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STEM CELLS AND SOCIETY

An Interactive Qualifying Project Report

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ABSTRACT

The issue of stem cells is highly debated and controversial. Although growing research continues to promise new hope for those suffering with debilitating diseases, stem cells continue to spur ethical concerns because of the controversial source of one type, embryonic stem (ES) cells. My analysis discusses the effect of this controversial technology on society and some common misconceptions. Work with adult stem cells is not new, and hematopoietic stem cells have been used clinically for over forty years in treating leukemia and blood disorders, while raising few ethical issues. My analysis emphasizes the two distinct types of stem cells, adult stem cells and ES cells which have different moral and legal statuses. Furthermore, my analysis reveals that there are genuine medical potentials in both adult and ES cells for diseases such as heart disease and Parkinson's disease. In terms of ethics, all major world religions allow adult stem cell research. But the ethics of ES cells is scattered, with the Roman Catholic Church declaring ES cell research immoral, while the Jewish and Muslim traditions encourage it. In terms of policies, the United States federal government under George Bush has taken a restrictive approach towards ES cell research, whereas other nations such as the United Kingdom, Australia, Singapore and China have embraced adult and ES cell research. Thus, stem cells have had a major impact on society, both in their medical potential, and the ethical and political fallout.

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PROJECT OBJECTIVE

The objective of this IQP project was to examine the topic of stem cells, and to discuss the effect of this controversial new technology on society. The purpose of chapter-1 was to explain why all stem cells are not alike and the basic characteristics of the various types of stem cells. The purpose of chapter-2 was to explain the kinds of experiments that stem cells have successfully been used for, sorting junk reports from bonafide studies, and discussing the medical application of stem cells on a host of human diseases. The purpose of chapter-3 was to examine the ethics surrounding this controversial topic. And the purpose of chapter-4 was to examine the laws governing stem cell use. Finally a conclusion is made by the author regarding the use of stem cells, and which laws best represent the author's point of view.

Chapter 1: Stem Cell Technology

Medicine has advanced greatly over the last 30 years, and the twenty-first century has ushered in a new approach to solving medical challenges. Our quest for treating and curing all ailments has always remained the same but the approach to such ailments has taken on a new direction. Medicine in the early and mid twentieth century was dominated by the development of drugs that could treat the symptoms of certain diseases. For example, the intent was to stop the pain of arthritis by using pain killers, but not to regenerate or repair the thinning cartilage of the joints. Another example is the treatment of type 1 diabetes where insulin is given to patients in order to maintain insulin levels vital for blood sugar levels. But the insulin was just a treatment that quelled the symptoms of type 1 diabetes and it did not correct or cure the underlaying autoimmune destruction of the pancreatic beta cells. However, scientists have always been searching for alternative ways to approach human diseases such as diabetes, leukemia, and Parkinson's disease.

Although diabetics still take insulin, and patients with osteoarthritis still rely on pain killers to make life more normal, new research has been geared at *regenerative medicine* which seeks to repair or correct the diseased tissue or organ by introducing healthy tissue to carry out the function that was ailing or lacking in the diseased patient. This new research is centered around stem cells which are the unspecialized cells that are able to become specific tissues like liver, heart or brain cells. Stem cell research has opened new doors that were once closed to medicine, and has introduced hope to many suffering from chronic or debilitating diseases. However, stem cell research has stirred moral and ethical debates that have shaped the way stem cell research is progressing. Unfortunately, the debates that continue to grow concerning stem cells are plagued with inaccuracies, hype, and misconceptions, and more often than not, a lack of

understanding of what stem cells are. In my analysis, I will first explain what stem cells are and what types are present, to demonstrate that not all stem cells are alike. Next, the potential and current applications of stem cells will be discussed, with a focus on discriminating hype from reality. And finally, the complex topic of stem cell ethics and legalities will be investigated, especially in view of the large varieties of stem cells available.

Key Stem Cell Features

In order to understand what stem cells are, it is important to lay down the key characteristics that makes stem cells unique. In order for a cell to be a stem cell it must not be specialized—that is they do not have a specific function but have the ability to become a specialized cell such as a skin or liver cell. Another key characteristic of stem cells are their important ability to self-renew and multiply indefinitely (NIH, 2006). Stem cells are often described as biologically "immortal" in that they can multiply indefinitely if given the right conditions.

Stem Cell Classifications

Despite these key characteristics stem cells vary in origin, ability, and potential, and these differences are critical in how scientists use them and the way the public builds their perceptions. Most people are unaware that there are different types and categories of stem cells that can be derived from different sources and have different properties. Stem cells are classified by their source and ability to differentiate into various types of cells. There are two main types of stem cells. The first are *adult stem cells* which are stem cells found in specific parts of our adult

bodies. The second, and the most controversial, is the *embryonic stem (ES) cell* which is derived from a 5 day old fertilized egg called the blastocyst.

Stem cells can also be classified on the basis of their potency—that is the ability of a stem cell to differentiate into different kinds of specialized cells (Figure-1). A stem cell is called *totipotent* (top cell in the figure) if it can differentiate into all the cells in the human including the placenta. The only totipotent cell is the fertilized egg (zygote). When the sperm and egg unite they form a single cell that has the ability to differentiate into all the cells of the human including its placenta. Stem cells that can differentiate into many different types of cells is called *pluripotent* (ISSCR, 2005) (second cell in the figure). Pluripotent cells are more limited than totipotent but still harness an amazing ability to specialize into a multitude of specialized cells. ES cells are considered pluripotent. *Multipotent* stem cells (lower left in the figure) are limited to differentiating into more specific types of cells that have a common function. The most popular example of multipotent stem cells is the hematopoietic stem cell which is the precursor cell of all the types of blood cells, such as red blood cells, platelets, and white blood cells, etc. Finally, *unipotent* stem cells usually differentiate only into one other type of cell. Epithelial stem cells are often considered unipotent since they usually make only other skin cells. Thus, it is obvious that stem cells are diverse, and that simplifications about their origins and abilities leads to common misconceptions and distortions.

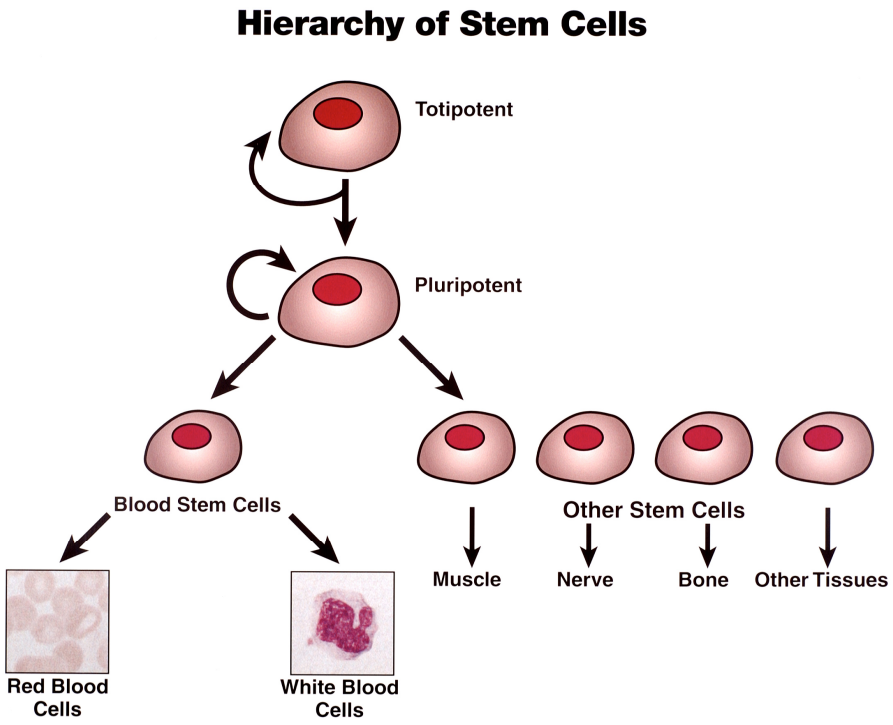

Fig. 1. *A diagram by the National Institute of Health (NIH) shows a hierarchy of the potency of stem cells. Totipotent cells can become all other cells in an organism. Pluripotent cells can form most other cells except the placenta. Multipotent stem cells such as hematopoietic (blood) stem cells can give rise to functionally related cells such as white blood cells and red blood cells. (NIH, 2006).*

Adult Stem Cells

The most common misconception is that all stem cells are derived from embryos. But in fact, stem cells are found in our bodies in various organs. Because cells in our body age and die, or are susceptible to diseases, cells are needed to replace them over the many years of life. Stem cells found in our organs such as skin, liver, brain, bones, and other organs are meant to specialize into that particular tissue, and continue the function of that organ when older or damaged cells die (American Federation for Aging Research, 2003). These stem cells that are found in the body are called adult stem cells. The "adult" does not suggest adult people but rather

stem cells that reside in specialized tissue. And most importantly, this adult classification is intended to distinguish these cells from the ethically controversial embryonic stem (ES) cells. So, a new born baby has adult stem cells in it's organs that respond to disease, damage or aging. In addition, umbilical cord blood hematopoietic stem cells are classified as adult. As result different types of adult stem cells reside in our body that are responsible for creating functional cells needed for health.

Hematopoietic Adult Stem Cells

Adult stem cells are not a new discovery, and in fact they have been used for over forty years as a treatment and therapy with little or no protest. Bone marrow transplants have been performed since the 1960's in order to help replace lost blood cells from radiation treatment for cancers, and for blood and immune system diseases in patients (NIH, 2006). The "active component" of bone marrow are adult stem cells, the hematopoietic stem cells (HSCs) that are multipotent and are able to produce all the types of blood cells including red blood cells, white blood cells, platelets, lymphocytes, and other immune cells (Abbott, 2003). The use of hematopoietic stem cells has been a very successful use of adult stem cells, at the forefront of our ongoing research of adult stem cells. HSCs can be found in the marrow of large bones or from umbilical cord blood.

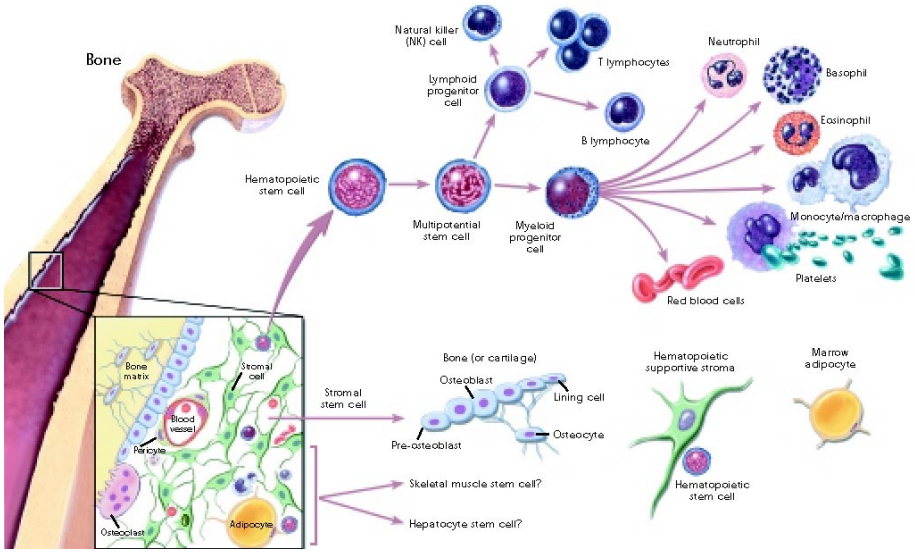

Fig. 2. ***Diagram of Hematopoietic Stem Cell Differentiation.***
Hematopoietic stem cells (diagram center) are found inside the marrow of large bones (left side of diagram). The figure shows that numerous blood and immune cells (right side of diagram) originate from these stem cells. They tend to be multipotent differentiating into blood components, although some recent research has indicated that they can also become other non-blood cells such as nerve cells.
(National Institute of Health, 2006)

HSCs are usually taken from the hip bone of a healthy individual and placed into the patient in need, however HSCs are also greatly enriched in the blood of the umbilical cord during birth (Viacord, 2007). This is a great advantage because cord blood can easily be extracted at birth (the cord is usually discarded) and it can be frozen for later use. Later if the person is in need of radiation treatment for cancer or develops a blood disorder or cancer such as leukemia, their HSCs can be used to replace diseased ones and give a second chance to the patient. Umbilical cord HSCs are a better alternative to marrow HSCs because it is the person's own stem cells when they were born, thus the patient's immune system will not reject the stem cells. Donated HSCs must match the patient, otherwise rejection or complication with the donated stem cells is a serious possibility. Because of the strong advantages of using cord HSCs, storage companies

such as Viacord have become financially feasible, and have offered services to preserve a baby's umbilical cord blood.

Because HSCs have been historically the most widely studied group of the adult stem cells, most of what we know about stem cell behavior comes from these cells. In fact, recent research on HSCs has determined that these cells may have the potential to become not just blood cells, but can also *transdifferentiate* into cardiac, liver, and skin cells (NIH, 2006). This ability is also known as *plasticity*. If this preliminary evidence holds true, the discovery of plasticity is a great advancement because it would open new non-controversial ways of utilizing adult stem cells for different organs and tissues, as a replacement for ES cells. It should be noted that some researchers have refuted this plasticity claim (Wagers et al., 2002), so more research is needed to clarify whether these cells can truly differentiate beyond blood cells.

Adult Neuronal Stem Cells

Although hematopoietic stem cells have been used extensively, other kinds of adult stem cells in our bodies are actually extremely rare and difficult to isolate. In spite of this, new research has focused on the potential of other adult stem cells, such neuronal, cardiac, and epithelial stem cells, as candidates for regenerative medicine. In the 1960's, about the same time the development of bone marrow transplant using adult HSCs began, some scientists noted that adult brains could undergo neurogenesis, the growth and development of neurons. Initially, this finding was mostly ignored because it was widely thought that neurons, the most important cells of the brain, could not regenerate if damaged (Cassidy and Frisen, 2001). The belief was that if a neuron died there would not be a replacement cell that could take its place. It was not until the mid-1990's that research uncovered that adult neuronal stem cells resided in adult brains, and

these can give rise to various types of cells including neurons. Although extremely rare, neuronal stem cells have been found in certain part of the brain. Recent research has indicated that neuronal stem cells are actually multipotent and can give rise to different types of brain cells (neurons, astrocytes, glia, etc) (Figure-3). The most obvious is the neuron, but also glial cells which are the support and packaging cells of the brain (Bjorklund and Lindvall, 2000). Research has focused on whether these stem cells can differentiate into functioning neurons if damage of the brain occurs. Most of the research still remains unsure, but experiments using mouse stem cells have shown the ability to migrate to injury sites and differentiate into new cells (Gage, 2000). However, the key question is whether the differentiated cell created is a viable and functional neuron that can fully replace the damaged brain tissue. This is still unclear but the push for finding out the abilities of neuronal stem cells continues.

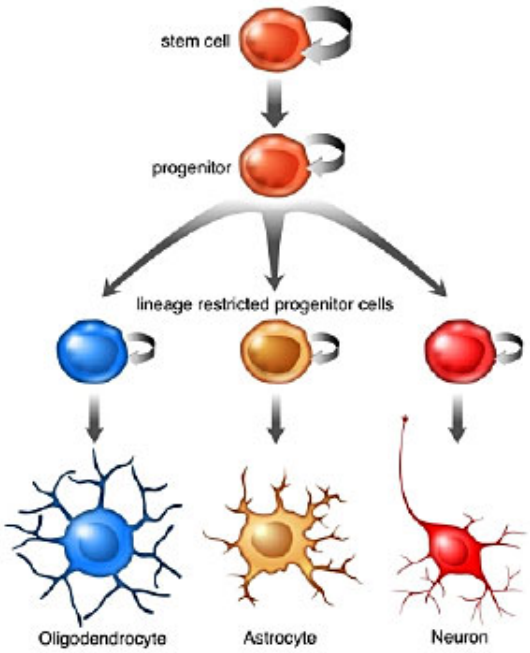

Fig. 3. The Fate of a Neuronal Stem Cell*. First,the neuronal stem cell (upper center) becomes a progenitor cell that heads towards one of three lineages. Neuronal stem cells can differentiate into glial cells (oligodedrocytes and astrocytes) as well as neurons. Plasticity experiments have demonstrated that neuronal stem cells can also become other cells such as muscle cells.* (Institute of Developmental Genetics, 2007)

Other research has emerged that has focused on the *plasticity* of adult neuronal stem cells. Suprisingly, scientists found that mouse neuronal stem cells could not only become brain cells, but they were able to become muscle cells when they were placed on a medium of muscle cells (Vogel, 2003). The plasticity of neuronal stem cells reiterates the potential that adult stem cells have. Despite the constant (but limited) availability of neuronal stem cells in adult brains, these stem cells alone cannot repair serious damage such as stroke or head trauma by themselves, so research must still be performed for amplifying these cells. However, ethical questions emerge on the feasibility of extracting adult neuronal stem cells. Because they reside deep in the brain, delicate surgical procedures are required to obtain them. Plus, their ability to grow outside the brain is more limited than for embryonic stem cells (NIH, 2006). Most of the research consequently has been done using mouse neuronal stem cells because of the obvious ethical issues involving invasive procedures in humans. Although the potential of neuronal stem cells are still being weighed, it is increasingly clear that not all stem cells are alike, and the similarities and differences can easily be mixed up.

Adult Cardiac Stem Cells

Like the brain, the heart was also thought to have no capacity to regenerate or renew if damaged by disease or natural aging. The common belief was that there are no cardiac progenitor cells — cells that eventually become the heart muscle (Beltrami et al., 2003). Most of this thought came from clinical experience with heart damage such as heart disease. Patients with heart disease would develop localized areas of cell death because of lack of blood flow to the area. The heart however, would attempt to repair the dead heart cells with scar tissue which is not able to beat or contract like normal myocytes (beating heart cells). Because of this, it was

believed that there are no stem or progenitor cells present in the heart that can proliferate into viable heart tissue. However, findings of other adult stem cells in other organs such as the brain and liver prompted more research into their existence in heart.

