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STEM CELLS

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ABSTRACT

This IQP describes the impact of stem cell technology on society. The different types of stem cells including adult, embryonic, and cord, along with the medical potential each type. The project concludes that although there is great potential with clinical stem cell therapies for curing disease and injuries, many legal and ethical obstacles need to be overcome for human ES cell therapies can be conducted.

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EXECUTIVE SUMMARY

In the human body, stem cells are known as the "master cells" of the body. Stem cells are undifferentiated cells that can differentiate into other types of the cells in the body to perform a specific function, thus they are a very exciting new field for biological research because they are long-lived and can proliferate many times, and can be "coaxed" into differentiating into a type of cell needed to cure a disease.

There are three different types of stem cells in the body. Embryonic or ES cells, adult stem cells, and cord stem cells. Adult stem cells are found in the body at any age but not in high quantity, while cord stem cells are found in the umbilical vein and the placenta. Cord cells are good to use because they offer less rejection by the human body, but the time in which they can be cultured in lab is short. The most promising type of stem cell is the ES cell which can be cultured for long amounts of time, and because it is completely undifferentiated it can be "coaxed" into differentiating into any type of cell needed for a given application. ES cells offer the most medical potential, but since the gathering of these types of cells involves the destruction of an embryo, there is much controversy around their use.

Stem cells have become a very hot topic in the scientific fields because of their unbelievable potential in curing disease and helping heal the body. Of course one must put aside fantasy and concentrate on the reality of what has really been accomplished to date. There will not be arms and hearts being grown in laboratories anytime soon. On the other hand, stem cell research has shown that clinical therapies involving both adult and ES cells can be used to treat and cure debilitating diseases such as Parkinson's disease

and diabetes. Research has shown that with the use of stem cells, the problem cells which cause these two fatal diseases can be repaired and thereby the patient cured. Stem cell therapies are also being developed to treat other health problems such as spinal cord injuries and damage to the heart done by heart attacks. Currently the majority of stem cell therapies include the use of adult stem cells, but slowly ES stem cell therapies are being brought from animal experimentation into human clinical use.

With stem cells and their research being such a controversial topic, it is not surprising that there are ethical obstacles that stand in the way of research being done, particularly with ES cells. The real question or controversy surrounds the use of blastocysts to attain the ES cells. Some call it murder, while some say a zygote is not a human being. This is a question that has created a highly publicized ethical issue in this country and throughout the world. Of the four major world religions, Christianity and Hinduism have a strong stance against the use of ES cells because in their doctrine life begins at conception and an embryo is considered life. Judaism on the other hand has a slightly more lax view of life since it considers life to begin much later than a 5 day old blastocyst, but in reality there is no clear stance by Judaism on the issue of Es cells and therapeutic cloning. Some jewish scholars agree with ES research, and some don't. Islam is the only major religion that shows strong support for the use of ES cells. Muslim doctrine states that an embryo is not considered life until 120 days after gestation, therefore the use of embryos for research is not considered unethical. There are some however who believe only leftover embryos should be used and new ones should not be created just for attaining stem cells. Of course each individual must make up their own mind.

The other major obstacle in the way of ES cell research is the legality of the research itself. After the discovery of ES cells in 1998, countries all over the world began implementing various statutes or restrictions because of the highly controversial way in which ES cells are attained. In the U.S. for instance, up until 2001, research was barely restricted, but on August 9, 2001, President George W. Bush announced an executive order which allowed federal money could be spent only for research on stem cell lines created before that date. Of course private funding was still available and still continues today to offset federal legislation. Many states began overriding that executive order. In 2001, California overrode the federal order and voters passed Proposition 71 which created a 3 billion dollar ES cell research institute. Many states soon followed including New Jersey and Massachusetts. There are still some states however who aligned themselves with the executive order and have banned ES cell research. In the US, it almost became a "red state vs. blue state" issue. With regards to the international community, European countries were also split on its stance on stem cells. The UK for instance allows therapeutic cloning in order to attain stem cells and is very lax, even offering compensation for women who donate embryos, but countries like Germany do not allow the research at all. Whatever the case may be, most countries now have some kind of statutes or restrictions in place, some very progressive and other very conservative. The legality of ES cell research will continue to be a major obstacle in the way of truly realizing the potential stem cell therapies can offer.

PROJECT OBJECTIVE

The purpose of this IQP was to examine the controversial topic of stem cells and their effects on society. Multiple stem cell categories and origins were investigated to show the reader that some stem cell research does not destroy embryos. Stem cell applications were analyzed to separate fact from fiction in this area, while ethics and legalities were also explained to demonstrate the full societal impact of this new technology.

CHAPTER-1: STEM CELLS: TYPES AND SOURCES

What Are Stem Cells?

Stem cells are the foundation cells for everything in your body. These are the cells that initially created your organs, tissues and other various cells your body requires. In general, stem cells have three main characteristics. First, these cells are long-lived. They persist *in vivo* throughout a person's life, and can divide in culture indefinitely. Second, they are the "master cells of the body", with the potential to change into other cell types. Embryonic stem (ES) cells) can give rise to all types of cells, while adult stem cells usually can generate only the tissue from which they were isolated. Thirdly, stem cells are unspecified cells, meaning they retain their primordial undifferentiated state, so are ready to differentiate into other cell types.

When cells can replicate numerous times it is called proliferation. Most cells such as heart and nerve normally cannot proliferate. Because stem cells can proliferate without change they are often described as being capable of long-term self-renewal. To say that stem cells are unspecified or unspecialized indicates that they do not have any kind of "tissue specific" molecules that would allow them to carry out a specialized purpose. This means that while the stem cell cannot pump blood like heart muscle, it can give rise to heart muscle to carry out that function (National Institute of Health, 2005). Basically, these are cells that haven't decided what they want to be yet and some can be made into virtually any cell found in the human body. These properties are why scientists are so excited about stem cells. They have the ability to cure life threatening diseases and the potential for even more, thus they are the basis for the new field of regenerative medicine.

Categorizing Stem Cells by their Locations

There are three main categories of stem cells that are distinguished by where they are located: adult stem cells, embryonic stem cells, and cord stem cells.

Adult Stem Cells

Adult stem cells are found in the tissues of adults. But they are also found in children and fetal tissue. The term adult is used because it refers to the maturity of the organ that it is taken from (Johns Hopkins Medicine, 2006). These stem cells are not found in large quantity however. This category of stem cells has not been found in all the vital organs. In the case of brain tissue adult stem cells are present, but are not very active. This results in a generally undetected response to a brain or spinal cord injury. Also, adult stem cells are typically only able to generate tissue similar to the one they were isolated from (ISSCR, 2004. An example of this are brain stem cells. They are usually capable of generating only brain tissue. A more complex example is bone marrow. Bone marrow stem cells can produce all the cellular components of blood, even though this includes a variety of cells such as red blood cells, several types of white blood cells, and platelets (ISSCR, 2004).

Embryonic Stem Cells

Embryonic stem cells are the inner mass of cells in a human blastocyst. About four to five days after fertilization the embryo is a hollow ball made up of approximately 150 cells, the blastocyst, composed of the inner cell mass (ICM), and the surrounding cells

the trophoblast (ISSCR, 2004). Research on embryonic stem cells is still in its infancy due to the fact that they were first isolated in humans in 1998, while adult stem cell research has been ongoing since the 1960s (National Institute of Health, 2006). Another potential source of embryonic stem cells are the germ cells of aborted fetuses. Embryonic germ (EG) cells are what develop into the egg and sperm cells. These cells show similar properties to ES cells when cultured, but there is also evidence that they may be limited in their capacity to produce a variety of cells due to the fact that the germ cells have developed for several weeks as opposed to five days. Although ES cells are the most important medically due to their ability to create a variety of tissues, because an embryo is usually destroyed to obtain them strong ethical issues surround their use.

Cord Stem Cells

Cord blood is the third known source of stem cells. These cells are collected from the umbilical vein and placenta after a child is born. This source is far more accessible compared to the other options since the cord is normally discarded at time of birth. In addition, cord stem cells typically are rejected less by the patient, demonstrating less graft versus host disease. However these stem cells can be cultured in a lab for a shorter amount of time than embryonic and adult stem cells (ISSCR, 2004). Cord blood banking has become more common in recent years. Today, it is quite easy to find a private or public cord blood bank to save and store this valuable material. Once harvested, the blood containing the stem cells is screened for infections and the tissue type is documented. The material then goes through processing, which involves removing the red blood cells, before being stored in liquid nitrogen. When a patient donates and uses his or her own

stem cells the treatment is called autologous. If the patient receives another donor's stem cells the treatment is called allogeneic. Receiving stem cells from your identical twin is referred to as syngeneic (Wikipedia, 2006). To date, Viacord, a well-known cord blood bank, has performed nineteen successful transplants (Viacord, 2004).

