible, to justify. If they feel that life begins later on, then they need to look at further issues before formulating an opinion on ES research such as whether the good of the potential treatments outweighs the destruction of the blastocyst. They need to form a moral status for the potential life, and decide if the research is justified. The thinking needs to then continue and consider the potential of adult stem cells, and see if they still feel ES research is justified, relative to the advances in adult stem cell research. They need to consider the instability of the ES cells as compared to more mature stem cells. The potential of ES cells to form tumors is quite alarming and should be carefully considered and neutralized if one wants to perform morally upstanding research on test subjects. The embryos that are destroyed to create ES lines are typically those obtained from *in vitro* fertilization (IVF) clinics that are in excess of what the couple needed, and going to be discarded and die. Since these are already doomed embryos, destroying them for research is just a different version of the same fate. The researcher is not destroying a potential life that would have otherwise been allowed to live a full life. This lessens the moral hazards of blastocyst destruction. A relatively new trend is the adoption of the extra embryos from IVF. Surrogate mothers are used to implant the embryo, and the children are raised as their own. This does not

imply that all of the stored embryos are saved, as a very small percentage is actually adopted. The adopted embryo children are often referred to as 'snowflake' children, in reference to the frozen embryos. While all these concerns are quite justified, it is still possible to conduct the research in good conscious.

Parthenote Ethics

Parthenotes only further cloud the morality of ES research. Because these artificial embryos are impotent to form a human, they have a lower moral status to most people. Because they cannot be implanted and grown to term, destroying a parthenote is not destroying a potential life. To decide the morality of ES research with parthenotes, one must decide where the line is between human life and cells containing the architecture for human life. If these embryos (the size of the period at the end of this sentence) are just a collection of cells, and not a human, then harvesting the inner cell mass is ethical. Parthenotes also have ethical issues due to the collection of the eggs. The eggs need to be harvested, using the same process as IVF. The donor takes drugs that regulate hormonal levels. The egg harvesting procedure increases the risk of certain cancers, such as ovarian and uterine cancer. With each donation cycle, the risks increase. Because of the rising health risks resulting from the egg donation, safeguards need to be placed to limit the number of times a woman can donate her eggs for research.

Inter-Species Ethics

There is also dissent to research that transplants tissue from one type of animal to another. This is not as clear of an issue as it might appear on the surface. By having the

ability to use stem cells from one animal to treat diseases or medical problems in another type of animal, researchers hope to one day possibly use animal stem cells to treat diseases in humans. By using animal ES or EG cells to treat human diseases, the researchers could have the boundless potential of pluripotent stem cells, without having to destroy a *human* life or potential life. One key issue here involves the potential transfer of animal viruses to human recipients, which is also a key ethical issue associated with xenotransplantation (the transplant of animal organs such as livers to humans).

Catholic Stance on Stem Cells

The religions of the world have quite varied opinions when it comes to ES and EG research. The Catholic Church's strict rules concerning reproduction, and its views on the start of life make it one of the strictest against EG and ES research. More liberal views come into play from Judaism and Islam, which might come as a surprise to many. Eastern religions, such as Hinduism and Buddhism, have objections that are not found in most western religions.

The Catholic Church feels that adult stem cell research can be conducted ethically. The Church's position is that the research can be conducted for the good of mankind, without taking human life. They also feel that human and animal tissues should be kept separate, as doing otherwise is too close to playing God. Some Catholic bishops are pushing for adult stem cell research as part of their crusade against ES and EG research.

