

STEM CELLS

An Interactive Qualifying Project Report

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ABSTRACT

Stem cell research is a controversial topic that strongly affects society, but misinformation to the public complicates the issue. This IQP clarifies the types and sources of stem cells, discusses their applications, and outlines the religious and political opposition that make support for the research difficult. We hope the public will read this report open mindedly to formulate their own educated opinion on this complex topic.

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EXECUTIVE SUMMARY

Due to misinformation released to the public on the topic of stem cells, many people believe the use of stem cells, no matter what their source of origin, was a bad idea. However, as more information is released on the subject, and as people are becoming aware of what already has been done with stem cells, many people are beginning to rethink their view on the current controversial research. Despite all the reported benefits, many people are still against using stem cells, including some major religions, which makes it all the more important to “shed light” on the subject of stem cells.

Stem cells are the starting cell type for every cell in the body. When developing in the womb, every cell started out as a stem cell and then developed into a specific cell type such as lung, heart, or tissue cell. Depending on the type of stem cell, some possess the ability to differentiate into one or many cell types, some stem cells can even develop into any cell type. Due to this ability (pluripotency), these cells are a very hot topic in regenerative therapies for all sorts of diseases such as Alzheimer’s, Parkinson’s, heart disease and many others (Frequently, 2004).

All stem cells can be classified under four different categories that describe their potency, or, the extent into which they can differentiate. These four categories are totipotent, pluripotent, multipotent, and unipotent. A totipotent stem cell can give rise to all the cell types in the body including the entire embryo and placenta; a fertilized egg cell is the only cell that is considered totipotent. A pluripotent stem cell is derived from a totipotent stem cell and can make up any type of cell in the body, except those types of cells used to make embryonic tissue (such as the egg). Embryonic stem (ES) cells are an example of this type. A multipotent stem cell is derived from a pluripotent stem cell,

they can develop into many related cell types found in the body but they cannot develop into all types. Finally, a unipotent stem cell can only develop into one type of stem cell, usually the same tissue it was extracted from. These types of cells are focused on one job. They develop into their specified and final cell type. The latter two types are often referred to as “adult stem cells” which will also be discussed.

Stem cells can also be classified by their source. There are two different types of stem cells based on source. The first and least controversial are adult stem cells. These stem cell types can be found in the brain, blood, cornea, retina, heart, intestines and several other areas (Weiss, 2005). The problem with all adult stem cells is that they are limited in their medical usage. They have already transformed into a specific type of cell, and are only found in one or very few areas, and thus could not be used to create any type of cell (Frequently, 2004). However, embryonic stem (ES) cells do not have this disadvantage. ES cells are pluripotent and therefore have the ability to become any cell type, making ES cells a primary target for medical research. The embryonic stem cell’s ability to develop into almost any type of cell is the primary reason why it is of great interest to scientists. Scientists hope to be able to make cell lines of all types, including: bone marrow, nerve cells, heart muscle, organ tissue, and many other types in the hope of curing diseases and increasing life expectancy.

Stem cell research shows great promise in both the adult and embryonic fields. Both areas have medical treatments currently in or on the verge of clinical trials, and they both have great results from animal testing in the labs. Despite the advances and promise of treatments, annual investments have dropped over the past couple years (Glaser, 2004). This is probably due to the constant debate over the ethical and moral status of ES

cells, and the current U.S. legislation blocking the derivation of new ES cell lines.

Unfortunately, sometimes all stem cell research gets incorrectly pulled into the debate of whether embryos should be destroyed for research, when this topic only pertains to ES cell research and not adult stem cells. It is imperative to remember that adult stem cell research and therapies use the person's own stem cells for treatment and do not involve any "killing" of embryos. With stem cell research being on the cusp of making life saving discoveries, it is even more important now than ever to try to understand all sides of the ethical and moral debate.

Various religions around the world also have mixed opinions about the use of stem cells in medical research. Some like the Catholic Church are very strict and are against all embryonic stem cell research. However religions like Judaism are for any medical advances that benefit the human race, so long as certain moral and ethical barriers are not crossed, and therefore are proponents of stem cell research. However, besides the obvious division of opinion about using embryonic stem cells between religions, there is also a debate between the members of the same religion. As Dr. Cheshire explains, "...how society decides to treat the least of human lives is a measure of how it chooses to value vulnerable and impaired human beings in general" (Cloning, 2006). As such, governments of countries capable of stem cell research are attempting to take political measures in the best interest of their country.

The United States currently allows federal funding only on ES cell lines derived before August 2001, but allows the private sector and individual state funding much more freedom (Weiss, 2005). The U.S. has struggled with the ethical stand point of funding human embryo work ever "since the advent of *in vitro* fertilization, which produced the

first ‘test-tube’ baby in 1978” (Dunn, 2005). The United States began making political and legal distinctions about stem cells in 1997 with the Dickey Amendment. This amendment was introduced by Representative Jay Dickey, and made it illegal to use federal funds for embryonic research (Johnson and Williams, 2006). One of the major political hurdles with stem cell research is whether the government should pay for it even though there are citizens of the country who may believe it unethical and do not want their tax dollars used for it. This was the reason for the Dickey Amendment. In addition to this, on August 9, 2001, Bush went and undid everything that President Clinton had done to expand and encourage embryonic stem cell research when he “announced that federal funding would now be restricted to a limited number of stem cell lines already created by that date” (Dunn, 2005).

Luckily state laws are able to sidestep both Bush’s regulations and the Dickey Amendment, and help fund ES research with their own money. California has especially taken a strong leading role with its state bond funding of an International Stem Cell Institute. Hopefully with more states supporting the research and a new election year approaching, expansion of funding will help keep the United States at the forefront of the research. Senator Edward M. Kennedy said it best: “There are some issues you just can’t get off the national agenda, and this is one...Stem cell research is going to happen. It will happen quicker with the President’s support, but all of us who are supporting this important research know that it is inevitable. It’s just a question of when” (Klein, 2006).

Stem cell research has advanced tremendously in the past few years, however religious and political opposition, in addition to ongoing scientific difficulties, make stem cells a very difficult field to work in. However, with continued support from private

companies and hopefully more support from state governments that have the technology to work with them, stem cell research will be able to make many more break-throughs and potentially help many patients around the world.

PROJECT OBJECTIVES

The objectives for this IQP are to explain why the topic of stem cells is a topic relative to society, to help prevent misinformation, and to help educate the public about its importance. To help better understand this topic we have divided this IQP into chapters to discuss issues such as the different types and sources of stem cells, their applications, moral and ethical issues, and political issues. The issue of stem cells is very current, and will continue to be an essential topic of discussion as more advances are made.

CHAPTER-1: STEM CELL TYPES AND SOURCES

The controversial topic of stem cells is a relatively new one. Scientists at the University of Wisconsin in Madison in November of 1998 reported that they had succeeded in removing cells from embryos donated from fertility clinics and had generated the first human embryonic stem cell line (Weiss, 2005). James Thomson and his team of scientists expected this feat of scientific ingenuity to be met with applause and admiration; instead the discovery was overwhelmed with controversy and debate. Many religious groups claimed the embryos that the young stem cells were obtained from are full fledged human beings, and as such are a member of society and should have all the rights to a free life as any other human being on earth. Some even went as far as to call it “cannibalism” (Weiss, 2005).

Due to misinformation released to the public on this new scientific endeavor, many people started believing that the use of stem cells, no matter what their point of origin, was a bad idea. However, as more information is released on the subject, and as people are becoming aware of what already has been done with stem cells, many people are beginning to rethink their view on the current controversial research. Despite all the reported benefits, many people are still against it including some major religions, which makes it all the more important to “shed light” on the subject of stem cells.

Stem cells are the starting cell type for every cell in the body. When developing in the womb, every cell started out as a stem cell and then developed into a specific cell type such as lung, heart, or tissue cell. Yet during this differentiation process, stem cells also retain the ability to make copies of themselves in an undifferentiated state. Thus they are considered “immortal” for the life of the organism, and can even be grown in

culture indefinitely. Depending on the type of stem cell, some possess the ability to differentiate into one or many cell types, some stem cells can even develop into any cell type. Due to this ability (pluripotency), they are a very hot topic in regenerative therapies for all sorts of diseases such as Alzheimer's, Parkinson's, heart disease and many others (Frequently, 2004).

Stem Cell Classification by Potency

All stem cells can be classified under four different categories that describe their potency, or, the extent into which they can differentiate. These four categories are totipotent, pluripotent, multipotent, and unipotent. A totipotent stem cell can give rise to all the cell types in the body including the entire embryo and placenta; a fertilized egg cell is the only cell that is considered totipotent. A pluripotent stem cell is derived from a totipotent stem cell and can make up any type of cell in the body, except those types of cells used to make embryonic tissue (such as the egg). An example of pluripotent stem cells are embryonic stem (ES) cells (Figure-1), one of the main focuses of this report (Frequently, 2004).

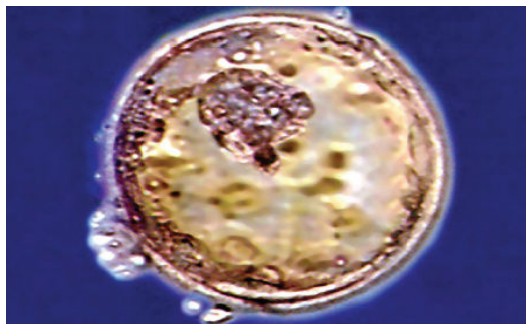


Figure-1: Human Embryonic Stem Cell (Marchant 2006)

A multipotent stem cell is derived from a pluripotent stem cell, they can develop into many related cell types found in the body but they cannot develop into all types. A good example in this category is hematopoietic stem cells (HSCs) that can form all the cellular components of blood. These types of stem cells are often referred to as “adult stem cells” which will also be discussed. Finally, a unipotent stem cell can only develop into one type of stem cell, usually the same tissue it was extracted from. These types of cells are focused on one job. They develop into their specified and final cell type. For instance, an epithelial stem cell can form skin cells. It then remains a skin cell for its lifetime (Frequently, 2004).