Recently, scientists have also found stem cells in baby teeth and the amniotic fluid surrounding the unborn baby. This discovery is very current but promising. More research must be done to determine the type of stem cell they are and find the full potential of these stem cells (ISSCR, 2004).

Categorizing Stem Cell by Their Potentials

Not all stem cells are created equally. While all types are important medically, some are better than others (Figure-1). Stem cells that have the potential to make any of the 216 types of cells in the human body are called totipotent stem cells (upper cell in the diagram). Totipotent cells are only found in newly fertilized eggs, called zygotes. It is these first few totipotent cells that will start to become specialized within days of fertilization and go on to form the approximately three trillion cells in the whole body. This is why totipotent cells are the most valuable (MedIndia, 2006)? From totipotent stem cells come all the other stem cells (The Why Files, 2006).

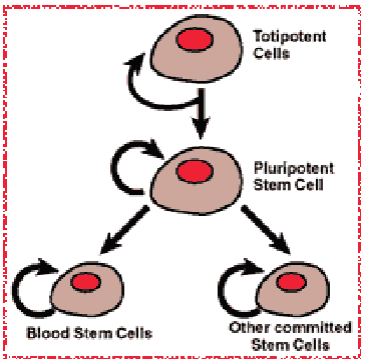


Figure-1: Stem Cell Potentials. All stem cells are capable of self-renewal (arrows to the left of each cell). Totipotent cells (upper cell in the diagram) can create all cells in the body. Pleuripotent cells (middle cell) can create several kinds of cells, while adult stem cells (lower right) usually generate only one type of cell. Picture courtesy of The Why Files Guide to Stem Cells.

The next rank of stem cells as far as potency goes is pleuripotent stem cells. These stem cells can produce a very large variety of cell types, but cannot develop a human being. Embryonic stem cells that were mentioned earlier are pleuripotent. Pleuripotent stem cells have the most potential medically speaking because they are more accessible and can still produce a myriad of tissue types (Wikipedia, 2006). Figure-2 shows an image of a colony of pleuripotent stem cells.

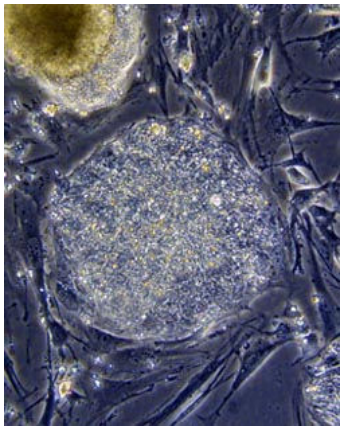


Figure-2: A Photomicrograph of a colony of Pleuripotent ES Cells (University of Wisconsin-Madison, 2006).

Multipotent stem cells can make a few cell types, but not as many as pleuripotent. A good example of multipotent stem cells is hematopoietic stem cells (HSCs). HSCs are found in a person's bone marrow and in cord blood, and are responsible for making blood cells. Bone marrow is found in the femurs, hips, sternum, and ribs primarily, the hips being the most common harvest site (Wikipedia, 2006). HSCs are the reason why patients with certain cancers or blood diseases receive hematopoietic stem cell transplants (HSCT), more commonly called bone marrow transplants. HSCT were first performed by Dr. Donnall Thomas in the 1970s. He was able to show that the HSCs are capable of repopulating the ill patients bone marrow and therefore produce new, healthy blood cells. This work later earned him a Nobel Prize (Wikipedia, 2006). Figure-3 shows an image of bone marrow stem cells.

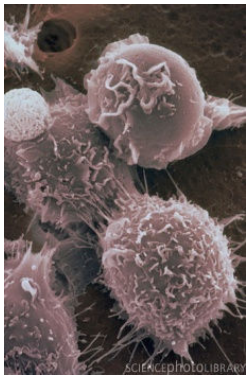


Figure-3: Micrograph of Bone Marrow Hematopoietic Stem Cells. Image courtesy of Leonard, Science Photo Library (2006).

The last type of stem cells and the least variable are unipotent cells. These only have the ability to make one type of cell but are still capable of self-renewal, a feature unique to stem cells. Two examples of unipotent stem cells are neuronal cells, which produce nerves,

and epithelial cells, that become skin cells. Figure-4 left panel is an image of neural stem cells while the picture on the right is of epithelial stem cells found in the mammary gland.

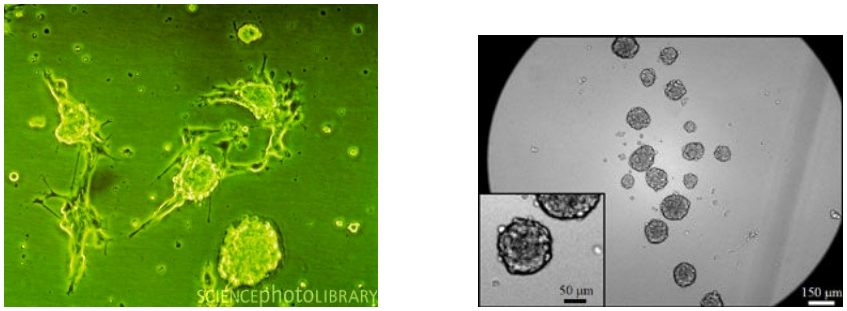


Figure-4: Micrographs of Neural Stem Cells (left panel) and Epithelial Stem Cells (right panel). Left image coutesy of Klaus Guldbrandsen/ Science Photo Library (2006). Right image courtesy of Mammary Stem Cells, NSC Home Page (2006).

Stem Cell Transdifferentiation

Although most adult stem cells are capable of only generating the tissue from which they were isolated, a recent theory, known as the "theory of stem cell plasticity", was announced. This theory suggests that some adult stem cells may have a greater potential to form more varieties of cells than was previously thought, which would extend their reparative capabilities to other kinds of tissue (Mammary Stem Cells, 2006). For example, some scientists claim that culturing hematopoietic stem cells (HSCs) on a feeder layer of neuronal cells (that secrete neuronal growth factors) can change (transdifferentiate) the HSCs into neuronal cells. Transdifferentiation is a topic highly debated among scientists. Some claim that it does not occur at all naturally, however the evidence is mounting that cells can transdifferentiate. In animal cases that involve missing parts being regenerated the evidence speaks for itself. A well-known example that occurs in salamanders and newts is the Wolffian regeneration. In this

experiment the lens of an eye was removed and subsequently a new lens forms from the dorsal iris. For this to happen the dorsal iris cells, which are naturally pigmented, must transdifferentiate into the characteristic transparent lens cells. While it's amazing that salamanders and newts can transdifferentiate cells, the questions remains can humans do the same (Theory, 2006)? Many laboratories are trying to perfect a way to convert tissue from the liver into pancreas tissue in humans. If this process can be developed this therapy would be used to treat diabetes patients. This would be an enormous discovery considering there are approximately 150 million diabetes patients worldwide currently with that figure expected to double to 300 million over the next twenty years (Transdifferentiation, 2005).

Stem Cell Isolation

You might expect that since stem cells are so valuable they would be difficult to harvest, but the processes are relatively simple. As mentioned before, the best-known stem cell harvest procedure is a bone marrow transplant. Under local anesthetic the bone marrow is removed usually from the top of the hips of the donor using a syringe. The process is typically less than an hour in length, and any pain afterwards can be alleviated with over the counter medicine. The recipient will then receive the new bone marrow intravenously (Abbott, 2006). A more recent option for purifying HSCs that does not involve bone marrow is called peripheral stem cell harvesting. Peripheral HSCs are found in small numbers in a person's veins. The donor is given medication in advance of the procedure to boost peripheral cell production thereby increasing the amount harvested per treatment. A needle is inserted into the donor's arm and tubes lead the blood to a cell-

separating machine to collect the stem cells. From there the blood is delivered back into the patient through a different needle in the other arm. The process takes two days, five hours each day, to complete one session and involves little to no pain for the donor. In either HSC-harvesting procedure the stem cells can be transplanted immediately or frozen until needed (Abbott, 2006).