The official Catholic perspective on ES research is one of the most rigid and strict. The Catholic Church teaches that life begins at the moment of conception- as the

sperm and egg fuse. This exact and early infusion of spirit and soul leads to a very staunch stance on ES research. The Catholic Church believes that human life is sacred, and ending a life even to save many others, is morally and spiritually wrong. Because Catholics believe that an embryo is a human life, destroying the embryo to harvest the ES cells is forbidden. This even applies to the destruction of the blastocyst, when harvesting the inner cell mass. The church believes that the greater good argument is not valid, and that only God has the power to decide when and which lives should end. The Catholic perspective is that the harvesting of embryonic cells is not just morally equivalent to murder, but is actually murder, due to the destruction of the blastocyst. This stance is not very surprising, as the Church is also firmly entrenched against abortion. The Catholic Church's stance against abortion leads them to also be against research with EG cells. The Church feels that aborted fetal tissue should not be used. They are even opposed to the use of tissue from abortions that happen without regard to research. They feel that the option of having the fetus donated for research may encourage women on the fence to decide to have an abortion. The Catholic Church is also against the creation and use of parthenotes, partially due to the closeness to IVF. The Church has strict rules regarding reproduction. They believe that reproduction is a gift from God and that it should only occur between a man and a woman, within the bonds of marriage. They feel that IVF occurs outside of marriage, and by removing intercourse from the equation violates God's will. This stance places the Catholic Church firmly against the use of the extra embryos created from IVF. The Catholic Church feels that parthenotes also violate God's will and are also too close to playing God, by creating 'life' outside of the way God intended.

Islam and Stem Cells

The Islamic faith does not have an official position concerning stem cell research. There is no one central authority from which the position could emanate, which makes determining the moral position more difficult. Iran, run by conservative Muslims, has officially allowed and supported ES research. If this can be considered an indication of religious backing of ES research, the research may find a promising new home in Muslim countries around the word. Iran is not the only Muslim country to openly support such research, Egypt and other countries also provide official support. Many Islamic scholars believe that life does not start until around the fortieth day. This position lines up with the Jewish perspective. Other scholars contend that life does not begin that early, they believe it begins around the one hundred twentieth day. This view is held by many Sunni and Shi'a Muslims, which believe ensoulment occurs around the 4^{th} month, when the baby has its first movements. These positions allow for little opposition to ES research, since life does not begin until the 40^{th} or 120^{th} day, destroying a blastocyst at day-5 does not constitute murder and is much more morally acceptable. Many Muslims also feel that, because the embryo cannot survive on its own outside of the womb, it has a lower moral status. Islamic scholars have described the process of becoming a person as gradual. This leads to an even lower moral status for the blastocyst.

However, there is some dissent among the Muslim community. This is mostly limited to arguments that this research is a slippery slope that could lead to morally questionable practices. They believe it could lead to the growth of humans for spare parts, the killing of babies for research, or other morally troubling situations. Muslims

feel that EG research is acceptable, as the aborted fetus is not yet a human, and therefore is not afforded the same moral protection as an adult would have. The EG cells are harvested from fetuses that are aborted in the 7th to 13th week, which is allowable in Islamic morality. Islamic law allows for abortions up until the 4th month, which is well past the 7th to 13th weeks required to obtain EG cells.

Church of the Latter Day Saints and Stem Cells

The Church of Latter Day Saints (LDS) has no official position on stem cell research. The Church has issued statements describing stem cell research as meriting cautious scrutiny. The LDS Church has a much more flexible position on the issues surrounding stem cell research than the Catholic Church does. The LDS Church typically has been quick to embrace and support new technology. The LDS Church believes that, prior to existence on earth, humans exist as a spirit child of God. The spirit and flesh are joined, and then life begins on earth (Clark, 2001) Senator Smith, a prominent Mormon politician, has gone on the record with a view of life beginning as a two step process. He believes that the flesh comes first and then the union of flesh and spirit. This separation of the creation of the flesh and the entrance of the spirit allow like minded Mormons to support embryonic stem cell research, because the embryo would be considered mere flesh, like an arm or leg, rather than a human life (Clark, 2001). To many in the LDS Church, implantation is the key. While being opposed to abortion, which is 'too much like killing' (Clark, 2001), embryonic research is acceptable since it is conducted prior to implantation. The unofficial position of the LDS Church is that there is a need for stem

cell research. The research must be undertaken in a very cautious manner, and much thought should be directed at maintaining the highest moral standards.

