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STEM CELLS

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ABSTRACT

Stem cells are the foundation cells for every cell, organ, and tissue in the body. Because of this bio-regenerative capacity, stem cells are promising therapies for diseases such as Alzheimer's, cancer, Parkinson's, type-1 diabetes, heart disease, stroke, and rheumatoid arthritis. However, some types of stem cells have ethical concerns and legal complications that make stem cell research a controversial topic. We conclude that many obstacles must be overcome before the potential uses of stem cells may be realized.

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EXECUTIVE SUMMARY

Stem cells are the foundation cells for every cell, organ, and tissue in the body. Stem cells are unspecialized cells that have the ability to differentiate into specialized tissues and organs with the appropriate chemical signaling. Stem cells are also self-replicating. These bio-regenerative characteristics are the reason that stem cells are promising therapies for diseases such as Alzheimer's, cancer, Parkinson's, type-1 diabetes, heart disease, stroke, and rheumatoid arthritis, among others.

Stem cells can be classified by the extent to which they can differentiate into different cell types. A totipotent stem cell (such as a fertilized egg) has the ability to give rise to all of the cell types in the body as well as all of the cell types that make up the extraembryonic tissues such as the placenta. Pluripotent stem cells (such as embryonic stem cells) are descended from totipotent stem cells, and develop about four days after fertilization. Pluripotent stem cells can generate all of the different cell types that make up the body, so they are of intense interest to the medical community. Multipotent stem cells (such as hematopoietic stem cells) are descendents of pluripotent stem cells. Multipotent stem cells have the ability to develop into more than one cell type in the body, but they can not make all tissues in the body. Unipotent stem cells, also known as progenitor cells, can only produce one cell type. Epithelial stem cells are of this type.

Stem cells can also be classified according to their sources. There are two main sources of stem cells, embryonic stem cells and adult stem cells. Embryonic stem (ES) cells are self-replicating, pluripotent cells that are potentially immortal. Adult stem cells

are undifferentiated multipotent or unipotent cells that are found in most adult tissues. These cells function to maintain and repair the body.

There are many common misconceptions about stem cell research. A common misconception is to confuse stem cell research with cloning. Stem cells can be used with or without somatic cell nuclear transfer techniques. Also, it is commonly thought that all stem cells have the same capabilities for treatment. Adult stem cells may not have the same capability as embryonic stem cells, but they have fewer ethical concerns, and many people are not aware they exist.

Many people falsely believe that stem cell research and applications have not saved a single life. Hematopoietic stem cells (HSCs) are multipotent adult stem cells that form all the cellular components of blood. HSCs have been used for over 40 years in bone marrow transplants to save the lives of thousands of patients with various cancers that have undergone radiation or chemotherapy. Stem cells found in umbilical cord blood are now being used because of several advantages over bone marrow HSCs.

Scientists are discovering that adult stem cells can be used to replace cells and tissues to restore function to various organs in the body including the heart, the nervous system, skin, and the liver. One type of adult stem cell therapy that has been successful is for heart disease. Other adult stem cell therapies that have provided very promising results are therapies treating patients with damaged nervous systems and patients with diabetes. In addition to adult stem cells, embryonic stem (ES) cells have the greatest medical potential of all the stem cells due to their ability to differentiate into any type of tissue, and these cells are only now being used on human patients.

Since embryonic stem cells are the most valuable medically, the ethical debate of using embryonic stem cells continues, and each major religion has its own views. ES cells are most commonly isolated from the inner cell mass of a blastocyst embryo generated by *in vitro* fertilization. But obtaining the ES cells destroys the embryo which has the potential for human life, so some classify the act as murder. The Roman Catholic Church is one of the religions in strongest opposition to the use of ES cells for research purposes. Catholic belief states that life begins at the moment of conception and that the embryo is the beginning of "personhood" no matter where it exists. The Jewish Biblical and Talmudic law state that personhood is acquired progressively, not immediately at conception. Judaism's beliefs place the beginning of life well after the 5-day stage needed to obtain embryonic stem cells, so this religion ethically supports using embryos for stem cell research. Muslims believe that the use of embryos for stem cell research is acceptable up to forty days after fertilization. Since the most common Hindu belief is that life starts at conception, the line involving the ethics of ES cell research becomes blurry.

The normal source of embryonic stem cells comes from unused embryos that are created through *in vitro* fertilization. However, embryonic stem cells can also be extracted from parthenotes. Parthenogenesis is a form of reproduction by which an egg develops without the fusion of sperm and egg. Because parthenotes cannot develop into an individual, there are fewer ethical concerns with their use. The authors of this IQP support research into the possible use of parthenote-derived ES cell lines as an alternative to *in vitro* fertilized embryos.

Since the exact time an embryo becomes a human being cannot be determined scientifically, or universally agreed upon religiously, most countries in the world have

developed their own policies for ES research ranging from either “permissive”, “flexible”, “restrictive” or “no established policy”.

One of the most liberal countries is Sweden, which is considered to be the world leader in stem cell research because of its strong public support, favorable bioethical climate, tradition of science and research, and strong government funding. The German parliament voted to allow the import of embryonic stem cells for scientific research, but only under close government control, while not allowing their derivation within the country. The United States’s ES cell policy set by President George W. Bush in 2001 stated that federal funding would only be allowed to support research using the 60 or so ES cell lines that already existed prior to August, 2001. However, individual states can adhere to their own policy on ES cell research, and California, New Jersey, and Massachusetts are leading the way to establish their own stem cell institutes.

Stem cell research has advanced enormously within the last five years. However, laws, regulations, misconceptions, ethical issues, and a decline in funding has made it more difficult for researchers in the United States to develop stem cell therapies. There are many obstacles that must be overcome before the potential uses of stem cells may actually be realized by patients.

PROJECT OBJECTIVE

The purpose of this IQP is to investigate the topic of stem cells, including their ethical and legal impacts on society, and to educate the reader about stem cells, a topic that could have an enormous impact on society in the future. Although not completely exhaustive, this IQP provides a broad spectrum of information about stem cells, identifies some misconceptions, and provides some insight on the opinion of the authors. The IQP is intended for people without a medical background, and provides enough information for the readers to form their own educated opinions about the main issues involved with stem cells.

CHAPTER-1: STEM CELL TYPES AND SOURCES

Stem cells are the foundation cells for every cell, organ, and tissue in the body (*Frequently Asked Questions*, 2004). There are two main characteristics of stem cells that distinguish them from other cells. Stem cells are unspecialized cells that have the ability to differentiate into specialized tissues and organs with the appropriate chemical signaling. Stem cells are also self-replicating. In general, they can replicate over the lifespan of an individual, and can also replicate indefinitely in culture (Mayo Clinic Staff, 2006). These characteristics are the reason that stem cells are promising therapies for diseases such as Alzheimer's, cancer, Parkinson's, type-1 diabetes, heart disease, stroke, and rheumatoid arthritis among others (*Frequently Asked Questions*, 2004).

Classification of Stem Cells on the Basis of Potency

There are many different types of stem cells. Stem cells can be classified by the extent to which they can differentiate into different cell types. These four main classifications are totipotent, pluripotent, multipotent, or unipotent. A totipotent stem cell has the ability to give rise to all of the cell types in the body as well as all of the cell types that make up the extraembryonic tissues such as the placenta. A fertilized egg is an example of a totipotent stem cell.

Pluripotent stem cells are descended from totipotent stem cells, and develop about four days after fertilization. Pluripotent stem cells can generate all of the different cell types that make up the body. However, pluripotent stem cells differ from totipotent stem

cells in that pluripotent stem cells do not have the ability to make any extraembryonic tissues. Embryonic stem (ES) cells (discussed in detail later in this chapter) are an example of pluripotent cells, and represent the type of stem cell most sought after for medical purposes due to their ability to form any tissue in the body. Figure 1 is an illustration depicting how pluripotent stem cells (center of the diagram) are derived from totipotent stem cells (upper left of the diagram). ES cells represent the inner cell mass of the blastocyst (upper right of diagram). This figure also illustrates the various differentiations of pluripotent stem cells (lower part of diagram) (*What's New*, 2001).

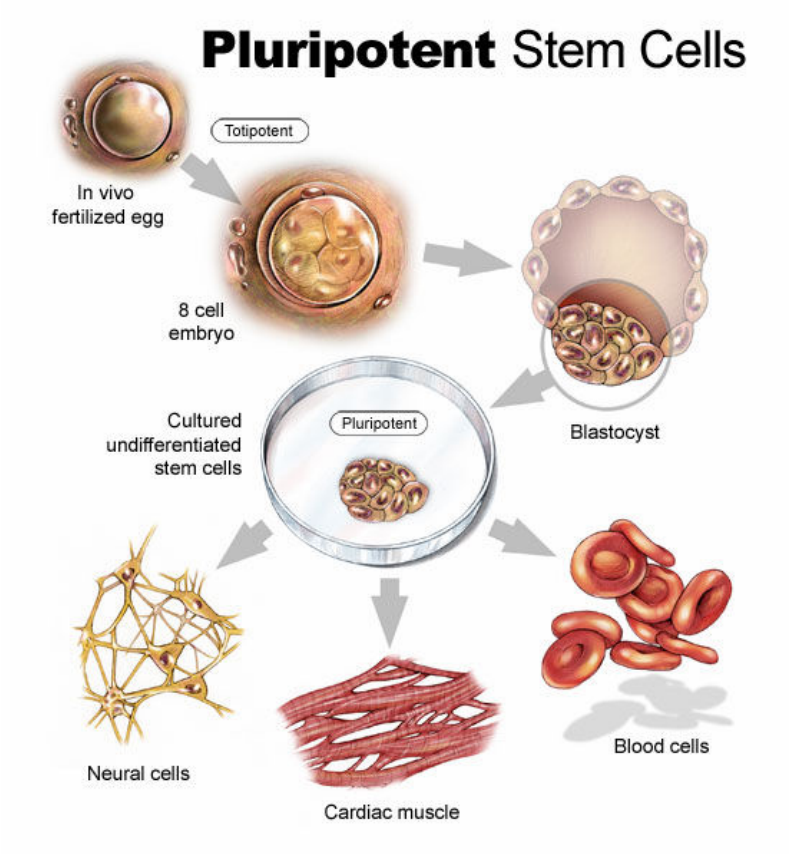

Figure 1: Pluripotent Stem Cells (*What's New*, 2001)

Multipotent stem cells are descendents of pluripotent stem cells. Multipotent stem cells have the ability to develop into more than one cell type in the body, but they can not

make all tissues in the body. Examples of a multipotent stem cell include neural stem cells and hematopoietic stem cells. Neural stem cells differentiate into the nerve cells and glia, neural support cells. Hematopoietic stem cells (HSCs) are primarily located in bone marrow and umbilical cord blood. HSCs differentiate into all of the cells found in blood, including red blood cells, platelets, and several kinds of white blood cells. Figure 2 illustrates where multipotent stem cells are located in the body. This illustration also shows that the differentiation of multipotent stem cells is based on their location in the body (*What's New*, 2001).