Once stem cells have been harvested they can be grown in a laboratory. The cells are grown in cultures at 37 degrees Celsius and under high humidity. The factor that varies is what the cells are grown on in culture. Different stem cells thrive on different food, or medium. The ultimate goals of growing the cells are to be able to grow large amounts of cells that are unspecialized, and to be capable of making them specialize when desired (ISSCR, 2006). Researchers at Yale University took it upon themselves to determine what the minimum nutritional requirements were to successfully grow human embryonic stem cells. The mixture, named HESCO, is reported to consist of a growth factor called Wnt3 and a basic fibroblast growth factor (bFGF). Also in the mix are cholesterol, transferring (a plasma protein that transfers iron in the body), a B-cell activating factor, insulin, and albumin (the major protein in the clear fluid portion of blood) (Emanuel, 2006). Recently however, researchers at the University of Wisconsin-Madison announced they had developed a way to successfully grow stem cells without the use of any animal cells for nourishment. Using this method the chance of contaminating the stem cell line with animal viruses and other undesired agents is eliminated. This in turn eliminates the risk of a patient receiving infected stem cells as part of their therapy (Devitt, 2006).

Human embryonic stem cells are moderately simple to grow in a lab. The cells grow on a layer of skin (epithelial cell feeder layer) and in the presence of serum. These provide the nutrients the stem cells require. If too many cells grow, some are transplanted to a different culture to continue growth. This process is called passaging and can be repeated forever in theory. With respect to culturing, hematopoietic stem cells are the exact opposite of embryonic cells. They tend to become specialized very quickly and are very hard to grow in culture. For these reasons, hematopoietic cells are usually not grown in labs (ISSCR, 2006), although a local biotech company (Viacell Inc.) founded by a former WPI Biology and Biotechnology graduate student Morey Kraus, has had some success amplifying cord HSCs.

Culturing neural stem cells is different in that they grow in suspension and not attached to the culture dish. They also do not require serum nutrients from blood. In culture, the neural cells grow to form a hollow ball called a neurosphere. Eventually the neural stem cells will develop into specialized cells (ISSCR, 2006).

If the cells are successfully grown *in vitro*, meaning outside the body, a stem cell line is established. A stem cell line is defined as "a population of cells which can replicate autonomously for long periods of time". These stem cell lines must keep their ability to form specialized cells after they are removed from the lab conditions that keep them from differentiating otherwise they are no longer considered a line (MedIndia, 2006). Embryonic stem cells easily fit these rules. Currently in the U.S. there are about eight to ten stem cells lines that are widely accepted as valid embryonic stem cell lines (ISSCR, 2006). A subsequent chapter in this IQP will examine whether these few ES lines are sufficient for supporting the ES research effort in the U.S.

Therapeutic Cloning

After understanding what a stem cell line is and how they work, you might be wondering how all of this relates to cloning. The honest answer is that working with stem cells is a form of cloning when it involves nuclear transfer. It is very important to say here that this is not the cloning depicted in movies or science fiction! While some concepts in the films may include elements of truth, they are still just movies and fiction.

There are two types of cloning: reproductive and therapeutic. Reproductive cloning is constructing a new individual from a single cell. This is accomplished by removing the nucleus in an egg and replacing it with the nucleus from another cell in the body. The nuclear transferred egg is then implanted in a surrogate mother to be carried full term, assuming all goes well (MedIndia, 2006). In theory, the resulting offspring would be a clone of the adult whose genetic material was used. In animals, the process has produced a large variety of transgenic animals that are useful medically, and has produced snuppy the worlds first cloned dog (Lee et al, 2005). However the cloning process is not efficient, and many oocytes are required, and the offspring can experience many problems. About one percent of clones that survive are normal and free of health troubles. Reproductive cloning is very inefficient, difficult, and initially made for agriculture reasons, not human applications (ISSCR, 2006).

Therapeutic cloning is the pertinent form of cloning for stem cell purposes. As with reproductive cloning, the nucleus of the embryo is replaced with one from another cell. For example, the goal is to take the nucleus from a patient's skin cell and clone an embryo to obtain ES cells for treating the same patient. Early claims to have achieved this

from Hwang's lab in South Korea (Hwang et al, 2005) were unfortunately withdrawn as fabricated. The major difference between reproductive and therapeutic cloning is that in the latter the embryo is never implanted into a surrogate and is not expected to mature full term. The goal of this therapeutic procedure is to obtain a blastocyst from which to isolate ES cells to repair damaged tissues (MedIndia, 2006). The chief benefit to this technique is the patient will not reject the stem cells because they are made of the same genetic material (ISSCR, 2006).

Parthenotes

Harvesting the embryonic stem cells by traditional methods involves destroying the blastocyst, which some consider murder. A different option that does not involve destroying the zygote is parthenogenesis. This method uses chemicals to fertilize the egg instead of fertilization from a male. Because partnenotes cannot produce viable offspring, their destruction creates fewer ethical considerations. To date, parthenotes have been achieved from primates (Cibelli et al, 2002) and humans (Cibelli et al, 2001), but ES cell lines have not yet been achieved with human parthenote blastocysts. This topic will be discussed further in Chapter-3 on Stem Cell Ethics.

CHAPTER-2: STEM CELL APPLICATIONS

Introduction

When discussing the potential stem cells have in healing the sick, wounded, or diseased, one must always be careful not to intertwine what's real and what's hype. With stem cells, much of the problem has been that people, usually the media, hypes stem cells to be a cure for all ailments and issues. This in turn leads people to believe the wrong things about what stem cells can do.

The reality is that it is true that stem cells have amazing potential to cure many high profile and fatal diseases such as diabetes and Parkinson's diseases, or to help regrow tissue and repair damage done to the nervous system. The mistake some people make is that they oversimplify how hard it is to extrapolate animal experiments to humans, and how hard it is to control the differentiation of the stem cells into desired tissues. Some say we'll just inject some stem cells, and eureka the disease is cured. This however is not the case, as stem cell therapies are only slowly being put into human clinical use. The main areas where stem cell clinical therapies are being made are in regenerative medicine, diabetes, Parkinson's disease, and spinal cord injury, so each of these disorders will be discussed in this chapter.

Since the body is essentially a machine made up of parts which work together, one can theorize that it is possible to replace a faulty part with one that is as good or maybe even better than the original part. This where stem cells come into play. Putting aside the nonsense of growing arms and eyes in a lab, the real work being done with stem

cells in regenerative medicine is at the cellular level. The theory behind this is that by using stem cells, either embryonic or adult, new tissue can be grown inside the body in place of any permanently damaged tissue.

Stem Cells and Diabetes

One of the biggest potential applications of stem cells is in the fight to cure diabetes. In the U.S., diabetes kills an estimated 200,000 people a year, and is considered the seventh leading cause of death (Stem Cells and Diabetes, 2005). Diabetes can affect any type of person, therefore combating it and fighting it is a hard process, which calls on one to constantly take medication, insulin shots and check their blood sugar periodically. Also leaving diabetes untreated can lead to a host of severe medical problems such as blindness, heart disease, and limb amputation from circulatory problems.

Currently there is no way to cure diabetes. Patients with Type I diabetes must inject insulin everyday, while those with Type II must take oral medication and be on a strict diet in order to control blood sugar levels. Some patients receive a pancreatic transplant which has shown promise, but because of the risky nature of transplant surgery, and the overall lack of pancreas organ supply, most diabetic patients must live day to day always taking care of themselves. With the discovery of stem cell therapies though, diabetic patients may have a chance at living a life where medications are not needed everyday to ensure a happy life.

Scientists and researchers have been going about creating stem cell therapies in many ways to combat diabetes using not only embryonic stem (ES) cells, but cells from adult and fetal tissue to reignite or restart a balanced insulin production. The research on

fetal tissue has not been as successful as the research done using adult and embryonic stem cells. In the case of fetal tissue, although results showed islet formation and insulin production, it was very difficult to expand the culture of the purified fetal cells, therefore logistically it was a hard therapy for normal clinical use (Beattie et al., 1997).

Adult stem cell therapies have shown great promise with regards to diabetes. Many different studies have been done with all different types of adult cells to reignite insulin production. One group of researchers actually isolated adult islet cells from cadavers and using genetic engineering, caused the functioning cells to proliferate into many insulin producing cells (Itkin-Ansari et al., 2001). Other researchers have been focusing on the ductal cells inside the pancreatic ducts. Several different teams of scientists have studied and experimented with these ductal cells and, through forced differentiation, have caused the proliferation of both more ductal cells, and insulin-producing endocrine cells. Tests have shown that these new endocrine cells have been producing insulin at levels very near the ideal amount needed per amount of glucose present (Stem Cells and Diabetes, 2005). However, one of the real problems with adult tissue is the fact that these new cells may form into tumors, but up until now, there has not been overwhelming evidence that this happens in the majority of cases.