Buddhism and Stem Cells

Buddhists traditionally believe that life begins at conception. They believe that conception requires three things. The first condition is a woman's fertile period. The second condition is it requires sex. The last requirement for conception is a 'being to be born', that is ready for life. Because of these beliefs, Buddhists are often against *in vitro* fertilization. However, this leaves a bit of wiggle room for the liberal Buddhist. If an embryo or parthenote is created outside of these conditions, such as in IVF, the traditional ethical rules do not directly apply to the embryo or parthenote. This could allow for a Buddhist to argue that ES research could be conducted in good conscious, provided the ES cells were the result of IVF or from parthenotes. Because one of Buddhism's main tenants is to avoid doing harm to other living things, they are firmly entrenched against abortion. Due to their moral objection to abortion, Buddhists are against the use of aborted tissue for EG research.

As do many religions that believe in reincarnation, Buddhists have moral issue with the leftover embryos from IVF. With ensoulment at conception, the soul remains in the body until death. With a leftover embryo, the soul would remain trapped inside the embryo, until it was disposed of, wherein it would return in another life. This is a disruption of natural order, as a soul could be reincarnated many times and never truly live. It would also be possible for the soul to be trapped, indefinitely, in a leftover embryo that was frozen. For these reasons, religions that believe in reincarnation tend to

have issue with the process of IVF and find it very morally troubling. This leads to a belief that they cannot, in good conscious, support ES research that uses embryos from IVF or parthenotes.

Hinduism and Stem Cells

Hindus do not have an all encompassing belief that dictates ethics for ES research. Hindus believe that life begins at conception. They do not believe that an embryo or fetus is growing into a human, but rather that the embryo *is* a full fledged human being. Their religion teaches that abortion is killing, and that it is among the worst of crimes. This belief is contradicted by the cultural preference for male children and the practice of selected abortion of female embryos. This practice is carried out because some feel that the burden of having a female child is greater than the wrongful killing a child. This is not meant to imply that it is considered acceptable, moral behavior, but rather to show that there is some leeway in the community. Hindus believe that in certain, absolutely necessary situations, it is acceptable to kill an embryo, provided that it is for the greater good (Reichhardt- 2004). In this sense, ES research does not qualify as ethical behavior, because the research itself is not strictly necessary, even though it is for the greater good. This view is also due to the ability of adult stem cells to form such diverse types of cells, rendering the destruction of embryos avoidable in most circumstances.

Chapter Conclusion

Each person needs to evaluate their own position on stem cell research. They need to take into consideration their religious, personal, and societal views, and formulate

their own standards by which they can determine what type of research is merited. Though there may never be a consensus on when life truly begins, the scientific community can still produce amazing, new advances in stem cell research. They can achieve this while taking religious and moral implications of the research into consideration.

CHAPTER-4: STEM CELL LEGALITIES

Because stem cells are ethically controversial, laws are in place regulating their use. The legalities dealing with stem cell research and applications vary from country to country. The national stem cell research policies found worldwide arise from a mixture of factors including the country's political and social climate, level of scientific and industrial development, and strength of economy. From a global perspective, every country has unique policies regarding stem cell research and clinical usage, but overall there are three main types of stem cell legislation categories which countries can be grouped in. In the first group there are more than ten countries, primarily located in Europe and Asia, which have passed liberal federal legislations allowing scientists in their boarders to openly conduct research into all areas of stem cell technologies, including somatic cell nuclear transfer (SCNT). SCNT is defined as the implantation of a nucleus from a somatic or body cell into an egg that has had its original nucleus already removed (Hoffman, 2005). Most of the nations that have approved this kind of open stem cell research are larger, more developed countries such as the United Kingdom, China, India, Japan, Sweden, and Israel.