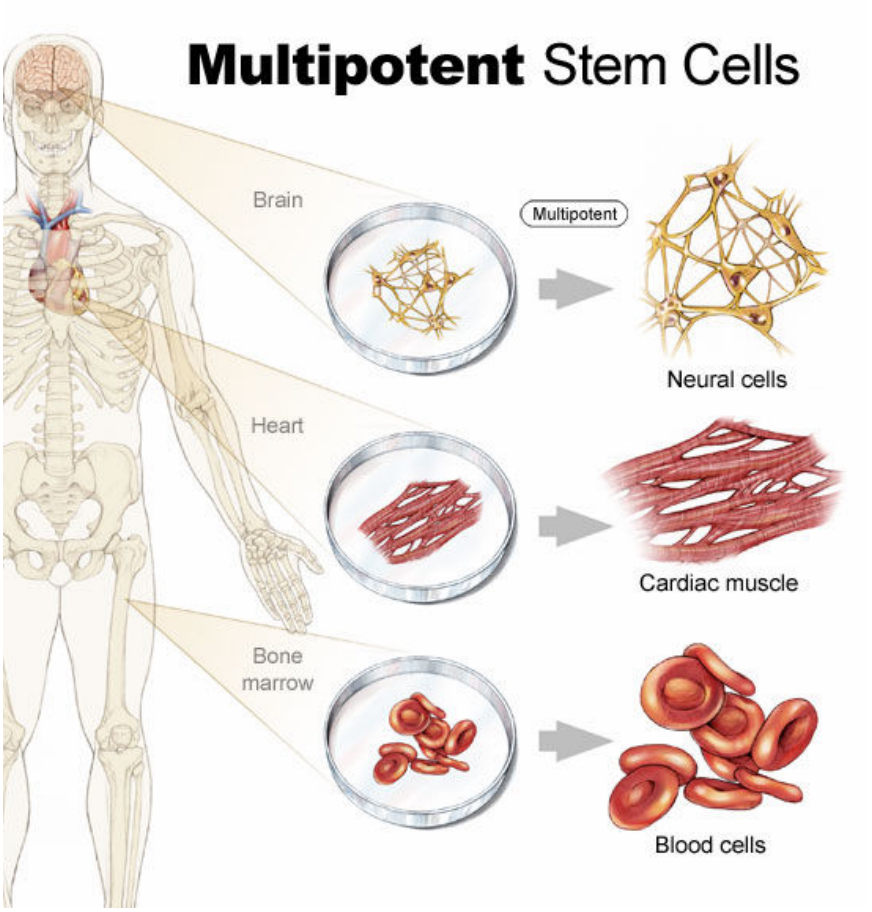

Figure 2: Multipotent Stem Cells (*What's New*, 2001)

Unipotent stem cells, also known as progenitor cells, can only produce one cell type. Examples of a unipotent stem cell are the erythroid progenitor cells that differentiate into only red blood cells, and spermatogenic stem cells that form sperm cells. Eventually, cells become terminally differentiated such as lung cells or liver cells. These cells are permanently committed to a specific function (*Frequently Asked Questions*, 2001).

However, it is debated whether progenitor cells are true stem cells. A true stem cell is self-replicating. Thus, a stem cell divides to make more stem cells and differentiated cells. A progenitor cell divides to produce only differentiated cells. Figure 3 demonstrates the difference between a true stem cell (upper left in the diagram) and a progenitor cell (lower left in the diagram) (*Adult Stem Cells*, 2006).

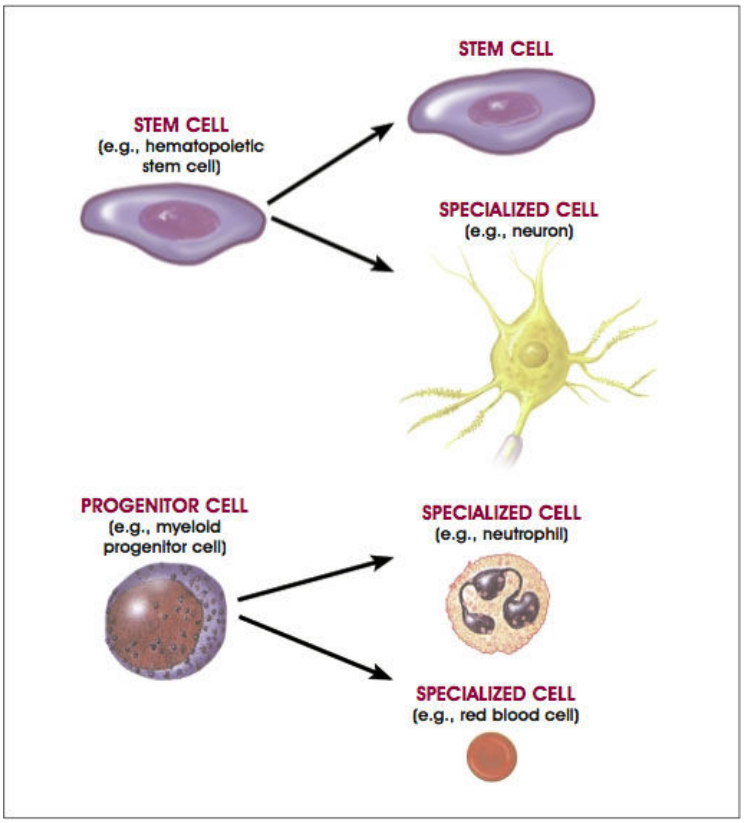

Figure 3: Distinguishing Features of Progenitor/Precursor Cells and Stem Cells (*Adult Stem Cells*, 2006).

Classification of Stem Cells From Their Source

Stem cells can also be classified according to their sources. There are two main sources of stem cells, embryonic stem cells and adult stem cells. Embryonic stem (ES) cells are self-replicating, pluripotent cells that are potentially immortal. Embryonic stem cells are derived from the inner cell mass of a developing blastocyst. These stem cells are obtained by transferring the inner cell mass from a blastocyst into a culture dish and co-culturing them with a feeder layer of inactivated fibroblast cells that help provide growth factors. The ES cells are allowed to divide. An embryonic stem cell line is created if after six months cells still continue to divide, remain pluripotent, and do not differentiate. The blastocysts used to create the embryonic stem cell lines are most frequently derived from frozen embryos produced by *in vitro* fertilization (IVF) that were

never implanted. These frozen embryos are consensually donated for research purposes (*Frequently Asked Questions*, 2001). Because the blastocyst is destroyed when the inner cell mass is obtained, the isolation of ES cells is categorized by some individuals as murder. This topic will be discussed in detail in Chapter-3. However, progress is being made on deriving ES cell lines from parthenotes, which are chemically treated eggs (not fertilized) that divide only to the blastocyst stage from which ES cells can be obtained. Because parthenotes can not develop into an individual, they have fewer ethical concerns with their use. Figure 4 exhibits embryonic stem cells from a mouse that have been stained green in order to clearly visualize them (*California Institute for Regenerative*, 2006)

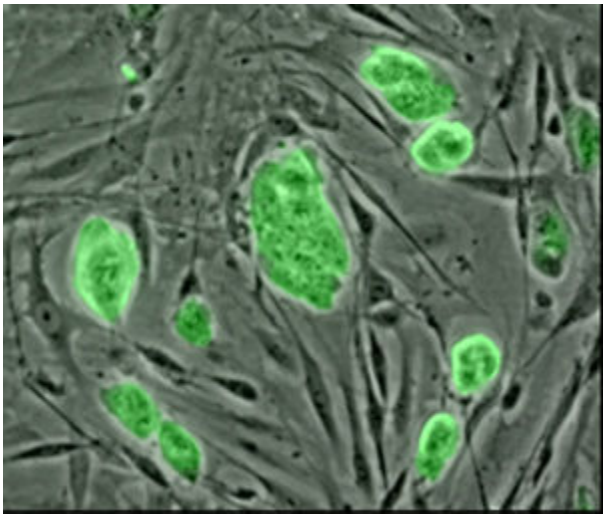

Figure 4: Mouse Embryonic Stem Cells
(*California Institute for Regenerative*, 2006).

Embryonic stem cells can divide indefinitely. The reason that embryonic stem cells are potentially immortal is due to high telomerase levels. Telomerase is an enzyme that acts to lengthen telomeres. Telomeres are repeating sequences of double-stranded

DNA located at the end of chromosomes. A long telomere length is associated with immortalized cell lines such as embryonic stem cells and cancerous cells. The telomere length shortens with each cell division. In most normal, differentiated cells, telomerase activity is very low and the ability to maintain telomere length decreases. Telomerase acts by adding hexameric repeating sequences of DNA onto the ends of the chromosomes. Therefore, a high telomerase level is essential to maintain the immortalization of stem cells. Figure 5 is an illustration of the long telomere length of embryonic stem cells as compared to the telomere length of the adult stem cells. In adult stem cells, telomerase is inactive. This prevents adult stem cells from dividing indefinitely. This figure also shows how telomerase adds repeating sequences of DNA onto existing telomeres (Kirschstein & Skirboll, 2001).