With regards to embryonic stem cell treatment of diabetes, the initial thought was that diabetes could be cured in a day or two. This if course in unrealistic but the optimism is valid as embryonic stem cells could one day drastically reduce the effects of diabetes. Although the biggest problem with adult cell therapies and/or pancreatic transplant has always been whether or not the patient's body would accept the new cells or would they fall victim to the immune system's defenses, with embryonic stem cell therapies, the cells

can be engineered from the start to not induce any immune response. The other big advantage of embryonic stem cell therapies is that through the correct steps and correct engineering of the cells, brand new islets can be formed which would reverse the effects of diabetes.

Most of the research done on embryonic stem cell therapies of diabetes until now has involved animal experiments. Many research groups have used different types of engineering, and have all found that with some engineering, embryonic stem cells can differentiate into insulin producing cells (Assady et al., 2005). The way in which they induce the differentiation can be different, but in the end many of the initial results show that insulin is being produced by these newly differentiated cells.

Although it may be years until there is a definitive stem cell therapy for treating diabetes, when digging through all the hype of the "magical two-day cure," one can see that there is actually great promise, and that research is moving along quite rapidly towards an end all treatment for diabetes. Although there has been some success in the human trials for combating Type I diabetes using adult pancreatic cell transplants, the fact still remains that Type I diabetes is caused by an autoimmune problem. This creates a major obstacle for scientists as some therapies may work good for the short term but over the long term, scientists need to make sure that these newly transplanted cells are not killed off by the immune system.

Stem Cells and Nervous System Disorders, Parkinson's Disease

The second major area where stem cell therapies have a potential of saving millions of lives and curing millions of people is in diseases and ailments of the nervous

system, such as Alzheimer's disease and Parkinson's disease. Up until very recently it was believed that brain cells and nerve cells could not easily regenerate, therefore any kind of damage to the brain and/or spinal cord was a permanent injury which could not be repaired. Recently though new research is showing that some regeneration does occur, and with the advent of stem cells, that regeneration can be elevated to the point where new nerve cells and brain tissue can be born.

Parkinson's disease is a disease, which affects a persons motor skills. It is a neurodegenerative disease, which occurs when the dopamine producing cells in the brain die. When this happens dopamine is no longer produced, which causes severe impairment of motor skills since dopamine is the brain chemical, which allows for the smooth coordinated movement of the body to occur. Currently Parkinson's affects about 1.5 million people in the U.S., and every year thousands more are diagnosed (Rebuilding the Nervous System with Stem Cells, 2005). What is especially devastating about the effects of Parkinson's, besides the tremors and impaired movement, is the slow onset of the effects, which can happen over a span of years causing one to have an altered life style. New stem cell therapies though have shown great promise in fighting and possibly even curing Parkinson's. Currently there are three approaches being undertaken by researchers in creating stem cell therapies for treating Parkinson's. They include tissue transplants, growing new neurons for implantation, and the reigniting of adult stem cells in the patient's brain to enhance the body's repair mechanism.

Fetal tissue transplants (containing neural stem cells) have been used since the mid 1980's as many groups have tried to transplant fetal tissue in order to restart dopamine production in the brain (Rebuilding the Nervous System with Stem Cells,

2005). Although many of these studies proved successful in that some of the transplanted dopamine producing cells did survive even after the death of the patient there was not enough dopamine produced to show a significant statistical difference (Rebuilding the Nervous System with Stem Cells, 2005). Nevertheless, there was hope and promise that with the right type of engineering, these dopamine producing cells could be productive enough to reverse the effects of Parkinson's.

The next major approach used with stem cells and Parkinson's is the growing of new neurons from undifferentiated cells. The theory is that if these new neurons are place in the brain, they will begin to produce a sufficient amount of dopamine needed for Parkinson to be reversed. Much of this line of work however involves using embryonic stem cells since they are the most undifferentiated stem cell known. Much of the research being done on this approach has yet to be completed but many groups have reported success so far with mouse and fetal embryonic stem cells (Freed et al., 2001). Also one privately funded group, the Geron Corporation, has shown much success using human embryonic stem cells. This group has shown results that they were able to coax human embryonic stem cells to form into mature neurons. Another group at the NIH also showed success in coaxing ES cells into becoming cells, which had the same behavioral and physiological characteristics as dopamine producing neurons (Kim et al., 2002). Of course these results are all in a laboratory setting, and the technology is probably years away from being ready for clinical use. Still there is much optimism that with the right engineering and methods, this type of stem cell therapy can be used to induce dopamine production and reverse the effects of Parkinson's disease.

The third major approach taken to combat Parkinson's using stem cell therapies is to actually induce the patient's own stem cells found in the brain to begin or restart the body's natural repair mechanism. This approach is the most current of three discussed, and is barely into the research phase, but scientists believe that if they could control and or enhance the migration of one's own stem cells into the damaged area by adding the appropriate growth factors, repair can begin sooner and can be more productive. It is known that when part of the brain is injured or impaired, stem cells migrate to the area (Rebuilding the Nervous System with Stem Cells, 2005). What scientists want to do is possibly merge approaches 2 and 3, and use adult or embryonic stem cells to further enhance this intra-patient migration and allow for real repair of the damage. This type of approach may also be useful not only in treating Parkinson's, but any kind of injury that affects the nervous system, even paralysis due to spinal cord injury.

Much of the work done with Parkinson's research seems to be more focused on using embryonic stem cells which offer the most potential since completely undifferentiated cells are needed, but when it comes to treating other injuries which affect the nervous system such as spinal cord injuries, scientists have actually put a lot of emphasis on adult stem cells, since they are available and can be used clinically. With spinal cord injuries, the difficulty seen is that many neurons are destroyed, therefore reconnecting these neurons to begin sending messages again is very hard. But what stem cells can provide is partial healing, at least for now, which would allow some semblance of movement.

Many different types of techniques are being used to treat spinal cord injuries with adult stem cells. Usually the process involves taking one's own adult stem cells and

re injecting them into the wounded area. For example a patient who had severe spinal cord injury was injected with stem cells from his own olfactory bulbs (Hughes, 2005). Soon he was able to gain some movement and control of the bladder. Of course with the rapid research in embryonic stem cells, one can be sure that embryonic therapies will also be developed which can possibly allow for even more healing than with adult stem cells, but that remains to be seen (Stem Cell Treatment, 2004). As of right now, adult stem cell treatments are being clinically used and have shown great success in allowing people to move and in some cases walk again.

Stem Cells and Heart Disease

The third major pathology area where stem cell therapy research is occurring is in the field of heart disease. One of the fast moving areas of regenerative medicine using stem cell therapies is in reversing the damaging effects of heart disease and/or heart failure. Heart failure affects about 5 million people in the U.S. Heart failure is basically caused by an inability of the heart to pump sufficient blood, usually caused by damaged cardiomyocytes (Can Stem Cells Repair a Damaged Heart, 2005). This damage usually occurs from heart attacks or other heart conditions. When these cells do not work properly, the body cannot be supplied with the blood needed for one to survive. Patients usually die within a few years. Although treatments are currently available to combat congestive heart failure, such as drug therapies and mechanical assistance, in the end they are only temporary, and the condition continues to remain fatal. Recently though new stem cell therapies have shown promise in allowing for the repair of these damaged cardiomyocytes and thereby almost curing the problem of a "weak heart".

The most current studies on repairing these damaged heart cells involved the use of adult stem cells or hematopoietic stem cells. As seen below in Figure-1, these adult stem cells are injected into the heart and cause the differentiation and birth of new cardiomyocytes.