The second group includes many more countries that have taken a milder stance on approving stem cell research, that mainly allows scientists to use stem cells that are harvested from embryos obtained from fertility clinic donations, as long as the harvesting is within federal guidelines. The embryos that are available for stem cell research are embryos that are leftover from *in vitro* fertility procedures that are no longer needed. Countries that fall into this category include Canada, France, Australia, Spain, and Brazil.

Again, each country in this group has individual policies, but all countries in this group meet the general standard of currently allowing the harvest of embryonic stem cells to some degree.

The final stem cell policy group has members such as the United States, Germany, Italy, Ireland, and Norway. Countries in this group either do not allow the harvesting or use of embryonic stem cells at all, do not have established policies dealing with stem cells, or strictly limit and monitor the use of human embryos and stem cell harvesting. Ireland and Norway are countries in this category that are on the stricter end of the spectrum, while the United States, Germany, and Italy are the more liberal countries in this group that closely monitor and regulate the use of human embryos in scientific research (Hoffman, 2005).

United States Stem Cell Legalities

Federal Stem Cell Research Policy

In the United States, stem cell research is governmentally regulated, and compared to many other nations the US falls into the most restrictive of the three categories as it holds fairly strict policies limiting what type of scientific research can be conducted with federal funds. However, aside from Federal guidelines, some individual states have established their own stem cell research policies by enacting statewide legislation.

As a whole, American stem cell research is regulated by the Office of Human Research Protections (OHRP), which is a division of the federal Department of Human

and Health Services (HHS). All American researchers wishing to conduct any sort of human or animal testing studies, whether it is federally or privately funded research, must abide by an assortment of government guidelines. These regulations require the institution at which the study will be conducted to be pre-approved for OHRP assurance that all testing will apply HHS guidelines and its human subjects protection regulations, and that all tests and devices used in the study must meet the standards set by the Federal Drug Administration that govern the use of investigational new drugs (INDs) and investigational devices (IDEs). Furthermore, clinical stem cell studies pertaining to the transplant of human fetal tissue into human subjects must abide by Public Law 103-43, which is titled, "Research on Transplantation of Fetal Tissue". There also may be state or local laws that can further regulate research conducted using human stem cells (Regulations and Ethical Guidelines, 2005).

The policies outlined by the OHRP for federally funded human embryonic stem cell research follow federal legislative regulation and the general criteria established by President George W. Bush in August of 2001. The OHRP regulations for federally funded stem cell research approve studies into the derivation and use of human embryonic stem cells as long as the stem cell lines used in the clinical trials were obtained prior to 9:00 PM (Eastern Standard Time) on August 9th, 2001, and that the stem cells were harvested from embryos that were created for reproductive purposes and are no longer needed (NIH's Role in Federal Policy – Stem Cell Research (2005). Other possible sources for embryonic stem cells are embryos produced by cloning, and embryos from aborted pregnancies, both of which are not approved ES cell sources in the United States.

According to President Bush's statement, by August of 2001, scientists from ten laboratories across the world were able to isolate, harvest, and store ES cells from seventy one genetically unique blastocysts. Blastocysts form between four and seven days after the embryo originates, and are hollow spheres surrounded by cells that result from the development of totipotent cells (Pelletier et al., 1999). To summarize the criteria outlined by President Bush, the United States government will approve federal funding for human embryonic stem cell research that uses stem cell cells from the seventy one different cell lines harvested before August 9th, 2001; any research that results in the harvesting of new human embryonic stem cells from any source will not receive federal funding collected from taxpayers (Pizzi, 2002). However, there is no federal legislation that absolutely forbids scientists from developing new stem cell lines with private funds, but the costs associated with ES cell harvesting are so high that no researchers have been able to successfully raise enough money to conduct privately funded research (Holden, 2002), although recent state bonds may alter this. In 2002, Stanford University announced plans to try and privately raise enough capital to become the only institution in the United States to privately fund their own stem cell research, possibly even forming their own ES cell lines (Check, 2002).