Stem Cell Classification by Source

Stem cells can also be classified by their source. There are two different types of stem cells based on source. The first and least controversial are adult stem cells, one of the most common being hematopoietic stem cells. Hematopoietic stem cells (Frequently, 2004) are the precursors of mature red and white blood cells that have the ability to replace bone marrow upon its destruction as well as produce mature blood cells. Other adult stem cell types can be found in the brain, blood, cornea, retina, heart, intestines and several other areas (Weiss 2005). Some advance has already been made in this field, such as the ability to perform adult stem cell replacement, through bone marrow transplantation, as a treatment for blood cancers and other blood disorders (Frequently, 2004). Another advance in this field has been the usage of umbilical cords, which contain many HSCs in them. These stem cells have the advantage of being much “younger” than bone marrow-derived HSCs, and therefore are less likely to be rejected by the patient. Thus far, umbilical cord blood stem cells have been used for stem cell

transplantation to reconstitute blood cell formation in patients that have been exposed to radiation, or given drugs for cancer or leukemia. Also, in some genetic diseases, a transplantation of umbilical cord blood cells can give them a new system that can form healthy blood cells (Frequently, 2004). These therapies will be described in more detail in Chapter 2.

Other types of stem cells found in bone marrow include endothelial stem cells and mesenchymal stem cells. Endothelial stem cells form the vascular system. Most, if not all, epithelial tissues contain stem cells. They are the primary mechanism for normal tissue renewal and for regeneration following damage (Slack, 2000). Mesenchymal stem cells form bone, muscle, fat, and cartilage (Glossary, 2004). Mesenchymal stem cells are also involved with repair in bone and cartilage. Once these cells divide, their progeny become committed to one function that is characteristic of a specific tissue type (e.g. cartilage) (Caplan, 1991).

Another type of adult stem cell is the neural stem cell; these can grow from adult brain tissue in culture media (Frequently, 2004) (Figure 2). Neural stem cells not only exist in a developing mammal, but they have also been found in the central nervous system of all developed mammalian organisms, including human beings (Gage, 2000). “The term ‘neural stem cell’ is used loosely to describe cells that (i) can generate neural tissue or are derived from the nervous system, (ii) have some capacity for self-renewal, and (iii) can give rise to cells other than themselves through asymmetric cell division” (Gage, 2000). Research by Clas Johansson has shown that new neurons are being continuously generated in specific areas of the adult nervous system. These neurons have been shown to be created by multipotent stem cells (Johansson et al, 1999). Some

research involving rats that had spinal cord injuries were shown to have increased ependymal cell proliferation. Ependymal cells give rise to cells that proliferate rapidly, they also generate neurons. This data lead the researchers to believe that these ependymal cells were in fact neural stem cells and are involved in the process of repairing central nervous system injuries (Johansson et al, 1999).

Potential Stem Cells with Neural Capability

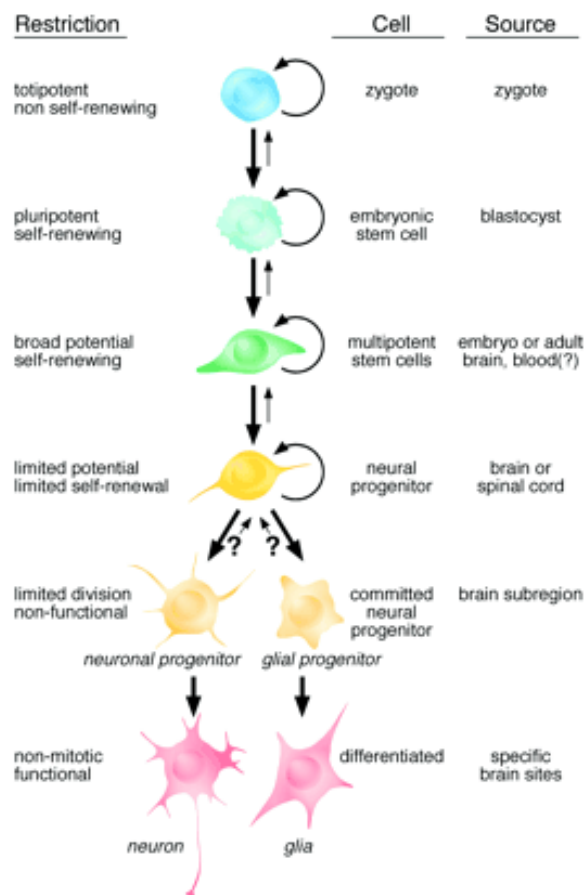


Figure-2: Possible Neural Stem Cells (Gage, 2000)

In the adult brain, the generation of new neurons, neurogenesis, occurs in just two regions (Bjorklund and Lindvall, 2000). These findings suggest the possibility that the brain has a latent capacity for self repair, however it is severely limited (Bjorklund and Lindvall, 2000). What is believed to perform these repairs is a type of neuronal stem cell.

This stem cell located in the central nervous system is limited in its mobility and accessibility, however it has been found to initiate and perform repairs (Johansson et al, 1999). If we were able to isolate and maintain a cell line of these neuronal stem cells, many degenerative brain diseases could be stopped and perhaps reversed. For example, the neurons required to treat Parkinson's disease can be obtained from the fetal brain (McKay 2000).

“James Thomson and Thomas Okarma suggested that human ES cells will someday provide a potentially unlimited source of cells, differentiated in vitro, for transplantation therapies involving the liver, nervous system, and pancreas. Irving Weissman alluded to the possible use of ESCs to enhance the success of whole-organ transplantation. If HSCs derived from human ESCs could be successfully transplanted into the blood system of a transplant recipient (by using immunosuppressive drugs), any further implant tissue (say kidney or pancreas) developed with the same ESCs would not, in theory, be rejected by the recipient because the immune cells produced in the recipient's blood by the HSCs would see the implant tissue as ‘self’” (Stem Cells, 2002).

Another example of adult stem cells are renal stem cells (stem cells from the kidney). These are an exciting topic for those working on adult stem cells due to their potential for treating a variety of kidney disorders; however, we are still not completely sure if they exist (Watorek and Klinger, 2006). There is however significant amounts of data that points to their existence and their possible use in kidney failure, renal diseases and cancer of the kidney (Watorek and Klinger, 2006). To determine if renal stem cells could generate the cell types found in the kidney, researchers examined the “differentiation potential of metanephric mesenchymal cells isolated on the first day of kidney development” (Oliver et al, 2002). The cells were examined and found to be “kidney-specific mesenchymal cells” (Oliver et al, 2002). They also found that the cells could indeed differentiate into the specific cell lines found in the kidney, suggesting that these stem cells were specific to the kidney organ (Oliver et al, 2002).

Research in the field of adult stem cells has given us much insight into what could be done with these cell lines, such as controlling and protecting vital organs from inflammatory and destructive autoimmune reactions (van Laar and Tyndall, 2006), treatment of cancers (Weiss, 2005), and their possible use in the treatment of several other debilitating disorders (Figure-3).



Figure-3: What are adult stem cells (Weiss, 2005)

The problem with all adult stem cells is that they are limited in their usage. They have already transformed into a specific type of cell, and are only found in one or very few areas and thus could not be used to create any type of cell (Frequently, 2004). However, embryonic stem (ES) cells do not have this disadvantage. ES cells are pluripotent and therefore have the ability to become any cell type, making ES cells a primary target for medical research.

ES cells, in some ways, are different from adult stem cells. Their origin is different and their potential use in medicine is much greater. The embryonic stem cell's ability to develop into almost any type of cell is the primary reason why it is of great interest to scientists. Scientists hope to be able to make cell lines of all types, including: bone marrow, nerve cells, heart muscle, organ tissue, and many other types in the hope of curing diseases and increasing life expectancy (Figures-4 and 5).

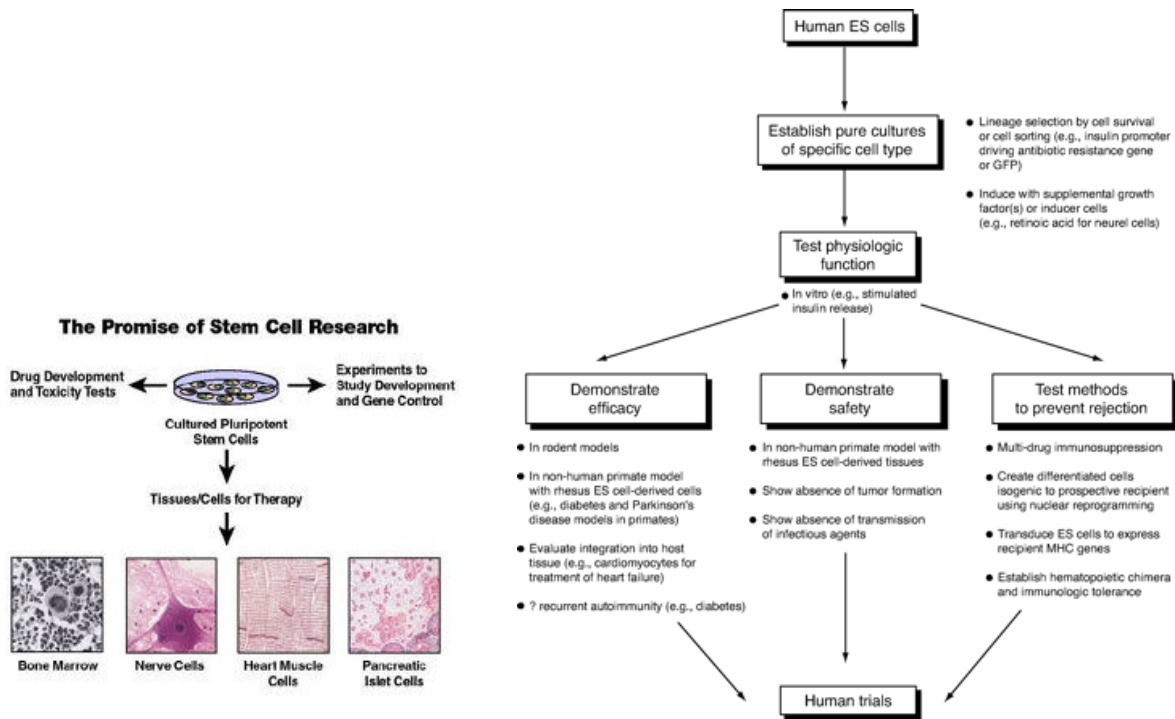


Figure-4: Stem Cell Potential (SoRelle, 2004).

Figure-5: Ideal progression of stem cell therapy (Odorico et al., 2001).