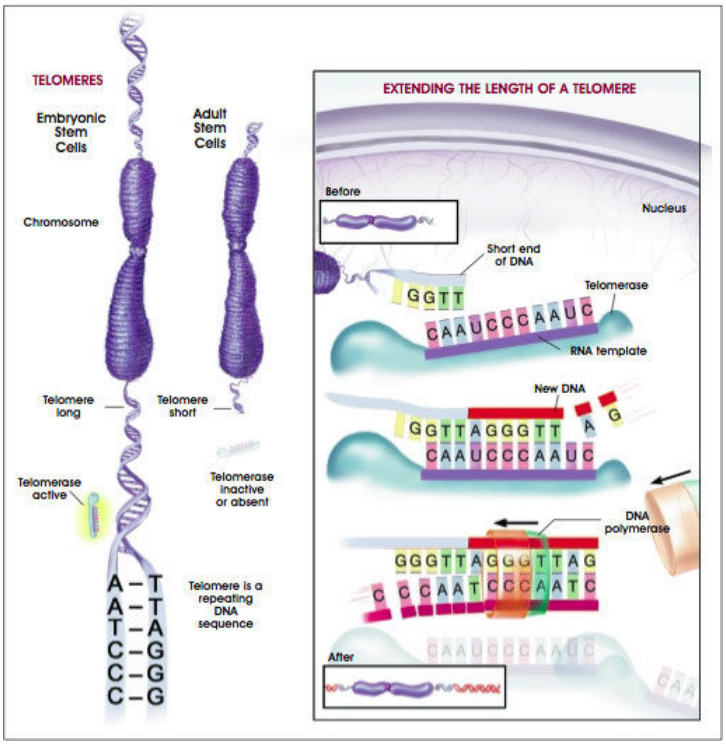

Figure 5: Telomeres and Telomerase Activity (Kirschstein & Skirboll, 2001).

Embryonic stem cells are also much more versatile than adult stem cells because they retain the ability to differentiate into every type of cell in the body. Therefore, embryonic stem cells could potentially be used as treatments to make new brain cells for a stroke or Parkinson's patient, new heart cells for a heart attack patient, or new liver cells for someone with liver cirrhosis (*Frequently Asked Questions*, 2001).

Adult stem cells are undifferentiated multipotent or unipotent cells that are found in most adult tissues. These cells function to maintain and repair the body. For example, hematopoietic stem cells in the adult bone marrow differentiate into mature types of blood cells. Other stem cells are also located in the bone marrow. These include endothelial stem cells and mesenchymal stem cells. Endothelial stem cells form the vascular system. Mesenchymal stem cells form bone, muscle, fat, and cartilage (*Glossary*, 2004). Other sources of hematopoietic stem cells include the placenta and umbilical cord blood. Although technically umbilical cord is not an adult tissue, cord stem cells are usually included with the adult stem cell category since their use does not destroy an embryo. Cells extracted from the umbilical cord have been shown to differentiate into neurons and bone cells. Figure 6 is a picture of adult human neural stem cells (*Stem Cells Open*, 2005).

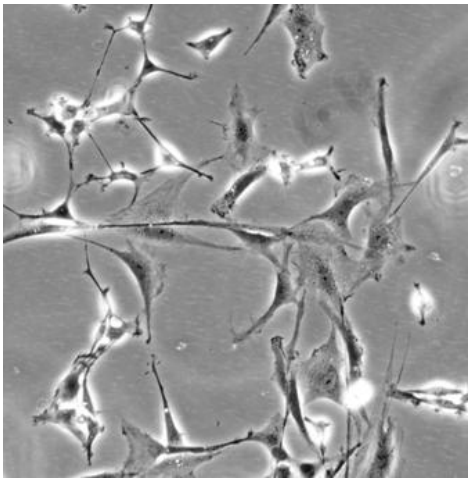

Figure 6: Human Neural Stem Cells (*Stem Cells Open*, 2005)

It is also possible for adult stem cells to be pluripotent. This adult stem cell plasticity is evidenced by the ability of hematopoietic stem cells to differentiate into neurons, glia, skeletal muscle cells, liver cells, and heart muscle cells. Adult stem cells have been derived from the brain, bone marrow, peripheral blood, spinal cord, blood vessels, skeletal muscle, epithelia of the digestive system and skin, cornea, liver, and pancreas, as well as others. Figure 7 illustrates the plasticity of adult stem cells. This figure shows how stem cells located in the bone marrow can differentiate not only into blood cells but into muscle cells, liver cells, and other types of cells (Kirschstein & Skirboll, 2001).

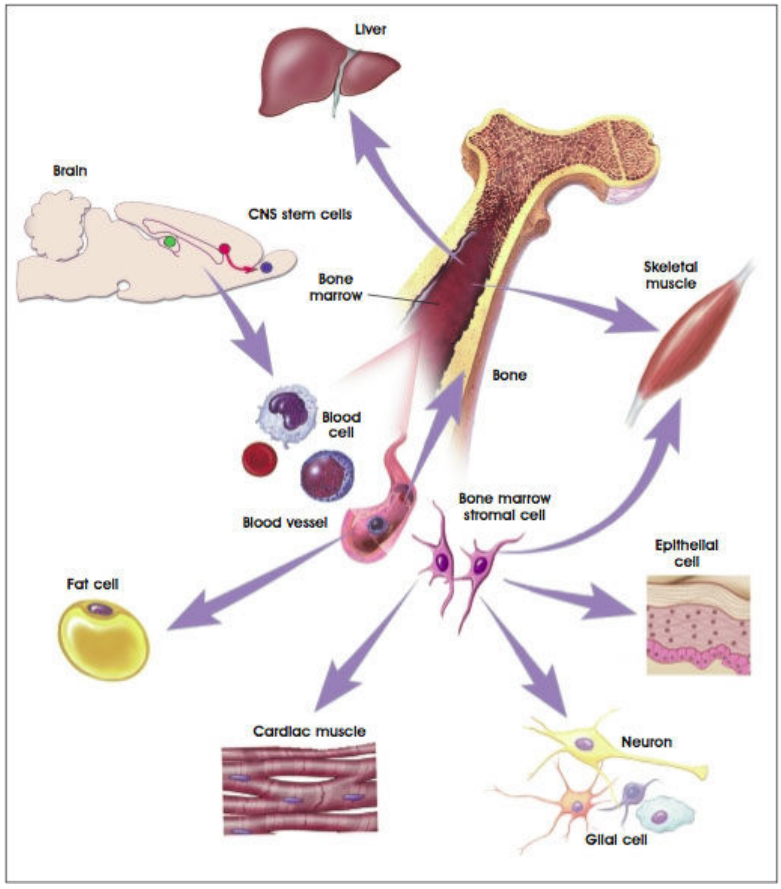

Figure 7: Preliminary Evidence of Plasticity Among Nonhuman Adult Stem Cells (Kirschstein & Skirboll, 2001)

Stem Cell Misconceptions

There are many common misconceptions about stem cell research. A common misconception is to confuse stem cell research with cloning. Cloning is used for the production of a cell or organism with the same nuclear genome as the host cell or organism. In this process, a nucleus from a skin cell from one individual is microinjected into an enucleated egg. The egg is then cultured to the blastocyst stage. At that point either the blastocycst can be used to derive ES cell lines for therapeutic cloning, or can be implanted into the uterus of a host for reproductive cloning purposes. Currently, reproductive cloning is banned in almost all countries, including the U.S. Although early reports from Korea indicated success with therapeutic human cloning, those reports have since been withdrawn, and human therapeutic cloning has yet to be achieved. If this can be achieved, ES cell lines could be derived from the skin cells of a patient to provide therapeutic tissues for that same patient.

Current stem cell therapies do not involve cloning. Current stem cell therapies use ES cell lines or adult stem cells derived from one individual (donor) to treat another patient (host). The confusion between cloning and stem cell research could be due to the fact that both stem cell research and cloning involve the use of embryonic cells. The confusion continues as therapeutic cloning was introduced as a means to produce embryonic stem cells from the same individual to help avoid immuno-rejection. However, stem cell research does not necessarily involve embryonic stem cells. While therapeutic and reproductive cloning includes the use of embryos, stem cell research uses

both embryonic and adult stem cells from an adult, embryo, umbilical cord, or amniotic fluid (*Frequently Asked Questions*, 2004).

Also, it is commonly thought that all stem cells have the same capabilities for treatment. Adult stem cells may not have the same capability as embryonic stem cells, but they have fewer ethical concerns, and many people are not aware they exist. Therefore, those individuals arguing against stem cell research should distinguish which stem cells they are against. It was originally thought that adult stem cells were only multipotent. However, the recent theory of adult stem cell plasticity claims that adult stem cells are more versatile than once thought. The advantages of using adult stem cells in possible treatment include the elimination of rejection to donor tissue or blood since the patient's own cells could be used. However, adult stem cells are rare in mature tissues, and it is more difficult to create large numbers of cells in culture compared to embryonic stem cells (*Frequently Asked Questions*, 2001).

Another common misconception is that all stem cell research destroys embryos. This is not correct. Only work with embryonic stem cells destroys an embryo. This is due to the fact that the inner cell mass is removed, and the embryo is no longer viable. However, there are other ways of obtaining embryonic stem cells that does not destroy an embryo. Parthenogenesis is a form of reproduction by which an egg develops without the fusion of sperm and egg (*Glossary*, 2004). This type of reproduction occurs frequently in nature among arthropods such as insects. In mammals, parthenogenesis does not create a viable embryo. Instead, a mass of about 100 cells called a blastocyst is created from

which embryonic stem cells can be extracted. Working with adult stem cells also does not destroy an embryo. Most adult stem cells are retrieved from the bone marrow, umbilical cord, or amniotic fluid (Philipkoski, 2003).

Another misconception is that no stem cells have ever saved a person's life. This also is not true. HSCs have been used for over 40 years in bone marrow transplants to save the lives of patients with various cancers that have undergone radiation or chemotherapy (*Frequently Asked Questions*, 2004). More than 15,000 bone marrow transplants are done annually in the United States alone (Beckestein, 2004).