Despite the federal legislation restricting stem cell research that has been passed, and lack of federal funding limiting ES cell research, the majority of the United States public supports additional stem cell research. Fifty-eight percent of Americans are in favor of the conduction of further stem cell research; with sixty percent of those questioned believing that the federal government should fund these projects (Langer, 2005). However the percentages determined in this poll are somewhat misleading as to

the beliefs of the voting public. National voter turnout rates range between just fifty five and sixty percent for most elections, including presidential elections. In the past couple of elections there has been strong conservative backing among the majority of the voting public, leading to the election of a republican into the presidential office and a republican majority in the senate (McDonald, 2006). Because republicans as a group are mainly pro-life and against ES cell research, and the majority of the voting public does not share the same views as the people questioned in the McDonald poll, it is unlikely that there will be any federal reforms to U.S. current stem cell legislation in the near future.

State Stem Cell Research Policies

The United States is different from other countries in regards to its policies on stem cell research because scientists must deal with federal guidelines that regulate government approval of stem cell research, as well as locally enacted state legislature. All states allow research into stem cell types such as HSCs, neural stem cells, mesenchymal stem cells, endothelial stem cells, etc. as long as the work meets the guidelines set by the FDA. In some states these local policies allow for scientists to have more freedom in their work, primarily dealing with ES cells. States such as California, Illinois, Ohio, and New Jersey have all passed statewide legislation allowing for more work to be conducted using ES cells, with Illinois going as far as to have issued an executive order that encourages further work with ES cells. All of these states allowing ES cell research have established a system of regulations and monitoring to ensure that the research being conducted meets the legal and ethical standards that have been established. However, almost half of the states in the U.S. have enacted state laws

restricting research on embryos in one way or another, ranging from the restriction of the sale of embryos in many states, to the prohibition of all research on embryos in South Dakota.

In 2004, Ohio became the first state to allocate state funding for research projects dealing with adult stem cells, and the state legislature is beginning to take further steps to set aside more state funds specifically for ES cell research (Ertelt, 2005). Shortly after Ohio began to support stem cell research in early 2004, the state of New Jersey enacted the first legislature that allocated taxpayer's money for ES cell research. New Jersey has given more than twenty million dollars to the New Jersey Stem cell Institute, and a state ballot initiative that would allow for the increase of its stem cell institute's funding to one hundred and fifty million dollars, as well as the allocation of two hundred and thirty million more dollars in research grants.

California became the next state to fund embryonic and adult stem research in 2004 with the passing of Proposition 71. Proposition 71 set aside three billion dollars in bonds that can be distributed yearly in amounts not to exceed three hundred and fifty million dollars, to stem cell research, including those projects dealing with ES cells (National Conference of State Legislatures, 2006).

In 2005, Connecticut also passed a bill through their State Assembly which allowed for state money to be used to fund both ES cell and adult stem cell research. The Connecticut stem cell bill allows for the distribution of one hundred million dollars of state money to Connecticut based stem cell laboratories over a ten year period (Associated Press, 2005). Rod Blagojevich, governor of Illinois, issued his executive order in April of 2006. The executive order that Blagojevich signed not only

appropriated ten million dollars in state funds for embryonic and adult stem cell research, but also resulted in the formation of the Illinois Regenerative Medicine Institute. Also in 2006, Maryland formed the Maryland Stem Cell Research Fund, and beginning in 2007, fifteen million dollars will be included in the state budget to be used for ES and adult stem cell research.

Other states like Massachusetts are taking steps towards the proposition of a bill before their state legislatures which would also support the funding of stem cell research. In 2005, the Massachusetts state legislature was able to override a veto by the governor and enact Senate Bill 2039. Bill 2039 resulted in the formation of a council to examine the use of public funds for the formation of a regenerative medicine institute within the University of Massachusetts Medical School (Worcester), and research on stem cells that have been harvested specifically from umbilical cord blood (National Conference of State Legislatures, 2006).