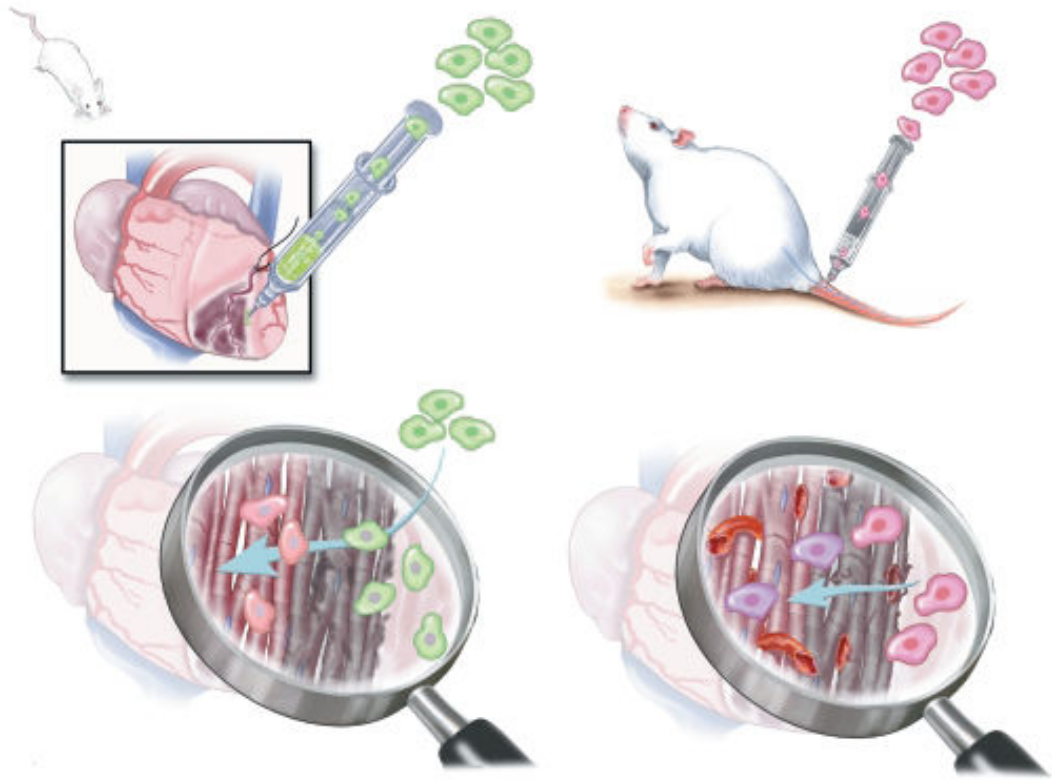


Figure-1: Diagram of the Injection of Stem Cells into the Heart. "Can Stem Cells Repair a Damaged Heart" (2005) NIH, Stem Cells, Chapter-9. http://stemcells.nih.gov/info/scireport/PDFs/chapter9.pdf

With the induction and introduction of these adult or hematopoietic stem cells into the heart, the stem cells differentiate into healthy cardiomyocytes, which can restore function

to the damaged part of the heart (Hematopoietic Stem Cells, 2005). This therapy has been shown to be very successful in rodent models and currently is being used in some places as a clinical therapy. In Germany for instance, a study done using 28 heart attack patients in 2003 showed much promise in using hematopoietic stem cells to induce cardiac regeneration (Britten et al., 2003). Each of the patients received his or her own hematopoietic stem cells into their hearts about 5days after the patient had suffered a heart attack. 26 of the 28 patients showed improved pumping efficiency and decreased dead tissue. This study showed that these stem cell therapies can work clinically but the procedure needs to be improved upon in order for the heart top return to its normal efficiency.

In the US, these same types of trials are occurring as well in order to gain an understanding of how and why these stem cells cause heart tissue regeneration. In 2003, a 17 year old who had his heart damaged from a nail gun accident was given an experimental treatment using an injection of his own stem cells in order to regenerate the damaged heart tissue. The experimental procedure was a success, and it was considered a victory for the stem cell community (Philipkoski, 2003). In 2005, The University of Pittsburgh Medical Center began a trial similar to the one done in Germany involving heart attack patients and the use of stem cells to help heal their damaged hearts however the results have yet to be produced (Novel Stem Cell Trial, 2004). Also in 2004-2005 researchers at the University of California, San Diego (UCSD) School of Medicine discovered specialized stem cells found in the heart of newborns (Rare Heart Stem Cells, 2004). Further research is needed to see what the full potential of these stem cells is, but

scientists predict that with the right type of environment and stimuli, heart stem cells can grow to become fully mature heart cells.

Other Stem Cell Applications

Aside from the research done in heart tissue regeneration, more research is being done on the regeneration of many other types of tissue using stem cells and tissue engineering. Since stem cells are a type of master cell in theory, they can differentiate into any type of cell in the body, which makes its potential even more grand. Of course when one thinks of regeneration, they get an idea of growing an entire arm out of a few cells, which is an unrealistic goal. The goal of the research being done now is to incorporate the regenerative properties and opportunities stem cells offer with the biomedical and tissue engineering work being done to allow for the growth of new skin tissue for example which resembles actual human skin instead of the biomedically engineered grafts available on the market.

The real research being done on regenerative medicine seems to be done in private sector as slowly companies are combining the power of privately funded stem cell research with the most recent advances in medical devices and implants which will not only prolong life, but actually repair damage. For instance a company in Lincoln, RI, called Nephros Therapuetics created a device called the RAD which consists of a bioartificial tube lined with stem cells which differentiates into the cells which line the renal tubules and performs the same functions as a kidney (Glaser, 2003). Tests showed that when this implant was put into place it took the place of injured tubules, and allowed them to heal naturally without any interruption of normal kidney function. Other similar

therapies are being created as well. Researchers at the University of Pittsburgh are working on a therapy to take stem cells from a patient's eye and create an engineered ocular surface (Glaser, 2004). This could go a long way in providing a treatment for those with severe eye injuries. There is much more potential for using stem cells in regenerative medicine, such as in the liver and other organs, but these are all progressing slowly since there is still so much to be understood about the stem cell, how it works and how much work they can do. Even more recently, with the successes that stem cell therapies are producing, companies are offering to bank the stem cells found in a new mother's umbilical cord blood, which can later be used if any stem cell therapy is needed on the child (Viacord, 2002; Viacell, 2002).

Chapter Conclusion

Stem cells obviously offer an amazing amount of potential in all of the fields discussed and in many more. The main point one needs to understand is how to separate the reality of this potential from the fantasy. In five years scientists will not be able to grow appendages or entire organs in a laboratory, but they may be able to use stem cells to help heal neurons damaged from a spinal cord injury to allow for some use of one's legs or arms. Stem cells offer amazing potential in allowing real healing to occur in the body. With the incorporation of stem cells with the current biomedical and tissue engineering research being done, there maybe be even more of a potential for stem cells in healing and regeneration of the body.

CHAPTER-3: STEM CELL ETHICS

Just because we know how to do something, doesn't mean it is necessarily right. Some people know how to steal a car, but they don't because they know its wrong. There are many who know how to use a gun, but they don't shoot others because it is against the law. But what if you're being attacked and you need to save your life? Do you still shoot the person? What if a scientist was studying how to use stem cells and it could save hundreds of lives, but it involved destroying embryos that have the potential to become individuals? The research could save many lives and improve the quality of life for even more. If that embryo is a life, do you destroy it to save another life? These are the questions we have to ask ourselves as this new frontier in medicine continues to open. How far are we willing to push the moral envelope, and at what cost? Every person has their own opinion based on their morals and what they perceive as right and wrong. Many of our morals are taught to us based on our religious beliefs. This chapter will explore how the four major religions of the world view stem cell research and what position each takes. It must be stressed that the opinions of one religious leader cannot be mistaken for the opinions of every follower associated with them.

The benefits that stem cells present are numerous and promising. Scientists believe stem cells may be effective therapies or even cures to several diseases including diabetes, heart disease, liver disease, muscular dystrophy, Alzheimer's disease, Parkinson's disease, spinal cord injuries, and stroke. The list goes on, and may continue to grow as we learn more about the capabilities of stem cells (Potential, 2005).

As an example of a recent stem cell application, just recently, scientists at the University of California, Los Angeles AIDS Institute and the Institute for Stem Cell Biology and Medicine were able to able to genetically manipulate an embryonic stem cell into a T-cell. T-cells are one of the body's main defenses against disease and infection. This is a dramatic breakthrough for the treatment of blood diseases, including human immunodeficiency virus (HIV) and AIDS, acquired immunodeficiency syndrome, diseases that specifically target T-cells (Stem Cell Research Raises Hopes, 2006). While this is a tremendous breakthrough using embryonic stem cells, there are drawbacks that surface with stem cell research.