There are many different types of stem cells that perform many different functions in the body. The use of stem cells can potentially have many applications in modern medicine. Most specialized cells in the body can not be replaced by natural processes if they are diseased or severely damaged. Stem cells can be used to help generate healthy, functional cells without the risk of rejection. Adult and embryonic stem cells can also be used to treat various diseases. In Parkinson's patients, stem cells may be used to form nerve cells that secrete dopamine. These nerve cells can then be transplanted into the patient, where they will theoretically be able to restore function in the brain. However, there are many obstacles that must be overcome before the potential uses of stem cells may be realized (*Frequently Asked Questions*, 2004), as will be discussed in later chapters in this report.

CHAPTER-2: STEM CELL APPLICATIONS

Stem cell research has opened possibilities for curing diseases that doctors would otherwise only dream of curing with traditional medicine. Ongoing research on stem cell therapies gives hope to patients who would normally not receive treatment to cure their disease but just to alleviate the symptoms of their chronic illness. For this reason, and because of the ethical issues that will be discussed in the next chapter involved with embryonic stem cells, research and use of stem cells have received a massive amount of attention from the media and the public. Yet as we learned in Chapter-1, not all stem cells are alike, so it is important to distinguish therapies that are well established versus those that remain future hopes. It is extremely important to differentiate hype from reality when it comes to the scope of what is currently possible and what may be possible in the distant future.

Uses of Adult Hematopoietic Stem Cells (HSCs)

Many people falsely believe that stem cell research and applications have not saved a single life. What many people do not realize is that stem cells have already been used to save thousands of lives for almost forty years in the form of Bone Marrow and Umbilical Cord Blood Transplants. Hematopoietic stem cells (HSCs) (discussed in Chapter-1) are multipotent adult stem cells that form all the cellular components of blood. HSCs can be isolated from bone marrow (the traditional source), umbilical cord blood, or peripheral blood from individuals treated with hormones to mobilize the HSCs from the marrow to move into the peripheral blood. Patients with cancers of the blood (leukemia

and lymphoma), inherited blood disorders (aplastic anemia and sickle-cell anemia), and other immune deficiency diseases have malfunctioning stem cells that do not produce enough blood cells or produce defective blood cells.

The classic way to collect HSCs for a transplant is from bone marrow. The HSC donor is usually put under anesthesia to relieve any pain during the process and the bone marrow cells are collected by puncturing a bone, usually a hipbone, with a syringe. When the marrow is transplanted, the cancerous HSCs in the patient are destroyed usually through chemotherapy or irradiation, and the healthy HSCs are infused into the patient's bloodstream then migrate to the cavities of the large bones (*Hematopoietic Stem Cells*, 2005).

More recently, specifically within the last three years, doctors have been using peripheral blood as their main source of HSCs. "As a source of HSCs for medical treatments, bone marrow retrieval directly from bone is quickly fading into history" (*Hematopoietic Stem Cells*, 2005). Researchers have always known that HSCs existed in small numbers in peripheral blood, but within the last ten years "they have discovered that they can coax the cells to migrate from marrow to peripheral blood in greater numbers by injecting the donor with a cytokine, such as granulocyte-colony stimulating factor (GCSF)" (*Hematopoietic Stem Cells*, 2005). The patient is injected with GCSF a few days before the HSCs are collected, and the cells are collected through one of the donor's veins. "Richard Childs, an intramural investigator for National Institutes of Health (NIH), says peripheral harvest of cells is easier on the donor – with minimal pain,

no anesthesia, and no hospital stay – but also yields better cells for transplants" (*Hematopoietic Stem Cells*, 2005). He also states that there is evidence that patients receiving peripherally harvested cells have a higher survival rate than bone marrow recipients do because the peripheral cells contain twice as many HSCs and engraft more quickly.

Alternatively, stem cells found in umbilical cord blood are now being used because of several advantages over bone marrow HSCs. First of all, the collection of the stem cells is simple and painless because the blood is collected shortly after birth from the mother's umbilical cord and placenta, which are usually discarded. Second, cord and placenta blood are both rich sources of HCS. Third, cord HSCs appear to be more primitive than marrow HSCs so are less likely to be rejected by the patient. Because of these reasons the use of this source has been increasing quickly since the early 1990s. "The New York Blood Center's Placental Blood Program, supported by the NIH, is the largest U.S. public umbilical cord blood bank, and now has 13,000 donations available for transplantation into small patients who need HSCs" (*Hematopoietic Stem Cells*, 2005).

Other Adult Stem Cell Therapies

HSCs are not the only kind of adult stem cells. Scientists are discovering that adult stem cells can be used to replace cells and tissues to restore function to various organs in the body including the heart, the nervous system, skin, and the liver. Although

most of these therapies have only been tested on mice, some have successfully treated humans in clinical trials.

Heart Stem Cell Therapy

One type of adult stem cell therapy that has been successful is for heart disease. Ever since researchers discovered that stem cells could be coaxed in laboratory culture dishes into developing into cardiomyocytes and vascular endothelial cells scientists have been looking to exploit that ability to provide replacement tissue for a damaged heart (*Can Stem Cells Repair a Damaged Heart*, 2005). The ability to do so provides tremendous advantages over a heart transplant procedure since the heart is not viewed as foreign by the patient's immune system. Heart stem cell therapy was first tested using mice as models. The scientists would tie off a major blood vessel to the mouse's heart to induce a heart attack. In a study done in this manner by Ortic and colleagues they injected stem cells from the mouse's own bone marrow into the damaged wall of the ventricle (Figure-8). These stem cells lead to the formation of new cardiomyocytes, vascular endothelium, and smooth muscle cells. "The newly formed myocardium occupied 68 percent of the damaged portion of the ventricle nine days after the bone marrow cells were transplanted, in effect replacing dead myocardium with living, functioning tissue" (*Can Stem Cells Repair a Damaged Heart*, 2005).

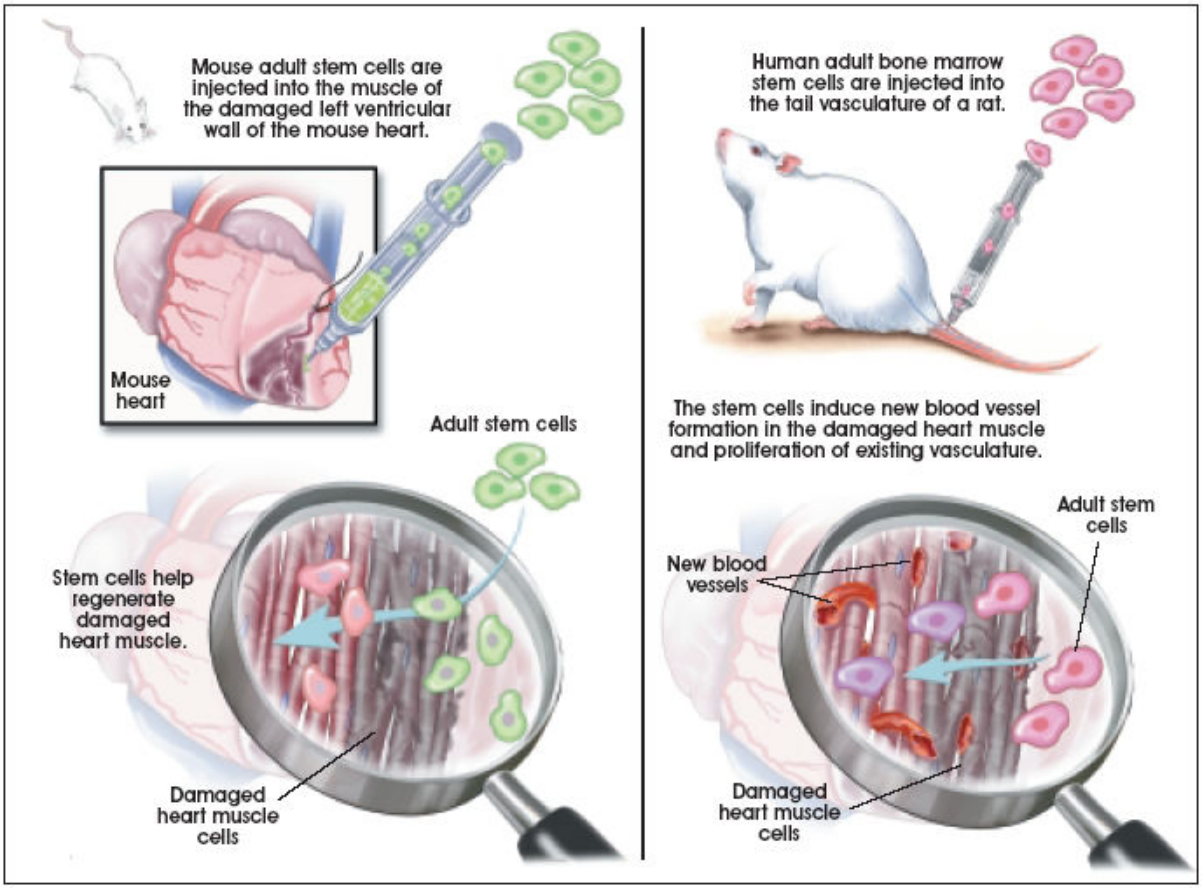

Figure 8: Heart Muscle Repair with Adult Stem Cells (*Can Stem Cells Repair a Damaged Heart*, 2005)

Another study published in the Proceedings of the National Academy of Sciences used pigs as models. Stem cells from a donor pig's bone marrow were transplanted into the damaged heart of a host pig. "After just two months, the stem cells had helped restore heart function and repaired damaged heart muscle by 50 to 75 percent"(*Trials to Test Safety of Stem Cell Therapy for Heart Damage*, 2005). These animal models allow scientists to study the effects of a certain treatment without actually putting humans in danger and pave the way for trials on humans to be conducted.