Recent research in mammals, including humans and other organisms, has discovered small quantities of cardiac stem cells in the heart. These stem cells are multipotent and can give rise to different heart cells including the myocytes which are the contracting muscle cells that allow the heart to beat and pump blood throughout the body, and smooth muscle found in arteries and veins, and endothelial cells which form coverings over the organ (Beltrami et al., 2003). Cardiac stem cells are found mostly in the right ventricle of the heart, and in extremely small quantities (March, 2004). But recent research has indicated that these cardiac stem cells can actually be isolated and reintroduced for possible therapeutic purposes (Hidemasa et al., 2003). Because it is difficult and risky to extract these stem cells from humans, rats have been extensively studied. Their cardiac stem cells have been shown to grow into mature myocytes that possess the ability to contract/beat like the rest of the heart (Beltrami et al., 2003). These promising findings have accelerated the search for a feasible way of extracting human adult cardiac stem cells from human heart. In one novel way, Johns Hopkins School of Medicine uses a catheter that is inserted into a vein in the neck and followed to the heart (March, 2004). Because the right ventricle seems to be the richest in cardiac stem cells, these can be removed and cultured to multiply. This technique and other methods will greatly enhance our knowledge of cardiac stem cells.

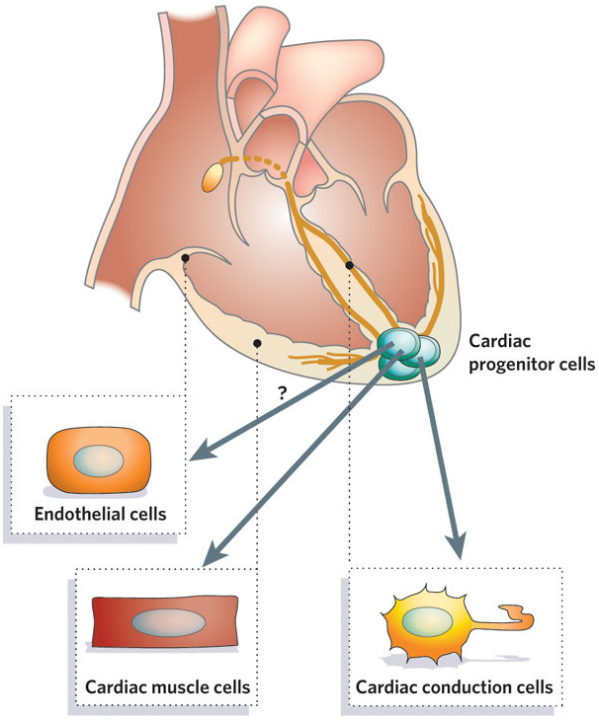

Fig. 4. Cardiac Stem Cells are Multipotent and Have the Potential to Form Different Types of Heart Cells*. The stem cells can be found in very small quantities in the heart especially in the right ventricle. Cardiac muscle cells (myocytes) are key for heart contraction. Their regeneration in heart disease patients could restore normal heart function. There is an estimated 1 stem cell for every 100,000 specialized cells in the heart making them hard to find.* (Srivastava and Ivey, 2006)

However, as approaches to finding and isolating cardiac stem cells grows, research has taken a step back at researching lower order animals such as the zebrafish and salamander. Most people are aware that a salamander can regenerate a limb or tail. Zebrafish have also recently been shown to regenerate heart tissue (Lepilina et al., 2006). Because of this amazing ability, researchers have been curious whether cardiac stem cells are responsible for the heart regeneration. When scientists subjected the zebrafish hearts to injury they observed myocardial progenitor cells—essentially cardiac stem cells at the injury site. These cardiac stem cells were

able to regrow the missing heart tissue (Lepilina et al., 2006). Not only did the heart regenerate its muscular tissue, it also regrew new blood vessels that feed the new tissue. In some ways, the zebrafish's ability to regenerate its heart is analogous to our ability to regenerate our liver if pieces are taken. Although, scientists are not sure whether the cardiac stem cells found in the zebrafish are similar to mammalian stem cells, or whether mammalian cardiac stem cells plasticity is as versatile, the implications of research with zebrafish will help understand the boundaries that cardiac stem cells have.

Adult Epithelial Stem Cells

Unlike the brain and the heart, our skin is constantly regenerating. Our skin bears the brunt of injuries, infections and the environment. Most everybody has experienced a cut on their skin and watched it heal back within a couple days or weeks. Our skin is comprised of mainly epithelial cells which form the continuous layer enveloping our body. Epithelial cells also are found inside our bodies, lining the cavities, organs and blood vessels (Cancer Research UK, 2002). These epithelial cells found inside also bear the brunt of injuries and also require prompt repair. It is no surprise that because of this harsh treatment some sort of cell must be present to replace the lost ones. Scientists have determined that adult epithelial stem cells are present in skin and other epithelial tissue that play an important role in the ability of epithelial cells to repair skin (Clayton et al., 2007). Although there are various types of epithelial cells, research has pointed to one source, epithelial stem cells. They are multipotent, are self renewing, and are able to become various skin and epithelial cells found inside the body (Sting et al., 2006). Although the plasticity of epithelial stem cells is still vague, most scientists point to skin grafting as epithelial stem cell's greatest potential (Slack, 2000).

However, very recently three teams of researchers have uncovered a new phenomenon in stem cell research. Using skin fibroblast cells from mice, which are not epithelial but are connective tissue cells found in skin, researchers were able to take a fully differentiated fibroblast cell and, using a relatively simple procedure, turn this adult cell into a pluripotent stem cell that behaves similar to ES cells (Cyranoski, 2007). This is an odd discovery because it is essentially the reverse of what classical stem cell research has been doing. In classical stem cell research, scientists look for stem cells that can differentiate into certain cells of interest such as heart, liver or ski n cells. Conversely, this recent discovery takes the differentiated cell (i.e. skin cell) and makes it into stem cell that then can be re-differentiated into another type of specialized cell such as a heart cell. If this finding holds true, these cells could serve as an alternative source of ES cells.

Despite these amazing abilities of adult stem cells, these cells have limitations and difficulties, and some scientists even cast doubt on the ability of adult stem cells to transdifferentiate and grow effectively in culture (Vogel, 2002). Most scientists point to embryonic stem cells as having the greatest potential in reaching the goals of regenerative medicine.

Embryonic Stem (ES) Cells

Perhaps the most discussed and debated type of stem cell is the embryonic stem (ES) cell. However, the debates are usually obscured because of the lack of understanding of what ES cells are and how they are derived. Also, frequently the debate about ES cells is generalized to include all stem cells. It is clear from the previous descriptions of adult stem cells that different types of stem cells exist, each with their own characteristics. In order to make an informed stance

on the stem cell debate, it is vital that one understand the origin and theory behind ES cells. There is no doubt that scientists in this field of research believe that ES cells are the most fascinating and hold the highest potential for regenerative medicine. Consequently, scientists have geared much of their research to ES cells, and numerous tantalizing discoveries have taken place since the unearthing of ES cells.

An embryo is formed when a sperm from the male unites with an egg from the female. Each carries half of the genetic information that is combined to form a cell that contains the full set of chromosomes. This fertilized egg is called the zygote which is unicellular and totipotent (Viegas, 2003). This cell (zygote) has the potential to form every cell of the organism. After fertilization the zygote starts to divide into more cells. In animals, the division of the zygote into a new entity is called the embryo. This developing and growing mass of cells in humans is usually called the embryo for seven to eight weeks after conception.

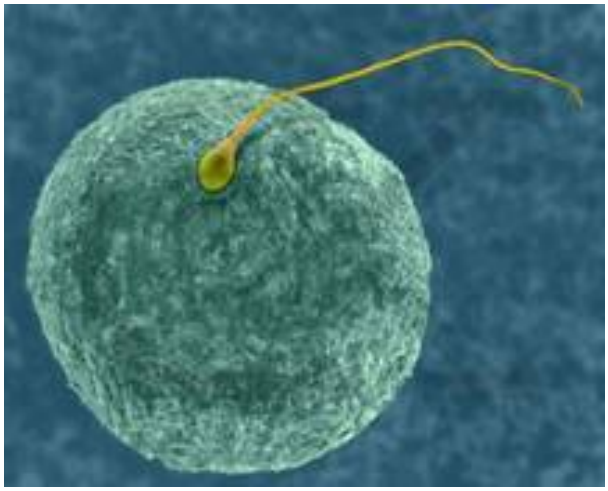

Fig. 5. Sperm Interacting With the Human Egg. *Only one sperm (yellow) will fertilize the egg (green) that will create the zygote and subsequent embryo* (Kunkel, 2001).

During these eight weeks, the embryo grows in complexity and specialization. Usually by the eighth week the entity in the womb is called a fetus and has much more recognizable features.

The cells used for embryonic stem cells come from a particular stage of the embryo called the blastocyst (NIH, 2006). The blastocyst is a ball of cells made up of about 70 to 100 cells. This blastocyst is usually formed around five days after conception in humans. At five days the blastocyst is a hollow ball of cells that has three main features (Figure-6).

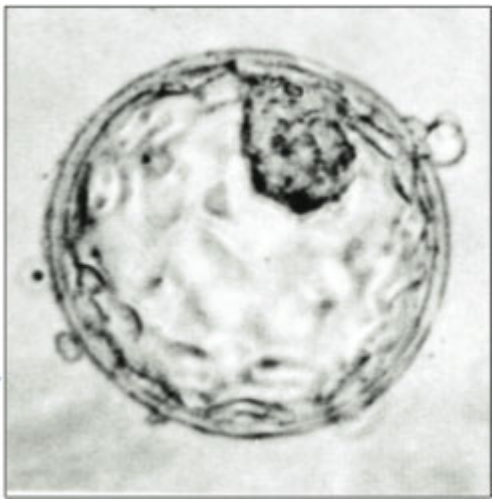

***Fig. 6**. **A Human Blastocyst at 5 Days**. Notice the outer layer of cells that is the trophoblast, the inner cell mass at the top, and the hollow interior. The bundle of cells that is the inner cell mass is where the embryonic stem cells are taken from* (NIH, 2006).

The first is the outer cells that form the ball and is called the trophoblast. These cells develop the placenta. The hollowed inside is know as the blastocoel. The third feature is a mass of cells inside the hollow of the blastocyst that is attached at one side of the blastocyst (NIH, 2006). This mass of about 30 cells is called the inner cell mass and is the location where the pluripotent embryonic stem cells are taken from. The blastocyst is only about the size of the period at the end of a sentence, and has no characteristics of a fetus or a baby. It is simply a ball of 100 cells that has not differentiated into specialized tissue such as nerves, muscle, or bones. The stem cells from the blastocyst can only be taken from the inner cell mass and not the other structures of the

blastocyst. Because of this, scientists must extract the stem cells from the inner cell mass and consequently destroy the embryo (Panno, 2005) (Figure-7).

However, there is often a misconception as to where ES cells come from. Many think that the embryo is taken from the womb of a mother. This is not true. All embryonic stem cells are taken from donors or from IVF clinics and fertilized via *in vitro* fertilization (NIH, 2006). *In vitro* means that it is done outside the living organism. So, scientists take the sperm and egg from consenting donors and create the zygote, and allow the embryo to develop for around four to five days until it becomes a blastocyst. This is all done in a test tube and the blastocyst stage is the farthest the embryo will ever go.

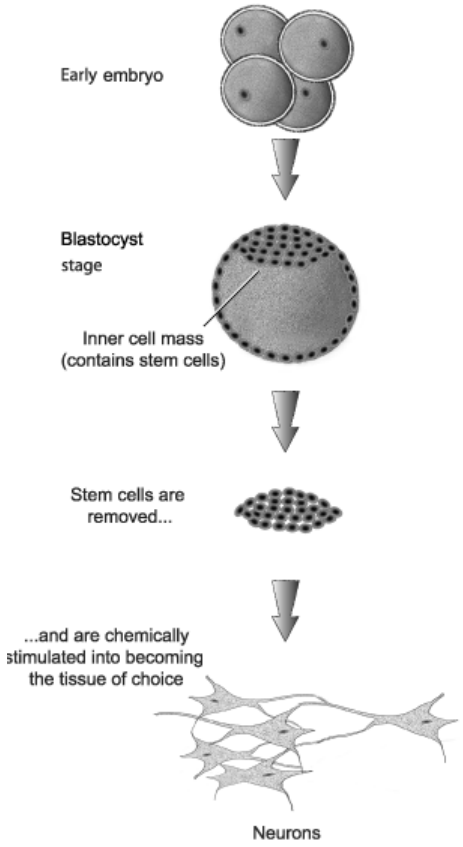

Fig. 7. Isolation of ES Cells. *This drawing shows the basic pathway that embryonic stem cells follow. They are extracted from a blastocyst, and coaxed into specialized cells. This drawing shows the ES cells being turned into neurons. Notice that the blastocyst has no physical features that resemble a human or any other animal* (The President's Council on Bioethics, 2002).

Once the stem cells from the inner cell mass have been removed, they are cultured on dishes using certain chemicals that allow them to multiply. Commonly, human ES cells are put on mouse embryonic skin cells (called feeder cells) so that these ES cells can proliferate. With the right combinations of chemicals and feeder cells the ES cells can multiply indefinitely. These ES cells are "immortal" and can multiply without differentiating into specialized cells as long as the right conditions are provided. This is an important characteristic that embryonic stem cells have (Okarma, 2001). A small amount of ES cells taken from a blastocyst, say about 15 cells, can in only six months produce millions of stem cells that have the same potency as the first 15 cells. The mass quantities of ES cells establish what are called lines. ES cell lines are ES cells that came from one source (embryo) and were grown (in vitro) into large quantities (ISSCR, 2005). The ability of ES cells to grow in large numbers without specializing allows researchers to culture and freeze certain ES cell lines, and transport them to other labs for more experimentation. Another key characteristic of ES cells is that they are pluripotent and can give rise to all different types of tissue including nerve, cardiac, bone, blood, pancreas and other tissues we possess (NIH, 2006). This allows for a much broader potential than adult stem cells which are more specific and have an uncertain plasticity. Also, adult stem cells such as hematopoietic stem cells lack the ability to grow indefinitely while maintaining the stem cell identity. Adult stem cells will grow undifferentiated for awhile, then spontaneously begin to specialize.

Because of the capacity of ES cells to self-renew and possibly become any cell in the body, numerous hypothetical possibilities have emerged in treating or curing diseases of all kinds. Despite the vast interest and research in ES cells, much about molecular and cellular mechanisms remain unknown, and much about this type of stem cell is enshrouded in

controversy. Because of the tense ethical debate involving ES cells, scientists have been turning to other possibilities that address the medical potential of ES cells but minimize the ethical concerns.

Parthenotes and Stem Cells

Because human ES cells are highly controversial, new methods of obtaining stem cells that have the same potential as ES cells are being developed. Adult stem cells currently do not have the same plasticity and availability as ES cells. A new method that has claimed the potential of ES cells is stem cells derived from parthenotes. Parthenotes are unfertilized eggs that are able to divide and form an embryo, and in some species an organism. Various animals naturally are able to reproduce asexually without a male sperm. This phenomenon is known a parthenogenesis. Animals such as turkeys, chickens, some reptiles, and some insects such as aphids are able to undergo parthenogenesis producing their progeny without a male. However, mammals, including humans cannot successfully undergo parthenogenesis naturally, and rely on sexual reproduction to form their progeny.

Scientists however, have found that eggs donated from a mammalian female can undergo parthenogenesis. They achieved this by chemically stimulating an egg (usually with strontium chloride) before it has been fertilized while it still contains all its chromosomes (Figure-8). As a result the egg began to divide forming an embryo (Cibelli et al., 2001). This embryo is grown until it reaches the blastocyst stage. Researchers have been able to extract the pluripotent ES cells from the inner cell mass, much like normal ES cells are isolated. However, the advantage of parthenotes in mammals and humans is that they soon die off after the blastocyst stage and can never form viable offspring (Kiessling, 2005). Thus, human parthenotes can never be humans but

can only develop up to the blastocyst stage enough to take the stem cells from them. This possibly avoids the ethical concerns of destroying life because life is never possible in human parthenotes. Because the stem cells come only from the female, these stem cells will genetically only match that particular female. However, male parthenotes are also being researched. Scientists using animals are trying to determine whether knocking out the genes of the egg from a female and putting in the chromosomes from two sperm will allow the resulting parthenote to be genetically similar to the male (Weiss, 2001). If parthenote-based stem cells dodge ethical concerns, banks of eggs from women could emerge, similarly to umbilical cord blood, that may be ready if disease affects the individual (Keissling, 2001). There is much more research that must be done to know whether stem cells from parthenotes are as viable or hardy as typical ES cells. Recent research has been able to create ES cell lines from human parthenotes that seem to behave like normal ES cells but seem more difficult to handle (Marchant, 2006).

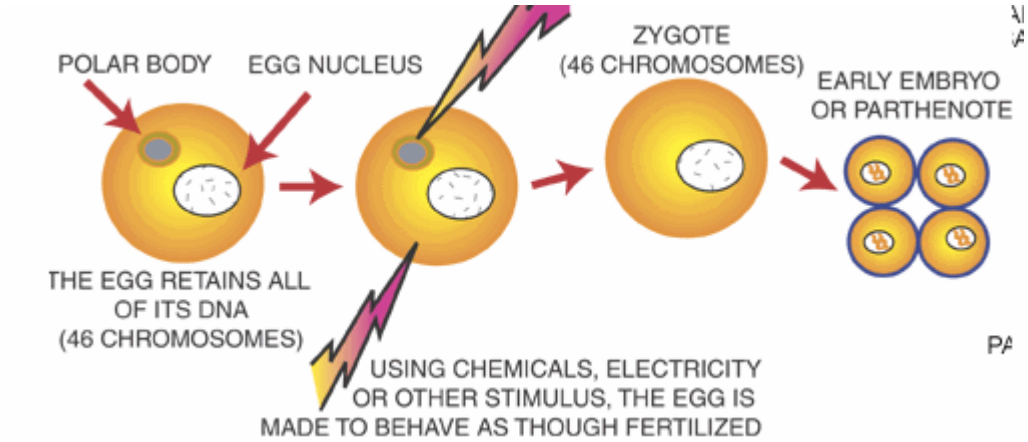

Fig. 8. The Basic Strategy of Creating a Human Parthenote*. The early egg with its full complement of chromosomes (left) is treated with chemicals or electricity to stimulate cell division. The early embryo (right) can go on to produce a blastocyst where the ES cells can be taken from and cultured* (Center for Genetics and Society, 2003).

Stem Cells and Cloning

Cloning has also been a controversial technique in biotechnology. Most recall the cloned mammal — Dolly the sheep (Wilmut et al.,1997). Cloning has also had its share of misconceptions and hype. Over the last few years numerous mammals have been cloned including a horse, dog, mule, rat and a pig (Lee et al., 2005). These mammals were successfully cloned using a technique called somatic-cell nuclear transfer (SCNT). In general, this technique is done by taking the nucleus and somatic cell such as udder cell in Dolly's case. The nucleus holds all the genetic information of the animal. The somatic cell with its nucleus is then placed (injected) into an egg of another animal (the egg's nucleus is removed previously). Through an electrical charge the somatic cell and the egg fuses together to form one cell that has the somatic cell's nucleus in the egg. This egg is then stimulated to start dividing and forming and embryo, and subsequently a genetically identical animal as the one the somatic cell was taken from (AAMC, 2007). Although the success rate for cloning is quite low, this method has opened new possibilities for cloning that was not possible without SCNT technology.