The problem with ES cells lies with having to terminate a potential human life in order to obtain the cells. Most ES cells are extracted from embryos created by *in vitro* fertilization (IVF); in vitro fertilization is the “fertilization of an egg in a laboratory dish or test tube” (In Vitro Fertilization, 2006). After the zygote is created, it progresses

through several cell divisions until it becomes a blastocyst which takes five days (Figure-6).

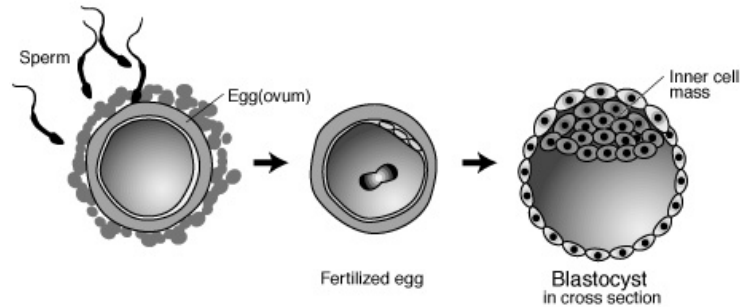


Figure-6: Development of a Blastocyst (The Amazing Beauty, 2006).

At 5 days, the embryo consists of an inner cell mass (ES cells) and the outer cell mass. Extracting the inner cell mass from the embryo destroys it. Usually during IVF procedures, excess embryos are created. If they are not used by the parents, with their signed consent they can be donated for research purposes (Weiss, 2005). Many scientists see the possibility for the usage of ES cell lines in regenerative treatments for organ transplants.

Stem cell research isn't all hype however. Scientists are making progress in the field of embryonic stem cell research. Typically the process of producing a stem cell line looks like the following (Figure-7).

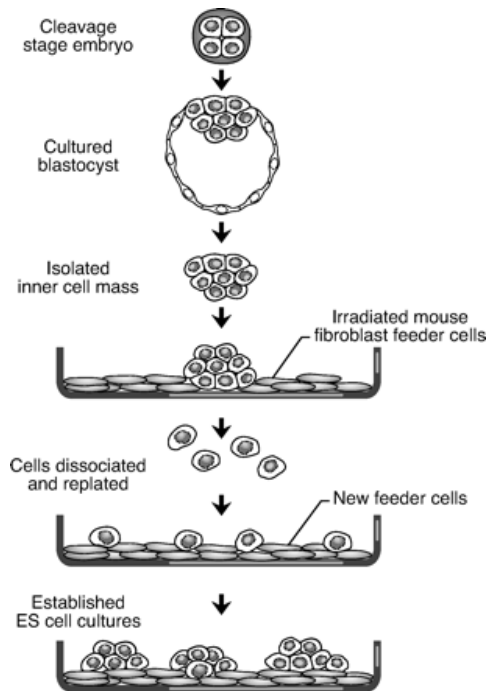


Figure-7: Stem Cell Line Production (Odorico et al, 2001).

The isolated inner cell mass cells are plated on a feeder layer (typically irradiated mouse fibroblast cells) that provides growth factors to feed the ES cells. More recently, protocols have been developed for growing ES cells on human feeder lines to prevent contamination of animal (mouse) proteins with the human lines. Once the ES cell cultures are established research can commence. The cells in this state are still undifferentiated, meaning that they are still capable of becoming any cell type in the human body. Scientists are still unsure about how to force the ES cells into becoming certain types of target cells (i.e. heart muscle), however that is one of the primary research areas (Odorico et al, 2001).

Unfortunately there is a lot of resistance to ES research. Most of it ethical, either from personal moral views or from religious stand points. Many people see the donating of these embryos to science as terminating a possible human life. However, is this

embryo which is smaller than the period at the end of this sentence and which contains no heart beat, no nervous system, no brain, a life? Advocates of stem cell research point out that IVF clinics worldwide are “bulging with thousands of unwanted embryos” that would be slated for disposal via autoclaving (Weiss 2005). So if the cells are going to be destroyed anyway, why not use them for science that could help save lives? This topic will be discussed in more detail in Chapter 3.

Parthenotes

Part of the resistance to stem cell research is due to misunderstanding. Despite all the facts released to the public, misconceptions are still very frequent. One of the largest misconceptions is that *all* stem cell research destroys embryos. This is untrue, only ES cell research destroys embryos. Luckily, there is an ethical solution to this exact problem that has already been experimented with. “Using chemicals that mimic a sperm's arrival, scientists in recent years have triggered parthenogenesis...” (Weiss 2001).

Parthenogenesis is the process in which an egg develops into an embryo without the fertilization of the sperm (Cibelli et al, 2002). ES cell lines have been established from monkey parthenote embryos (Cibelli et al, 2002) and murine parthenote embryos.

Although human parthenote embryos were created in 2001 (Cibelli et al, 2001) ES cell lines were not established at that time. Very recently, human ES cell lines have been created by Tiziana Brevini and Fulvio Gandolfi at the University of Milan. They used 104 eggs donated by women at fertility clinics (Marchant, 2006). Brevini and Gandolfi were able to create two separate ES cell lines, which is a huge step forward in human parthenotes and stem cell research.

In the monkey parthenote research by Jose Cibelli, four out of 28 eggs (14%) developed to the blastocyst stage which is the necessary stage to retrieve the stem cells. The stem cells were removed from the inner cell mass and plated. After 1 week cell proliferation was noted in three of the inner cell mass cell lines, and a stable cell lines called “Cyno-1” was developed. Although only 14% of the eggs developed long enough to reach the desired stage of development, the possibility of using parthenotes in exchange for embryonic stem cells was shown to be viable (Cibelli et al, 2002).

These parthenotes always die before they can be implanted in the womb, but live long enough to be able to extract the inner cell mass which contains the embryonic stem cells. “Those cells [stem cells obtained from the parthenotes] turned into intestine, skeletal muscle, retina, hair follicles, cartilage, bone and other cell types -- even heart cells beating in unison. Some turned into nerve cells that secreted the brain chemical dopamine, the kind of cell that is gradually lost by Parkinson's patients. The idea ... is to grow replacement cells and tissues from a female patient's own eggs so they are genetically so similar to the woman that they won't be rejected by her immune system” (Weiss 2001). Since the parthenotes can not live long enough to be born there are fewer ethical concerns because it can never become a human being (Marchant, 2006). Human eggs are still destroyed in the process however. So perhaps parthenote embryos can serve as an alternative source for ES cells until we can develop other procedures.

Despite the advances and prospect of the research, many people still object to parthenote research, some even more so than embryonic stem cells. "The same people who were up in arms about doing research on embryos were up in arms about research on Parthenotes ... They correlated this with virgin birth. They correlated it with Christ"

(Weiss 2001). Since the word parthenogenesis is translated to “virgin birth” from Greek, many Christian religions are even more upset about parthenote research than stem cell research because they see a parthenote as being born virgin, just like Christ.

Despite the political, moral and scientific battles that are being waged over the issue of stem cells, research is continuing and progress is being made. We have already talked about many instances in which stem cells save lives or show great signs of promise. Results like these will be discussed in Chapter-2, and continue to produce optimism for the advocates of stem cell research. The hope that stem cells will save many more lives may soon be realized.

CHAPTER-2: STEM CELL APPLICATIONS

Stem cell research has opened the door to an entirely new realm of medical research. Although we have only begun to understand the mechanism in which stem cells work, much progress has been made in the field. However, as we learned in Chapter 1, not all stem cells are alike and therefore each stem cell type has a different potential for research. It is important to distinguish between those types to get a better understanding of what is in the distant future. In addition, much misinformation has been published on stem cell successes, making it difficult to distinguish fact from hype. In this chapter, exploring what has been done, what can be done, and perhaps most importantly distinguishing fact from fiction will allow everyone to understand more about stem cell research and allow the general public to obtain a clearer and more objective view on this topic.

Adult HSC Treatments

One of the largest misconceptions is that stem cells have not saved a single life. This is untrue; people forget that bone marrow and umbilical cord blood transplantations have been saving lives for decades (Verfaillie, 2002). More than 70 diseases and disabilities are treatable with adult hematopoietic stem cells (HSCs) (discussed in chapter 1), such as breast cancer, leukemia, and sickle cell anemia (Earll, 2005). Stories from patients receiving these HSC treatments have given hope to researchers searching more ways to use stem cells in medical research. For instance, 16 year-old Nathan Salley is alive today because of stem cells transplanted from an umbilical cord. Nathan suffered

from Acute Myloid Leukemia, an often fatal childhood form of Leukemia (Earll, 2005); such blood-based diseases are the type HSC treatments are best designed to treat.

Many other lives have been improved through adult HSC stem cells. “Thirty-six-year old Susan Stross is one of more than 20 MS patients whose conditions have remained steady or improved after receiving an adult HSC stem cell transplant. The same results are reported with several hundred patients worldwide” (High, 2001).

Umbilical Cord Blood HSCs

Umbilical cord blood is an excellent source of HSCs, no anesthesia has to be delivered as with bone marrow-derived HSCs, and the cells are less likely to be rejected by the patient (Viacell, 2006). Obtaining bone marrow includes putting the donor under anesthesia, injecting a syringe in a bone (typically the hip) and removing some of the bone marrow cells. The cells are then injected into the patient whose own HSCs have been destroyed by irradiation (or by chemotherapy for killing off the cancerous HSCs). The injected HSCs progress through the bloodstream and are able to recolonize the patient’s bone marrow, and produce more healthy blood cells that the patient lacked before. The idea is to replace defective or non-existent blood cells with new progenitor cells that can produce healthy blood cells to replace the deficient ones (Hematopoietic Stem Cells, 2005). Since an umbilical cord blood can easily be removed at birth (and is normally discarded), there is no need for a donor as long as the parents of the child decide to store the blood from the umbilical cord with a clinic that offers such a program. The collection of the umbilical cord blood is simple and painless; it also has more primitive HSCs than bone marrow, making it more likely the donor will accept the transfused

blood. The New York Blood Center's Placental Blood Program, which is supported by the National Institutes of Health is the largest umbilical cord blood bank in the United States, and has over 13,000 donations available to those who need it (Hematopoietic Stem Cells, 2005). In fact, umbilical cord blood HSC transplantations have become so successful, scientists are looking at them as an alternative to bone marrow transplantation (Gluckman, 2000). The storing of umbilical cord blood for years until needed can seem expensive, however after factoring in the difficulty in finding a compatible donor for a bone marrow transplant, it can be a very wise choice, perhaps even life saving.