The first successful case of heart stem cell therapy was the case of sixteen year old Dimitri Bonnville from Royal Oak, Michigan. Dimitri was shot in the heart with a nailgun while repairing a home. After the accident he underwent open-heart surgery at William Beaumont Hospital and then suffered a massive heart attack. Doctors came to the conclusion that he needed a heart transplant. William O'Neill, Beaumont's chief of cardiology, said before the procedure "we did cardiac MRI studies and we found that basically the entire front wall of his heart was dead" (Philipkoski, 2003). The only alternative offered to Dimitri's parents was for Dimitri to be a test case for stem cell therapy which his parents agreed to. The teenager's therapy began with a four-day regiment of a drug that stimulated the production of hematopoietic stem cells in his blood. Doctors then harvested Dimitri's HSCs and transplanted them into the artery that supplies blood to the front of the heart. He was discharged about a week later to recuperate at home. His doctors say they have never seen a recovery like this, and O'Neil states that "many other patients we have observed like this have never seen any improvement" *(Philipkoski,* 2003). Since then, studies have shown that "Dimitri's heart ejection fraction, a measurement of how well the heart is functioning based on the percentage of blood pumped out of the heart's main pumping chamber, is now at 40 percent. This compares to 25 percent following the nail gun incident. The normal ejection fraction is 50-75 percent" (*Teen Stem Cell Transplant Patient Shows Improvement*, 2005). German heart specialist Bodo Eckehard, who has also successfully treated a heart patient using adult stem cells, claims that "even patients with the most seriously damaged hearts can be treated with their own stem cells instead of waiting and hoping on a heart transplant" (Earll, 2005).

Adult Neuronal and Pancreatic Stem Cell Therapies

Other adult stem cell therapies that have provided very promising results are therapies treating patients with damaged nervous systems and patients with diabetes. First exhibiting impressive results in mice models, there are now about 60 documented cases of quadriplegic and paraplegic patients regaining some mobility, bladder control, and sensation in their limbs from stem cell treatments (Earll, 2005). Dennis turner, a man from California with Parkinson's disease, experienced a more than 80 percent reduction in his symptoms after he received an injection of his own neuronal stem cells (Earll, 2005). A study published in the *Medical Post* concluded that "11 out of 15 Type-1 diabetes are 'completely off insulin' after receiving adult pancreatic cell transplants." Researcher Denise Faustman at Harvard Medical School stated "It was astonishing! We had revered the disease without the need for transplants" when they used animal adult stem cells to grow new islet cells to produce insulin and combat diabetes (Earll, 2005).

Embryonic Stem (ES) Cell Therapies

As discussed in Chapter-1, embryonic stem (ES) cells have the greatest medical potential of all the stem cells due to their ability to differentiate into any type of tissue, however scientists are still looking for a way to unlock their mysteries. They would like to do so because unlike adult stem cells these cells have the potential to differentiate into any type of cell in the body and they posses the unique ability to replicate in culture. Unfortunately ES cells do not have as good a track record as adult stem cells. Even though there are researchers in other countries such as China and North Korea that claim to have successfully treated patients using ES cells, this is primarily just hype, and these

researchers have either failed to show evidence that would support their claims or have been exposed as frauds. “Embryonic stem cells have not cured or successfully treated a single patient.” (Earll, 2005).

However, embryonic stem cells have provided results in mouse models. Bernat Soria and his colleges at the Universidad Miguel Hernandez in San Juan, Alicante, Spain, successfully reversed the symptoms of diabetes in mice (Figure-9). They implanted ES cells with added DNA containing the insulin gene, and found that the cells differentiated and where able to respond to changes in glucose concentration by increasing insulin secretion nearly sevenfold (*Stem Cells and Diabetes*, 2005).

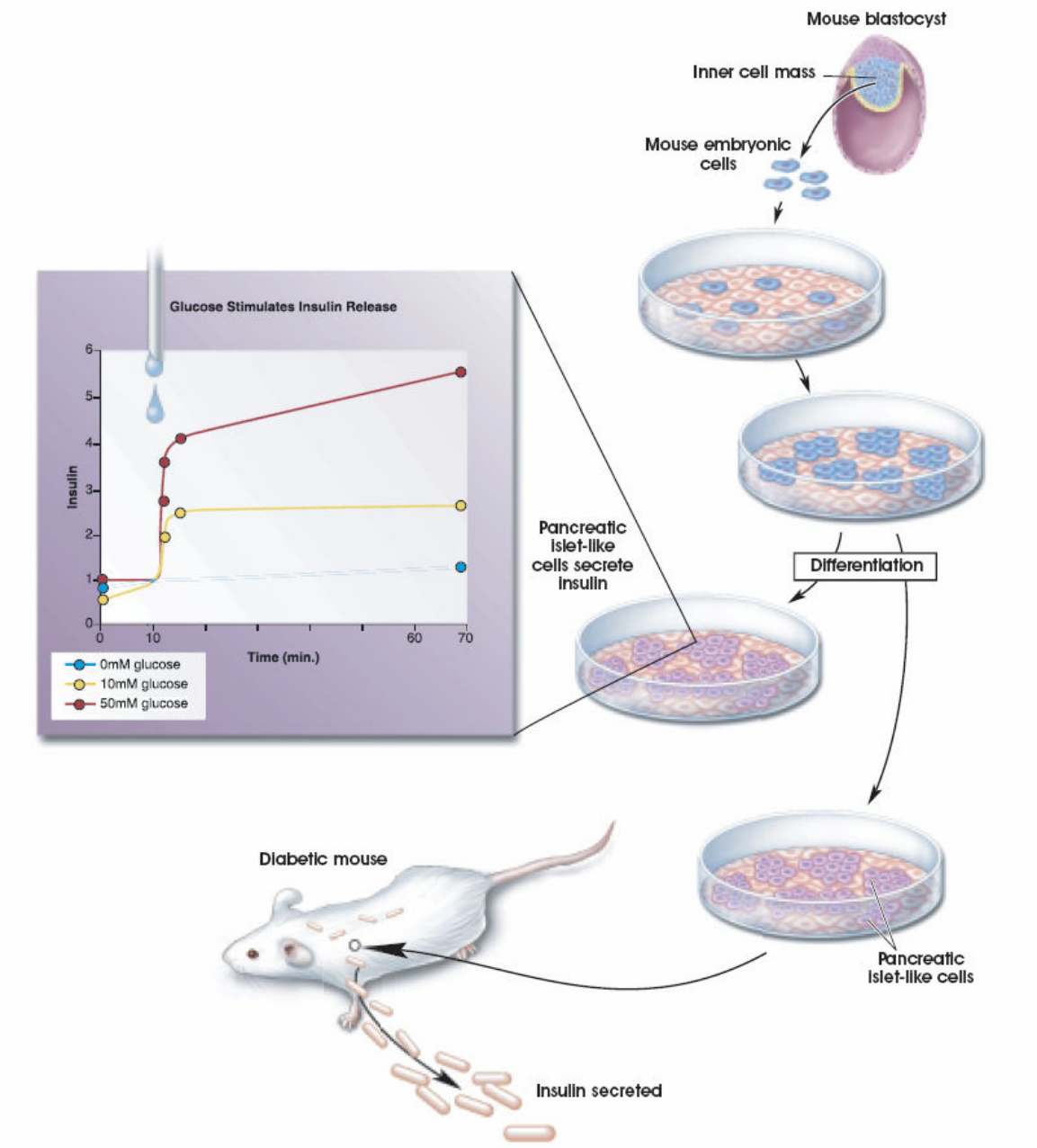

Figure 9: Development of Insulin-Secreting Pancreatic-Like Cells From Mouse Embryonic Stem Cells (*Stem Cells and Diabetes*, 2005)

Researchers at John Hopkins University reported evidence that embryonic stem cells can restore movement in an animal model of amyotrophic lateral sclerosis (ALS). The rats used in the study where exposed to the Sinbis virus which destroys the motor neurons in the spinal cord, essentially paralyzing muscles in their hindquarters. The group

used embryonic stem cells from human fetal tissue because they had trouble sustaining stem cell lines from rat embryos (*Rebuilding the Nervous System with Stem Cells*, 2005). They injected the stem cells into the fluid surrounding the spinal cord of the rats.

> "Three months after the injections, many of the treated rats were able to move their hind limbs and walk, albeit clumsily, while the rats that did not receive cell injections remained paralyzed. Moreover, at autopsy, the researchers found that cells derived from human embryonic germ cells had migrated throughout the spinal fluid and continued to develop, displaying both the shape and the molecular markers characteristic of mature motor cells"(*Rebuilding the Nervous System with Stem Cells*, 2005).

Conclusions

Even though the stem cell research has advanced enormously within the last five years, laws, regulations, misconceptions, ethical issues, and a decline in funding has made it more difficult for researchers in the United States to develop stem cell therapies. Embryonic stem cell research has come under fire both politically and religiously over the past years, as we will discuss in Chapter-3, and the public typically incorrectly stereotypes all stem cell research as using the controversial embryonic stem cell. This image could be a reason why the annual investment in tissue engineering dropped in 2002 from $610 million to $506 million in the United States (Glaser, 2004). These are some of the reasons why Robert M. Nerem, Ph.D, warns that the United States could fall behind with 40% of the 33 new tissue engineering firms started since 2000 located outside of the U.S. (Glaser, 2004). Looking ahead… "Research and development efforts need to focus

primarily on developing reliable sources of stem cells and progenitor cells, learning how to control cell function, developing interactive biomaterials, engineering three-dimensional constructs that, early on, serve as better model systems for studying cells in vivo, scaling up manufacturing processes, and creating off-the-shelf products" (Glaser, 2004).

With this in mind, Michael Lysaght, Ph.D., claims that "stem cells and regenerative medicine are hard-wired for success, but human therapies are likely to be 20-50 years from clinical adoption" (Glaser, 2003).

CHAPTER-3: STEM CELL ETHICS

Bioethics is the study of the ethical and moral implications of new biological discoveries and biomedical advances (*Bioethics*, 2006). Because of their enormous medical potential yet controversial method of obtaining them, stem cell research has been a constant issue of bioethical debates. Stem cells are self-replicating, undifferentiated cells that sometimes have the ability to become any cell in the body. Due to these special properties of stem cells, it may be possible to develop treatments for Alzheimer's, cancer, Parkinson's, type-1 diabetes, heart disease, as well as many other illnesses (*Frequently Asked Questions*, 2004). However, there is little consensus on the ethical uses of stem cells among the major religions of the world- Christianity, Hinduism, Judaism, and Islam.