As a result of this SCNT technique, scientists hope to be able to create genetically identical ES cells to a person. One of the biggest hurdles of normal ES cells is that they are genetically different than the patient since the ES cells come from another person. Thus, the human body would reject this different tissue if it were transplanted into the patient. However, if the patient's somatic cell such as a skin cell is taken and fused is an enucleated egg from a donor, this egg would have the exact genetic code as the patient. This egg then could be stimulated to divide into an embryo using parthenogenesis. The embryo can then be matured to the blastocyst stage, and the pluripotent stem cells can be taken from the inner cell mass and cultured. These

stem cells would have the same genetic code as the patient and could be used without the fear of rejection (Newton, 2007).

This type of cloning is called therapeutic cloning because the goal is to harvest stem cells that can potentially be used to grow tissue necessary for the patient. On the other hand, cloning such as the one that created Dolly has been dubbed reproductive cloning (ISSCR, 2005). Although different animals have been cloned, the success rate is low and still poses challenges. For example it took over 276 attempts to create Dolly (Freudenrich, 2004). Therapeutic cloning poses even more of a challenge, and to date no successful human stem cell lines have been harvested using SCNT. Furthermore, therapeutic cloning does not alleviate the ethical dilemmas that normal ES cells have since it still uses an egg. However, the potential of this technique may in theory have a profound effect on medical treatments and regenerative medicine.

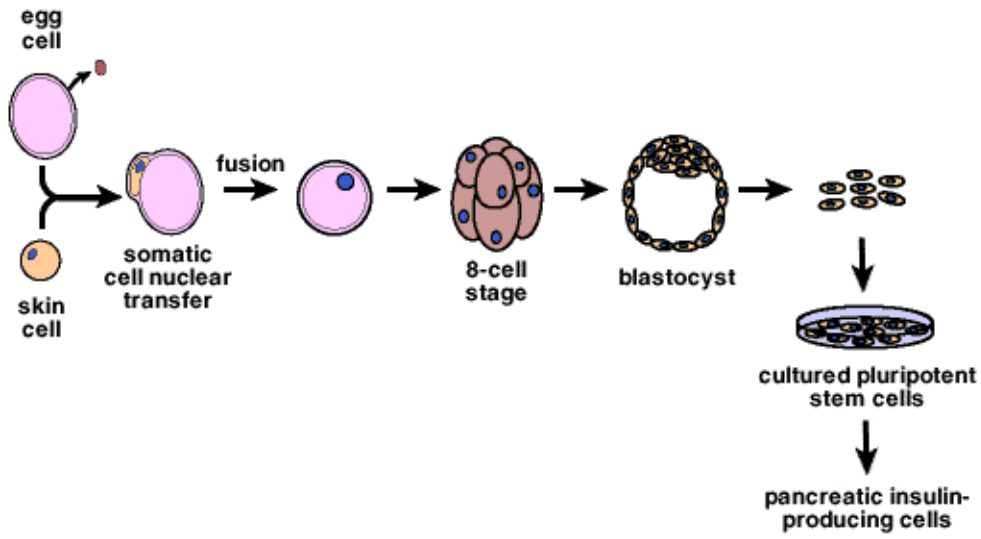

Fig. 9. ***Diagram of Therapeutic Cloning***. *The first step involves removing the egg's nucleus and fusing a somatic cell such as skin cell to the egg (left side of diagram). This egg is then stimulated to divide and grow into an embryo (diagram center). When it matures into the blastocyst stage, scientists can remove the ES cells from the inner cell mass (upper right) and culture them and stimulate them to specialize into the cells of interest (lower right). This drawing shows insulin producing cells being produced which could potentially treat people with juvenile diabetes (type 1)* (NIH, 2006).

It is quite apparent that there are different types of stem cells, and each has different sources and potentials. However, claims such as "I am against stem cells" carries a premature understanding of the complexity and assumes all stem cell to be the same, in this case it assumes that adult stem cells are ES cells. In fact, we have seen that adult stem cells are vastly different in origins and potential than ES cells. So claims such as the one above should be more specific such as "I am against embryonic stem cells etc.". However, this should also come with correct knowledge and a basic understanding as discussed earlier. I believe that stem cell research of all kinds is irreversible, and the continued research will open new understandings of stem cells. Much about stem cells is still unknown, and the research is in its infancy. Yet the possible applications has already been discussed and numerous possibilities for their use in medicine has been researched, hypothesized, and some has been hyped. In the next chapter I will discuss the applications that stem cells have and may be used for. Further, I will discuss what has been hyped to the public, and the current clinical standpoint on the different types of stem cells.

Chapter 2: Stem Cell Applications

The current focus of most of stem cell research lies in their potential medical applications. Our increasing knowledge of stem cells has continuously created new exciting possibilities for numerous ailments, but has also raised puzzling questions on the behavior of stem cells, and it is often hard to decipher fact from fiction for various lab claims. Despite the relatively infantile knowledge of stem cells, the push to introduce them as a treatment for disease has been enormous, and much of the research has been geared at making the exiting possibilities of regenerative medicine come alive as soon as possible. Yet it is often obscure of what are these medical potentials are and what scientific research has actually been able to accomplish in hopefully bringing these cells from the lab to local clinics.

Another important question that arises here is what are the limits to stem cells, if any? People on all sides of the debate have sometimes brought confusion to what the actual medical potentials are. Again, a clear understanding of different types of stem cells plays a critical role in their medical potentials. On both sides of the debate, claims and disclaims of medical promise have circulated that have added to the fogginess of the stem cell issue. But the medical potentials go beyond treatments for diseases to include applications in the pharmaceutical industry that may also enhance our medical understandings. Using the previous chapter-1 as a basis, in this chapter I will discuss what stem cell medical potentials are, what has been done up to now, and what applications must remain as future hopes.

Stem Cells and Disease Treatment

Hematopoietic Stem Cells and Blood Disorders

Most scientists believe that full scale use of stem cells for disease therapy is at least 10 to 20 years away. However, the use of stem cells is not as futuristic as it may seem. The use of hematopoietic stem cells for treating those with leukemia, a cancer of the blood and other blood disorders has been in use for over 40 years. People with leukemia have been able to receive stem cells transplants from others, or more recently from their own blood, and this has given them a true second chance. The transplant of hematopoietic stem cells has been a hallmark success story for stem cell based therapy, and has highlighted stem cells' potential for treating not just blood disorders but other diseases.

One of the first applications using stem cells involved using hematopoietic stem cells (HSCs) for treating patients with leukemia. Leukemia which comes in many forms is essentially a cancer of the blood. More specifically, white blood cells that are part of the immune system start to divide uncontrollably and result in highly immature white blood cells, and a cancerous blood stream that can spread and kill the individual. In the late 1950's and 1960's physicians and scientists devised a method that involves the transplant of HSCs to treat leukemia patients that had the life threatening cancer (Thomas et al., 1957). The first step in treating the leukemia was to irradiate the patient to kill the cancer. However, because powerful radiation/chemotherapy was required, the radiation and chemotherapy destroys many of the other blood and immune cells, and renders the patient's blood useless. Thus a replacement of blood is needed to provide fresh blood and immune cells if the patient is to survive. After radiation (and/or chemotherapy), bone marrow containing HSCs (that form all the cellular components of blood) was taken from a

donor (usually a close relative) and injected into the patients blood stream. The hope was that these HSCs would start to grow and divide, and produce the necessary blood and immune cells. Although there was some significant risk in rejection or failure for the HSCs to develop, the procedure was a life saving treatment.

However, early on when HSC transplants were performed, anti-rejection drugs had not been developed, and rejection, even by a close relative, was a large problem and hindered the total success of this therapy. Another way that leukemia was treated with HSCs was by taking the bone marrow from the leukemia patient, irradiating the entire patient then re-administering the bone marrow back into the patient hoping the leukemia mostly resided in the peripheral blood, not the marrow. Again, the goal was for the HSCs to re-populate the blood stream with the various types of blood and immune cells that would ward off infection and carry a healthy blood supply. This method was good because it reduced the risk of rejection, however, there was a risk that the cancer may still reside in the bone marrow even after a cleansing treatment, and the patient could regain the leukemia.

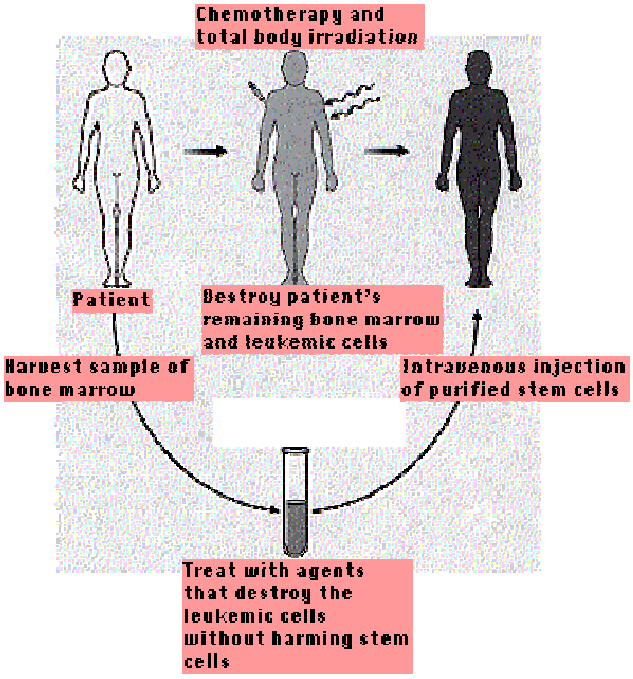

Fig. 10. Autologous HSC Transplant for a Leukemia Patient. *This diagram shows the general procedure involved in bone marrow transplant from the patient themself. The patient's own bone marrow is removed, then treated with chemotherapy drugs to kill residing cancer. The patient is then irradiated and given powerful chemotherapy that kills off the cancerous white blood cells. The treated bone marrow is then re-injected into the patient in which it will start to develop into mature blood cells and restore blood function* (Transplants of Hematopoietic Stem Cells, 2006).

The remarkable thing about HSC transplants was that for many leukemia patients it was a lasting cure (Thomas, 2000). As anti rejection drugs were developed (cyclosporine etc.), the success for bone marrow transplants increased substantially, and the application spread to other blood diseases that previously were incurable and fatal.

As more experience and knowledge was gained on HSCs, new methods for isolating and transplanting them into patients started to emerge that further improved success. One method was isolating HSCs from the peripheral blood. This method removed the need for painful bone marrow extractions and also allowed faster treatment time than the conventional bone marrow transplant. The other source that was introduced in 1989 was HSCs from umbilical cords (Glukman et al., 1989). Both of these greatly improved the availability of HSCs, and helped to curb complications associated with bone marrow transplants. Currently, various types of leukemia are treated with peripheral blood HSCs and cord blood HSCs, but rarely from bone marrow. Although early on, stem cells were largely unknown, scientists recognized the potential that these stem cells offered especially in treating blood diseases and restoring the numerous types of blood cells.

With an upsurge in HSC research in the 1950's and 1960's, new discoveries were made on the compatibility of HSCs transplants. On of the main problems was the lack of compatibility

of the donor to the patient. In the beginning the transplants were marred by unsuccessful transplants because doctors were unable to determine a proper match. The main finding that propelled HSCs was the HLA groups (van Rood et al., 1958). These human leukocyte antigens (HLA) were specific markers that enabled the body's immune system to distinguish self from foreign matter. If a matching HLA type was used in the bone marrow transplant the likelihood that the patient would reject the HSCs was reduced which greatly improved the success of HSCs transplants. This elevated it from an experimental last resort treatment to a primary therapy for millions that suffer from a host of blood disorders.

The most famous treatment involving HSCs in the United States took place in 1984. The patient did not suffer from Leukemia but rather a rare genetic disease known as SCID (Severe Combined Immunodeficiency). This disease, which occurs in only 1 in 100,000 people, is rare but usually fatal soon after birth. However, the patient, David Vetter a young boy who had SCID was living in a germ-free bubble his entire life that protected him from getting infections that would kill him. SCID is a disease in which the primary immune system defense cells (B and T lymphocytes) are not present and thus the patient cannot fight off infections (SCID, 2006). Vetter, who became known as the "bubble boy" was given HSCs in the hope that he could be removed from the bubble and live a normal life. With the success of HSC transplants in the past and Vetter's difficulty living in the bubble, HSCs posed the only chance at overcoming SCID. The procedure started with extracting bone marrow from his sister that had a matching HLA. Then her bone marrow was injected into the "bubble boy". The hope was that the HSCs would begin to specialize into the immune cells needed especially the B and T lymphocytes and giving him a new immune system correcting the genetic defect. Although the transplant was a success, it was discovered that the Vetter's sister had a virus called Epstein-Barr present in her bone

marrow. Because his immune system was not developed, he could not fight the virus and subsequently succumbed to it and died only 15 days later. Had there been no Epstein-Barr in his sister's bone marrow, Vetter, may have been cured from his condition.

Fig. 11. David Vetter (Bubble Boy) in his Bubble*. This picture shows Vetter looking out from his germ free bubble that had confined him for his entire life because of a genetic blood disorder called SCID. Although it was hoped that a HSC transplant would rescue him from this confined space, Vetter died as a result of a dormant virus in his sister's bone marrow which was transplanted into him. Vetter received a lot of media coverage and was an amazement to the public during the 1970's and early 80's and even spawned a movie entitled "Bubble Boy" dramatizing the life in a bubble* (Texas Children's Hospital, 2004).

The tragedy of this however, was not caused by the failure of the HSCs but rather by a lack of identification of pathogens in the bone marrow that led to the failure. Previously, more than a decade before Vetter, scientists were successful in using HSCs to cure SCID in another patient (Gatti et al., 1968). This was in fact the first successful procedure using hematopoietic stem cells in the United States and highlighted the further potential of HSCs in treating not just leukemia but also genetic blood disorders. Even today, after years of research and experience, patients with SCID are given HSC transplants from donors that are able to restore immune function and

allow the patient to live a normal life. However, today bone marrow treatment for SCID has been replaced with peripheral or cord blood and advanced blood testing to prevent the tragedy that occurred to Vetter.

Over the 40 years of HSC transplants, numerous blood diseases that were once death sentences have been cured which has revolutionized medicine. Various diseases such as aplastic anemia, beta-thalassemia, Blackfan-Diamond syndrome, globoid cell leukodystrophy, sickle-cell anemia, X-linked lymphoproliferative syndrome, and Wiskott-Aldrich have all found a viable treatment with HSCs (NIH, 2001). The significance of HSCs transplants in treating everything from leukemia to SCID has been noted as one of the most significant medical achievements in the 20th century. In fact, one of the most prominent pioneers of HSC applications, E. Donnall Thomas (cited in the experimental treatment of leukemia above), received a Nobel Prize in medicine for a truly revolutionary way of treating blood disorders. However, research on HSCs has not stopped and new uses has broadened it capabilities on various blood disorders and other diseases. One of the new modifications that has improved HCSs is gene therapy. Gene therapy aims at modifying the genetic information in a cell so the defect in the cells can essentially be corrected. Using gene therapy, HSCs can be modified so that they can grow in culture which normally is difficult to do. One advantage to this, if successful, is HSCs will be able to be grown in large quantities and remain potent relieving the constant demand for donations. More recently, gene therapy has also showed promise in a different way using hematopoietic stem cells to treat SCID. Although the older treatment of using a matching donor's HSCs was a major success, the complications was still prevalent and was still a lengthy and risky procedure with the risk of rejection. In 2000 researchers came up with a novel way to cure SCID without using another person's hematopoietic stem cells (Cavazzana-Calvo et al., 2000). The researchers extracted the

SCID patient's own bone marrow that was genetically incapable of producing B and T lymphocytes. Using a virus (Maloney retrovirus) as the introduction vector, researchers took the correct gene and inserted it into the bone marrow cells (HSCs) of the patient. The corrected HSCs were then reintroduced into the patient's bone marrow cells. The results were remarkable. Both patients in the trial began to produce normal levels of T and B lymphocytes, and sustained this normal level. The real advance here is that the SCID patients did not need an allogenic (donor) transplant and thus did not receive many of the complications associated with normal HSC transplants. What is more is that these gene therapy HSCs were able to produce antibodies to a host of pathogens that previous SCID transplants were unable to do (Gene therapy, 2000). This story demonstrates the limitless potential that HSCs have and their power as an effective treatment. Combined with modern techniques such as gene therapy, HSCs have whole new host of potential applications which includes modifications and new possibilities for new treatments of other disorders.

As the wealth of knowledge on hematopoietic stem cells increases, researchers have constantly been ambitious at pushing the capabilities of medical application of HSCs. Although HSCs have been widely successful at treating leukemia, a cancer of the blood, research has shown that HSCs can also be an effective therapy for treating other cancers such as lung, prostate, liver, pancreas, kidney and a other common cancers (NIH, 2001). In one study, patients suffering from renal cancer (kidney cancer) were given injections of peripheral HSCs from a donor (Childs et al., 2000). The results were promising; about half of the patients in the study survived for at least a year and some for almost 3 years. Although half did not survive, and the cancer progressed, there was notable remission in the other half that indicated that HSC transplants may in fact have a cancer fighting effect and could be implemented as a another tool

in combating cancer. Although there has been over 40 years of working with HSCs, and has been vital in the treatment of blood disorders saving millions of lives, the mystery and usefulness has not been exhausted. Like the example of fighting numerous cancers, HSCs have been studied as a potential treatment for other diseases such as heart disease and diabetes which is discussed below. Among stem cells, hematopoietic stem cells has be the exemplar of success of what stem cells can do while at the same time avoiding the tangle of ethical controversies associated with embryonic stem cells.

Stem Cells and Parkinson's Disease

Although hematopoietic stem cell therapy is the only currently available stem cell treatment, researchers have been working on using different types of stem cells to bring effective treatments to Parkinson's disease and begin clinical trials. Parkinson's Disease (PD) is a neurological disease that affects a certain part of the brain known as the substantia nigra. This region in the brain contains neurons which secrete a chemical neurotransmitter called dopamine. Dopamine is an important chemical for motion and posture, and is important for making movements. People with Parkinson's Disease have degenerate dopeminergic (dopamine secreting) neurons and thus cannot make enough dopamine essential for normal movement. This lack of dopamine causes worsening tremors or shaking throughout the body, and also difficulty walking or maintaining normal posture. This neurodegenerative disease (meaning that it progressively worsens) affects about half a million people, most over the age of 50 (The National Institute for Neurological Disorders and Stroke, 2007).