The positives to stem cell research are abundant and provide strong emphasis for doing good things for mankind, but there are also several drawbacks. One of these is the lack of variability in adult stem cells. Because the use of adult stem cells does not destroy an embryo, such cells have fewer ethical considerations, and all four main religions support their use so long as they are used to better mankind. However such cells have less medical potential than ES cells because they can only generate the same kind of tissue they were isolated from. Because researchers have yet to find a way to expand the variability of adult stem cells (i.e. they can not induce their trans-differentiation into another type of tissue), the emphasis is shifts to embryonic stem cells, which in theory can generate any tissue in the entire body. The greatest drawback to using embryonic cells is of course destroying embryos or obtaining the cells from aborted fetal tissue. While some people feel that this is necessary step in order for the greater good to benefit, others see destroying the embryos as murder, and therefore should be against the law. This then leads to questions like: when does an embryo become a

person, and what rights does the unborn embryo have? There is no one right answer to these questions, but some kind of compromise has to be met. That is possibly the only way the benefits of stem cell research can be accessed while minimizing the drawbacks.

Christian Stance on ES Cells

Christianity is currently the largest religion worldwide, boasting 2.1 billion members or approximately 33 percent of the world's religious followers (Major Religions, 2005). Christianity is a "one god" religion based on the teachings of Jesus of Nazareth that were recorded in the Gospels (Christianity, 2006). Christian religion accepts the use of adult stem cells under the condition that they are only used for benevolent purposes. In his speech to the Diplomatic Corps Pope John Paul II stated, "…research using adult stem cells, moreover, offers the promise of considerable success (Pope John Paul, 2005)."

The Christian concern is the use of embryonic stem cells. Most Christians believe that life begins at the moment of conception. Before forty days and before birth, a fetus has a soul and is entitled to the same rights as an adult. As quoted in the Holy Bible, from John the Baptist, "For he will be great in the sight of the Lord, and he will drink no wine or liquor; and he will be filled with the Holy Spirit, while yet in his mother's womb (Luke 1:15)." This clearly explains that a fetus has a soul prior to birth. While it is not stated directly, other excerpts from the Bible suggest that ensoulment occurs at conception. Therefore, to destroy a blastocyst (day-5 embryo) intentionally and with premeditation, even for the benefit of the masses, constitutes murder in the eyes of most Christians, especially the Catholics (Shannon, 2006).

Parthenotes are also not approved by Christian religion. In 1987 the Church's Magisterium condemned parthenogenesis in the Instruction *Donum vitae*; words that "set forth the central content of Gods revelation and the sacredness and inviolability of human life (Dios, 2000)." While this approach cannot produce a viable human embryo, and therefore murder is not committed, Christianity is extremely opposed to human embryo manipulation. The bottom line here is that the Christian faith is opposed to all forms of research involving human embryonic stem cells (Cheshire, 2003). It should be noted however, that Christianity encompasses many divisions. The views may vary between divisions, say from Catholic to Protestant. Catholics agree with the aforementioned policies while some Protestants think that its okay to use embryos "that cannot be used for reproductive purposes, within a 15-day window from fertilization (General, 2006)."

Healing is greatly encouraged in Christianity. In the Bible there is a passage from the gospel of Matthew saying, "News about him spread all over Syria, and people brought to him all who were ill with various diseases, those suffering severe pain, the demon-possessed, those having seizures, and the paralyzed, and he healed them (Matthew 4:24)." This begs the question, if remaining embryos from IVF are going to be discarded anyway, should they instead be used to heal, as Jesus did? Not all Christians are opposed to embryonic stem cell research (Faithful, 2005). Some Christians, like members of the Christian Alliance for Progress and similar organizations, support embryonic stem cell legislature as well as other controversial topics (i.e. equality for gays/lesbians and abortion) (Issues, 2006).

Hindu Stance on ES Cells

Hinduism has an estimated 900 million followers worldwide, making it the third largest religion in the world, as well as being the oldest religion on earth (Major Religions, 2005). Like Christianity, Hinduism teaches, “Conception is the beginning of a soul’s rebirth from a previous life,” and therefore marks the beginning of personhood (General, 2006). Thus it stands to reason that Hindus reject the use of embryonic stem cells as Christians do. This also includes obtaining stem cells from aborted fetuses. The dilemma Hindus face is where to draw the line between right and wrong. Hindu teachings say to do good actions in the world, but they also say to respect the holiness of creation (Hinduism, 2006). Do the benefits of healing the ill outweigh the negatives of destroying embryos? Each person and their interpretation of Hindu teachings can only answer this question.

Hinduism clearly supports the use of adult stem cells as long as they are taken with consent and used morally. According to a top Hindu spiritual leader, “Any knowledge can be used or misused. Atomic power can be used for the benefit of mankind, or it can be misused to destroy mankind with atomic bombs. The only issue is how it is being used (Dharma, 2003)." Adult stem cells present a feasible alternative to ES cells in the Hindu faith as long as they are not misused.

Hinduism considers another ethical side to stem cells: the fiscal aspect. Hindu scriptures say that followers should take notice to how money is earned. The focus should be on helping others and not increasing wealth. A concern with stem cell therapy is that it will be too expensive and only be afforded by the rich, and the focus may shift to greed (Manickavel, 2006). This is a real concern considering that President George Bush

restricted federal funding for research in the US while India, where about 890 million Hindus live, is becoming a major biotechnology power. If the possibilities of stem cells turn out to be realities, many people stand to gain a lot of money (Mishra, 2005). So despite accepting adult stem cells as an alternative, the other ethical dilemma is whether or not the considerable financial gains of some are good for the soul.

Muslim Stance on ES Cells

Islam is the next largest religion in the world after Christianity, having roughly 1.3 billion followers (Major Religion, 2006). Islamic supporters, called Muslims, are guided by a central religious text called the Qur'an. The angel Gabriel delivered the Qur'an, or Koran in English, from God to the prophet Muhammad. The Shari'ah is the portion of the Koran that contains the legal text (Islam, 2006). As far as stem cell research goes, the Islamic faith is arguably the biggest supporter. Two key excerpts appear in the Koran that support stem cell research. The first,

> "We created (khalaqna) man of an extraction of clay, then we sent him, a drop in a safe lodging, then We created of the drop a clot, then we created of the clot a tissue, then We created of the tissue bones, then we covered the bones in flesh; thereafter We produced it as another creature. So blessed be God, the best of creators (klaliqin) (Weckerly, 2006)!"

This statement, explaining the creation of man, is important because of the phrase "thereafter We produced it as another creature." It is interpreted to mean that the fetus is not seen as an actual life until later on in the pregnancy. Under Islamic law, an embryo is not considered a person but is acknowledged as potential life. Actual life is given more protection than potential life. Potential life becomes actual life after 120 days of

pregnancy, well after the blastocyst stage from which ES cells are derived. This is described in the Koran in the excerpt,

> "Each of you possesses his own formation within his mother's womb, first as a drop of matter for forty days, then as a blood clot for forty days, then as a blob for forty days, and then the angel is sent to breathe life into him (Weckerly, 2006)."

These two passages from the Koran are interpreted to mean that an embryo is not a human life until after 120 days of gestation and therefore it is not an infringement of Islamic law to use embryos in stem cell research (Weckerly, 2006).

While Islamic law allows research on stem cells, there are some concerns held by Muslim scholars. One fear is that just because it is acceptable to destroy embryos for research, scientists may create the embryos for the sole purpose of destroying them. A solution is to only use frozen embryos left over from *in vitro* fertilization, provided the owners give full consent. Also, some kind of "monetary safeguards" should be set when compensating the donors; for example: donors can release the embryos to researchers with no compensation, or choose to have them eliminated from storage. This ensures that no embryo donor can receive money for the donation, eliminating money as a motivation. In addition, some Muslim scholars believe that there should be a limit to how many embryos are created. This would prevent excessive amounts than needed being created in hopes they would be donated. Lastly, it is recommended that adult stem cell research continue in hopes that science will progress to the point where embryos are no longer needed (Siddiqi, 2002).

As with every religion, these are general rules and do not apply to every Muslim. Inevitably, some may feel stem cell research is wrong, while others may want to do more

to aide researchers. It is important to realize that the opinions of some people are not the opinions of all people.

Judaism Stance on ES Cells

Judaism is the smallest of the four major world religions, comprised of roughly 15 million followers (Major Religions, 2006). Jewish followers obey laws and commandments revealed to them by God in the form of the Torah. The Torah contains 613 laws, of which only about 300 are still applicable today (Judaism, 2006). When the issue is stem cells, one can find laws that both support and discourage stem cell research. Once again, there is no dispute over the use of adult stem cells or cord blood. The problem is with embryonic stem cells and those obtained from aborted fetal tissue (Jakobovits, 2006).