Most of the moral confusion is centered on embryonic stem cells. The use of adult stem cells does not pose as much of a moral dilemma due to the fact that adult stem cells can be taken from umbilical cords, placenta, or bone marrow and not from an embryo (*Frequently Asked Questions*, 2004). Thus, research with adult stem cells does not destroy human embryos. Using adult stem cells for research and possible treatments is therefore supported by all of the major religions. However, there are disadvantages in using adult stem cells over embryonic stem cells. Adult stem cells cannot divide indefinitely, and are also not as versatile as embryonic stem cells. Since embryonic stem cells would potentially prove more valuable for medical purposes, the ethical debate of using embryonic stem cells continues, and each major religion has its own views. The remainder of this chapter will focus on the ES cell debate.

Christianity and ES Cells

The Roman Catholic Church is one of the religions in strongest opposition to the use of embryonic stem (ES) cells for research purposes. The largest dilemma surrounding the use of ES cells is the definition of when life begins. Catholic belief states that life begins at the moment of conception and that the embryo is the beginning of "personhood" no matter where it exists. The church states that every embryo should have the opportunity to grow into a mature human being (*Background Information on Stem*, 2005). The Catholic Church's prohibitive stance on ES cells is based on the 1987 document entitled the "Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation", which was published by the Congregation for the Doctrine of Faith. This document states that attempts at the manipulation of an embryo are characterized as a violation of the dignity of the human embryo that is granted personhood from the moment of conception (Frazzetto, 2004). The Vatican also released a document entitled the "Declaration on the Production and the Scientific and Therapeutic use of Human Embryonic Stem Cells" in August of 2000 claiming that the use of human ES cells is immoral.

> "On the basis of a complete biological analysis, the living human embryo is - from the moment of the union of the gametes - a human subject with a well defined identity, which from that point begins its own coordinated, continuous and gradual development, such that at no later stage can it be considered as a simple mass of cells" (*Declaration on the Production*, n.d.).

However, the notion of life beginning at the moment of conception evolved fairly recently in the church. In the medieval church, the definition of personhood was different. The church believed that an embryo acquired a soul only when it took a recognizable human form. In 1869, Pope Pius IX declared that an embryo obtained full personhood from the time of fertilization. Since that time, the Catholic Church has stood strong on this position and has declared the destruction of an embryo after conception as murder no matter if the embryo is conceived naturally or through *in vitro* fertilization (Frazzetto, 2004). Pope John Paul II also was a strong advocate against the use of ES cell research. He also supported the belief that life began at conception. However, Pope John Paul II did not point to a specific biblical text that supports the belief that life begins at conception (Weckerly, n.d.).

There are also many different opinions about stem cell research that is raised from the Protestant sect of Christianity. Several denominations, such as the Southern Baptist Convention, believe that the embryo is the smallest form of human life and that it should not be destroyed. However, other denominations, including the American Presbyterian Church, conclude that the research is acceptable if the goals of the research cannot be reached in any other way. The majority of the Protestant denominations favors stem cell research, but also maintains that the research must be limited to the embryos that cannot be used for reproductive purposes. In other words, embryos within a 15-day window from fertilization are the only embryos that can be used (*Background Information on Stem*, 2005). Still other denominations, such as the Unitarian-Universalists, the Episcopal Church, the Evangelical Lutheran Church, the United Methodist Church, and the Church

of Jesus Christ of Letter Day Saints, have no official position on the use of stem cells (Derbyshire, 2001).

Judaism and ES Cells

The Jewish Biblical and Talmudic law state that personhood is acquired progressively, not immediately at conception. Jewish traditions do not give human status to an embryo until it has reached forty days of gestation. However, the fetus only receives personhood at birth. Therefore, since Judaism's beliefs place the beginning of life well after the 5-day stage needed to obtain embryonic stem cells, this religion ethically supports using embryos for stem cell research (*Background Information on Stem*, 2005). Rabbi Yehiel Ben Ayon, a column writer for the *Canadian Jewish News* writes that "Judaism teaches that life begins at birth; hence the possibility to kill life can only begin at the same time that life begins. In Judaism, an unborn child is not life, but the potential for life" (Ayon, 2002).

According to the Torah, the Jewish people have an obligation to seek knowledge. The Torah is the central and most important document of Judaism. The Torah primarily refers to the first five books of the Hebrew Bible. However, the term is also sometimes used in the general sense to include both of Judaism's written law and oral law. Therefore, the Torah encompasses the entire spectrum of authoritative Jewish religious teachings throughout history (*Torah*, 2006). In Jewish law, a strong value is placed on human life. *Pikuach nefesh* meaning, "the preservation of life", is paramount in the Jewish religion. Rabbi Yehiel Ben Ayon says that the "Torah teaches us the supremacy of

life. It tells us that guarding life is more important than even guarding the Torah itself" (Ayon, 2002). This belief causes stem cell research to be viewed almost as a mandate in order to help better human life. Most Jewish ethicists and medical and religious personnel agree that in Jewish tradition, it is permissible to destroy an embryo for the purpose of benefitting other living human beings (Yearwood, n.d.).

Islam and ES Cells

The source of Islamic beliefs comes from the Qur'an, the central religious text. According to the Qur'an, the use of embryos for stem cell research is acceptable up to forty days after fertilization. Beyond the fortieth day, well after day-5 blastocyst formation from which ES cells are obtained, most Muslims agree the fetus becomes a human being. The Shari'ah, the religious law of the Muslims, says that an embryo acquires a soul 120 days after fertilization, which is towards the end of the fourth month of pregnancy. Many Muslims also believe that obtaining personhood is a developmental process. This belief is similar to that of Judaism (*Background Information on Stem*, 2005). Also like Judaism, Islam's beliefs place an obligation to seek out knowledge since it is a part of human nature on its followers. Dr. Abdulaziz Sachedina, a professor of Islamic Studies, states that "…in Islam, research on stem cells made possible by biotechnical intervention in the early stages of life is regarded as an act of faith in the ultimate will of God as the Giver of all life, as long as such an intervention is undertaken with the purpose of improving human health" (Weckerly, n.d.).

The Shari'ah also makes a distinction between potential life and actual life, and that actual life should be afforded more protection than potential life. Under most interpretations of the Shari'ah, the embryo is considered potential life and is not yet considered a person. Therefore, using an embryo to create stem cell lines would not violate Islamic beliefs. The majority of the two major Islamic groups, the Sunni and the Shi'ite, do support regulated use of embryonic stem cells (Frazzetto, 2004).

Hinduism and ES Cells

In traditional Hindu beliefs, conception is defined as the beginning of a soul's rebirth from its previous life. However, some Hindu beliefs place the beginning of personhood between three and five months of gestation. Few Hindus believe that incarnation can occur as late as seven months after conception (*Background Information on Stem*, 2005). Therefore, again there is little consensus as to when life begins. However, there is consensus on the main belief of ahimsa or nonviolence. Hinduism respects the sanctity of all life. Since the most common Hindu belief is that life starts at conception, the line involving the ethics of ES cell research becomes blurry.

However, there are Hindu stories in which it is praised to destroy one life to save another life for the greater good. This act is supposed to bring about good karma. For example, there is a story about a sage named Dadhichi, whose bones were needed by the gods in order to eliminate a demon. Since the demon had to be destroyed, Dadhichi readily gave up his life for the good of the world. The Hindu tradition glorifies his sacrifice and labels him a martyr. Therefore, in the eyes of Hinduism, embryonic stem

cell research must be used for the greater good of the world in order to justify the sacrifice of embryos (*Hinduism and Modern*, n.d.).

IVF ES Ethics

The normal source of embryonic stem cells comes from unused embryos that are created through *in vitro* fertilization. Currently, there are over 400,000 unused frozen embryos in fertility banks across the United States. These embryos are not used by the parents for implantation if the parents deem they have enough children, or if the mother has health problems, so these embryos are normally discarded, and never go on to develop into a mature adult. Even though these embryos are not used, many people feel it is still unethical to use these embryos for obtaining ES cells. However, since these embryos are normally discarded anyway, it may prove more ethical to try to save lives with these embryos regardless of ES cell research purposes (*Frequently Asked Questions*, 2001).

It is possible to donate the excess frozen embryos for stem cell research. The Stem Cell Resource (SCR) is a non-profit, independent organization, founded by reproductive medical professionals and academic researchers in order to gain further knowledge in the field of human embryology and cell therapy. The SCR provides service to physicians who have patients seeking to donate surplus embryos that are otherwise destined for destruction. In order to donate excess frozen embryos, the couple must consent. The couple is provided information to ensure that they understand the ethical and scientific issues surrounding such donations, and supplies informed consent

documents for the donors to sign. These donors are not paid for donating excess embryos (*Frequently Asked Questions*, 2001).

Parthenote Ethics

Parthenogenesis is a form of reproduction by which an egg develops without the fusion of sperm and egg (*Glossary*, 2004). The term parthenogenesis comes from the Greek word meaning "virgin birth". This type of reproduction occurs frequently in nature among arthropods such as insects, especially ants and bees. In mammals, parthenogenesis does not create a viable embryo. Instead, a parthenote is created. A parthenote is a chemically treated egg (not fertilized) that divides only to the blastocyst stage from which embryonic stem cells can be extracted. Because parthenotes cannot develop into an individual, there are fewer ethical concerns with their use, and much research is focused on using them as a replacement source for ES cells. Figure 10 depicts the division of a monkey parthenote after the egg was chemically treated (Vrana et al., 2003).