There are only a few available treatments for Parkinsonism, one of which is giving L-dopa a precursor of dopamine to the patient. However, this treatment is transient, and carries

significant side effects, and the disease will eventually progress. Another option available is transplanting fetal midbrain tissue into the patient's brain. The fetal brain tissue differentiates into dopamine producing neurons at the transplant site (NIH, 2001). However, using fetal brain tissue is ethically controversial because it involves working with aborted fetuses, and this tissue is difficult to acquire. Thus this fetal transplantation technique is even more ethically controversial than working with ES cells (which are derived from day-5 embryos the size of a period at the end of this sentence. The final or alternative current option is deep brain stimulation in which a stimulating electrode is implanted into the brain. Again this procedure may not work for all patients and carries the burden of repeated surgeries and equipment inside the brain that could cause complications (NIH, 2001).

Because of the growing number of people with Parkinson's Disease and the unreliability of current treatments, researchers continue to look for an effective treatment or cure for this debilitating ailment. Because of stem cells' ability to differentiate into different types of cells such as neurons, researchers have been working on whether stem cells could be coaxed into forming the dopamine producing neurons. Using a rat model of Parkinson's Disease that shows similar symptoms to the human case, researchers have been able to transplant mouse ES cells into the midbrain of the PD rat (Kim et al., 2002). They found that these ES cells differentiated into neurons that were able to produce dopamine. Further they observed a better movement of the treated rats showing that the stem cell transplant had been able to repair some of the lost function of the diseased rat.

Another method by other researchers used ES cells from mice and differentiated them *in vitro* into more specific neuronal stem cells, then transplanting them into the PD rat's brain

(Bjorkland et al., 2002). Again this study found that these stem cells became dopamine producing cells, and caused an improvement in the rat's behavior and motor function.

In a more dramatic experiment, researchers used human embryonic stem cells and transplanted them into the rat PD model. They also observed behavior improvement, and when the brains were analyzed they found the human ES cells had become dopaminergic neurons in the rat midbrain (Ben-Hur et al., 2004). Also, the stem cells did not grow out of control which would have hindered the results. These studies demonstrated that ES cells have the possible potential to treat Parkinson Disease in rats. Although this shows that ES cells are a viable PD treatment, it still has only been shown in rodent models. This treatment has still not entered human clinical trials and remains in the pre-clinical stage where more research must be done.

However, there has been one study involving one patient suffering from Parkinson's that yielded interesting results. In a senate testimony a lone patient who had suffered with Parkinson's recalled his procedure using stem cells. The doctor that performed it took neuronal stem cells from the patient's own brain, cultured them, and then inserted them back into the patient's brain. According to his testimony, the patient described his regain of control and coordination, and overall very quiescent tremors (US Senate Committee…, 2004). Because this study was only for one patient, it is still unknown whether a human case of Parkinson's disease will be able to be successfully treated using adult stem cells. Another hurdle in entering possible human treatment is immune system rejection of ES cells. Even in the rat treatments, the rats were given powerful anti-rejection drugs in order for ES cells to be accepted by the rat. The importance of this research is its implications; because not only were they able to make dopaminergic neurons, but the marked improvement in the rat points to possible long term treatment or remission in PD patients.

Most of the PD research uses ES cells, but some scientists have investigated the possibility of using adult neuronal stem cells extracted from the patient and reintroducing them as viable dopaminergic neurons that would eliminate the problem of rejection. In both cases, the prospect of stem cell therapy in humans is about 10 years away from beginning clinical trials. If proven successful in humans, stem cell therapy may be able to provide a more hopeful and long term treatment to those who suffer with Parkinsonism.

Stem Cells and Alzheimer's Disease

Another neurological disease that has been at the forefront of the stem cell debate is Alzheimer's Disease (AD). The possibility of using stem cells for treating Alzheimer's was introduced to the public after the death of Ronald Reagan who suffered from Alzheimer's for numerous years. His wife Nancy became a great advocate for stem cell research in Alzheimer's disease treatment. However, AD poses a great challenge for stem cell based therapies. Alzheimer's is a neurodegenerative disease that predominately affects the elderly, and is the leading cause of late life dementia (Alzheimer's Association, 2007). It is caused by a protein buildup called amyloid plaques which accumulate in the brain and cause neuron damage and death. The connections between neurons called synapses are also destroyed because of these plaques, which results in deteriorated communications between neurons. These plaques cause many of the prevalent symptoms, such as loss of cognitive function, memory, and judgment (Lindvall and Kokaia, 2006). Eventually, patients with Alzheimer's within ten years of the onset of the disease will die as a result of the progression of the disease. The challenge for stem cells with Alzheimer's disease is that unlike Parkinson's (which affects only one part of the brain), Alzheimer's can affect different regions in the brain, and has no definitive pattern of progression

(Panno, 2005). So treating AD with stem cells is a great challenge because the practicality of introducing stem cells into different parts of the brain may have unknown consequences.

However, continued research on the applicability of stem cell based therapy for Alzheimer's and other neurological diseases has shown that stem cells introduced into the brain of mice via a direct injection were able to form new and functional neurons and supporting glial cells (Deacon et al., 1998). Furthermore, they also found that these stem cells formed connections or synapses with other neurons in damaged areas in the mouse brain. Both of these findings enhance the potential of stem cells becoming a possible treatment for Alzheimer's. Yet the question of whether these new neurons will be able to alleviate the symptoms is still unknown. Because much of the research is preliminary, all preclinical research has involved mice and other animals that have conditions similar to Alzheimer's or simply have a defect in the brain. Alzheimer's according to many stem cell researchers poses a great challenge for stem cell transplantation because of its widespread development and the nature of the disease itself (Panno, 2005). Thus, Alzheimer's is not a very suitable candidate for stem cell transplants so far. However, new theories have emerged that are currently in testing that may utilize stem cells in a different way. Because stem cells have the odd ability to migrate to the injured regions of the brain, researchers have been contemplating using genetically modified stem cells that are able to produce key neuronal growth factors that can repair damaged neurons (Tuszynski et al., 2005)). In this case stem cells would not be used as the therapeutic treatment but rather a delivery (vector) tool for administering growth factors that have been shown to improve Alzheimer's patients. This technique again is a very early stage of preliminary investigation and may take years before clinical trials begin.

Another key hurdle is scientists must first fully understand the mechanisms by which Alzheimer's progresses. There has been much debate about the actual mechanism of the disease that has still left a fog on effective treatments for this disease. Overall, stem cell based therapy for Alzheimer's is many years away, if any. No human clinical trials have begun, and basic research is being done on mice and in culture dishes. However, for people like Nancy Reagan, stem cells offer a last resort for hope for the millions in the United States and around the world who suffer from Alzheimer's.

Stem Cells and Spinal Cord Injury

One of the most exciting and anticipated applications of stem cells is spinal cord trauma. Perhaps it is because of the dramatic effect that this type of treatment could have on a paralyzed person who goes from a wheelchair to possibly walking again. Those hopes have inspired intense research in this very aspect of stem cell therapy. One of the most famous people to open the possibility of this research was the late Christopher Reeve. A horseback riding accident left the former "Superman" with severe spinal cord trauma, and consequently a quadriplegic (paralyzed from the neck down). His inability to breathe, walk, or urinate without the aid of sophisticated equipment stimulated many emotions and longing for an effective treatment or cure. Because of the high profile of Reeve's case, it led to many rumors about the ability of stem cells to repair spinal injury that may not be true.

So what are the potential for stem cells in treating spinal cord injuries? What has been done in treating spinal cord injuries? In order to answer these questions, it is vital that we understand the basis of spinal cord injury and the current research that will put into perspective the hope that stem cells may offer and the science behind it. Spinal cord injury usually is caused

by a serious accident such as a car accident, a fall, a blunt force, a bullet wound, or in Reeve's case falling off a horse. These accidents cause the vertebrae which houses the spinal cord to misalign and damage the spinal cord. The spinal cord is the main communications thoroughfare for nerve impulses from the brain to the rest of the body. These communications are accomplished through neurons that are long, and conduct electrical impulses to muscles, organs and other nerves. The neurons rely on a type of sheath called myelin that insulates the electrical current much like the rubber sheathing a wire. Both of these cells, the neurons and myelin (oligodendrocytes) must work in unison to ensure a correct message is sent to or from the brain. Thus in an injury of the spinal cord, the vertebrae (or another object) impedes the spinal cord which causes damage and neuronal and myelin death at the spot of injury. Because of this damage, messages sent from the brain or being received by the brain cannot correctly be sent. A good analogy of this situation would be if there was an accident on the highway, that accident would not allow the rest of the cars to get to their destinations. Fortunately, in the car accident case, emergency personnel can clear the accident on the highway and resume normal travel. However, in the spinal cord injury case, communication to the area below the injury site is cut off, and neither sensory information nor information to the area can be received. Thus the person becomes paralyzed and is unable to move, feel or continue some organ function. Those who have an injury in the neck region (cervical) lose function and feeling of the entire body below the head and are called quadriplegic, like Reeve. If the injury is in the middle of the back (thoracic) it affects usually the legs and bladder function, and leaves the person unable to walk or feel their legs. The great difficulty and the road block in spinal cord injury is that once it is injured, the spinal cord tissue has the inability to repair itself—consequently the inability to reestablish

correct messages. The injury site will form scar tissue instead of neurons or oligodendrocytes, and the immune system will attack the injury site further damaging the connections.

Because the spinal cord cannot heal itself, little can be currently done to restore normalcy. The only treatment presently that may help is administering a steroid called methylprednisolone immediately after the injury (Lindvall and Kokaia, 2006). This has shown in some cases to help in partial recovery in patients. Another treatment is intensive physical therapy that may also give some improvement to the patient. However, both of the current treatments stop short of repairing or enabling significant recovery.

Because of the stem cell's ability to transdifferentiate, the prospective of stem cells being able to become neurons and glial cells has opened a new possibility in treating spinal cord trauma patients and hopefully restoring function and feeling to those who have lost it. Current research on stem cells has come a long way in making stem cells a true hope for many suffering with spinal cord injuries. Although much more research must be done, recent research has shown that stem cell therapy may be a viable option in helping repair spinal cord injury. In 1999, a landmark experiment involving stem cells and spinal cord injury found that ES cells transplanted into spinal cord injury site improved rat mobility (McDonald et al, 1999). The researchers in this study took rats and used a metal rod and created a lesion in the rat's spinal cord. This simulated a classical spinal cord injury and the rats lost movement to their legs. They then took embryonic stem cells treating them with retinoic acid, and injected them into the injury site. After two weeks, some of the ES cells had differentiated into neurons and oligodendrocytes. The most remarkable result was that not only did neurons and myelin develop, the researchers also observed that the rats has regained limited mobility of their legs that had been previously lost. This research opened the possibility that indeed stem cells have the potential of remitting at least

partial paralysis. However, again this study was done on rodents (rats) only, and these rats had to take heavy doses of anti-rejection drugs for the ES cells to survive. The implication of this research is still debated. Some believe that indeed these stem cells were able to grow into neurons and myelin cells and restore some of the connections (NIH, 2001). However, others have pointed to the ES cells stimulating growth factors that may have helped to re-grow the connections in the spinal cord.

In 2005, another team of researchers made another breakthrough in stem cell treatment of spinal injury. Researchers used human embryonic stem cells that were coaxed into becoming early stage oligodendrocytes (myelin) *in vitro*, then injected them into rats at seven days after spinal cord damage and 10 months after the injury (Keirstead et al., 2005). Two months post-treatment, they observed marked improvement in the ability of the rats walking which they were not able to do without the stem cell treatment. However, this improvement only occurred in the rats given the stem cells injection after seven days, not in those with a 10 month old injury. It appears that these precursor oligodendrocytes were able to wrap around the 7 day injured neurons and reestablish nerve impulses. The 10 month old injured rats were unable to recover from their paralysis because scar tissue had filled in the damaged areas of myelin, and the new cells (from the hES cells) could not wrap around properly. This finding was significant because, one, it used human ES cells, thus opening the potential for treating humans. Second, it emphasized that myelin is crucial in spinal cord recovery and repair. Third, the stem cell treatment was only effective in early injury not in older cases. Thus, this finding instills hope on future spinal cord injuries, but perhaps not for those who already have spinal cord injuries, unless treatments can be developed for removing scar tissue prior to stem cell transplant. The outcome from this research seems to be to proceed with stem cell based treatment for recent injuries.

However, again this study was only performed on rat models and not on humans, and extensive use of anti-rejection was required.

Some medical practitioners around the globe have been able to apply stem cells to human patients with some remarkable results. One of the most controversial methods is by the pioneer Dr. Carlos Lima who has used stem cells found at the top of the nasal cavity, known as the olfactory mucosa which has rapidly diving cells, and implanting them into the injury site in the spinal cord. These olfactory stem cells are adult stem cells that are taken from the patient with the spinal cord injury, they are crushed up and then injected back into the patient's spinal cord. The goal of this method is to harness the potential of the stem cell and help grow the axons of neuron which are like the wires of the spinal cord. At a senate testimony, a patient that suffered a spinal cord injury that left her paralyzed waist down summarizes the potential of this application on spinal cord injuries. The patient testified she was able to hold her bladder and control her bowels, as well as walk with the aid of a brace. Prior to Dr. Lima's treatment she was confined to a wheelchair and could not move her legs or control her bladder (US Senate Committee …, 2004). This partial recovery outperforms any typical treatment today. The significant thing about this experiment was that the stem cells were from the patient themselves, and there was no threat of immune rejection, and few ethical dilemmas. The positive results also indicate that the stem cells were able to take hold in the spinal cord and restore some of the connections. Further, this procedure was done on humans that had suffered from the spinal cord injury many months or years before the treatment. This holds the possibility that even those who have suffered from the injury have some hope of being able to walk or live a normal life. However, this procedure has not been able to restore full normalcy, and the mechanism of how it

works is still unknown. Despite this, many more years of research is required for clinical applications.

Both ES cells and adult stem cells show great hope for spinal cord trauma. The biggest challenge will be translating the positive results from rats to humans, which will require a more in depth knowledge of the spinal cord and the mechanisms by which stem cells work.

Stem Cells and Heart Disease

Heart disease is the leading cause of death in the world and in the United States. Heart disease and other heart ailments affect millions of people, and the number of cases is increasing. Heart disease or heart failure occurs when the heart cells called cardiomyocytes die as a result of lack of blood flow to the heart (i.e. blockage of coronary arteries). Less of these cardiomyocytes which are the main cells that make the heart beat (pump) puts more strain on the heart to pump blood to the rest of the body. When the heart is over-strained, the heart may stop beating and a heart attack may result. Heart attacks (myocardial infarction) worsen the condition of the heart and progresses heart disease. The main problem with heart disease is that because of the low blood flow, the cells begin to die but are unable to be replaced, thus weakening the heart. Instead of new cardiomyocytes the area where the cells die is replaced with scar tissue which does not have the contractibility of cardiomyocytes. Because there is no treatment for heart disease, the disease slowly progresses until the heart dies, and the only option is a heart transplant. Heart disease has major consequences on lifestyle and can incapacitate a person. Transplants for those with advanced heart failure are difficult to attain, and most do not survive more than five years (NIH, 2001).

Although there are numerous drugs for treating heart disease, such as nitrates, these drugs only slow the progression, or alleviate symptoms, and little recovery is possible. Recently, physicians and healthcare experts have opted for a preventative platform to combat heart disease. These include lifestyle changes such as more exercise, healthier diets, and awareness of leading causes of heart disease such as high blood pressure, diabetes, and obesity. Yet, the disease incidence has still risen, probably because of the lack of public awareness and lack of applying these preventative measures.

Because of the ability of stem cells to differentiate into different types of cells, the hope of applying stem cell treatment for heart disease has spawned extensive research to find a better treatment for the globe's deadliest disease. The research that has emerged has involved adult stem cells and embryonic stem cells, each holding their own potentials for treatment. One of the first findings in heart stem cells research was that mouse embryonic stem cells were able to differentiate into beating cardiomyocytes (Kehat et al., 2001). Although this was in culture (in vitro), the ability of the murine stem cells to become beating heart cells and carry all the characteristics of normal heart cells was a milestone, and meant that indeed ES cells have ability to become viable heart cells. In 1996 researchers extended this mouse research by differentiating mouse ES cells into cardiomyocytes and then injecting them into the heart of heart attack induced mice (Klug et al., 1996). They observed that these heart cells integrated into the heart and repopulated heart tissue. This research indicated that not only did ES cells have the potential to become cardiomyocytes, but also that it is feasible to inject these stem cells into the heart with possible benefit to heart disease patients. Another important finding was that ES cells were able to become vascular endothelial cells (Klug et al., 1996). These cells form blood vessels and feed the heart blood. They are significant because not only does a damaged heart need new

cardiomyocytes but it needs a sufficient blood supply to that area to keep the cardiomyocyte healthy. So both cardiomyocytes and vascular endothelial cells are vital for repair of a damaged heart from heart disease.

Other research has utilized adult murine stem cells, namely hematopoietic stem cells (HSCs) as an effective stem cell therapy for heart disease (Figure-12). Researchers took mice and created a heart attack (myocardial infarction), then injected HSCs into the area of damage. The researchers observed that the HSCs were able to differentiate into cardiomyocytes and vascular endothelial cells in the damaged portion of the heart (Orlic et al., 2001). The amazing thing was that these cells replaced 68 percent of the damaged area, and the cardiomyocytes were functional. They also found that that arteries and capillaries formed around the area. In essence, the diseased area in the heart was partially repaired. This was followed by the results that the mice that received the HSC treatment had a greater number of survivors than those who received no stem cell treatment. This study emphasized the plasticity that adult stem cells have, and their potential in treating ailing hearts. Other researchers have explored the plasticity of human hematopoietic stem cells and have found that indeed human bone marrow HSCs can become cardiomyocytes and endothelial cells in rodent models. When these human hematopoietic stem cells were injected into rats with a damaged heart, the researchers observed that the area of damage became more vascularized, meaning that the blood flow to the area had increased (Kocher et al., 2001).