HSCs for Treating Heart Disease

Promising (but not proven) applications have also been obtained using HSCs in the treatment of heart disease. "Sixteen-year-old Dimitri Bonville had been accidentally shot in the heart with a nail gun while doing home repair, undergone open-heart surgery and suffered a massive heart attack, when doctors told his parents he needed a heart transplant" (Philipkoski, 2003). The doctors mentioned an alternative to a heart transplant; it had never been done before and was extremely new but showed promise. The doctors offered to perform an experimental stem-cell therapy that would inject Dimitri's own HSCs directly into his heart. The theory was that the stem cells ability to differentiate into any cell type would allow the stem cells to differentiate into the heart cells that were destroyed. As the doctors described,

"The teenager's therapy began Feb. 17 with a four-day regimen of a drug that stimulated the production of stem cells in his blood. On Feb. 21, doctors harvested Bonville's stem cells. Using a heart catheter, they transplanted the stem cells into the artery that supplies blood to the front of the heart. He was discharged about a week later and is now recuperating at home. His doctors say they have never seen a recovery like his (Philipkoski, 2003)."

The treatment worked perfectly, Dimitri's stem cell therapy had saved him from having to obtain a heart transplant, and perhaps it even saved his life entirely.

Treatments such as this show that injecting specific adult stem cells into the damaged area is sometimes enough to instigate repair of the damaged area. Research like this is becoming an important point for those against ES cell therapies, stating that ES cells would be totally unnecessary if sufficient adult stem cell types can be discovered. They also state that many lives have already been saved by adult stem cells, but that very few lives have been affected by ES cell research (Philipkoski, 2003).

Adult Neuronal Stem Cell Applications

Umbilical cord blood and bone marrow aren't the only adult stem cell treatments to show promise. Significant advances with adult neural stem cells have also been achieved. Michel Lévesque is a physician, neuroscientist, and neurosurgeon based at Cedars-Sinai Medical Center in Los Angeles. He is also an Associate Clinical Professor of Neurosurgery at the UCLA School of Medicine, and member of the UCLA Brain Research Institute, the founder of NeuroGeneration, a biotechnology company pioneering autologous neural stem cell therapies, and Chairman of the Foundation for Neural Repair, a not-for-profit foundation, and sponsoring translational research to accelerate human trials using neural stem cells. Dr. Lévesque testified to the Senate Committee on Science on the current usage and research of adult neural stem cells, as well as current and future research. He stated that, "Since 1996, our laboratories have been involved with the isolation and characterization of human adult-derived neural stem cells, obtained from patients undergoing neurosurgical procedures. In the adult brain, these cells cannot on

their own trigger repair responses. However, if placed in experimental laboratory conditions stimulating certain genes, these neural stem cells can be “awakened” and begin to divide and replicate events of normal development” (Levesque, 2005). If neural stem cells could be coaxed into triggering a repair response, many degenerative brain diseases could potentially be cured by the neural stem cells in brain. This is entirely possible because the human brain has the capacity to repair itself, but for some reason it lacks the means to activate the proper cells to do so. Dr. Levesque has found a way to activate these adult neuronal stem cells into “turning themselves on” which could possibly lead to several treatments of brain disorders. Levesque went on to say, “These newly created neural stem cells can grow for several months in laboratory conditions reaching several millions in number, a process called cell expansion. Their ability to self-replicate and form all types of cells found in the central nervous system can be verified *in vitro* under controlled conditions. They can be placed in storage or maintained in sterile incubators until ready for use” (Levesque, 2005). These new cells have been able to correct deficits in rat models of human Parkinson’s disease (Björklund et al, 2002). The studies showed that, “human adult neural stem cells do not divide once differentiated, do not form aberrant tissue or tumors after chronic transplantation, and have normal karyotypes (number of chromosomes)” (Levesque, 2005).

Adult neuronal stem cell use is very promising for the treatment of degenerative diseases just like Parkinson’s in rat models, but the big question is can it be used to treat diseases in humans? The answer is yes; “... [Dr. Lévesque] transplanted a patient with advanced Parkinson’s disease with differentiated neurons derived from an initial needle biopsy. At three years post-operatively, the overall Unified Parkinson’s Disease Rating

Scale (UPDRS) improved by 81% while ‘on’ additional medication, and 83% while ‘off’ medication. We demonstrated here the long-term clinical remission of Parkinson’s disease symptoms in a single patient” (The Testimony, 2004).

Results like the ones Dr. Levesque obtained in his study are very promising for the treatment of degenerative brain diseases, as well as other non-neuronal diseases if the neuronal stem cells can be coached to trans-differentiate into other kinds of tissues. Dr. Levesque believes that, “The current debate between the ES cell proponents and those who are opposed to their use distracts from other avenues with promising outcome, such as adult stem cell therapy,” (Levesque, 2005). But he does believe in the potential of all stem cell research, including ES cells (Levesque, 2005). The aforementioned research is about to enter Phase II clinical trials with the Food and Drug Administration.

ES Cell Therapy

Although adult stem cells have the ability to differentiate into one or several cell types, and have fewer ethical concerns than embryonic stem (ES) cells, they don’t have the ability to differentiate into all cell types, and that is where ES cells get their “power”. Scientists hope to be able to control ES cells in hopes of harnessing their pluripotency ability.

“Stem cells have been widely touted as eventual cures for neurodegenerative diseases such as ALS and Parkinson's. The conventional wisdom is that they would be grown to produce the particular nerve cells that are lost in each disease, which would then be grafted into the nervous system to repair it. But researchers currently understand little about the signals that make stem cells differentiate into particular cell types, nor are they sure how to get grafted cells to integrate effectively into tissues and organs (Zandonella, 2005).”

Research involving animal models for ES cell therapies has shown promising results, and has brought the potential use of ES cells in humans even closer to a reality.

At the Washington University School of Medicine, scientists transplanted differentiated mouse ES cells in a rat nine days after a spinal cord injury. Two to five weeks later, the rat was examined via histological analysis and the results showed that the ES cells transplanted into the animal not only survived but differentiated in astrocytes, oligodendrocytes, and neurons. Also, further analysis showed that only the rats that were treated with the ES cells showed hind limb and weight support while the other rats who were also afflicted with the same injury, did not (McDonald, 1999). Other animal models using ES cells have also shown potential. Scientists injected mouse ES cells into rat models of Parkinson's disease. The ES cells that were injected differentiated into dopamine producing neurons which are in severely low numbers in Parkinson's patients. The results encourage the use of ES cells in cell-replacement therapy for Parkinson's disease (Kim, 2002).

The pluripotency of ES cells makes them difficult to work with however. Since ES cells can differentiate into any cell type, controlling them can be a challenge. Neuroscientist Clive Svendsen said that, “‘You have to learn to control that power in the dish’ before thinking about putting the cells into patients ... For that reason, most groups say they are at least five or, more likely, 10 years away from ES cell clinical trials” (Vogel, 2005). A company by the name of Geron (Figure 8) is attempting to significantly shorten that timeline. It hopes to put therapies using ES cells into clinical trials as early as possible (Geron, 2004). It is currently talking with the FDA to set up guidelines for the therapies. But even advocates of ES cell research are skeptical about this. They don't want an already unstable and controversial field to have a failed clinical trial and lose the little support they have now.

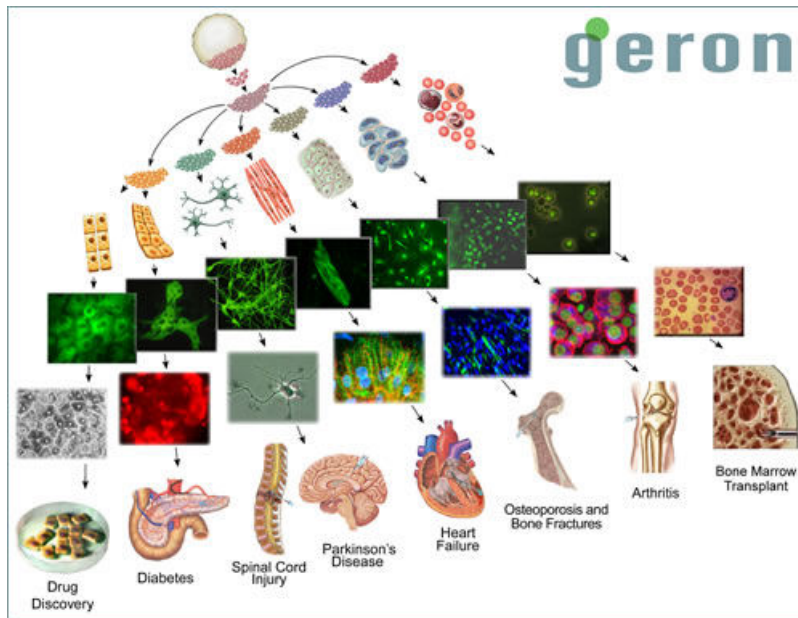


Figure-8: Geron's Possible Treatments Using ES Cells (Geron, 2004)

Geron is pushing ahead ever hopeful that their treatment to treat spinal cord injuries will be a complete success (Vogel, 2005). Geron has “developed a protocol that encourages hES cells to differentiate into cells called oligodendrocyte precursors. These cells can form oligodendrocytes, the cells that, among other functions, produce the protective myelin sheath that allows neurons to send signals along their axons. This sheath is often lost during spinal cord injuries” (Vogel, 2005). Geron's treatment as previously described, would involve directly injecting human ES cells into a damaged spinal cord, the stem cells would then differentiate into the proper cell lines necessary to repair and maintain a healthy spinal cord. Geron's research showed tremendous results in their animal models tested last year. Geron reported that,

“For newly injured rats, the results are promising. In animals that received oligodendrocyte precursors 7 days after their injury, the cells survived and apparently helped repair the spinal cord's myelin. Within 2 weeks, treated rats scored significantly better on standardized movement tests than control animals, which had received human fibroblasts or a cell-free injection. But when the researchers injected cells 10 months after the injury, they saw no effect--sobering news for people like Langevin suffering from old injuries. The cells survived but were apparently unable to repair the long-term

damage. For that reason, Keirstead says, Geron's proposed clinical trial would target newly injured patients” (Vogel, 2005).