Figure 10: Monkey Parthenotes (Vrana et al., 2003)

The method of creating a parthenote begins with an egg obtained before ovulation in a woman. This is preferred because before ovulation a woman's egg has a full DNA complement with forty-six chromosomes. This is referred to as the diploid number. Alternatively if the egg was retrieved after ovulation, the egg would retain only twenty-three chromosomes. This is referred to as the haploid number. It is possible to stimulate a haploid egg to replicate its set of genes to return to a diploid number of forty-six chromosomes, but it is easier simply to harvest while the full complement is present. After an appropriate egg is obtained with the correct number of chromosomes, a chemical trigger is introduced. One such trigger is a small electrical shock that tricks the egg into believing it has been fertilized. The egg then begins to divide. The egg continues to divide into the blastocyst stage. It is at this stage that the embryonic stem cells can be obtained (McConchie, 2005). Figure 11 illustrates the process of parthenogenesis (*Reproductive Cloning Basic*, 2003).

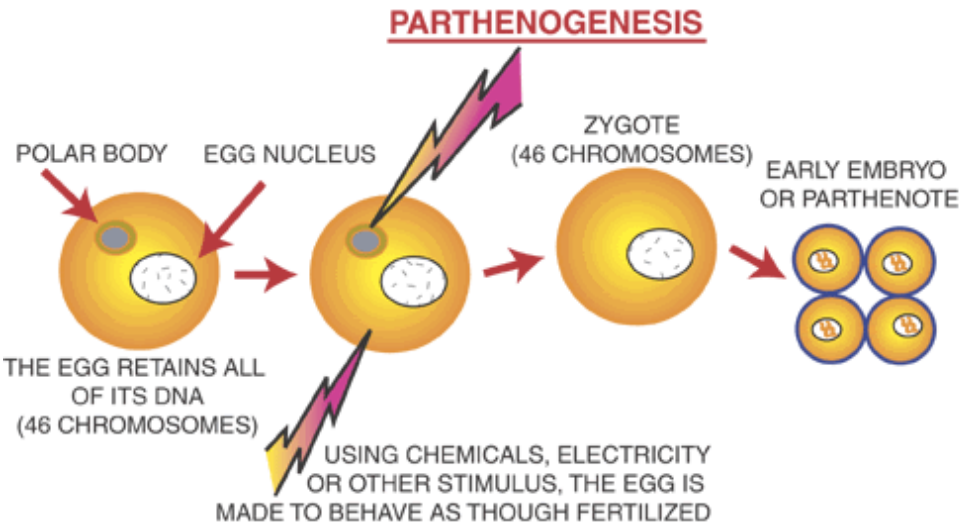

Figure 11: Parthenogenesis (*Reproductive Cloning Basic*, 2003)

Although parthenotes may some day serve as replacements for fertilized eggs as a source of ES cells, there are technical challenges presented with the process of obtaining stem cells through parthenogenesis. The first challenge is that the genetic structure of the parthenote is relatively unstable. This may lead to potential problems in the use of parthenote-derived ES cells as treatment. One problem with using genetically flawed embryonic stem cells is the potential increase in cancer. Cancer is normally caused by mutations in genes regulating cell division. Since embryonic stem cells divide indefinitely, using stem cells already poses a risk of cancer. However, if the stem cells being used have flawed genes, the potential risk of cancer increases. In addition to faulty genetics, the pool genotypes for research of embryonic stem cells would be limited only to fertile females that could provide viable eggs. Viable eggs are difficult to obtain from postmenopausal women. This is unfortunate since older women are more likely to develop degenerative diseases needing stem cell treatments than younger women (McConchie, 2005). In spite of the potential limitations of parthenote use for acquiring embryonic stem cells, it still has its advantages and should be considered as an alternative to using traditional methods. However, there are still ethical issues surrounding parthenote use.

The largest ethical issue involving the use of parthenotes is the distinction of whether a parthenote is considered a true embryo. Some argue that it is only embryo-like due to the fact that it is not an embryo created by the union of sperm and egg. Others claim that even though the embryo was not created by normal means, it should still be treated as a true embryo (McConchie, 2005). This would mean that it is just as unethical

to obtain embryonic stem cells from parthenotes as it would be from true embryos. However, naturally occurring parthenotes do occur in mammals. These naturally occurring parthenotes are often destroyed without ethical concern. Parthenogenic embryos in mammals are referred to as a teratoma or tumor. These embryos are surgically removed because there is no treatment available to help the embryo to survive, and removing the embryo saves the mother's life (Jones, 2003).

An embryo created through parthenogenesis does not complete gestation naturally. One way a parthenote could complete gestation is if the embryo was combined with trophoblastic cells. These cells normally comprise the outer ring of cells in the early embryo, which function to form the placenta. The lack of ability of a parthenote to form a placenta may be due to the fact that there is a lack of paternal imprinting genes. These genes normally direct placenta growth in mammals. However, since combining trophoblastic cells with a parthenote may potentially lead to survival of the embryo to gestation, another ethical dilemma is raised equivalent to the original use of fertilized embryos (Jones, 2003).

The parthenote is an exact genetic match to the woman from whom the egg was removed. If the embryo survived through the gestation period, the child would be a genetic clone of the mother. This once again leads to the common misconception of embryonic stem cell research and its relatedness to cloning. Since the parthenote is an exact genetic duplicate of the donor female, many people find this fact in itself to be unethical. The people that are against cloning fear that the use of parthenotes may lead to

the first cloned human. However, no lab-created monkey or human parthenote has ever survived past the blastocyst stage to date, so most scientists argue there are few concerns associated with the ability to create a parthenote embryo that can survive to maturation.

Some researchers believe that two haploid nuclei from two different eggs can be forced to combine and develop. This could make it possible for same-sex female couples to conceive a child that is a combination of two genomes. However, the same research that could make it possible for same-sex female couples to conceive a child, could also make it possible for men to benefit from parthenote-based therapies. Currently, only fertile women can benefit from parthenote based therapy. Research in animals suggests that male parthenotes can also be created. Two sperm are inserted into an enucleated egg. The egg is then stimulated to start dividing. The resulting parthenote would be a near genetic match to the donor male patient (Jones, 2003).

Religion plays an important part in the ethical questions raised by parthenogenesis. It is difficult to answer ethical questions of when life begins when it comes to parthenogenesis. One must first answer the question of whether or not the embryo is a true embryo or if it has less value because it is not the combination of a sperm and an egg. If one views a parthenote to have the same value as a true embryo, then Christianity is against the use of parthenotes since life begins at conception. Hinduism also believes life begins at conception but may find justification for destroying one life for the greater good of the world. Judaism and Islam believe that life begins well after the blastocyst stage as been reached. Thus, the question of whether or not a

parthenote deserves the same rights as a true embryo does not need to be answered because a parthenote does not survive to the point when life is considered to begin. However, if a parthenote is not considered a true embryo, religious views may find other controversies with using this method. For instance, parthenogenesis is associated with "virgin birth". Since Christ is also correlated with a virgin birth, parthenogenesis is correlated with Christ. Therefore, using parthenotes for research is highly unethical based on that view (Weiss, 2001).

Even though parthenogenesis is meant to be an alternative to the highly controversial traditional method of acquiring embryonic stem cells, the use of parthenotes is also surrounded by many ethical concerns. However, it has been shown in animals that parthenotes have great potential for therapeutic purposes. The parthenotes that were created from monkey eggs, which can be seen in Figure 1, went on to differentiate into intestine, skeletal muscle, retina, cartilage, hair follicles, bone, and more extraordinarily, heart cells that beat in unison, and nerve cells that secreted dopamine. It is these kinds of nerve cells that are gradually lost in Parkinson's patients. As much as parthenogenesis raises ethical questions, it also raises amazing possibilities (Weiss, 2001).

Conclusions

The author of this chapter agrees with the world's four main religions that working with embryonic stem cells is an ethical dilemma that should not be taken lightly. However, the author believes that embryonic stem cell research is warranted so long as the cells are used to try to save lives. The author also feels that working with

parthenotes, although not without ethical concerns, should be encouraged as an alternative to working with fertilized embryos whenever possible, until an alternative source can be found. The author also believes that working with ES cells from IVF embryos is warranted, so long as full parental consent is provided, the donors are not paid, and the cells are used to try to save lives. Research on adult stem cells should also be pursued for potential medical therapies.

CHAPTER-4: STEM CELL LEGALITIES

One thing that every country in the world has in common is that they agree that taking a human's life is one of the worse crimes that can be committed. Since the exact time an embryo becomes a human being cannot be determined scientifically, or universally agreed upon religiously, and most laws and regulations are based on ethics, Embryonic Stem (ES) cells bring forth many legislations that researchers in many countries are forced to adhere to.

Most countries in the world have developed its own policy for ES research, and their policies range from either "permissive", "flexible", "restrictive" or "no established policy". Figure 12 displays a map of the world with each color representing which type of ES policy the country enforces. According to this map, more then half of the people in the world, about 3.5 billion, have either a permissive or a flexible policy on ES cell research (Hoffman, 2005). Almost all countries have banned human cloning for the purpose of reproduction (reproductive cloning), but have not banned human cloning all together (therapeutic cloning). Therapeutic cloning involves either the derivation of ES cell lines from *in vitro* fertilized (IVF) eggs, or the transfer of a nucleus from an adult cell (either from a patient or another donor) into an enucleated egg (somatic cell nuclear transfer, SCNT. The former procedure is less controversial than the latter (Hoffman, 2005). Since few countries, if any, ban use of the less controversial adult stems, we will focus on the legalities of the more controversial ES cells in this chapter.