Until the fetus is born, the mothers life takes precedence, and if threatened, aborting the pregnancy is not considered criminal. So in this case, actual life takes precedence over potential life. However, aborting a fetus due to unwanted pregnancy or to obtain stem cells to save someone else is not allowed. Some believe that abortion violates the law of hurting oneself, while others say it defies the law of "wasting seed" (Eisenberg, 2006).

Another aspect to consider is that Jewish law clearly states that prior to forty days gestation a fetus lacks humanity. In relation to abortion, rabbis vary in their opinion. Some say it violates the law because it was not a threat to the mother's life, while others disagree arguing it was not entitled to the rights of a person yet, and is therefore not

murder. Some rabbis do not even justify the forty-day mark because it would violate wasting male seed, which is forbidden before conception occurs (Melman, 2001).

Because there isn't an official Jewish statement concerning the use of embryos in stem cell research, opinions vary. Some believe that embryos left over from *in vitro* fertilization and genetic screening may be used in research that may lead to saving many lives. In regards to creating embryos for the sole purpose of destroying them and using the stem cells, once again there is no official response (Eisenburg, 2006). It must be stressed once again that these opinions are not unanimous and do not represent the opinions of the Jewish community as a whole, just some of its leaders.

Chapter Conclusions

While the opinions of some religious leaders appear to be close-minded or too capricious, we may now have a better understanding of what their views are grounded in. It appears that the Christian point of view and the Islamic point of view will never come to a total agreement, but the most one can hope for is that everyone comes to some compromise. For example, a good compromise would be to agree that adult stem cells should be used instead of ES cells whenever possible. There will always be some who completely disagree with that future compromise, but that is to be expected (it is impossible to please all at one time). When you realize the immense numbers of people suffering from disease and genetic disorders that could be alleviated or cured, you understand that a compromise must be made for their sake; to end their suffering. Assuming that all we think stem cells can do is correct or even better, the outcome may outweigh the sacrifices. Because there is no single clear conclusion that unifies the

religious stance on stem cells, perhaps in the end it boils down to individual consent, and working towards the common good. The authors of this IQP think that adult stem cells should be used instead of ES cells whenever possible, and that research funding should be substantially increased for adult stem cell research. We also think that excess embryos in fertility clinics are an acceptable source for ES cells (after all they are going to be destroyed anyway), so long as both parents provide consent, no money was paid to the donors, and the embryos were not created exclusively for stem cell purposes.

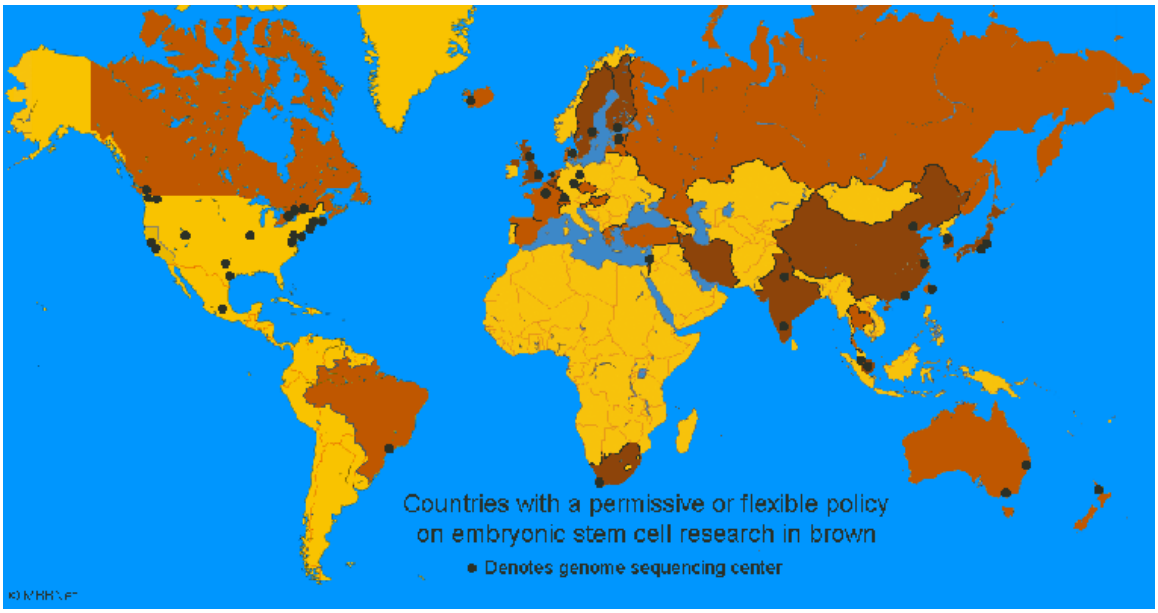
CHAPTER-4: STEM CELL LEGALITIES

Introduction

With any new medical or scientific technological advancement, there are always obstacles that must be overcome, whether they are technological, ethical or legal. In the case of stem cells, as we have seen the first two clearly apply, and maybe the biggest obstacle remaining is the legality of stem cell research. Although lawmakers in almost every country in the world understand the power that stem cells offer, the issue remains a very controversial one. The reality is that lawmakers have not necessarily outright banned stem cell research, but lawmakers in many countries have setup guidelines and/or restrictions on federal funding for this type of research.

As discussed before, ES cells are probably the most advantageous of the three types of cells due to their ability to make almost all other kinds of cells. Although their discovery was fairly recent, 1998, the advancements already made, and their potential for further advancements has opened up the legal floodgates. Since most ES cells are gathered from embryos created through *in vitro* fertilization, the ethical issues discussed earlier have also become legal issues. Lawmakers are basically forced to make a distinction of when life actually begins, and act on it. If lawmakers believe that life begins before day-5 when ES cells are obtained from an embryo, then obtaining ES cells constitutes "murder". These controversial issues surrounding stem cells have forced lawmakers to impose certain restrictions on federal funding for laboratories which derive ES cells. Certain countries and/or regions of the world offer different ideas. Some European countries for instance, particularly Scandinavian countries, are more liberal or

progressive when it comes to supporting ES cell research knowing the end result may save hundreds of millions of lives, while other countries, due usually to major ethical or religious reasons, are very conservative about stem cell research. Figure 1 below shows a color coded map of the world along with an explanation of colors showing which areas of the world are liberal about stem cell restrictions and which are very restrictive or conservative.



Map Explanation

- **"permissive"** = various embryonic stem cell derivation techniques including somatic cell nuclear transfer (SCNT), also called research or therapeutic cloning. SCNT is the transfer of a cell nucleus from a somatic or body cell into an egg from which the nucleus has been removed. [**Options 4 & 5 in Walters, LeRoy**, in References, below] Countries in this category include the United Kingdom, Belgium, Sweden, Iran, Israel, India, Singapore, China, Japan, South Korea, South Africa, and others. [**Walters, LeRoy**, National Academy of Sciences, Oct. 12, 2004. See References, below] These countries represent a global population of more than 2.7 billion people.
- **"flexible"** = derivations from fertility clinic donations only, excluding SCNT, and often under certain restrictions. [**Option 3 in Walters, LeRoy**, in References, below: "Research is permitted only on remaining embryos no longer needed for reproduction."] Countries in this category include Australia, Brazil, Canada, France, Spain, The Netherlands, Taiwan and others.
- Restrictive policy or no established policy. Restrictive policies range from outright prohibition of human embryo research, to permitting research on imported embryonic stem cell lines only, to permitting research on a limited number of previously established stem cell lines. Countries with a restrictive policy include (among the most restrictive) Austria, Ireland, Norway, Poland, (among the less restrictive) Germany, Italy, and the United States.
- Map is designed to reflect **national policy** and whether or not public funds may be used to pursue stem cell research using IVF embryos donated from fertility clinics.

Figure 1: World Map Color Coded For ES Stem Cell Policy.
(Hoffman, 2005)

The United States Stem Cell Policy

The U.S. has always been considered front runners in medical and scientific advancements, and it was no surprise that when ES cells were first discovered in the U.S. many private and public research institutions pledged much of their time and money to investigating the possibility that these ES cells could be used and manipulated to cure diseases such as diabetes and Parkinson's. Unfortunately with all this excitement over these new medical possibilities, the legal and political webs began to form in the country. Many conservative groups considered the destruction of embryos as illegal and unlawful, while liberal groups stated that an embryo is not alive, and were normally discarded anyway.