Providing this treatment safely will be a challenge however. In some of the earlier trials, ES derived cells would sometimes differentiate into the wrong cell type, or would sometimes migrate away from the injection site. “In its spinal cord trial, Geron plans to inject ES-derived cells that can form just a single cell type, an approach that may circumvent some of these problems. For a full recovery, patients are likely to need new neurons as well as other support cells called astrocytes, but using precursors that differentiate into all three types of nerve cells can be problematic” (Vogel, 2005).

Another and very serious problem may be the accidental creation of tumors.

“One of the defining characteristics of ES cells is that they form disorganized tumors, called teratomas, when injected in undifferentiated form under the skin of immuno-compromised mice. ‘The ES cell is basically a tumor-forming cell,’ says neuroscientist Anders Bjorklund of Lund University in Sweden. ‘This aspect has to be dealt with seriously before the cells are applied in the clinic.’ Even a benign tumor in the central nervous system would be serious, says Svendsen: ‘Any sort of growth in the spinal cord is not good news’” (Vogel, 2005).

Geron scientists have stated that they have several protective measures in place to prevent this from happening in the clinical trials; however they do state that the procedure is still being worked on for improvements. Despite the issues brought up by other scientists such as contamination issues, and avoiding more research being the first company to perform this type of therapy, Geron’s research shows promising results, and they are hopeful that even if their research doesn’t work the first time it will set standards for research in the future so companies that want to start this research won’t have to start from square one (Vogel, 2005).

Stem Cell Applications as Support Therapy

Other researchers believe that stem cells have even more potential than they're currently being used for. Evan Snyder, who works at the Burnham Institute in La Jolla, California stated that, "... cell replacement is an exciting future prospect. But apart from replacing lost cells, he notes that stem cells have other, more subtle roles that could be exploited therapeutically. Snyder has evidence that, in the nervous system, stem cells can act as 'chaperones' that nurse sick and injured neurons back to health" (Zandonella, 2005). Neural stem cells can secrete biochemicals that improved the function of neurons, as well as promote survival, decrease inflammation, and encourage the growth of blood vessels. Research has shown that neural stem cells taken from rats secrete glial cell line-derived neurotrophic factor (GDNF) which protects the cells and aids in the recovery of symptoms from Parkinson's disease. Snyder argues that, "You are not trying to replace the lost cells ... instead, you are trying to protect what is there" (Zandonella, 2005). Using this therapy, researchers plan to take this approach to the FDA in hopes of treating Amyotrophic Lateral Sclerosis (ALS), which is better known as Lou Gehrig's disease (Zandonella, 2005).

Chapter Conclusions

Stem cell research shows great promise in both the adult and embryonic fields. Both areas have medical treatments currently in or on the verge of clinical trials, and they both have great results from animal testing in the labs. Despite the advances and promise of treatments, annual investments have dropped over the past couple years (Glaser, 2004). This is probably due to the constant debate over the ethical and moral status of ES

cells. Unfortunately, sometimes all stem cell research gets incorrectly pulled into the debate of whether embryos should be destroyed for research, when this topic only pertains to ES cell research and not adult stem cells. It is imperative to remember that adult stem cell research and therapies use the person's own stem cells for treatment and don't involve any "killing" of embryos. With stem cell research being on the cusp of making life saving discoveries, it is even more important now than ever to try to understand all sides of the ethical and moral debate (to be discussed in Chapter 3). We need to work together as scientists and as a community to come to a mutual agreement on the status of embryonic and adult stem cell research so that the experts in this field can delve ever deeper into unlocking the mechanisms to control and utilize stem cells to their full potential.

CHAPTER-3: STEM CELL ETHICS

Now that the world has started to have the knowledge, ability and skill to use stem cells, an important question is, should we? In September of 2005 a Gallup poll of 1,002 adults nationwide, as seen in Table-I on the next page, asked people's opinion about the origins of human life, how much this opinion affects their life, and whether their religious and scientific beliefs conflict (CNN, 2005). It shows that 84% of people believe that God had at least some role in the evolution of humans, and 76% of people have thought about the origins of man at least a moderate amount (CNN, 2005). Though this only illustrates the idealism of a monotheistic, or the belief in a singular entity, religion like Christianity or Judaism, this poll shows that the United States could be even more divided on whether humans should interfere with the "natural process of life," especially when 66% of the people polled believe that their theological beliefs about creation mean a great deal or moderate amount to them (CNN, 2005). There are some religions that believe that stem cell usage is murder and that scientists are playing god (Ayon, 2002). What makes this question even more complicated is due to the different types and levels of stem cells, as discussed in Chapter 1 and 2, and how their religious beliefs could conflict with only some or all of the levels of stem cell use. As the poll shows, 35% of people find that their religious and scientific beliefs conflict with each other (CNN, 2005). Almost all religions may be accepting of adult stem cells, but some believe that the use of embryonic stem cells is sacrilegious. As it can be imagined, religious controversy about stem cells is a major obstacle for the continuation of its research. For this reason stem cell ethics is a worthwhile discussion.

"Which of the following statements comes closest to your views on the origin and development of human beings? Human beings have evolved over millions of years from other forms of life and God guided this process. Human beings have evolved over millions of years from other forms of life, but God had no part in this process. OR, God created human beings in their present form exactly the way the Bible describes it." Options rotated					
	Evolved, God Guided %	Evolved, God Had No Part %	Exactly As Bible Describes %	Other (vol.) %	Unsure %
9/8-11/05	31	12	53	1	3
"How much have you, personally, thought about these different explanations for how human beings came to exist on earth: a great deal, a moderate amount, not much, or not at all?"					
	A Great Deal %	A Moderate Amount %	Not Much %	Not At All %	Unsure %
9/8-11/05	41	35	17	6	1
"How much does it matter to you which of those theories is correct: a great deal, a moderate amount, not much, or not at all?"					
	A Great Deal %	A Moderate Amount %	Not Much %	Not At All %	Unsure %
9/8-11/05	40	26	19	14	1
"Which comes closer to your view about the relationship between science and religion? They generally agree with each other. They generally conflict with each other. OR, They are not related to each other in any meaningful way."					
	Generally Agree %	Generally Conflict %	Not Related %	Unsure %	
9/8-11/05	24	35	36	5	

Table I: CNN/USA Today/Gallup Poll. Sept. 8-11, 2005.
N=1,005 adults nationwide. MoE ± 3 (CNN, 2005)

Christianity and Stem Cells

The first religious stance that should be looked at is Christianity. The world's largest religion, they have the most conservative and restrictive views on stem cell research. When speaking about embryonic stem cell research, Archbishop Francis E. George stated that "history has shown that it is always the dispossessed, those whose lives are easily overlooked, who are subjected to the worst abuses of scientific research," and that the "so-called 'spare' human embryos are particularly vulnerable to this kind of moral blindness because so many people seem to have difficulty identifying with their humanity" (US Bishops, 2006). Christians believe that life begins at fertilization, which is when the egg and sperm combine and create a new genotype. Biologically speaking, this is believed to be the beginning of a new human life (Shannon, 2006). Professor

Thomas Shannon goes on to explain that “together with this affirmation is the correlative presumption that this is the time of the infusion of the soul. Although there is no official doctrine on this position, the attitude of the Church is that moral priority should be given to this position” (Shannon, 2006). The Church believes that no matter how insignificant in size it may be, it is still life says Bishop Donald Wuerl, " while (a stem cell) is a tiny speck, it nonetheless contains the elements out of which comes the fully developed human person" (US Bishops, 2006).

Pope John Paul’s II address to the diplomatic corps on January 10, 2005 seems to exemplify the catholic position:

“Conflicting views have been put forward regarding abortion, assisted procreation, the use of human embryonic stem cells for scientific research, and cloning. The Church's position, supported by reason and science, is clear: the human embryo is a subject identical to the human being which will be born at the term of its development. Consequently whatever violates the integrity and the dignity of the embryo is ethically inadmissible. Similarly, any form of scientific research which treats the embryo merely as a laboratory specimen is unworthy of man.” (Pope, 2005)

The Pope goes on to explain that the “Scientific research in the field of genetics needs to be encouraged and promoted, but, like every other human activity, it can never be exempt from moral imperatives; research using adult stem cells, moreover, offers the promise of considerable success” (Pope, 2005).

With this being said, there are a few within the Christian and Catholic Church that support embryonic stem cell research, arguing that the embryo is the potential for life but does not yet have the moral status of a born child. This stance argues embryos should not be bought or sold (Farley, 2000), but can be used to save lives. Doctor Ronald Cole-Turner of the Pittsburg Theological Seminary and a member of the Protestant denomination, the United Church of Christ, explains that the majority of the members believe “that embryos have an important but less status” (Cole-Turner, 2000). The

General Synod, the church-wide counseling body which is the voice of the church on particular issues, released a statement that the “human pre-embryo” should be treated with the utmost respect but that it has only the “potential to develop into full human personhood” and thus supports “human pre-embryo research, including research that produces and studies cloned human pre-embryos through the 14th day of fetal development.” Human blastocysts from which ES cells are obtained are usually day-5. The only limitations were that the embryos are treated respectfully, they are not implanted, and that there is public discussion of current and future research (Cole-Turner, 2000). Thus, the Christian faith seems to be divided slightly on their views about embryonic stem cell research, but the majority believes it to be immoral. They only all support the usage of adult stem cells as a community.

Judaism and Stem Cells

A more liberal ethical stand on stem cell research is that of Judaism. A main theological certainty is that they accept “both natural and artificial means for overcoming illness” and that doctors are both “the agents and partners of God in the ongoing act of healing” (Dorff, 2000). It is Jewish belief that they “have a duty to God to develop and use any therapies that can aid us in taking care of our bodies, which ultimately belong to God” (Dorff, 2000). The second major controversy about stem cell research is when life begins. Rabbi Yehiel Ben Ayon confirmed that “Judaism teaches that life begins at birth; hence the possibility to kill life can only begin at the same time as that life begins (Ayon, 2002). In Judaism, an unborn child is not life but the potential of life. Certainly an unborn child may not be aborted, but to do so is not killing. It is wrong. It is forbidden,

but it is not killing.” (Ayon, 2002). Dr. Rabbi Elliot N. Dorff, of the University of Judaism, explains that “Genetic materials outside the uterus have no legal status in Jewish law, for they are not even a part of a human being until implanted in a woman’s womb, and even then, during the first 40 days of gestation, their status is ‘as if they were simply water’” (Dorff, 2000). Therefore, Jewish law and religious beliefs allow for embryonic stem cell research. They also believe that the use of adult stems “is always accepted and even welcomed” (Ayon, 2002). Rabbi Yehiel Ben Ayon continues that “Judaism does not see the artificial growth of human cells on a laboratory dish as a human life” and that “it is routine in medicine today to grow human skin for use in skin grafts. Growing stem cells should then be seen in the same light” (Ayon, 2002). These quotes show that followers of Judaism believe that embryonic and adult stem cell research is moral and should be encouraged as long as it is done for the common good.