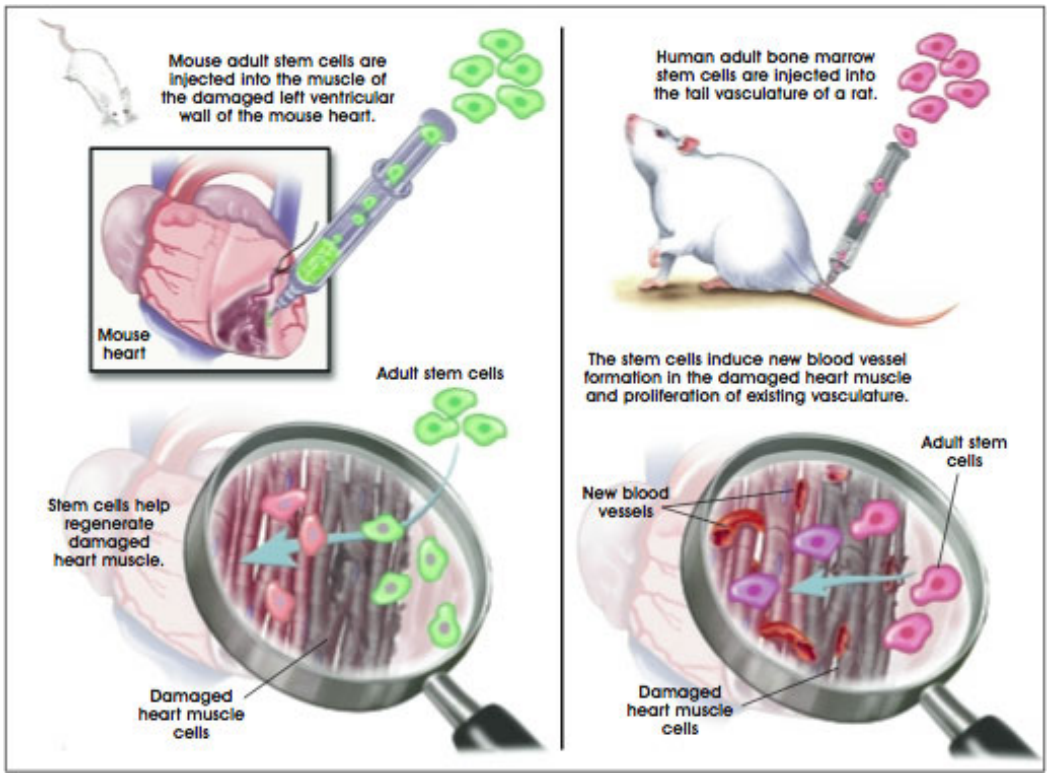

Fig. 12. Adult Stem Cell Therapy in Heart Diseased Mouse. *This illustration shows how adult stem cells such as the hematopoietic stem cells are injected into the damaged portion of a mouse heart, which induces repair of damaged heart tissue tissue and growth of a fresh blood supply to the area (The National Institute of Health, 2001).*

Because of the success in treating heart damage with HSCs in rodent models, some researchers have begun to implement this method in human trials. In various places around the world, small trials have been initiated that involve injecting the patient with their own hematopoietic stem cells thus eliminating rejection. Most of the patients that are in these trials are at the advanced stages of heart disease and this treatment is the last option. In one study, two groups of patients suffering from heart failure were given either the HSC injection or a placebo injection (Schächinger et al., 2006). The course of recovery was examined, and the results had mixed signals. For the group that had the stem cell injection, after four months they had a 2.5 percent better pumping ability of the heart compared to the control group that received the

placebo. This according to heart specialists is a meek number, but does spell that there may be some benefit. The human studies have not seen the dramatic improvement seen in the rodent studies. Other studies have found that there was no statistically significant difference in the treatment compared with those that did not receive any treatment (Lunde et al., 2006). Yet, many heart specialists don't doubt that they do have an effect. They point to a lack of enough stem cells being injected that are attainable through the hematopoietic method. Thus, researchers believe that ES cells have the capacity to produce large numbers of stem cells that can be implanted. However, not enough research has been done yet, and ethical obstacles remain before human studies using human ES cells may proceed. Larger studies are needed before HSC treatment can become a widespread clinical option for those suffering from advanced heart disease.

The research has suggested that both adult and embryonic stem cells hold high potentials in treating those who suffer or may suffer from heart disease. However, the research is preliminary, involving mostly rodent models, and the limited human trials have not yielded spectacular results. It seems that the preventative measures are still the key to avoiding heart disease, but stem cells may in the future be able to effectively help restore the viability to damaged and weak hearts.

Stem Cells and Type I Diabetes

Diabetes has become a major health crisis in the United States, affecting over 18 million people, and the cases are growing each year. There are various types of diabetes, but the major types are type I (or juvenile) and type II diabetes. Type I diabetes is caused by an immune system attack on the beta-cells found in the pancreas that produce insulin (Figure-13).

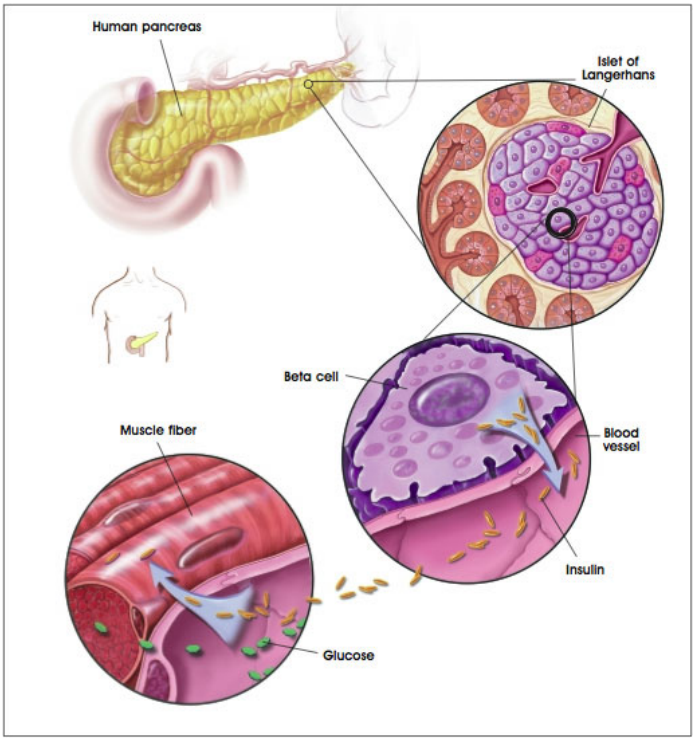

Fig. 13. General Anatomy and Physiology of Pancreatic beta-cells*. This diagram illustrates the location of insulin producing beta-cells and their function in the pancreas. The beta-cells are found in structures within the pancreas called the Ilets of Langerhans (diagram upper right) which responds to glucose in the blood. Beta-cells dump insulin into the blood stream which and shuttles the glucose from the blood to inside cells, in this case a muscle cell (fiber) (lower left). In a diabetic (type 1) the beta-cells are destroyed thus no insulin can be produced* (The National Institute of Health, 2001).

Insulin is a vital hormone that shuttles glucose our main energy source from our blood into the rest of the body's cells. However, because the autoimmune attack kills the beta cells, insulin cannot be produced, and consequently glucose cannot be taken in by other cells. The direct consequence of this is an elevated level of glucose in the blood, and little glucose in the body's tissues and organs that need it such as the brain and muscle. This dilemma leaves the person suffering with type I diabetes with no energy, and high levels of glucose in the blood that become toxic to various organs and the brain.

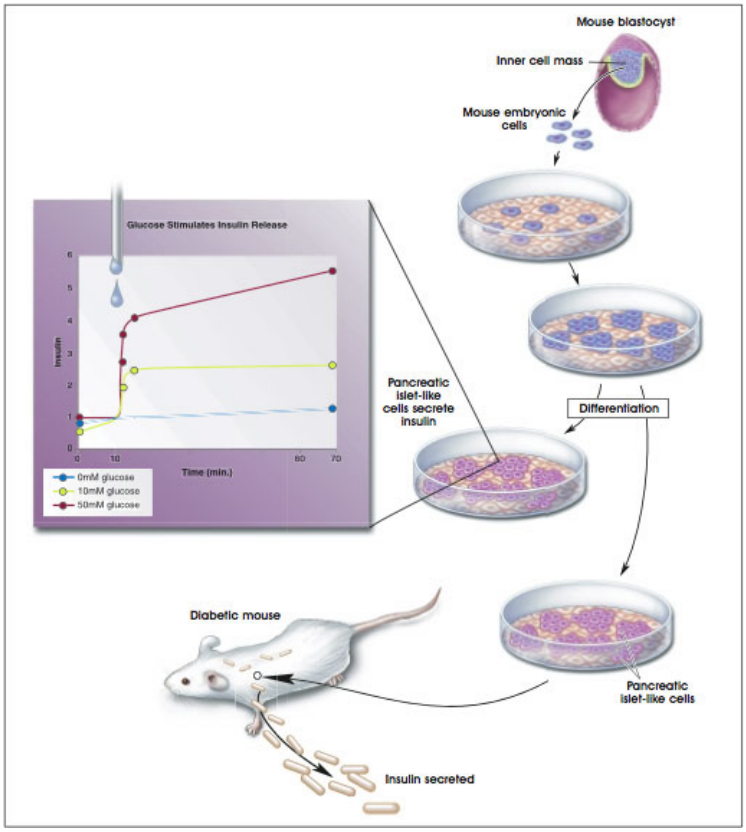

Fig. 14. General Procedure for Using ES Cells to Treat Diabetes. *This illustration shows the general concepts involved in using ES cells to treat a diabetic mouse. The ES cells are taken from the ICM of the blastocyst (upper right) and cultured on petri dishes (middle right). Then after an adequate proliferation, the ES cells are stimulated to differentiate into beta-cells that form islet like clusters which respond to glucose in vitro (left). They are then injected into the mouse (bottom of diagram) where these beta-cells produce insulin every time the mouse consumes glucose thus keeping glucose levels normal* (National Institute of Health, 2001).

If left untreated, the patient with type I diabetes cannot survive. The common treatment for those who suffer with type I diabetes is direct injection of insulin. Although this allows the patient to live, it does not alleviate the symptoms, or the long term complications of blindness, kidney failure, heart disease, or death (American Diabetes Association, 2007). New methods have proven successful in remitting the type I diabetes. The most notable is whole pancreas

transplant from a cadaver. In this case, a new pancreas has in some cases eliminated the diabetes. However, because it is a transplant they are extremely rare and only a small percentage may have chance to receive one. Also, they must be put on heavy doses of anti-rejection drugs that compromise their immune systems. Furthermore, there is the risk of the immune system attacking the new pancreatic beta-cells rekindling the onset of diabetes.

Because of the lack of effective treatments, stem cell research has naturally been at the forefront of a potentially effective treatment for type I diabetes. Like the diseases already discussed above, the theory behind using stem cells to treat diabetes is quite simple. In theory, ES cells can be transplanted into the pancreas or other organ, become differentiated into islet cells, then secrete insulin in response to high blood glucose levels. In following with this theory, researchers have been able to take mouse ES cells in culture and stimulate them into insulin producing beta-cells (Lumelsky et al., 2001). When glucose was introduced in the culture medium, the beta-cells responded by producing insulin. Morphologically, these beta-cells were clustered similarly to the pancreatic unit called the islet. Researchers have also been successful in using ES cells that have become beta-cells and injecting them into diabetic mice (Figure-14). The diabetic mice had been poisoned to destroy it's beta-cells, and injection with new ES cell derived beta-cells was able to stabilize its glucose level, in effect diminishing the hallmark of diabetes, high blood glucose (Soria et al., 2000). This research is significant because first, it illustrates that indeed stem cell derived beta-cells are able to produce insulin. Second, the beta cells were able to survive in the mouse and effectively clear glucose from the diabetic blood. Despite the mice being under heavy immunosuppressants, the basic principal of transplanting functional beta-cells has been demonstrated (in mice), and thus is a feasible goal in diabetes treatment.

There are however hurdles that must be overcome even in mice before ES cell therapy can be used in patients. First, immunosuppression must be minimized or eliminated. Second, the area must become properly vascularized meaning a sufficient blood supply must be established for the transplanted cells. Third, it has to be demonstrated that the treatment is long term and symptoms do not return. And fourth, the underlying factor of adverse effects (i.e. side effects) on the body has to be assessed. ES cell research on diabetes is in its preliminary stages and so far has shown a potential in eventually treating humans, although more research on mice and other animal models are needed before a safe and reliable approach can be tested on humans with type 1 diabetes.

Those in the realm of adult stem cell research have also explored the possibility of using adult stem cells to treat type I diabetes. In a murine study, researchers genetically induced mice to become diabetic (NOD mice) thus damaging the pancreas and beta cells. These mice had high blood glucose and little insulin. The researchers took bone marrow stem cells (hematopoietic stem cells) and injected them into the blood stream of the diabetic mice. After two weeks, they observed that the glucose levels had dropped to normal levels, and insulin production had risen (Hess et al., 2003). When the researchers analyzed the pancreas (using markers) they found that the growth of beta-cells were from the pancreas and not from the hematopoietic stem cells. Thus, although it is unknown what in the bone marrow stem cells stimulated growth of beta-cells, it underscores that there is some secreted factor that may help repair damaged pancreatic tissue.

With respect to using stem cells in patients, because hematopoietic stem cells have been used extensively for treating blood disorders, trying this on people with type 1 diabetes is practical and lacks the ethical strings associated with human clinical trials. Indeed researchers have already extended this method to a small number of patients with type 1 diabetes. In one

small study, 15 newly diagnosed type 1 diabetics were injected with their own hematopoietic stem cells (isolated from peripheral blood) and tracked. The researchers found that 14 of the 15 did not need to take insulin and the diabetes had remitted (Voltarelli et al., 2007). Most were insulin free for a number of months before needing to take insulin again and regaining diabetic symptoms. This study although small is quite significant because it underscores that indeed hematopoietic stem cells do have the potential to help repair pancreatic function. A larger study is needed, and also an investigation of why most of patients in the study regained their diabetes is needed. One advantage of using hematopoietic stem cells is that the stem cells come from the very own patient receiving the treatment and thus immune rejection is no threat or burden.

Both ES cell research and hematopoietic stem cell research has given hope that possibly type 1 diabetes may have met its match. The key to any of these hopes is more research that will broaden our understanding of stem cell treatment on type 1 diabetes.

Stem Cells and Diseases Conclusion

Stem cells may also some day be able to treat other diseases, such as ALS, multiple sclerosis, stroke, and macular degeneration. Although there has been amazing progress in stem cell research, more research is needed. Because of stem cells apparent unlimited potential, many people and scientists have hyped the potential of stem cells as being some sort of whiz-bang magical cure. This is not the case as we have seen with the cases presented in this chapter. Stem cell treatment involves multiple complex steps to take it from the lab to hospital. In addition, there are technical challenges that come along with all treatments and stem cells are no exception. Most likely when stem cells becomes a treatment option for patients, this will involve extensive and risky procedures, and may be a last resort treatment. However, to a patient that

has a life threatening disease such as diabetes, stem cells may be the only hope for a priceless normal life. Although hematopoietic stem cells are currently the only widely used stem cell therapy (for leukemia and blood disorders), it is not known when stem cells may become an available human treatment for many of the other human diseases, but many years remain before the predominant murine studies can be replaced with human clinical trials.

Other Stem Cell Applications

Stem Cells and Pharmacological Testing

Although much of the interest in stem cells has revolved around using them for treating diseases, there are many other applications that stem cells may provide a solution for. One of these applications is using stem cells for testing the toxicity drugs have on various tissues. In order for a drug to make it to the pharmacy, pharmacological companies must extensively test their products for safety standards set by the government and for consumer quality expectations. Drug testing is a lengthy and expensive process that may take years and cost billions of dollars for a single drug to be allowed on the market. Commonly, when a drug is tested it first is tested using animals, usually mice. Animal testing however, does not reveal the full toxicity the drug may have, and thus toxic drugs may make it to human clinical trials or to widespread use (Sinha, 2005).

Animal testing has raised concern from animal rights organizations who want the use of animals in research banned. Stem cells may serve as a solution for both, and may in fact help to increase the safety and lower drugs testing time and cost. The rational behind using stem cells is that ES cells are able to multiply indefinitely allowing for large quantities of cells for testing. In

addition, ES cells from humans can be stimulated to differentiate into important types of cells such as liver, heart or brain cells (Okarma, 2001). Then the drugs can be administered to these cultures directly determining the toxicity or adverse effect the drug may have on specific types of tissue. This would eliminate the need for animal testing, and speed up the time from stem cell testing to human clinical trials (Newton, 2007). Furthermore, using human ES stem cells will eliminate the discrepancies between animal trials and human trials, giving a more accurate picture of a drug's potency. Some scientists have acknowledged that this application of stem cells may be the most immediate and have a great impact making better and cheaper drugs that millions of people depend on.

Stem Cells and Whole and Artificial Organs

The field of regenerative medicine has many ambitious goals in order to augment treatment for various diseases. In the above discussion of various disease applications of stem cells, the primary focus was on cellular transplantation of stem cells into the affected patient or animal model. In other words, scientists have been studying the effects of injecting stem cells into a patient in hopes that these stem cells will target the diseased area(s) and repair or differentiate into new cells that can carry the vital function that is lacking in the patient. Although this method has shown some exciting progress, some scientists have higher goals namely using stem cells to create a whole new organ and then transplant the organ into the diseased patient thus eliminating the disease. The theory is a challenging but possible one. If some one for example has advanced heart failure and needs a new heart but cannot receive a match or because donations are in short supply, a stem cell derived heart may be the answer. In this hypothetical scenario, stem cells first must be cultured to differentiate into all the different

types of cells that make up the heart. The key into creating the organ is there must be a three-dimensional scaffold or skeleton that the stem cells can grow on that will make the shape and functionality of the organ—in this scenario the heart. The stem cells must be coaxed into developing the right type of cells in the right spots on the scaffold heart for the heart to be normal. After the cells have been coaxed into the right spot and grow into mature cells, this heart must be proven to be functional, and can then be transplanted into the patient's chest. The scaffolding will most likely have to be a biodegradable material that can breakdown in the body as the organ develops (Glaser, 2003). When transplanted, the organ then must be able to proliferate and grow a sufficient blood supply. As one can see, although in theory it is feasible, there are complex and large challenges in order that stem cells can give rise to a functional and long lasting organ. One simple reason is that organs are complex and contain a multitude of tissue and cell types that come together in a very specific manner to perform its task(s). A second reason is that a well established knowledge of cellular interaction at the molecular level is required for both stem and mature cells, and there is currently a lack of this knowledge.

However, the main question is whether current research has been able to meet the challenges of whole organ construction? And, what are the implications of this research on the future of regenerative medicine? Because of the extreme complexity of the research, researchers from various disciplines including biomedical engineers, biologists, and physicians, have collaborated in beginning to understand what is needed, and experimenting on building whole organs. For example, researchers have been able to construct a bladder for children that have spina bifida. They achieved this by taking biopsies of the bladder tissue from the patient. These cells are then grown on a biodegradable scaffold and then implanted into the patient where it grows a blood supply, and the scaffold breaks down leaving a functional bladder-like organ

(Cross et al., 2003). Although they did not use stem cells directly, researchers point that stem cells may also work in creating this bladder. The bladder is a much simpler organ than the heart or liver but the main concepts remain the same.