These political lines were drawn almost as soon as the potential of these newly discovered ES cells were announced. Since the issue was one of much social importance, soon it made its way to the Washington DC where lawmakers began discussing all matters relating to the embryos and how they were to be used.

As the development of ES cells began in the late 1990's, Congress felt it needed to act immediately to setup some kind of guideline for federal funding towards this new technology. In 1995, the Dickey Amendment was passed which called for federal funds not to be awarded to ES cell research where human embryos were either injured or destroyed (Stem Cell Laws 2005). In its original form, the Dickey Amendment was really a law passed only for embryo research, but in 1998 when the first ES cells were isolated from embryos, the wording on the law was changed to only prohibit funding for research which directly causes embryo injury or death. This slight amendment to the law allowed for more research to be done with these newly discovered ES cells.

More amendments were on the way but were put on hold when the newly elected Bush administration decided to take some time and "review" the issue. In 2001, President George W. Bush announced that federal funding would be allowed for ES cell research on stem cell lines created before August 9, 2001, but none for lines created after that date (White House 2001). This was a major compromise since it protected the further destruction of embryos while still allowing research to be performed on existing ES cell lines. At first this seemed like a very good thing for the community but soon it was realized that the existing cell lines were not as plentiful as originally thought, therefore the act actually slowed the fast paced advancement of U.S. ES cell research (Stem Cell Laws 2005). What basically happens now is if one wants to do research, they would need to check with the stem cell registry at the NIH to get funding for research and must prove that the line being used was created before the August 9 date (NIH 2005).

President Bush also created in 2002 the Council on Bioethics whose purpose was to discuss and assess matters regarding stem cell research, the ethics behind the research techniques, etc. At first, the council was fairly balanced with both those for and against stem cell research, but in 2004, two of the council members were replaced with the staunchest advocates of restriction free stem cell research.

The stem cell issue was brought up again in 2005 and 2006 when both the House and Senate passed a bill, which eased restrictions on stem cell funding. The bill was actually a three-part bill, which called for federal funding for stem cell harvesting from embryos left over from *in vitro* fertilizations. The second part made it illegal to grow embryos specifically for stem cell harvesting, and the third part called for more research to be done using umbilical and adult stem cells. Unfortunately the first part of this bill,

which may be the most important part, was vetoed by President Bush. The issue remains unresolved as to whether Congress will actually obtain enough votes to overturn the veto (Stem Cell Controversy 2006).

States Stem Cell Policies

Some states in the United States are in the process of passing laws that override the federal funding restriction on newly created ES cell lines. There are also some states that abide by the federal law or are even more conservative in that they completely forbid research on embryos.

Some of the more "liberal" states, which have laxed laws against stem cell research, include California, Connecticut, Massachusetts, New Jersey and Rhode Island. These states have laws for instance, which allow the cloning of embryos for research. Also in these states, state funding is available for stem cell research (Johnson 2005). California was the first state to override the 2001 federal legislation. In 2004, voters approved Proposition 71, which created a 3 billion dollar publicly funded institute for stem cell research (LAO 2004). Unfortunately the full amount of money has yet to be granted due to legal delays. In 2004, New Jersey appropriated state funds for research in both embryonic and adult stem cells. Massachusetts, Connecticut and Maryland all followed suit and passed laws appropriating fund for stem cell research. Most of these states have also setup Research centers and/or institutes to further research all types of stem cells.

There are however some states which are not in favor of stem cell research. For instance Missouri does not allows the use of state funds for reproductive cloning

(although reproductive cloning is not used to obtain ES cells), and Nebraska law does not allow state funds to be used for ES cell research. Other states such as Indiana do allow stem cells research from a placenta or amniotic fluid, but does not allow research on embryos and completely forbids cloning. It seems as though with some states being in favor of embryonic stem cell research and some being against it, the issue of saving lives has become a political one, where the "red states vs. blue states" issue is also being pulled into the debate (Johnson 2005).

European Policy on Stem Cells

European countries have always had the reputation of being more progressive in research, specifically research related to saving lives. The standards and or obstacles that European products have to pass are much less stringent that those of the FDA in the US. When it comes to stem cells though, there appears to be a large separation in which some countries have very permissible policies on ES cell research, while some have very restrictive policies which all but outlaw ES cell research of any kind or at least research where the cells have been harvested from destroyed embryos.

The most permissive countries in Europe include the United Kingdom, Belgium and Sweden. The UK has been very progressive about its policies with regards to ES cell research. In 2001 it passed an addition to The Human Fertilization and Embryology Act which had originally been passed in 1990 to deal with IVF treatments (The Human Genome 2002). The 2001 addition allowed for the creation of embryos solely for research and examination, thereby legalizing therapeutic cloning. It is illegal however for this newly created embryo to be implanted into a woman for reproductive cloning. Even now

in 2006, the UK acts as a progressive beacon for stem cell research. Recently the government has allowed women to donate some of their unused eggs during the IVF process for research, and in return they receive a discounted rate from the clinic for its services (New Scientist 2006).

In Sweden the same permissive situation exists, where it is completely legal to therapeutically clone embryos for the sole purpose of harvesting ES cells (Sweden's Stem Cell Success 2002). Also other countries such as Singapore and Israel are slowly trying to become the stem cell giants that Sweden and UK are. With very little political debate in these countries about morals or ethics, the new research is really breaking ground on possible treatments using these stem cells. Some European countries are not completely permissive of cloning, in Spain and France for instance eggs no longer needed for reproduction can be used to create stem cell lines, but eggs themselves cannot be collected for the sole purpose of therapeutic cloning.

While Sweden and the UK act as progressive countries that have put aside political squabbles to get this new technology moving, there are still many European countries that are staunchly against the legalization of therapeutic cloning. Countries like Poland, Austria and Norway are extremely restrictive allowing almost no stem cell research, not even on cell lines that were previously established, while countries like Germany and Italy have restrictive policies similar to the U.S. where only a certain number of established cell lines can be used for research and no therapeutic cloning can be newly performed (Kim 2002). Germany and Italy are very vocal about their stance against therapeutic cloning going so far as almost blocking the European Union from giving any funding for stem cell research (Deutsche Welle 2006). These restrictive

countries did have a small victory though as the EU awards funding on a case-by-case basis.

The legal challenges that face stem cell research, specifically embryonic stem cell research don't seem like they will end any time soon. With such a controversial way of attaining ES cells involving the destruction of embryos, one can always imagine that there will be some kind of resistance, but it seems as though slowly some states are becoming more and more progressive in understanding the importance of this research. It may a long time before any kind of common ground is found, but what is known is that this is a topic that will be discussed in legal circles and legislatures for many years to come.

CONCLUSIONS

The ultimate goal of this IQP is neither to convince nor dissuade readers about the potential of stem cells, but to give them the knowledge and facts to form and defend their own opinions. Hopefully some readers now know that some types of stem cells come from adults and do not destroy embryos to obtain them so are not opposed to that type of stem cell therapy, the difference between therapeutic and reproductive cloning, and recognize parthenotes as an alternative ES cell therapy.

Another of our objectives was to dismiss any myths or fantasies surrounding stem cell applications. While Hollywood and the media portray this research to be incredible and able to make copies of limbs, organs, or even whole people, the viewer must remember that what they are watching is fiction combined with a shred of fact. With enormous amounts of animal research and human clinical testing, stem cells may allow victims of spinal cord injuries to use their limbs and perhaps walk again. Growing them a brand new limb or spine is not currently possible. We also tried to shed light on the reasons why some religions allow or forbid certain types of stem cells. Understanding a person's beliefs could ultimately lead to acceptance and tolerance. Once again, it is important to remember everyone associated with a particular religious group may not hold the same beliefs.

Lastly, we hope to have clarified the legal status regarding stem cell research, documenting which countries have lenient policies, which countries have moderate policies, and which countries do not allow any form of ES cell research. While some

readers may still be opposed to this research, the authors of this IQP feel it is in the best interest of society to support stem cell research through federal funding. In order to do this however the current U.S. policy regarding ES cells must be less restrictive, and allow new ES cell lines to be derived. If these steps are not taken, it is our opinion that the U.S. will fall behind dramatically in this field of medical advancement. As said before, these are our personal opinions. It is not our aim to persuade everyone to agree with us, but to educate people and allow them to make their own decisions. Being ignorant or misinformed is no longer an excuse.

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