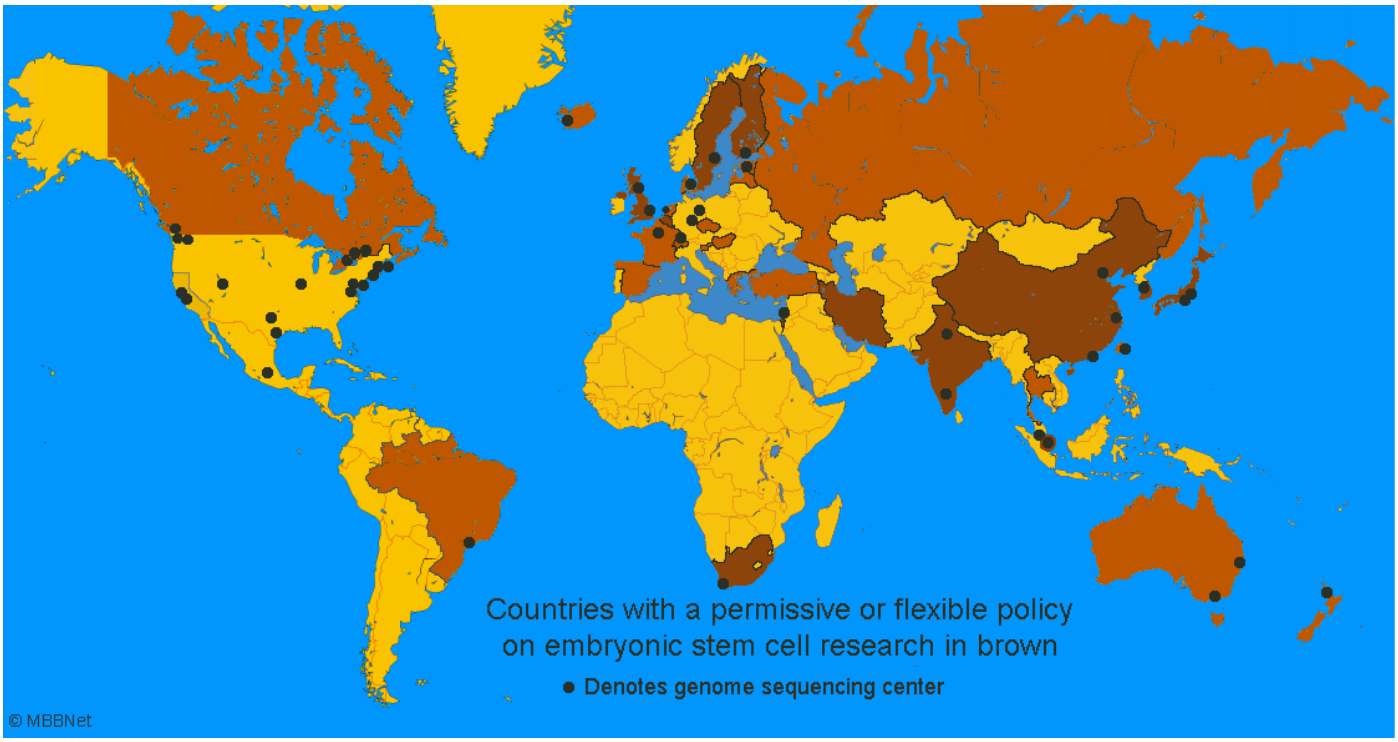

Figure 12: World Map of ES Research Policy (Hoffman, 2005).

- Permissive
- Flexible
- Restrictive policy or no established policy

"Permissive" countries allow research on various ES cell derivation techniques, including SCNT (Hoffman, 2005). This group includes major countries such as the United Kingdom, Belgium, Sweden, Iran, Israel, India, Singapore, China, Japan, South Korea, South Africa, and others, and represents a global population of about 2.7 billion people (Hoffman, 2005).

"Flexible" countries allow, under certain restrictions, research on ES cells derived from fertility clinic donations only, while excluding SCNT (Hoffman, 2005). In these countries, "research is permitted only on remaining embryos no longer needed for reproduction" (Hoffman, 2005). This group includes Australia, Brazil, Canada, France,

Spain, The Netherlands, Taiwan, and others, and represents about 700 million of the world's population (Hoffman, 2005).

"Restrictive" countries have a range of different conservative policies they enforce, or have no established policy at all disallowing their use. Austria, Ireland, Norway, and Poland are among the most restrictive in the restrictive group, and Germany, Italy, and the United States are among the less restrictive within the restrictive group. Some restrictive countries outright prohibit any type of human embryo research. Other countries, like Germany, limit researchers to use only imported ES cell lines. The last group of countries, which includes the United States, permits research on a limited number of previously established stem cell lines. Even though Dr. Necati Findikli reported the first known derivation of human embryonic stem cells from donated blastocyst-stage embryos in Turkey, the country along with several others does not define any guidelines or specific regulations when it comes to ES cell research (Hoffman, 2005).

Sweden

One of the most liberal countries is Sweden, which is considered to be the world leader in stem cell research because of its strong public support, favorable bioethical climate, tradition of science and research, and strong government funding (Sweden's Stem Cell Success, 2002). With regards to legislation, Sweden is ahead of many countries because the framework for the legislation was worked out quickly and quietly without the debate found in most other countries around the world.

Germany

In Germany researchers are feeling more constrained than ever with new restrictions that tighten the import of ES cells. The German parliament voted to allow the import of embryonic stem cells for scientific research, but only under close government control. "Although the German parliament's decision to allow the limited import of embryonic stem cells may appear to be a liberalization, the vote actually signifies a tightening of restrictions for researchers" (Kim, 2002). The law restricts researchers to use stem cells that have already been created, and prohibits German researchers from creating their own ES cell lines. The embryonic protection law that was passed more then a decade ago did not account for the discovery of stem cells, and therefore did not explicitly ban their importation. Regine Kolleck, the deputy chair of the National Ethics Council, states that "the import was not prohibited before, it was completely free. Now we'll have a very restrictive law on the way the import is regulated, and that is more than we had before" (Kim, 2002). Alexander Kekulé, director of the Institute for Medical Microbiology in Halle, finds the new law "a handicap in Germany" saying that the parliamentary resolution is a "clear restriction" on scientists and that "historically, research has hardly been restricted in Germany" (Kim, 2002). Some scientists fear that Germany's decisions on ES research could affect smaller countries such as Austria, Portugal, and Ireland. Kolleck states that "Germany certainly has some sort of a leading role. But as long as the German embryonic protection law is in place, other countries will stay with their restrictive regulations as well" (Kim, 2002).

United States

The United States's ES cell policy was set by President George W. Bush on August 9, 2001. The President stated that federal funding would only be allowed to support research using the 60 or so ES cell lines that already exist "where the life and death decision has already been made" (White House Press Release, 2001). This statement seemed promising, but unfortunately it was later discovered that the number of usable stem cell lines are actually fewer than 10 (Philipkoski, 2003). Recent discoveries suggest that the approved ES cell lines may not be useable at all because they were grown in direct contact with mouse cells (which are used as "feeder cells" that provide growth factors) and may have contracted viruses that would preclude their use in clinical trials on humans (Pizzi, 2002). Thus many scientists in the U.S. stem cell community argue for a loosening of the Bush 2001 policy.

Individual States

Even though President Bush authorized research with these existing stem cell lines, it is up to the individual states to their own policy on ES cell research. Some states, like South Dakota, strictly prohibit research on embryos regardless of the source, while a number of states have already passed legislations and established state constitutional rights to pursue ES cell research. In early 2004 New Jersey became the first of these states to appropriate funds specifically for stem cell research (Johnson, 2005). Over the last 2 years, about $23 million of New Jersey's general revenues have been allocated to the New Jersey Stem Cell Institute. Also $150 million in capital funds to build the Stem

Cell Institute of New Jersey, and a $230 million ballot for stem cell research grants have been proposed (Johnson, 2005).

Many other states quickly followed New Jersey and sought out legislation that would allow ES cell research to be funded. Proposition 71 gave researchers in California the right to pursue ES cell research including SCNT. Proposition 71 was approved by California voters on November 2, 2004, and includes $350 million annually in ES cell research funding for 10 years, up to 3 billion dollars (Johnson, 2005). A similar legislation was passed in 2005 in Connecticut under Senate Bill 934 which created a fund to provide $10 million a year in grants for 10 years.

Massachusetts

In Massachusetts, legislators overrode governor Mitt Romney's veto when they enacted Senate Bill 2039 which created a set of ground rules for stem cell researchers and also set up a biomedical research advisory council (Johnson, 2005). The council will examine the appropriateness of public funding for stem cell research, and assess the feasibility of creating an institute for regenerative medicine at the University of Massachusetts Medical School in Worcester (Johnson, 2005). Richard Hynes, a Professor of cancer at the Massachusetts Institute of Technology, says that these ground rules are important because "the Massachusetts law makes it clear to people in this state what they can do" (LeBlanc, 2006). For example, a key section of the law removes the requirement that scientists who want to engage in ES cell research must seek the approval of the local district attorney first (LeBlanc, 2006). These regulations where meant to

encourage research on ES cells and set an example to other states, but some researchers are finding them to be a burden. Robert Lanza, Vice President of Research for Advanced Cell Technology in Worcester, says "the law is hindering the company by barring them from sufficiently compensating women who donate eggs, making it difficult for the company to obtain the eggs vital to stem cell research" (LeBlanc, 2006).

Conclusions

It is hard enough to get through the technical complications involved with something as complex as stem cell research without adding the complications and expense of government restrictions and regulations. It is the opinion of the authors of this IQP that the United States should loosen the restriction on ES cell lines created only before 2001, and should extend its federal funding to develop new clean stem cell lines to work with.

CONCLUSIONS

Even though stem cell research has advanced enormously within the last five years, laws, regulations, misconceptions, ethical issues, and a decline in funding has made it more difficult for researchers in the United States to develop stem cell therapies.

As far as ethical issues involved with ES cells, the authors of this IQP agree with the world's four main religions that working with ES cells is an ethical dilemma that should not be taken lightly. However, the authors believe that embryonic stem cell research is warranted so long as the cells are used to try to save lives. Working with parthenotes, although not without ethical concerns, should be encouraged as an alternative to working with fertilized embryos whenever possible, until an alternative source can be found. Working with ES cells from IVF embryos is also warranted, so long as full parental consent is provided, the donors are not paid, and the cells are used to try to save lives. Research on adult stem cells should also be pursued for potential medical therapies, and once their use is perfected they should serve as alternatives to ES cells.

It is hard enough to get through the technical complications involved with something as complex as stem cell research without adding the complications and expense of government restrictions and regulations. It is the opinion of the authors of this IQP that the United States should loosen the restriction on using federal funding for ES

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