Stem Cell Legalities in Countries Outside of the United States

Unlike North American nations which mainly have strict stem cell policies, there are many countries in the world that fit into all of the three categories that describe the strictness of their national stem cell research policies. The United Kingdom, South Korea, and Sweden fall into category I. Category I consists of the countries that are the most permissive to all types of stem cell research and have very liberal national policies that regulate stem cell research. France, Spain, Australia, and Canada are the larger countries grouped into category II, where stem cell research is supported by the

government, but is also closely monitored and regulated. Finally, Germany and the U.S. head up category III, consisting of countries which all have fairly strict stem cell legislation and regulations, mostly pertaining to ES cells, some of which are similar to those stem cell policies found in the United States.

Category I Policies

The United Kingdom was one of the first countries in the world to pass legislation that dictated what experiments researchers could legally conduct with human embryos with the enacting of the Human Fertilisation and Embryology Act of 1990 (Garfinkle, 2004). The purpose of the 1990 Act was mainly to set legal guidelines for researchers studying the use of embryos in reproductive procedures. In 2001, the previous Act was reexamined and expanded to include sections with regulations for ES cell and other types of embryonic research. This new act included the development of a national cell bank that will be run by the country's Medical Research Council, and will contain an assortment of embryonic stem cell lines that are available to English researchers. The bank will receive these cell lines from laboratories which are granted yearlong licenses that permit the isolation and harvesting of individual cell lines. These licenses are awarded by the United Kingdom's Human Fertilisation and Embryology Authority. Once the license expires, scientists are restricted by a policy somewhat similar to that found in the United States where research can only be conducted using the cell lines harvested before the expiration of that license, unless a new license is granted. Several licenses have been granted to English research facilities beginning in early 2002 with London's King's College (Garfinkle, 2004).

Sweden might have one of the most desirable political and scientific climates for stem cell research. Stem cell research, including ES cell studies, has been widely supported by the public and the government for years, dating back to the 1980's with early treatment methods of Parkinson's disease, which has resulted in some of the most liberal stem cell legislation found in the world. Overall, there are more than thirty research groups and ten institutions located in Sweden conducting widespread stem cell research. Sweden established a national cell line bank shortly before the United Kingdom, which made it the first of its kind in the world. Laws have been established that allow the harvesting of ES cells from embryos created during *in vitro* fertilization procedures, as well as the use of cloning for therapeutic purposes. Both of these areas of research are highly debated in most countries due to ethical concerns, but have received very little opposition from Swedish citizens. As a result of their country's very open stem cell policies, Swedish researchers often receive monetary support from sources in other countries, including America. Charities in other countries that support research into the treatment of diseases such as Parkinson's disease and heart disease give money each year to Swedish researchers because they are allowed to conduct research which would not be permitted in the charity's home country (Sweden's Stem Cell Successes, 2002).

In 2005 South Korea decided to expand on Sweden's idea of a national stem cell bank, and announced the formation of a worldwide stem cell bank. This cell bank would provide access to pre-made unique and diverse cell lines for scientists all over the world, including those located in countries like the U.S. that do not allow further harvesting of ES cells. The cell bank will be part of the "World Stem Cell Foundation" and was headed by Woo Suk Hwang (prior to his recent resignation), who was the first scientist to

ever clone a human embryo for the purpose of harvesting its ES cells. The World Stem Cell Foundation is located at South Korea's Seoul National University, and will hopefully be able to produce more than one hundred stem cell lines per year. Using the SCNT technique, scientists can also produce stem cells that are based on specific DNA provided by the buyers, so that the resulting cells will have the genetic characteristics necessary for their study. The development of this worldwide cell bank is important because it will provide an avenue for scientists to obtain ES cells without obtaining government funding to pay for the harvesting process, essentially circumventing many country's legislation that is aimed at preventing this type of research on ES cells (Kaplan, 2005).