Currently no organ has been grown from stem cells, although various companies and researchers have been working on developing prototypes (Glaser, 2004). Most researchers believe that embryonic stem cells offer the best possibility at growing whole organs because they have the flexibility to become any type of tissue and are able to grow extensively in culture or on a scaffold. The prospect for whole organ growth from stem cells is many years away and is in its preliminary research stages. However the development of functional organs using stem cells may save many lives, and eliminate waiting lists for precious organ donations. Again, there is the misconception among some of the public that growing an organ is a whiz-bang thing. Conversely it is highly difficult, and perhaps is the most challenging feat for stem cell research and regenerative medicine.

Hybrid Organs

Although creating whole organs may be the most ideal of treating human diseases, using artificial or hybrid organs have also found a solid foundation in stem cell research and application. An artificial organ is a non biological instrument that does the similar function of the organ. For example, a kidney dialysis machine is an artificial organ since it can aid in filtering blood that the kidney's normally would do. However, the dialysis machine is bulky and does not have the same capacity as the kidney. However, researchers have developed a more dynamic artificial organ that uses both stem cells and normal artificial materials (a "hybrid") such as polymers into a device that is able to temporarily replace a failed kidney. The device uses stem

cells that are seeded in a tube that differentiates into kidney cells that are able to produce urine and cleanse the blood (Glaser, 2003). The advantage is that blood can be redirected to this device outside the body where actual kidney cells can extract toxins and produce urine. Researchers have been successful with this organ and are in clinical trials.

The remarkable thing about stem cells is that there is a limitless potential on their applications. The amount of research on stem cells is staggering with thousands of papers published shedding more light on their potential. Stem cell will not be an answer for all diseases, but it will and already has revolutionized medical thought and medicine.

Chapter 3: Stem Cell Ethics

One of the most famous twentieth century sociologists of science, Robert K. Merton, argued that science is influenced, and is part of, the larger sociological infrastructure. He argued that social institutions, religion, economics, and politics all influence the way science has and will develop. This is clearly seen in today's scientific community where pressure to conform to policies and religious dogma has raised serious questions on science's ability to flourish. The reality of ethical concerns from religious groups and the public has dominated stem cell research. Perhaps no other biological scientific discovery has created such an atmosphere of ethical apprehension. Avoiding these ethical concerns will not solve any problems since science is intrinsically bound by society. The key is understanding the viewpoints of different religions which will give a clearer picture on what the grievances or ethical boundaries are.

When it comes to the major ethical questions on stem cell research, two main questions need to be answered from different religious perspectives. The first is whether scientists should work with stem cells of all kinds? The second is whether the medical benefits that have been seen outweigh any ethical questions? The best way of answering these questions is by analyzing the religious points of views on stem cells, and drawing an overall conclusion on what the ethical concerns are and how it impacts stem cell research. These questions are vital to the future of stem cell research because it will most likely shape the way research will progress and be performed. In this chapter I will elicit the perspectives of the five major religions namely, Christianity, Islam, Judaism, Hinduism and Buddhism on stem cell research which will bring out the dynamics of the ethical controversy surrounding the stem cell debate.

Religious Views of Adult Stem Cell Research

Earlier (Chapter 1) I made the distinction between adult stem cells and embryonic stem (ES) cells. Adult stem cells are those that are taken from a developed human being, or from blood from an umbilical cord, not from an embryo. One of the most significant applications of adult stem cells is hematopoietic stem cells (HSCs) that have been used for over forty years to save lives in bone marrow transplants. However, during that time there were no ethical voices from any group or religion concerning research and treatment using these adult stem cells. Even today as new research on adult stem cells have emerged, religious groups have not condemned this research. In fact, adult stem cell research has become a platform for many religions as the "moral" alternative to embryonic stem cells. All major religions of the world, Christianity of all denominations, Islam, Judaism, Hinduism, and Buddhism are not against adult stem cell research. The Catholic Church has been outspoken in the stem cell debate voicing their opposition to ES cell research. However, when it comes to adult stem cells, even prominent Catholic officials representing the Vatican have actively supported adult stem cell research. In a treatise written by the Vatican on stem cells in 2000, it expressed support and hope for adult stem cells saying, "*The possibility, now confirmed, of using adult stem cells to attain the same goals as would be sought with embryonic stem cells - even if many further steps in both areas are necessary before clear and conclusive results are obtained - indicates that adult stem cells represent a more reasonable and human method for making correct and sound progress in this new field of research and in the therapeutic applications which it promises. These applications are undoubtedly a source of great hope for a significant number of suffering people.*" (Correa and Sgreccia, 2000). This affirms the support by the Catholic Church for adult stem cell research and a moral acceptance of using adult stem cells for treating diseases.

The Protestant Churches have also come out recently to clarify their stance on adult stem cell research. For example, the conservative Evangelical Covenant Church bolstered its support for adult stem cells saying, "*Use of adult stem cells from bone marrow currently seems the most promising. Since these are some of the easiest cells to isolate and cultivate, they provide a promising beginning for regenerative therapy*." (Reichenbach, 2004). The key factor of adult stem cell research for many Christians is that it bypasses the moral dilemmas that ES cells face, but still holds the door open for treating human diseases and helping humanity. A prominent women's Christian group that has been vocal on the stem cell debate expresses their optimism for adult stem cells citing numerous medical advances with adult stem cells saying, "*The alternative of adult stem cells is greatly needed in a scientific community willing to go to nearly any length for medical advancement.*" (Elliot and Porowski, 2005). Thus, in areas that are influenced by Christian traditions, both Catholic and Protestants, adult stem research should be welcomed as a morally licit scientific venture. However, many times the Christian point of view is fogged by the more controversial ES cell debate and draws conclusions by scientists and by the public that Christians are wholly against *all* stem cells and scientific advancement, and are insensitive to helping advance medical treatment.

Although the Christian voice on the stem cell debate in United States has been the most prominent, other religious views and ethical concerns have become an important in an ever diversifying society and scientific community. The Jewish beliefs on adult stem research have also been researched by Jewish scholars, and have concluded that adult stem cells do not violate Jewish law. The common conclusion by Jewish Torah scholars in conjunction with Jewish scientists is that "*While there are few Jewish legal objections to deriving the stem cells from adult or umbilical cord tissue, the problems arise, however, with deriving stem cells from the*

embryonic tissue." (Jakobovits, 2006). The ethical argument in adult stem cell research is diminished in Jewish traditions because there is no question of whether there is a taking of a life but rather only saving one. So naturally, saving a life is common to Jewish practice as well as natural human trait. The statement above however does not imply that Judaism is against ES cells necessarily, but that ES cells raises ethical questions that needs to be answered in more detail, whereas adult stem cells do not.

Scholars and scientists in Islam have also explored the ethics of adult stem cell research in Islamic law and scripture. Again, like the Jewish philosophy, Muslims see no hindrance to faith, and see this sort of research as obligatory because it may help relieve suffering or help people. The logic is that adult stem cells do not harm another person, and helping others is a "religious duty" and thus adult stem cell research should be pursued (Siddiqi, 2002). A prominent Muslim scholar expressed the Islamic perspective on adult stem cells saying, "*And, as far as stem cell research is concerned, adult stem cell research is allowable (and actually praiseworthy, for its goal of providing health benefit)…*" (Sachedina, 2000). Thus, Islam does not simply accept adult stem cell research, but rather encourages it as a religious responsibility that has few ethical strings.

Hinduism and Buddhism which both share similar worldviews have also expressed acceptance to adult stem cell research. Both religions view science and knowledge as part of a spiritual force that if harnessed for good can be allowable. A Buddhist scholar drew his conclusion that, "*In terms of general principles, however, it seems that in accordance with other world religions Buddhism would hold that: a) there is no ethical problem in principle with the therapeutic use of adult stem cells…*" (Keown, 2001). Hindu scholars also view adult stem cell research as permissible since it does not violate natural order like ES cells do. The consensus of

these two religions is that there are no moral or ethical problems with adult stem cell research, and nor does it disturb life or nature and thus this research is encouraged as valid way for medical treatment. Thus, no major world religion is against working with adult stem cells, so long as they are used to try to save lives.

Religious Ethics of Human Embryonic Stem Cell Research

Although adult stem cell research has lead to little ethical controversy, embryonic stem (ES) cell research has produced a phenomenal amount of ethical concerns from various religious and religio-political groups. Unlike the unanimous agreement of the major religions in favor of adult stem cell research, ES cell research is divided among the religions, and even within religions, that adds to the complexity of the ethical issues. The issue of ES cell research has caused a reevaluation of religious doctrine and its ethical role in guiding stem cell research. It would be immature to adopt only one religious view on ES cells as the moral and ethically correct way. Rather, an evaluation and understanding of the basis for support or opposition must be considered from all religious perspectives that will provide a path so that ES cell researchers can ethically pursue advances in this exciting field.

The main question that surrounds the issue of the ES cell debate is when life begins. For all of the religions discussed, life is when ensoulment takes place. In other words, what is the time when the spirit meets the biological entity? The answer to this question by in large is the moral calculator to whether ES cell research is moral or immoral. The next moral question is whether the destruction of an embryo/ blastocyst is morally unacceptable or acceptable even when the potential of saving other lives is the goal? This question is the looming question that I

mentioned earlier on the battle between potential medical benefit and the ethical detriments that arises in some religious views.

Before discussing the various religious standpoints on ES cell research, it would be helpful to briefly recap the scientific basis of conception and ES cell technology. When a sperm and egg meet in a human they fuse to form one cell called the zygote. This cell starts to divide into more cells over the course of days, and by the fifth day it is made up of about a few hundred cells shaped into a hollow ball called the blastocyst (Figure-15) which is about the size of a pinhead.

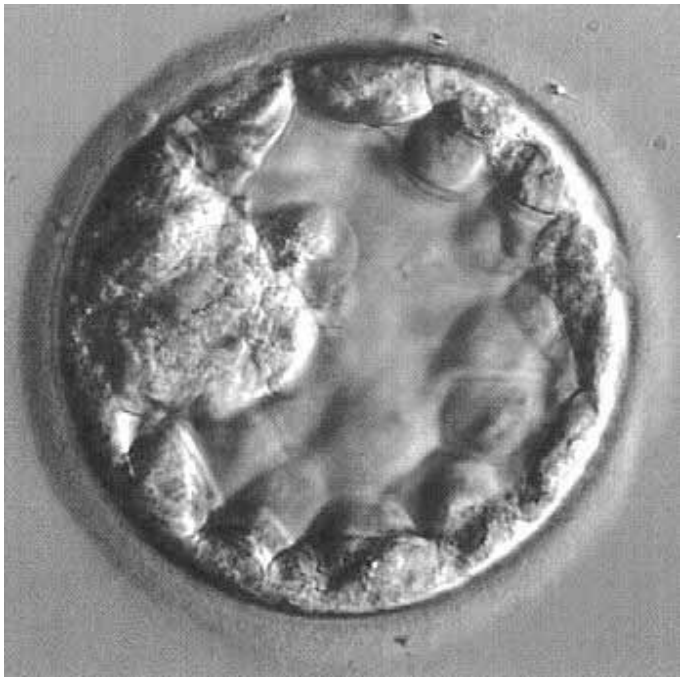

Fig.15. Human Blastocyst at 5 Days. *The main ethical question for hES cell research is if this embryo shown here, is a living human with a soul and entitled to the same rights that a normal person has. If so, would killing this ball of cells the size of a pinhead be just as morally wrong as killing a fully developed person?* (Advanced Fertility Center of Chicago, 2007).

At this stage, the there are three main features of the embryo, the trophoblast, blastocoel, and the inner cell mass. Pluripotent ES cells can be extracted from the inner cell mass (ICM), and be grown on Petri dishes indefinitely. In order that the ES cells can be extracted, the blastocyst (embryo) must be destroyed in the process. Normally, the only source of these embryos is by *in vitro* fertilization produced in IVF clinics that usually use IVF technology for couples with fertility problems. Because excess embryos are produced (the success rate is not very high and couples often produce extra embryos in case they are needed), the extra embryos are frozen in the IVF clinic. These excess embryos will likely never be used, and are usually destroyed following consent by the donors. Thus, scientists can use these banks of excess embryos to create more ES cell lines for further research. Another method is by taking the sperm and egg from the donors and developing them to the blastocyst stage without the intent of reimplantation, then extracting the ES cells. Both these methods are done *in vitro* meaning in a test tube or Petri dish and never from the womb of a mother.

Christian (Catholic) Ethical Perspective of Human Embryonic Stem Cell Research

As I mentioned earlier, the main question for the Roman Catholic Church is when life begins and whether the destruction of this "life" warrants it as immoral and murderous. Catholic edict claims that life is started at conception, when the egg and sperm unite (Correa and Sgreccia, 2000). Thus blastocyst embryos which are 5 days old are "humans" and are entitled to the same rights that any human walking around has. The main opposition is that because hES cell extraction destroys the embryo (blastocyst) this human is being murdered and denied the right to develop and live (Pellengrino, 2000). The equation is the same as killing a person in a homicide, and thus is religiously immoral and sinful. In Catholicism, the embryo is not just a ball of cells

but a living entity that has a soul and human dignity that cannot be denied, and subsequently isolating hES cells violates this right by destroying the human embryo. However, the argument has arose that because the end goal of ES cell research is good and genuine could this justify ES research? But the stance of the Catholic Church is that just because the end goal is good and moral it does not make the action right, and thus even with the medical potential of hES cells research it is still unethical and morally wrong according to most Catholic scholars. Thus, in the Catholic perspective, the detriment outweighs the medical benefit of hES cell research should not be a morally licit endeavor.

Both the late Pope John Paul II and the current pope Benedict XVI have spoken critically against both hES cell research and those who conduct this research. In an address Pope John Paul issued a clear statement that summarized the Catholic leaderships' position on hES cell research saying, "*The challenge to life has grown in scale and urgency in recent years. It has involved particularly the beginning of human life, when human beings are at their weakest and most in need of protection. 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*." (Pope John Paul II, 2005). Like Pope John Paul II, Pope Benedict XVI has also issued his view on the ongoing hES cell research saying, "*Scientific research must be encouraged and promoted, so long as it does not harm other human beings, whose dignity is inviolable from the very first stages of existence*." (Pope Benedict XVI, 2007). Both Popes emphasize the criminality behind

"killing" an embryo as more cruel for the fact that they are "innocent" and "defenseless" which naturally makes the crime graver.

In the United States, Catholic officials have also tried to pressure politicians and the public that ES cell research cannot be tolerated saying that, "*We hope and pray that President Bush will return to a principled stand against treating some human lives as nothing more than objects to be manipulated and destroyed for research purposes. As we face a new century of powerful and sometimes even frightening advances in biotechnology, we must help ensure that our technical advances will serve rather than demean our very humanity.*" (American Catholic, 2001).

This stance however is not unanimous in the Catholic tradition. Various Catholic leaders and scholars have voiced different opinions concerning hES cell research that actually support its advance. These Catholics have justified their support for hES cell research from older historical traditions (Catholic) that believed that life and ensoulment occurred after conception not during it as is believed by the church today (Newton, 2007). Also, these Catholics acknowledge the scientific understanding of human development and believe that, like human development, spiritual development follows likewise. Thus, the fully developed human in their view is more superior than a pin sized human embryo and carries different rights. Margaret Farley a prominent catholic and scholar of Catholicism expresses the proponent view of hES cell research saying in a bioethics testimony, "*A growing number of Catholic moral theologians, for example, do not consider the human embryo in its earliest stages (prior to the development of the primitive streak or implantation) to constitute an individualized human entity with the settled inherent potential to become a human person. The moral status of the embryo is therefore (in this view), not that of a person, and its use for certain kinds of research can be justified.*" (Farley, 2000). Another

view from another well known Catholic scholar, Thomas A. Shannon, uses the basis of development of a human and the distinction between phases of being human. His justification stems from using "common nature" that is characteristic of all humans and "individual nature" which defines a person. An embryo is thus in common nature to us sharing the same genes. But it lacks individuality that only a developed person will have and are given rights to. So, the embryo is not at the same as a person and cannot be given the same status and rights, but can be respected as being in "common" with us (Shannon, 2001). Although he does not approach the question of ensoulment (when the soul is joined with the physical being), he implies that in effect the embryo is soulless and thus can be used for stem cell research. These views however form the minority of Catholic belief, and the opposition including key figures such as the Pope have defended their interpretation as the true "Catholic" understanding. Farley noted the division in hES cell research among Catholics in her bioethics testimony, "*We have, then, two opposing cases articulated within the Roman Catholic tradition. It would be a mistake to conclude that what this tradition has to offer, however, is only a kind of draw. It offers, rather, an ongoing process of discernment that remains faithful to a larger set of theological and ethical convictions…*" (Farley, 2000). According to this assessment, the Catholic view of hES cell research is not uniform, and opinions that have analyzed the religious texts and ethics have come with different conclusions. Thus, labeling Catholicism as against embryonic stem cell research may not be the appropriate conclusion. However, the pontifical (Pope and hierarchy etc.) stance is clear—that is embryonic stem cell research is unacceptable, and other techniques such as adult stem cell research must be supported and undertaken.

Catholic Stance on Parthenotes

However, the ethical debates have not stopped at just using fertilized embryos but also new techniques such as human parthenogenesis and therapeutic cloning that have been shown as possible alternative ways at creating blastocysts from which hES cells can be isolated. Both these techniques have complicated the ethical debates and have spurred a new layer of ethical concerns that needs further evaluation. Human parthenogenesis for example has raised new questions on the meaning of life and the destruction of it. Human parthenotes are eggs that are stimulated to divide without the male contribution (sperm) and contain only the females genes. One of the hallmark properties of a human parthenote is that it cannot naturally grow into a viable human being and dies soon after stimulation. Scientists have been able to grow these human parthenote embryos to the blastocyst stage and have isolated ES cells from them (Cibelli et al., 2001). Thus, the question is raised as to whether the parthenote is a human being and warrants the rights just as a person or even as a normal embryo? The Catholic perspective has again been split, but conclusions have been made on the legitimacy of the parthenote and whether this type of research is moral or not. Because the parthenote dies early and does not have potential to become a person, scientists have hoped that this technique may avoid the ethical concerns so prevalent in normal ES cell research. However, the Roman Catholic Church has been critical of parthenote based research. One reason is because they claim that because parthenotes are able to grow to the blastocyst stage like the fertilized embryo it thus has the same right of being human as the fertilized embryo. The second reason is that since it has not been fully proven that a human being cannot be produced by natural or artificial means from a parthenote, the *possibility* that a human may be able to be formed leaves it morally questionable and undesirable (Latkovic, 2006). A third reason is some see this manipulation of an egg as reducing the human sanctity of

life to just a biological phenomenon, and doing odd things such as parthenogenesis shows disrespect to the living human entity including a parthenogenic embryo. As a result of these three reasons, human parthenotes for the Roman Catholic Church are not an ethically sound source for hES cells. However, because the science on this is still vague and new, there has not been a consensus on this issue, and those Catholics that are proponents of hES cell research will be sure to debate the rational of the hierarchy.