Buddhism and Stem Cells

Buddhism is quite unlike the religions already spoken about because of one main fact; Buddhism is polytheistic, meaning that they believe in many gods. Christianity and Judaism are monotheistic where they believe in one godly creator. Buddhism does not believe in a “divine creator, whose plan might be distorted by human tinkering with nature” (Frazzetto, 2004). They follow the teachings of the Buddha Śākyamuni. Buddhist ethics are not followed because it is law instead the Buddhist philosophy that is “designed as expressions of indisputable human rights or as a consequence of dignity inherent in every human being. Ethics are much more a matter of personal choice; principles like the one of ‘non-harming’ should be followed as guidelines” (Schlieter,

2004). Therefore, there are many interpretations of when life begins and what the consequences are to your karma. Karma is believed to be a sum of all of your actions in your current, past and future lives. Therefore, how you act in one life will affect your reincarnation, or rebirth.

Damien Keown, who is known as an expert on Buddhist biomedical issues explains that “Buddhism teaches that life may come into being in a variety of ways, of which sexual reproduction is but one, so sexual reproduction has no divinely sanctioned priority over other modes of procreation” (Frazzetto, 2004). Buddhist teachings about embryology assume “that the transmigration of consciousness is sudden rather than gradual” (Hughes and Keown, 1995). However, an article by James Hughes, from the MacLean Center for Clinical Medical Ethics and by Damien Keown, of the University of London, explains that there are a variety of views of when Buddhist believe ensoulment occurs:

“Based on the findings of modern neuro-embryology Buddhists today might maintain that the fetus does not fully embody all five *skandhas* and the illusion of personhood until after birth; this is the argument developed by most Western ethicists to defend abortion. If the fetus is not yet a fully embodied person, then the karmic consequences of abortion would be even less than the killing of animals, which Buddhism teaches do have moral status. This neurological interpretation of the *skandhas* may be more consistent with Western Buddhism, which often sees the doctrine of rebirth as peripheral or interprets rebirth metaphorically rather than literally” (Hughes and Keown, 1995).

Consequently, the actual definition of when life begins is not an exact time. Therefore there are two main interpretations about this in Buddhist teachings. A small segment of Buddhists believes that incarnation or conception “does not occur until as late as the seventh month.” Though there is another larger segment that believes the “transmigration of consciousness occurs at conception, and therefore that all abortion incurs the karmic burden of killing” (Hughes and Keown, 1995). Though abortion occurs later in the development of the fetus, it could be inferred that this segment of the

Buddhist would believe that stem cell research would have the same moral effects as abortion because the status of the fetus is the same at any point of its development. Though this might seem a reasonable rationale, it is still not so clear what Buddhism's view on stem cells is. Buddhism "encourages placing a strong value on respecting every living being, which includes fertilized embryos that are used for, or originate in, research activities" (Frazzetto, 2004). Though, Yong Moon, a gynecologist at the University of Seoul and the lead author of the South Korean cloning paper, explains that "cloning is a different way of thinking about the recycling of life. It's a Buddhist way of thinking" (Frazzetto, 2004). This goes to show that stem cell research and usage would be just the continuation of life in a different way and thus would be supported. Alternatively, Keown disagreed with Moons' comments because "therapeutic cloning involves experimentation on immature human beings, it might be thought clearly contrary to Buddhist ethics" (Frazzetto, 2004). This illustrates that there really is no one Buddhist opinion about embryonic stem cell research. Conversely, adult cell research is approved by the Buddhist community explains Robert Hood, a practicing Buddhist and an editor of the Journal of Buddhist Ethics (Holmes, 2004).

Islam and Stem Cells

Similar to that of Buddhism, Islamic beliefs are based on textual information, mainly the Qur'an, without a major religious institution to guide the opinions of the followers. Instead the Shari'ah, or the religious law of Muslims, is open to interpretation (Sachedina, 2000; Frazzetto, 2004). There are two schools of thought, the Sunni and the Shi'ite. The Sunni make up the majority of the Islamic followers and interpret the text in

a more traditional way than the Shi`ite (Sachedina, 2000). Both sects do believe that they have an obligation serve society by using the knowledge that was given by God to help the common good (Frazzetto, 2004). There many ideas about when the embryo reaches the moral status. A majority of Muslims believe that ensoulment occurs 120 days after conception (Frazzetto, 2004). The Shari'ah go further to make “a distinction between actual and potential life, determining that the former should be afforded more protection than the latter. Under most interpretations, the embryo is therefore not considered to be a person, and using it to create stem-cell lines would not violate Islamic law” (Frazzetto, 2004). Hassan Hathout, of the Islamic Organization for Medical Sciences in Kuwait, is quoted by Bill Broadway saying that “Islam opposes creating embryos with the intention of using them for research” (Broadway, 2001). However, Dr. Abdulaziz Sachedina of the University of Virginia explains that “it is correct to suggest that a majority of the Sunni and Shi`ite jurists will have little problem in endorsing ethically regulated research on the stem cells that promises potential therapeutic value, provided that the expected therapeutic benefits are not simply speculative” (Sachedina, 2000). It would be right to presume that both Islamic sects would support the use of adult stem cells since no life is destroyed in the process of cultivating them.

There is also some Muslim disagreement over who could use the stem cells. This is due to the fact that there is a great emphasis “on inter-human and familial relationships” (Frazzetto, 2004). Giovanni Frazzetto explains that “the preservation of the parent–child lineage is of utmost importance to Muslims, as are the spousal relationships that encourage parental love and concern for their children. Dr. Abdulaziz Sachedina explains further that “[The] Muslim focus of the debate on genetic replication

and embryonic manipulation is concerned with moral issues related to the possibility, through these technologies, of creating incidental relationships between a man and a woman without a spiritual and moral connection between them” (Frazzetto, 2004). Consequently, Islamic law prohibits surrogate parenting and adoption, but would allow “the adoption of human embryos,” when excess embryos exist, for research purposes as long as they are used only by the couple who created them (Frazzetto, 2004).

Parthenote Ethics

A relatively new way to obtain embryonic stem cells is through ‘parthenogenesis.’ This process is also known as ‘virgin birth’ because chromosomes from the female egg are used without any fertilization from the male sperm. “Scientists instead deceive the female egg cell into believing fertilization has taken place. Using the chromosomes already present within the egg cell, cell division and embryonic development begins” (Cloning, 2006). This process is very controversial due to the fact that there is no consensus if this “half-embryo” is considered life. In an article by the Family Research Council it was stated that “scientists...destroy the embryos for their stem cells, discarding human dignity to satisfy scientific curiosity (Cloning, 2006). As it can be seen there is already quite a bit of debate about parthenogenesis. However, because the topic of human embryo parthenogenesis is so recent, thus far there has not been much written from the religions that were previously mentioned. Instead the ethical and moral status of “embryos” created by parthenogenesis will be discussed by the opponents and proponents of the research.

Proponents of parthenotes believe that this process is a way to save fertilized embryos from destruction. Guido de Wert and Christine Mummery continue to explain that:

“As the parthenote undergoes the first divisions normally and is at these stages not distinguishable from embryos derived by normal fertilization, we would argue that it should be regarded as a non-viable embryo. In the light of its non-viability, the potentiality argument is not applicable. The moral status of parthenotes may therefore be regarded as very low, lower even than that of normal viable embryos at the same stage (see earlier). Thus, although not an ‘embryo-saving alternative’, all other things being equal, parthenogenesis may be regarded as ethically preferable to the generation of viable embryos by fertilization or nuclear transfer (for instrumental use)” (de Wert and Mummery, 2003).

Proponents also believe that parthenotes are not living beings because “the embryo is unable complete gestation due to genetic components absent in the parthenogenesis process” (Cloning, 2006).

However, Dr. William Cheshire retorts that “careful examination of all the medical evidence, however, fails to demonstrate conclusively that the living human parthenote cannot be a human being”, and that labeling a parthenote as “ambiguous humanity” does not justify its exploitation (Cloning, 2006). Opponents believe that “the individual developing parthenogenetically would be genetically distinct from its mother” either by only having half of the mothers genetic code would make it an individual, or that through “normal development...the shuffling of genes will have produced peculiarities in the makeup of the offspring that altogether distinguish it from its mother (Latkovic, 2006). Thus, these embryos would have the same moral status as any human being. Though no successful human parthenote implantation has been attempted, the question as to whether this chemically modified embryo could successfully be implanted and thus be a distinct human being is unknown. The only Catholic religious relationship to parthenogenesis mentioned was that because Christ was believed to be born though a

“virgin birth,” there are many Catholics that believe that embryos created through parthenogenesis have an even greater ethical status than embryos used from IVF clinics (Weiss, 2001).

As seen by the many quotes of prominent religious figures and scholarly writers, the ethical and moral considerations of stem cell use and policy are decidedly complex. There is not only a division of opinion about using embryonic stem cells and parthenotes between religions, but also between the members of the same religion. As Dr. Cheshire explains, “...how society decides to treat the least of human lives is a measure of how it chooses to value vulnerable and impaired human beings in general” (Cloning, 2006). There will never be a national consensus on the ethical or moral status and rights of embryos used in embryonic and adult stem cell research, but it is imperative for the continuation and progress of stem cell research that we understand and respect these beliefs.

CHAPTER-4: STEM CELL LEGISLATIONS

Ever since the successful creation of the first stem cell line by James Thomson in November of 1998, ethical and political turmoil engulfed the world and especially the United States (Weiss, 2005). Now that the ethical controversy over embryonic and adult stem cell use has been discussed, it is understandable how difficult it is for a country or state to decide what their political or legislative regulations should be. As figure-9 illustrates below there are many “varied political climates” (Weiss, 2005). The United Kingdom, China, Korea and Singapore (shown as dark orange with the permissive countries in the figure) have lenient regulations and have provided the most money towards stem cell research, while Germany (shown with the restricted countries in light yellow) has prohibited the research straight out. United States stands in the middle. The United States allows federal funding only on certain stem cell lines but allows the private sector much more freedom (Weiss, 2005).