Category II Policies

Australia is a major player in global stem cell research, with Australian research teams conducting studies using stem cells to test the effects of drugs on human cells using *in vitro* studies, as well as experiments studying the effects of stem cell therapies on diseases such as heart disease and leukemia. Australia is considered a middle of the road country in terms of how strict its policies are dealing with stem cell research, resulting in it being grouped into category II. National policies found in countries from category II slightly resemble those found in both the category above and below it. Federal policy was established by lawmakers by the enacting of two acts in 2002, the Prohibition of Human Cloning Act, and the Research Involving Human Embryos Act. The first act bans all human cloning, regardless of purpose, while the second act sets precedent allowing state approved laboratories to harvest ES cells from embryos obtained from fertilization

clinics. Australian researchers that meet the strict conditions for research approval stated in the Research Involving Human Embryos Act may apply for a government license to harvest ES cells that is awarded by the National Health and Medical Resources Council. Like the UK and South Korea, Australia also established a national group which received the bulk of national funding for stem cell research in 2003 called the Australian Stem Cell Center (Stem Cell Research in Australia, 2003).

The other larger countries grouped into category II have all passed similar legislation. These countries are not as open to the outright funding of ES cell research, they all have some sort of stringent guidelines in place to ensure that only approved research is being conducted. Essentially all of these countries with moderate policies do allow further harvesting and research of ES cell lines, like legislation found in category I countries, but all have stricter laws to regulate these studies, similar to those policies found in category III countries.

Category III Policies

Category III countries all have stem cell policies similar to those found in the United States and Germany. Germany is a country that has been at the front of technological and scientific advances for hundreds of years, but with very strict stem cell research regulations, is likely to struggle to keep up with countries like South Korea and the UK in the future of stem cell technology. Germany has had federal legislation in place for more than a decade that outright bans research on human embryos. This means that German scientists were never able to harvest any ES cells, and as a result they do not have any cell lines in storage that were established by their scientists. However, German

researchers have been able to import cell lines from other countries, as these cell lines and their import had not been explicitly prohibited by German law. Unfortunately for German scientists, in 2002 the German parliament passed legislation that severely limited their ability to import cell lines. The new legislation does allow the import of ES cells under strict regulations and monitoring by the German government. Many of Germany's citizens and politicians favor an outright ban of ES cell importation, with the new legislation narrowly being approved by Parliament, and receiving a lot of criticism from German Catholics and Protestants who support an outright ban of ES cell research (Kim, 2002).

It is likely that as long as countries like the United States and Germany continue to impose strict legislation regulating ES cell research, many other countries will also uphold similar stem cell legislation, as these two world powers are often looked to set precedent for legislation found in other countries.

CONCLUSIONS

Stem cells are long-lived cells in the body that have the ability to differentiate into a specialized cell to create new tissues. Because of this tissue regenerative capacity, stem cells are currently at the forefront of medical research and development. It is believed that as stem cell research and therapies continue to advance, doctors will be able to offer more effective treatment methods for many of the diseases that affect humans. Based on a substantial amount of animal research with both adult and ES stem cells, doctors around the world have already conducted human research studies that have yielded positive results, however it is likely that these early clinical trials and applications have just begun to scratch the surface of what science will be able to use these "master cells" for in the future.

However, as with all change and technological advancement, stem cells have presented new moral dilemmas that are as diverse as the research being conducted. Ethical concerns relating to moral and religious objections to stem cell research are being debated among politicians, theologians, and average citizens on a daily basis. Most of the world's main religions support adult stem cell research, however only the Muslim and Jewish faiths support ES cell research.

As a result of these beliefs, most countries have chosen to take a national stance on stem cell research, enacting some sort of federal legislation to set regulations for their researchers to follow. Due to unique political and ethical climates, national stem cell policies typically vary from country to country; and in cases like the United States, state policies can help compensate for a stifling federal ES policy.

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