Catholic Stance on SCNT

The other technique that has been discussed is therapeutic cloning which uses somatic cell nuclear transfer (Discussed in Chapter 1), essentially cloning a cell and growing it to the embryo stage where the ES cells can be taken out. Because this method eliminates rejection of the transplanted stem cells from a donor since the cells have the patient's same genetic information, it has been a well sought after goal in stem cell research that if successful could revolutionize regenerative medicine.

However, the Roman Catholic stance on therapeutic cloning is much the same as normal embryonic stem cell research. For example, a statement by the Vatican responding to the legitimacy of therapeutic cloning said, "*The answer is negative, for the following reason: Every type of therapeutic cloning, which implies producing human embryos and then destroying them in order to obtain stem cells, is illicit; for there is present the ethical problem examined above, which can only be answered in the negative.*" (Sgreccia and Correa, 2000). Here they say, because the cloned embryo is developing into a fully developed human, this is the same as destroying the fertilized embryo and thus is just as grave. So two implications can be made this statement. One is that this cloned embryo is living and ensouled. Second, the cloned embryo has

the same status as the fertilized embryo, and thus therapeutic cloning is just as morally wrong as any other embryonic stem cell research. This method seems to be even more ethically alarming because it involves a very sensitive and ethically troublesome topic of cloning. Therefore, the issue of therapeutic cloning is highly entangled in two ethical conundrums. It is unlikely that the Vatican and other Roman Catholic officials will sway to the arguments made by Margaret Farley and Thomas Shannon. It has yet to be determined if the Roman Catholic's view will impact the direction of future ES cell research. However, The Roman Catholic's ethical concerns have echoed to other religions and have cast a moral cloud that hangs over hES cell researchers.

Protestant View of Human Embryonic Stem Cell Research

Like The Roman Catholic Church, most protestant denominations have come out against hES cell research and have labeled it immoral. However there has been shifting views, and some denominations have said that hES cell research is acceptable. The conservative Evangelical Church and Baptists have supported the views of the Catholics, calling the destruction of a living embryo immoral and sinful. For example, a statement by a protestant ethicist claims that, "*Human embryos are living human beings in their earliest stage of development. They don't have to be viewed as human persons for us to realize they are more than just biological specimens*." (O'Mathúna, 1999). This belief falls along the same lines that Catholics argue. The argument by protestant opponents of hES cell research is that the fertilized egg is a human being with all the rights that accompany it. The destruction of an embryo is just as grave as the killing of a person and thus is immoral. Some Christians see the unethical nature of stem cell research as taking one life to help another. One Christian view says in offense of hES cell research, "*The*

underlying utilitarian belief that some humans need to be sacrificed for the betterment of others is morally and ethically wrong." (Vick, 2000).

Some Christian denominations have supported hES cells research. Churches such as the United Church of Christ, Episcopalian Church, and Unitarian Church have joined forces to provide an alternate Christian view of the ethics of hES cell research. Groups such as the Christian Alliance for Progress have cited their reasons for their support and ethical platform. There view is starkly in contrast to the anti-hES cell Christians saying, " *I don't believe for a minute that cells that would be thrown away from fertility clinics have the same essence as real, living human beings endowed with the Spirit of their Creator.*" (Faithful Progressive, 2005). Their rational is although these embryos from IVF clinics are living and even ensouled, throwing them away or keeping them frozen indefinitely, they believe, is not the best way of utilizing them and should be used to benefit humanity at least. So for these Christians the ethical questions is not whether the embryo is living or not, it is a matter of utilization of these embryos that rationalizes hES cell research. They also see that hES cell research may also save lives and is a form of being "pro-life".

Both proponents and opponents in the Christian religion have been trying to influence political leaders on their ethical opinion and why their belief should be enacted as part of the law. The current President George W. Bush for example who has strong religious beliefs as a Christian (United Methodist) has weighed on his opinion and has rallied behind the opponents of hES cell research. His strong ties with the Evangelical Church who are opposed to embryonic stem cell research has not only backed his own opinion but also has enacted legislation in 2001 that limits the funding and research capabilities of hES cell research. Bush has openly stated his opposition saying, "[the pro hES cell research bill] *would support the taking of innocent human*

life in the hope of finding medical benefits for others." (Bush, 2006). His spokesman also reiterated Bush's ethical concern for this research saying in a press conference, "*The President believes strongly that for the purpose of research it's inappropriate for the federal government to finance something that many people consider murder. He's one of them. The simple answer is he thinks murder's wrong.*" (Snow, 2006). The legislation that this statement is referring to is a bill bought by congress that would allow federal funds for hES cell research. Bush's own legislation in 2001 which he claims was lead by his ethical conscience limited funding of all hES cell research after August, 2001. Thus he took his ethical belief and enacted legislation in order to cease funding for what he would call "murder" of an embryo, and subsequently the government should not take part in this action. Whatever the position, the ethics of hES cells has become a political battle that has crossed party lines and has spawned a number of federal and state bills that will influence the way hES cell research will develop (discussed in Chapter-4).

Fig. 16. Political Cartoon on the Ethical Dilemma of hES Cells. *This political cartoon poignantly expresses the complexity of the ethical dilemmas faced with human ES cell research. The cartoon raises the question of whether the life of an embryo is as valuable as the life that may be saved from stem cell therapy* (Illinois Family Institute, 2007).

Jewish Perspective on Human Embryonic Stem Cell Research

Although Christianity is by far the largest religion in the United States, other religions have also weighed in on the ethical standpoint of the embryo and hES cell research based on their religious traditions. Unlike the Catholics and other Christian denominations, there has been little debate within the Jewish faith on the status of the embryo and the religious ethics that back their standpoint. Almost all Jewish sects seem to come to the same ethical conclusion on hES cell research. The Jewish ethical conclusion based on scripture and rabbinic interpretations concludes that hES cells research for the purpose of finding medical treatments is allowed and encouraged (Dorff, 2000). The first reason for their acceptance is because the overall goal of hES cell research is to save lives, which is the chief law in the Judaic Laws (Tendler, 2000). The second reason deals with the status of the embryo. Jewish scholars have investigated biblical texts and have found that the embryo has no moral status for the first 40 days of conception. Judaic texts have called these first 40 days of the embryo as "mere water" and not ensouled and granted essentially the same moral status, if any, as water. However, an embryo that is implanted in the mother's uterus gains a moral status that cannot be manipulated. Rabbi Moshe Dovid Tendler states the Jewish view on the morality of the embryo saying, *Thus, There are two prerequisites for the moral status of the embryo as a human being; implantation and 40 days of gestational development. The proposition that humanhood begins at zygote formation, even in vitro, is without basis in biblical moral theology*." (Tendler, 2000). The moral status of the embryo for the first 40 days even in the womb is like water but cannot be aborted and removed. This does not pose a challenge to hES research because embryos are first used from spare embryos in IVF clinics fertilized outside the mother. Also, hES cells are taken from the blastocyst stage which is only a five day old embryo and thus has no moral status. The

conclusion is then that because there is no moral status of an embryo as a human, using these embryos is not murder and is legitimate (as long as the embryo is *in vitro*). Jewish scholars often note that working with ES cells is not just acceptable, but is also mandated, because it is working towards helping humanity which is a key part of the Judaic laws (Dorff, 2000). Unlike the Catholics belief that life begins at conception, Jews believe ensoulment starts at 40 days, and only then is the destruction immoral and grave as murder. In general, the Jewish tradition overwhelmingly supports hES cell research, and scholars feel it does not impede on any religious decrees. Jewish scholars also see no objection to both human parthenogenesis or therapeutic cloning since the embryo is not a living being (Zoloth, 2000). The Jewish approval of hES cell research has been a banner for bringing pro hES cell legislation into law that still respects ethical concerns. The Jewish acceptance and support has given an alternate view (from the Christians) of ethics based on biblical texts and modern ethical reasoning. The difficulty in drafting legislation based on different ethical concerns is that the legislation is going to have to favor one ethical or religious point of view in order that a meaningful resolution can be reached.

Islamic Perspective on Human Embryonic Stem Cell Research

Islam which is the second largest religion in the world after Christianity has also dealt with the ethical concerns that arise in the issue of hES cells. Like the Jewish tradition, the Islamic tradition is based on holy texts (Quran, Sunnah) which make up the social and religious laws, and scholarly thought when scripture does not explicitly say what is lawful. Islamic scholars have come to a similar conclusion as Jewish scholars and have said that hES cell research is permissible based on religious text and inference made by religious scholars. Islamic law views life as two groups, potential life and actual life (Siddiqi, 2002). Potential life is an

embryo or a fetus that is not ensouled and has the *potential* to become a human later on. In Islam, potential life is not given the same status as actual life. In fact, Islam views the human embryo as having no significant status for the first 40 days (or 120 days depending on interpretation) of gestation whether in the womb or in a test tube. Thus, similarly to the Jewish perspective, Islam believes that there is no ensoulment in an embryo for the first 40 days, and that Islamic scripture has described the 40th day as when God "breathes his soul" into the embryo thus making potential life into actual life consequently making the destruction of this actual life unlawful (Sachedina, 2000). So, scholars have advanced Islamic laws into making logical conclusions on the modern issue of the ethical nature of hES cell research. The first is because Islam believes that ensoulment occurs after the 40th day, destroying the embryo is not unethical or immoral and is allowed. Second, the use of spare embryos from IVF clinics are allowed, and thus extracting ES cells from the blastocyst (in vitro) which is a five day embryo does not violate any Islamic laws (Siddiqi, 2002). Thus manipulation of the blastocyst is not a crime and in fact has been called "obligatory" to do this research for it seeks to help treat disease and help humanity overall (Weckerly, 2006). Islam however, does not permit insemination of an egg that does not belong to a married couple and thus either spares from the couple or IVF embryos for research must come from consented married couples (Siddiqi, 2002). The conclusion from an Islamic ethical perspective is that hES cell research does not infringe on any laws, and that not only is it allowed but it should be a high priority for Muslims since is seeks towards saving lives and bettering humanity.

We have seen two religions, Judaism and Islam that have no ethical problem with using human embryos for medical research. It is a common misconception that religions or religious people of all faiths are against this "immoral" act. However, we see an interesting phenomenon

in which Judaism and Islam which are heavily governed by religious laws see no moral conflict. Both of these religions have very similar explanations of why their religions allow this research. It seems that the Christian ethical concerns has silenced Jewish and Islamic encouragement of hES cell research, and has created a battle between religion and science that in these two faiths does not really exist.

The other moral question that will need to be answered, is what religious ethical doctrine will be accepted in society as law making? Despite the US being a largely Christian country, will the public and law makers support ethical positions held by Jews and Muslims? Or can a consensus be reached among the three "Abrahamic" faiths (Christianity, Judaism, and Islam) that endorses a pro- hES cells ethical understanding? Already, those Christians in support of hES cell research have come together with Jews and Muslims in the hope that hES cell research is not compromised. In other countries that have large populations of Jews and Muslims such as Israel, there has been an explosion of hES cells research as well as adult stem cell research that is a testament to the support both Judaism and Islam have for all forms of stem cell research.

Buddhism's and Hinduism's Perspectives on Human Embryonic Stem Cell Research

The religions of the east, Buddhism and Hinduism have also had to grapple with the ethical issues that come along with hES cell research. Buddhism and Hinduism have a tradition of natural laws in which nature is the ultimate power and force—and that the goal as a person is to understand nature in its entirety. Both these religions also have a different definition of life than other western religions such as Christianity. Buddhists and Hindu's believe in the concept of reincarnation in which the soul of an individual is passed on to different creatures or people in search of enlightenment (understanding nature). The question here is then is, does the embryo

constitute a human being that is ensouled? Buddhist scholars believe that the reincarnation (rebirth) means that life is started at conception when the sperm and the egg meet. The scholars cite that this living individual which is in the form of an embryo contains *karma* (the good and the bad one will do) from a deceased individual (because of reincarnation) and thus this karma present in the embryo would make this embryo the same moral status as an adult person (Keown, 2004). The conclusion from this is that destroying this embryo is taking away a life and this is not desired in Buddhism. Buddhists however, sees not only destroying embryos for research as unacceptable, but the spare embryos created in IVF clinics that will be frozen or destroyed as a violation of the embryos rights and also not allowed (Keown, 2004). Consequently, working with hES cells is immoral in Buddhism and should be avoided. Buddhist scholars also note that although the goal may be good and help people, the action is still not permissible. One Buddhist scholar said this, "*Destroying a human embryo gives a person bad karma, even if the person believes he or she is doing it for the greater good. One cannot be free from the consequences of the action itself.*" (Bhikkhu, 2007). The stance for most Buddhists is that hES cell research is immoral because it destroys life and subsequently cannot be supported.

Hindu scholars have also said that the embryo from conception is a reincarnated soul and thus must be treated as though this soul was a living person. Killing the embryo is tantamount to killing a person and thus is prohibited in the Hindu tradition (Jyoti, 2007). Hindu's also are critical of hES cell research because it disturbs the natural balance that nature has set forth. One Hindu scholar said in response about the morality of stem cell research, "*If we disturb the balance of nature, the only place it will lead us is to destruction. Whatever has been created by God has been done after a lot of consideration, keeping in view the requirements of man.*" (Saraswati, 2003). The emphasis in Hindu ethics tends to be that manipulating nature is not

beneficial and does not in the end provide any good, even if the goal is to help the sick. Another Hindu scholar also criticized hES research saying, "*We have no right to kill anyone deliberately… As for destroying embryos in the process of working for the greater good, I don't believe a greater good will be achieved through research that's directed toward fabricating new, commercial medical therapies.*" (Jyoti, 2007). Although Hindus believe that human embryos should not be used for research because it kills a life, they also believe that animals that are used for testing or research should also be treated with some respect since the reincarnated soul may also preside in other creatures (Hug, 2006). Thus Hinduism is opposed to using human embryos for research and to a lesser extent animal research as well, and considers it immoral to take away life from the embryo violating natural law.

hES Cell Research and American Public Opinion

The United States tends to be a religious country, and in one poll 91% of Americans said they believed in God (Braiker, 2007). Another poll indicated that 82% of Americans identified themselves as Christians. This brings out an interesting question. Does the ethical view by the Catholic and Protestant churches largely opposing ES cell research reflect the public ethical opinion? Surprisingly, although the majority of Americans are Christians, polls asking Americans whether hES cell research is ethical has found that a healthy majority of Americans are in favor of hES cell research and would like to see further research. In an ABC News poll in 2007, when asked whether they support or oppose human embryonic stem cell research, 61% support hES cell research, while 38% oppose it (ABC News/Washington Post, 2007). This is an interesting observation on the ethical mindset of Americans. Although most say they are Christian, which is mostly against ES cell research, individuals seem to go against this religious

teaching and favor hES cell research. Thus, the ethical mindset for some Americans may be influenced by family illnesses where a hope for a cure or effective treatment has made a strong argument. It seems that the chief ethical concern among the public is not dealing with whether killing an embryo is murder or not, but rather whether science can find a way to relieve suffering to the millions of fellow citizens that deal with numerous diseases. It also shows that the political thrust may not lie with religious figureheads, but with individual opinions and concerns. In fact, polls that have questioned the approval of George Bush's tightening of federal funding for hES cell research, and have found discontent among the majority of Americans, and one poll said that 52% disapprove and only 31% approve of his 2001 legislation (Newsweek, 2006). Again, we see that the public stance is not parallel to that of ethical beliefs held by Bush in which he calls the destruction of a human embryo murder. Because public opinion is a vital part of American politics, it may inevitably be the main ethical voice for politicians who will draft legislation on the ethical ground of research using human embryos.

Chapter 4: Stem Cell Legalities

The stem cell debate discussed in the previous chapter has not remained in the theological realm. Because ethics is a great part of all societies, and in some countries religion bares much influence on the political system, governments have had to deal with drafting laws that accommodate ethical concerns and scientific opportunities. The debate within the political system on stem cells has been even been more heated than the theological debates, and has further complicated the stem cell issue. However, religious and political concerns are not independent, but intertwined. The result often brings out religious views imposed on the scientific community that dictates the ethical boundaries and scientific ventures that can be performed.

Laws that regulate stem cell research are a vital force in the progression of stem cell research, and by the flick of a pen, research on certain stem cells research can be set back years. On the flip side, stem cell research has shaped the way politics is waged, and especially in the United States it has become an issue that has been a banner for legislators that both opponents and proponents of stem cell research have rallied around. Because laws play an important role in the way stem cell research is performed, this chapter will analyze the laws that regulate stem cell use in the US and abroad, and discuss whether these laws infringe or support stem cell research while characterizing the political (and many times religious) rationale behind some of the legislation.

United States Legislative Policy on Stem Cell Research

President Bush's 2001 Legislation

In the last chapter I briefly touched on President George W. Bush's decision in 2001 restricting human embryonic stem cell research. Although in 2001, hES cell research was still relatively new, lawmakers were in full swing in making sense of the ethics and drafting legislation accordingly. Actually, the public was in support of hES cell research. In an ABC News poll July 26, 2001, when asked if they supported or opposed stem cell research, 63% said the supported hES cell research, while only 33% were opposed to it (ABC News/Washington Post Poll, 2001). Despite seemingly popular support among the public, President Bush on August 9, 2001 signed into law a bill that has become the most important piece of legislation governing stem cell research. Bush shared his views on national television on August 9, 2001, in primetime explaining his decision for passing this landmark bill.

Bush's August 9, 2001 bill outlined an ethical perimeter for federal tax dollars being spent for hES cell research. He declared that stem cell lines (he declared 60 lines) that had already been derived prior to his 9:00 PM announcement could continue to receive federal tax monies for their research. However, the conditions were that the embryos the hES cells were derived from must have been produced for reproductive purposes and were not needed (spare IVF embryos) with the consent of the donors (Bush, 2001).

His second declaration was that any hES cell lines derived from a human embryo after August 9, 2001 would not receive federal money for its research. His rationale behind his decision was that because those lines prior to his announcement have already destroyed the embryo, it would be waste to outlaw those lines. Instead he argued, that those already existing

lines meeting the conditions mentioned above could be used under federal money to help save lives and further research (Bush, 2001). His rationale for restricting further isolation of hES cells from embryos stems from his ethical belief that was discussed in the previous chapter. Because Bush believes that destroying a 5 day old embryo destroys a human life and is tantamount to "murder", he argues that tax dollars and the federal government as well as public tax dollars should not take part in funding this "murder".