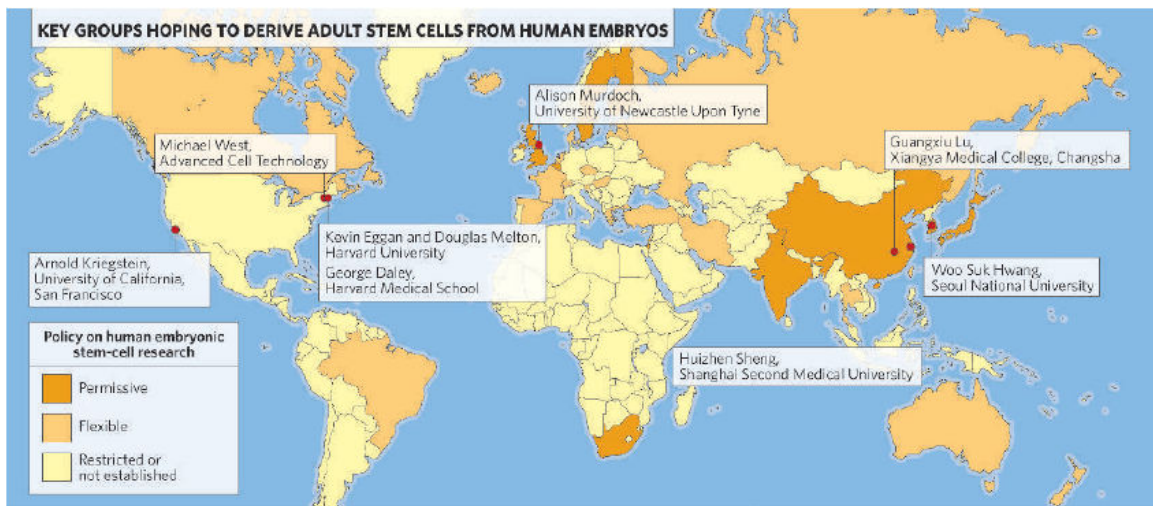


Figure-9: World Stem Cell Map (Check, 2005)

Stem Cell Policies Around the World

One organization that discusses issues of international law is the United Nations General Assembly (UNGA), which is a subset of the United Nations (UN) and is the only section of the UN in which all members are represented (United Nations, 2006). On March 8, 2005 the UNGA “approved a nonbinding resolution urging member states to adopt legislation ‘to prohibit all forms of human cloning in as much as they are incompatible with human dignity and the protection of human life’” (Johnson and Williams, 2006). This announcement led the European Union (EU) to clarify their own regulations and rules to still continue to fund embryonic research (Johnson and Williams, 2006). Other EU nations have gone further to limit the research (Germany), or prohibit the research (Austria, Ireland, or Lithuania), while others have no regulations, Czech Republic or Portugal (Johnson and Williams, 2006). Non-EU countries are just as diverse in their regulations; China, Japan and Columbia being the most liberal, and Ecuador being the most conservative.

From August 9, 2001 to May 23, 2004, 128 human embryonic stem cell lines had been created. A survey conducted by the Boston Globe also found that the majority of these were not created in the United States. Specifically “94 were created in labs outside the United States, and 34 (26%) were created in this country” (Johnson and Williams, 2006). However by July 2005 (Figure-10), 70 ES cell lines had been created in the U.S. constituting 45% of 155 worldwide (Weiss, 2005).

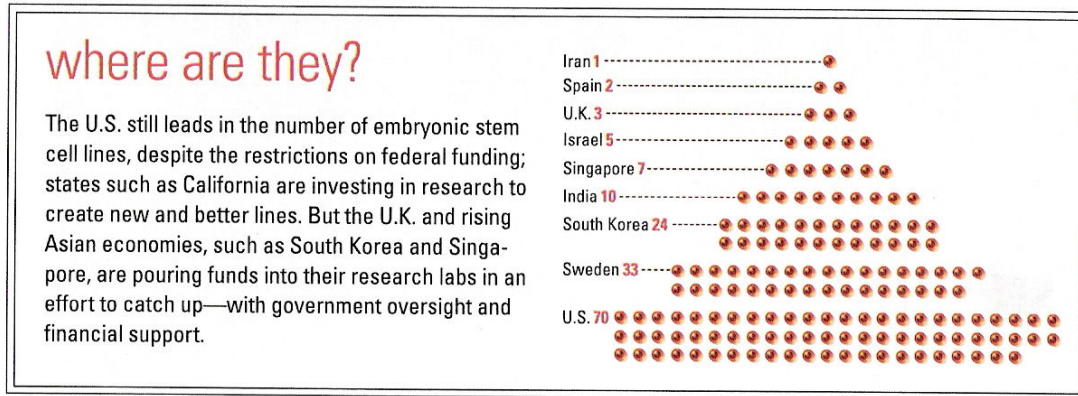


Figure-10: ES Stem Cell Lines as of July 2005 (Weiss, 2005)

Although 9 countries currently have ES cell lines, this does not mean that all countries necessarily have access to them for performing research; many countries have laws that limit or ban the distribution of stem cell lines created in their country. For example, stem cell lines cannot be shipped abroad from the United Kingdom until the UK Stem Cell Bank has processed them (Johnson, 2006). The United Kingdom’s Stem Cell bank is relatively new and was the first of its kind. Glyn Stacey, the director of the bank, explains that it was created by the UK as a way to “apply the same rigorous standards to all cells” (Weiss, 2005). Japan has much stricter regulations on their stem cell lines; they cannot be shipped to any laboratories in other countries (Johnson and Williams, 2006).

Stem Cell Policy in the United States

The United States has struggled with the ethical stand point of funding human embryo work ever “since the advent of *in vitro* fertilization, which produced the first ‘test-tube’ baby in 1978” (Dunn, 2005). The United States began making political and legal distinctions about stem cells in 1997 with the Dickey Amendment. This amendment was introduced by Representative Jay Dickey and made it illegal to use federal funds for embryonic research (Johnson and Williams, 2006). One of the major

political hurdles with stem cell research is should the government pay for it even though there are citizens of the country who may believe it unethical and do not want their tax dollars used for it. This was the reason for the Dickey Amendment.

During the Clinton Administration, when the first human embryonic stem cells were first created, Congress and Clinton reinvestigated the (Johnson and Williams, 2006). In 1993, Congress and President Clinton enacted the National Institutes of Health Revitalization Act which gave the National Institute of Health (NIH) “direct authority to fund human embryo research for the first time” (Dunn, 2005). The first step that the NIH took with this new power was to “establish a panel of scientists, ethicists, public policy experts, and patients' advocates to consider the moral and ethical issues involved, and to determine which types of experiments should be eligible for federal funding” (Dunn, 2005). By 1994, the panel, called the NIH Human Embryo Research Panel, presented their recommendations to the federal government. They came to the conclusion “that the destruction of spare embryos from fertility clinics, with the goal of obtaining stem cells, should receive federal funding” (Dunn, 2005). President Clinton took into consideration all of the NIH’s recommendations but believed that the NIH should “not to allocate funds to experiments that would create new embryos specifically for research” (Dunn, 2005). However, the Congress did not agree with President Clinton. In 1995 the Congress attached the Dickey-Wicker Amendment to the appropriations bill for the Department of Health and Human Services that “banned the use of federal funds for any experiment in which a human embryo is either created or destroyed” (Dunn, 2005).

The next milestone for both the political and scientific community was in 1998. James Thomson, of the University of Wisconsin, “successfully created the first human

embryonic stem cell lines” (Thomson et al., 1998; Dunn, 2005). Harold Varmus, director of the NIH, explained that “this [embryonic stem cell] research has the potential to revolutionize the practice of medicine” (Dunn, 2005). Finally, in 1999, the Dickey-Wicker Amendment which had been limiting all embryonic stem cell research to only private funding was overruled by Harriet Rabb, the head lawyer at the Department of Health and Human Services. Her legal opinion was that human embryonic stem cells “are not a human embryo within the statutory definition,” and therefore the Dickey-Wicker Amendment would not apply to them (Dunn, 2005). This conclusion allowed the NIH to allow federal funding for the research. By 2000 the NIH and the Clinton Administration created strict guidelines about the type of cell that would be given the funding (Dunn, 2005). The NIH guidelines also prohibit:

“(1) research in which human stem cells are utilized to create or contribute to a human embryo; (2) research in which human stem cells are combined with an animal embryo; (3) research in which human stem cells are used for reproductive cloning of a human; (4) research in which human stem cells are *derived* using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg; (5) research *utilizing* human stem cells that were derived using somatic cell nuclear transfer; and (6) research utilizing stem cells that were derived from human embryos created for research purposes, rather than for infertility treatment” (Johnson and Williams, 2006).

The Dickey-Wicker Amendment still applied though to one aspect of the research; no embryos could be destroyed in the process of creating the stem cells (Dunn, 2005).

Unfortunately by 2001, President Bush took over office before any of the grant applications submitted to the NIH for federal funding were approved. The Bush Administration reviewed all the policies that Clinton had created, and asked the NIH to prepare a “scientific review...of the status of the research and its applications” (Johnson and Williams, 2006). The NIH report supported the continuation of both embryonic and adult stem cell research, but did not make any direct recommendations to the Bush

Administration (Johnson and Williams, 2006). On August 9, 2001, Bush went and undid everything that President Clinton had done to expand and encourage embryonic stem cell research when he “announced that federal funding would now be restricted to a limited number of stem cell lines already created by that date” (Dunn, 2005). President Bush explained that his decision “allows us to explore the promise and potential of stem cell research without crossing a fundamental moral line, by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life” (Johnson and Williams, 2006). Under Bush’s regulations federal funds could “only be used for research on existing stem cell lines that were derived (1) with the informed consent of the donors; (2) from excess embryos created solely for reproductive purposes; and (3) without any financial inducements to the donors”, and could “not be used for (1) the derivation or use of stem cell lines derived from newly destroyed embryos; (2) the creation of any human embryos for research purposes; or (3) the cloning of human embryos for any purpose” (Johnson and Williams, 2006). On a positive note, the Bush Administration would support the continuation of stem cells “which do not involve the same moral dilemma,” as in those from umbilical cord blood, placentas, and adult and animal tissues (Johnson and Williams, 2006).

Unfortunately, of the 78 legally approved ES cell lines that are approved for U.S. funding, only 22 are actually suitable for the research (Figure 11).

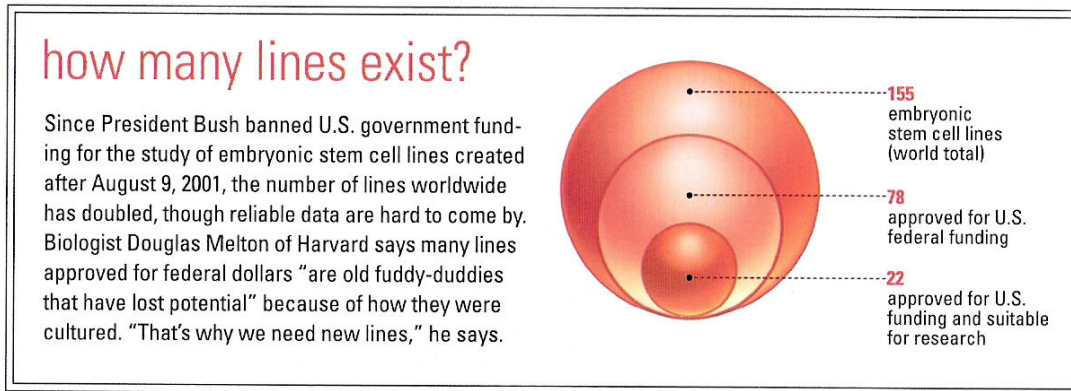


Figure-11: Stem Cell Lines (Weiss, 2005)

Many scientists believe that this restriction on stem cell lines will keep the United States from being at the forefront of the research. As quoted in figure-11, Douglas Melton of Harvard University says that many of the currently approved ES cell lines have lost the potential to differentiate due to poor culture conditions. Stephen Minger is the director of the Stem Cell Biology Laboratory at King’s College in London and feels that “the United States is in real danger of being left behind” because of the “political uncertainties in the United States (Weiss, 2005). Another problem with the Bush policy is the viability of the current stem cell lines that are approved for funding. All of them were developed using new techniques that created lines that are “harder to work with, not well characterized, and genetically unstable” (Johnson and Williams, 2006). For this reason, in 2004, over 200 Members of the House of Representatives wrote a letter to Bush asking him to change his current policy so to make use of the extra embryos created during IVF. Their largest concern was the stem cell line limitation that Bush set would keep the “research from being successful...[as US scientists] move to countries like the United Kingdom, which have more supportive policies” (Johnson and Williams, 2006). The NIH director sent a response that hinted that the research could do better with more stem cell lines, but Bush’s ethical reservations prevent him from loosening the

restrictions (Johnson and Williams, 2006). Some progress was made after the Senate did the same as the House of Representatives'. The NIH would create new centers whose main objective is to find out how stem cells could treat many diseases, as well as create a National Embryonic Stem Cell Bank, similar to that of the UK, that would collect stem cell lines eligible for federal funding. Unfortunately this progress was not progress at all to some. The President of the Coalition for the Advancement of Medical Research explained that "creating a bank to house stem cell lines created before August 2001 does nothing to increase the wholly inadequate supply of stem cell lines for research" (Johnson and Williams, 2006).

Then, on May 20th, 2005 Bush made it quite clear that he would not loosen his embryonic stem cell policy: "I'm a strong supporter of adult stem cell research, of course. But I made it very clear to the Congress that the use of federal money, taxpayers' money, to promote science which destroys life in order to save life is -- I'm against that. And therefore, if the bill does that, I will veto it" (Baker, 2005). By July 19th, 2006 both the House and Senate had passed an embryonic stem cell bill that would lift restrictions on federally funded embryonic stem cell research (Klein, 2006). But on July 20th the inevitable happened; Bush vetoed his first bill during his administration. Bush believed that "if this bill were to become law...American taxpayers would for the first time in our history be compelled to fund the deliberate destruction of human embryos" (Babington, 2006). It is definitely clear that there will be no progress in the expansion of federally supported ES cell research. However, almost 70% of the US population believes that the ethical problems that Bush sees in the research should not hold back the research (Figure-12).

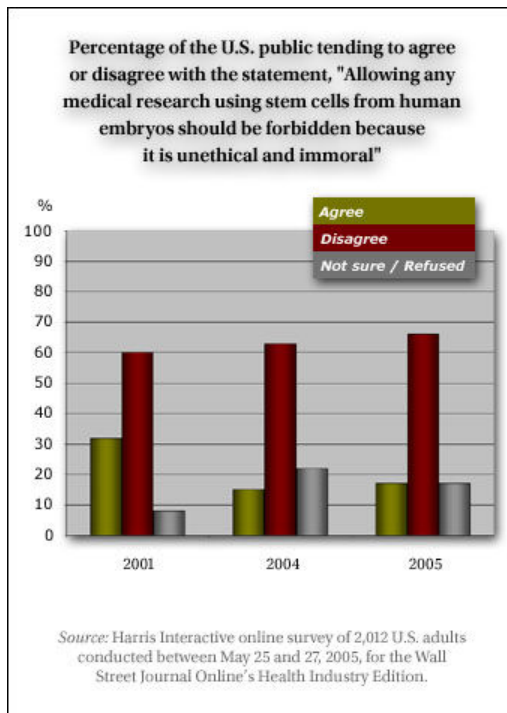


Figure-12: Public Support for Stem Cell Research Grows: Poll (Public, 2005)

State Policies

Luckily state laws are able to sidestep both Bush's regulations and the Dickey Amendment and help fund ES research with their own money. State policy is just as varied as countries around the world (Figure-13).

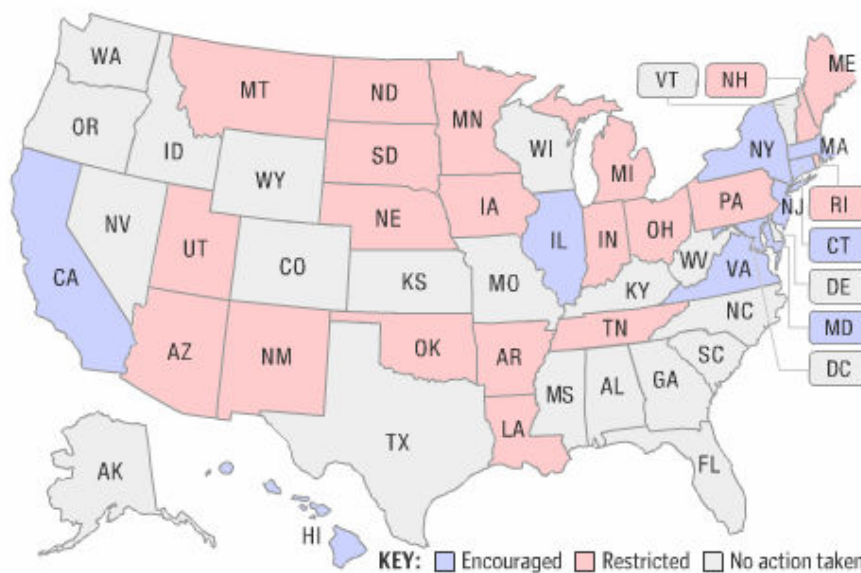


Figure-13: "Stem Cell Legislations in the U.S. by State" (Stem Cell Legislation, 2005).

California has led the way, promising 300 million dollars a year for the next decade on embryonic stem cell research (Wiess, 2005). Many states hope that by encouraging the research they will stimulate their economies and create much needed jobs (Weiss, 2005). Other states, like Connecticut, Massachusetts and New Jersey are doing the same, making them advocates of stem cell research as well. Here in New England, a Biomedical Research Advisory Council was created in Massachusetts through the enactment of Senate Bill 2039. This bill was vetoed by Gov. Mitt Romney, but luckily the Senate overrode his veto (Massachusetts, 2005). The council will “examine the appropriateness of public funding for research on stem cells from umbilical cord blood, and assess the feasibility of establishing an Institute for Regenerative Medicine at the University of Massachusetts Medical School” (State, 2006). The bill also will make it easier for scientists to conduct stem cell research by removing a requirement to get approval from the local district attorney before starting, as well as giving the regulatory controls over to the Health Department (Massachusetts, 2005). More recently, on July 31, 2006, Massachusetts is considering funding a life sciences center that would include stem cell research (State, 2006). It is the hope that this new legislation will bring Massachusetts to the head of ES stem cell research.

Chapter Conclusion

Hopefully with more states supporting the research and a new election year approaching, expansion of funding will help keep the United States at the forefront of the research. Senator Edward M. Kennedy said it best: “There are some issues you just can’t get off the national agenda, and this is one...Stem cell research is going to happen. It’ll

happen quicker with the President's support, but all of us who are supporting this important research know that it is inevitable. It's just a question of when."

CONCLUSIONS

Despite the numerous advances in both embryonic and adult stem cell research, both areas of stem cell research have had difficulties stemming from political and moral debates, lack of funding, and scientific hurdles that need to be crossed before major clinical advances can be accomplished.

We the authors feel that all stem cell research, including the research of embryonic stem cells and parthenotes, should proceed with few restrictions. We believe the benefits that can be obtained through the use of stem cells in applied medical therapies and treatments, such as possible cures for Alzheimer's and Parkinson's, are too great to ignore. In order for research to use embryos from IVF clinics, we believe that the parent of that embryo must consent to the donation of the embryo for research, and must be made fully aware of its use through written documentation.

We also believe that government and private funding should be allowed to help aid the already challenged field. We, the authors, believe that the current restrictions put in place by the US government in August 2001 are too strict and should be lifted to allow full federal funding for all stem cell research, including ES cells.

However, we do believe that some light restrictions are in order. We believe the research and consequent therapies to follow should only be used for medical research for the purpose of trying to save human lives. The use of stem cells for "cloning farms" or any other applications other than those in the medical field should be prohibited. We also think a government agency, FDA or perhaps a new agency, should oversee all stem cell related therapies being introduced into the market to ensure a certain level of quality and

adherence to standards. These standards would be set by that agency after a mutual consensus is reached by an expert panel on current stem cell research.

The medical promise of stem cell research is too great to be ignored, and unless we as a nation can come to a consensus on their use, the U.S. will fall behind other countries in stem cell research, and as such would fail to benefit from what many scientists argue is medicine for the new millennium.

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