President Bush saw his bill as a compromise between ethical concerns and scientific progress in the United States (Bush, 2001). This bill is significant to stem cell research because it limits the amount of federal money that researchers can get; and federal dollars are an essential part of any scientific project. Without significant federal funding, research is handicapped, and because stem cell research is so expensive, US research may start to lag behind. A series of public polls that followed President Bush's remarks outlining administration's stance in 2001, found that initially about half of those polled agreed with his solution to dealing with hES cell research. In one CNN/USA Today poll, 50% of those polled in 2001 agreed with Bush's decision to deny federal funding for future hES cell lines (CNN/USA, 2001). However polls taken in 2007 have shown that the public has distanced it's view on Bush's legislation. One poll which asked whether the federal government should or should not provide federal funding to hES cell research found that 53% believe that the government should provide funding, while 41% said it should not (CNN/Opinion Research Corporation Poll, 2007). Another poll asked whether the federal government should ease or tighten restrictions, 38% believed the government should ease restrictions, while only 20% sided with Bush's 2001 restrictions (USA Today/Gallup Poll, 2007). Although there has been a shift in public opinion on Bush's 2001 legislation, Bush himself has stood behind his rational and regulatory policy on stem cells even with increasing

congressional and public opinions differing from his view. Bush was aware that his decision to limit federal funding was risky for both his popularity and US scientific community. President Bush in November of 2001 created The President's Council on Bioethics made up of various religious, scientific and medical experts that would observe and follow the scientific breakthroughs, and report to the president its recommendation on the ethical basis of the continued stem cell research (The President's Council on Bioethics, 2002). Although his policy was implemented in August 2001, this council played a significant role in the president's further decisions. The Bioethics Council, however does no recommend legislation or way of dealing with the stem cell issue, rather is investigates and carries studies that are focused on ameliorating the ethical dilemmas that may overwhelm President Bush himself. However, the legislative policies and ethical philosophy were all crafted by Bush himself but in council with his bioethics committee. The President's Council on Bioethics is likely to make further influence on the President's outlook on stem cell research.

Figure 17. Political Cartoon expressing Bush's 2001 Legislation. *This cartoon shows Nancy Reagan (middle) a proponent of stem cell research exclaiming her husbands famous lines " Tear down this wall" referring to his restrictive 2001 policy limiting federal funding on further hES cell lines. It shows Bush (lower right) walking away from her plead to open the doors to stem cell research. The cartoon also depicts Bush walking away with the "religious right" symbolizing his ethical belief that destroying embryos is murder. Sentiment like this is*

widespread among public figures, and many believe that Bush has surrendered the medical promise of hES cell research for personal and religious reservations (Keefe, 2004)

2006 Stem Cell Research Enhancement Act

In September of 2006, both the House of Representatives and Senate passed a bill that would ease the restriction placed by Bush's 2001 legislation and allow consenting donors to use spare embryos from IVF clinics to create new hES cell lines with federal funds (CNN Politics, 2005). Standing his ground based on his 2001 legislation, Bush used his first Presidential veto, and vetoed the 'Stem Cell Research Enhancement Act' that was a bipartisan effort (Bash, 2006). In a press conference, Bush defended his veto of this bill by bringing small children who came from spare embryos in IVF clinics sensationalizing his decision to keep the 2001 restrictions in place. In the 2006 press conference, Bush reiterated his ethical stance and unwillingness to allow federal aid for new lines saying, "*This bill would support the taking of innocent human life in the hope of finding medical benefits for others…It crosses a moral boundary that our decent society needs to respect. So I vetoed it*." (Bush, 2006).

Using his backdrop of "spare" adopted babies, he further debated his rationale saying, "*These boys and girls are not spare parts. They remind us of what is lost when embryos are destroyed in the name of research. They remind us that we all begin our lives as a small collection of cells… 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, and I'm not going to allow it.*" (Bush, 2006). However, members of the house and senate even in Bush's own party, the Republicans, have criticized his opposition to expanding federal funding. The 2006 senate majority leader, Bill Frist who is a conservative Republican, said in response to

Bush's veto, "*I am pro-life, but I disagree with the President's decision to veto the Stem Cell Research Enhancement Act. Given the potential of this research and the limitations of the existing lines eligible for federally funded research, I think additional lines should be made available"* (Frist, 2006). Thus, although Bush sees his views as a legitimate conservative argument, other conservative legislators such as Frist have not stood with the rationale.

Figure 18. Bush Announces his veto of the 2006 Stem Cell Research Enhancement Act*. In this photo, Bush (right) defends his decision to veto a bill passed by congress that would have allowed further hES cell lines to be isolated. In expressing his defense he brought children who were from spare embryos and adopted into families. In one statement in his announcement, he says that these children behind him are "not spare parts". His veto leaves his 2001 legislation in effect and he threatened that more legislation advocating more embryo destruction would meet his veto pen* (Wong, 2006).

Bush's 2001 legislation on hES cell research which still remains in effect raises a series of questions that need to be answered in order that a rational conclusion can be met. The first question is whether we need more embryos for further research and why? Can we work with the "60" stem cell lines that President Bush has said are an adequate number of lines to work with? Second, is the law that was enacted by Bush in 2001 too restrictive? And, will his legislation affect the ability for the United States to stay ahead in stem cell research?

Before discussing whether we need more embryos—hence more ES cell lines, it would be helpful to understand what are stem cell lines and their capabilities. Stem cell lines are ES cells that have been removed from a single embryo and cultured multiple times. Because ES cells can grow indefinitely, cultures can be grown and re-grown and sent to different labs around the country or the world and remain in an undifferentiated state. President Bush argues that 60 human ES cell lines are genetically diverse and available for federally funded research (Bush, 2001). He believes that this number is sufficient for all the research since they can be cultured indefinitely and studied by different labs across the country. Thus, he believes there is no need for extra stem cell lines, and no need to destroy more embryos. However, there are a few problems to his rationale. The first is that although Bush explicitly mentioned there were 60 available lines prior to August 9 2001, it has been discovered that only 22 distinct lines exist according to the National Institute of Health stem cell registry (NIH, 2007). This means that only 22 lines not 60 lines are receiving or are eligible for federal funding. Even this number may be large, and the actual number may end up by some estimates to be only 15 or even 9 lines (Garfinkel, 2004). This discrepancy, is significant because President Bush believed that the number was 60 and thus enough and based his entire legislative policy on that number. Now that scientists are finding out that only a handful of lines are available for federal funding, the confidence level among many researchers been wracked with hesitation since the number of lines is so unsteady.

The other question is, even with 22 lines, is the number adequate for staying up to date with the ambitious goals of hES cell research? Although, theoretically these lines can grow indefinitely in their state, there are technical challenges that defy the ability for these stem cells to remain fully viable. The first technical problem with the current federally funded 22 lines is

that all these hES cells were grown on Petri dishes layered with murine embryonic fibroblast cells called a feeder layer in order that it provides a place for the hES cells to stick on and for providing nutrients to the hES cells. Scientists worry that these animal feeder cells will corrupt the hES cells and transmit pathogens such as viruses (AAAS, 2003). Using these potentially corrupted hES cells would make it risky to transplant them into humans and make working with these hES cells more difficult. Although a new method has been developed that does not need animal feeder cells, all the federally funded ones do (Basu, 2005). Thus, contamination of these lines may make it more difficult for progressive research to continue.

Solutions to the Stem Cell Restriction

The solution to this would be to isolate fresh hES cell lines from new IVF embryos that can grow on the non animal feeder cultures. However, President Bush's regulation will not allow federal funding for further hES cell isolation or research on those new lines. Consequently, his 2001 legislation is too restrictive, and new lines need to be developed if further research is to be made. Further, I believe that because Bush made his policy based on 60 lines when in fact it was close to 22, his policy must be adjusted including allowing the isolation of new lines (from IVF spare embryos) that are federally funded to aid in hES cell research. Also, I believe that researchers should have access to more federally funded embryonic stem cells. Although Bush bases his disapproval on his religious and ethical opinion, growing support from the public and bipartisan legislators has shown that the American public is willing to spend their tax dollars on further isolations that will ease the tight boundaries that Bush has implemented on researchers.

More importantly, most in the public as well as in Capitol Hill (Senate/US House of Representatives) have understood the potential medical benefit that hES cell research and all

stem cell research may provide and are ready to move forward in making these medical benefits a reality for those who suffer from grave diseases. Also, I believe that Bush's restrictions do set the US back and creates a vacuum in which there are many scientists who want to continue research but are hesitant or cannot carry out their research because federal funding is limited to only a few contaminated lines. It has also been the tradition that the US has held the torch in many scientific breakthroughs, and limiting such potential medical research would be a detriment to the whole worldwide scientific community. Thus, I believe that Bush's current legislation is much too restrictive and he has based his reasoning on personal religious and ethical beliefs. Although, there must be regulations, there should not be dates set that determine which line receives federal fund and which don't, or which line is "moral" and which is not. In order for the US to maintain its leadership in stem cell research, new embryos will have to be destroyed and new lines will have to be created under federal monies which poses little ethical concerns to the majority of Americans and US lawmakers.

I would, however, like to clarify that Bush' s 2001 legislation does not restrict *adult* stem cell research, and in fact Bush has supported adult stem cell research allocating $250 million in 2001 alone. Also, it would be an incorrect statement to say that Bush's legislation has outlawed hES cell research. New stem cell lines can still be isolated from IVF embryos with the consent of the donor, however, these lines will not receive essential federal funding. So it would be incorrect to say that that Bush has stopped hES cell research or that hES cell research is illegal, but rather he has restricted federal funding from new lines derived from embryos past August 9, 2001 which I believe is too restrictive for the technical challenges, the inconsistency in line numbers, his ethical ground, and the ramifications it may have on future stem cell research.

State Regulation of Human Embryonic Stem Cell Research

Because President Bush has restricted federal funding for more hES cell research, a number of states have taken it upon themselves to contribute their monies to further ES cell lines and research on these lines. Although most states do not posses the massive budgets of the federal government, states like California, New Jersey, and Massachusetts among others have responded to the scientific community's peril of the lack of federal funding and have seen the medical potential that stem cell research holds. Also, these states have seen stem cell research as an economic investment drawing biotechnology companies to their location providing jobs and economic growth in their states. Bush's legislation does not prohibit *states* from providing money to hES cell research from embryos destroyed after his August 9, 2001. Thus, these states have taken advantage of this and have pursued cooperating with researchers in allocating and funding institutions and companies that need more funding in their research. Some states however, have drafted their own laws that have restricted the research of embryonic stem cells, and some have even tightened restriction more so than the federal law that Bush has enforced. However, state funding in some cases has become the last bastion for embryonic stem cell research although it does not alleviate the need for federal funding.

California

The first state to respond to President Bush's restrictive legislation was California. California legislators responded in 2002 by drafting a bill that would explicitly encourage and fund further isolation and research of human embryonic stem cells using state money. The bill (SB 253) also established a biomedical advisory committee that will oversee and send

recommendations to lawmakers and scientists (SB 253, 2002). The bill was passed by the California Legislature and took effect.

A second bill that was proposed by a state Senator Deborah Ortiz sought to create a state institution that was responsible of allocating state funds and distributing them to researchers involved in stem cell research. However, the bill failed to pass the California Legislature, and was moved to a referendum placed on the 2004 election ballots. The California Stem Cell Research and Cures Initiative, called Proposition 71, would enable the creation of a California Institute of Regenerative Medicine that would be the main agency endorsing and overseeing public funds to be distributed to researcher working on new ES cell lines as well as adult stem cell and previous ES lines, even those not funded by the federal government. The proposition also said that if approved, 3 billion dollars of state bonds would be loaned over a 10 year time span that would be portioned by the California Institute of Regenerative Medicine (CIRM) to aid stem cell researchers providing salaries and research assistance to both established and start-up researchers in California. The proposition won a majority of voters 59% approving, with 41% disapproving the initiative on November 2, 2004 (Smart Voter, 2004). By 2005, proposition 71 was signed into law and California became the first state to fund and create a government (state) agency specifically for stem cell research. The motivation behind both the legislation passed in 2001 and 2005 was to create an atmosphere where researchers could stay competitive with the rest of the world and encourage more flexibility for scientists that Bush's legislation had clamped down on. Proposition 71 also put in place a committee called the Independent Citizens' Oversight Committee which will regulate the entire CIRM agencies operations, ethics, and funding procedures (CIRM, 2007).

The passing of the initial bill in 2002 (SB 253) and the establishment of the CIRM in 2005 was a huge boost to stem cell researchers still worried about Bush's 2001 federal legislation. Furthermore, it was drastic show of the level of both the public and Californian state legislators support and aspiration for freeing up the restriction on this potential revolutionary way of medicine. California has become a source for American researchers to keep American research up to the caliber of other nations. However, California has not remained to only state to encourage and fund hES cell research. Other states have followed suit in hopes that their states may become hubs for this exciting research and help to keep America up to par with the feverishly fast pace of current stem cell research.

New Jersey

Like California, The state of New Jersey, also alarmed at Bush's 2001 restrictive legislation, sought to enact their own state laws that would encourage and recognize hES cell research and adult stem cell research. New Jersey legislators crafted a bill that would develop a state agency called the Stem Cell Institute of New Jersey which would collaborate with local universities and institutions on stem cell research. The bill which was passed by the New Jersey Legislature on January 2, 2004 and signed by its governor James McGreevey formally made the state of New Jersey a supporter and magnet for stem cell research (Genome News Network, 2004). The bill placed special emphasis on using the newly formed Stem Cell Institute to investigate treatments for disease. The bill also, called for ample funding from state funds to help in propelling the therapeutic possibilities of all types of stem cells including hES cells and adult stem cells. Over 150 million dollars from the state of New Jersey's public money would go directly to the Stem Cell Institute in the form of a grant. An additional 230 million dollars would

be given to the Stem Cell Institute in the form of public bonds (Mansnerus, 2005). The bill promotes the further isolation of hES cells from human blastocysts and has set requirements to doctors treating couples with fertility issues, informing them of the option of using their spare embryos for stem cell research. The state of New Jersey hopes that its initiative will attract top stem cell researchers and create a flourishing scientific place on the east coast that will hopefully fruition into viable treatment for its citizens and also promote economic growth. Although, it does not compare to the 3 billion promised by California, New Jersey has created another outlet where researchers looking for more funding can find relief from federal restrictions.

The move by New Jersey is also significant because it emphasizes the widespread discontent that states across the nation have towards Bush's unrelenting will to disallow vital funding and the willingness of legislators to enact counter regulations in their state. Also, the ethical acceptance of using embryos for research in New Jersey and California and it popular support among these states has challenged the ethical beliefs held by the Bush administration. One could make the claim that New Jersey's acceptance to hES cell research and further isolation is liberal example. However, other states such as Massachusetts have had to deal with fierce opposition within state government, and have become a microcosm for the ethical and political battle that is seen at the national level.

Massachusetts

Massachusetts, which is known for being at the forefront of advanced science and healthcare, has also responded to federal restrictions as well as competitive atmosphere following Bush's stem cell policy. Seeing California and New Jersey among other states passing legislation encouraging stem cell research, Massachusetts legislators have also been concerned

about losing a competitive edge against other states. Also, because leading researchers and institutions are located in Massachusetts, encouraging and utilizing the knowledge and expertise would be an asset to the entire stem cell research and regenerative medicine field. In response to mainly these reasons, Massachusetts state legislators created a bill called the "Act Promoting Stem Cell Research" that would formally support stem cell research. The bill that was spearheaded by state senate chair Robert Travaglini, Cynthia Creem, and Harriette Chandler focused on providing support to already established institutions and companies involved in stem cell research (Senate Bill No. 25, 2005). The bill encourages research involving adult stem cells, any stem cell lines derived from spare IVF embryos, and also allows the research of embryos created from somatic cell nuclear transfer (SCNT) also called therapeutic cloning (Finer, 2005).

The bill also eases restrictions on researchers seeking stem cell research. For example, prior legislation required researchers wanting to research using embryonic stem cells needed to get the approval and licensing from their local district attorney. This was a difficult and bureaucratic path, and deterred researchers from pursuing research with hES cells. The bill proposed to eliminate this obstacle, and hand over regulation and oversight of stem cell research to the Massachusetts Health Department which is more suitable and less bureaucratic. This would in turn hopefully encourage researchers to pursue hES cell research and make it easier for them to pursue it. The law also explicitly bans the research of human reproductive cloning but cites it's support of therapeutic cloning.

On May 30, 2005, the Massachusetts state legislature approved the bill in the senate 35 to 2 (Finer, 2005). Although the Governor Mitt Romney initially had publicly been supportive of the bill and expressed optimism, he vetoed the bill because he believed the bill did not create safeguards against human cloning and the creation of embryos for the sake of research (Holden,

2005). Romney defended his veto saying, "*the law should prohibit all human cloning and the creation of new human embryos for the purpose of research"* (Romney, 2005). Although he claimed that he supports stem cell research, he specifically criticized creating embryos in the lab for research, and using cloning as a technique to obtain genetically specific hES cells. Despite Romney's veto the state legislature sought to override the veto.

On June 1, 2005, the state senate and house reconvened and overwhelmingly overturned Romney's veto surpassing the two-thirds majority needed. The state senate passed the bill 35 to 2 , while the state House exceeded the two-thirds 112 to 42 (Daily News Central, 2005). The bill supporting stem cell research was passed and became law in Massachusetts despite the Romney veto. The passing of this bill made Massachusetts the third state behind California and New Jersey to explicitly support further stem cell research including, adult, embryonic and therapeutic cloning. The bill however, did not create state institutes like California and New Jersey to oversee and distribute funds, but rather the bill focused on the state and its Health Department cooperating with the Harvard Stem Cell Institute and the University of Massachusetts Medical School as well as private companies who are already leaders in advanced stem cell research. The bill also did not appropriate any amount of state money that would go to funding stem cell research. However, senate chair Travaglini promised that more bills would push for state tax dollars to help institutions such as Harvard Stem Cell Institute expand stem cell research. The opposition by the executive branch in Massachusetts and the support by the legislature in some ways is analogous to the national debate between Bush and Congress. Also, polls in Massachusetts have shown that a solid majority (80%) of people in the state support the bill passed in 2005 and even the heavy Roman Catholic population in Massachusetts shows approval of the bill (Fenn, 2005).

Romney adamant about pursuing his restrictive policy again caused a stir in the state when he, in conjunction with the Massachusetts Public Health Council, changed the wording on the bill (An Act Promoting Stem Cell Research) on a particular section. The section originally discussed the prohibition of making embryos from a sperm and egg for the purpose donating it. The Bill originally was worded, *No person shall knowingly create an embryo by the method of fertilization with the sole intent of* ***donating*** *the embryo for research.* (Section 8.b., 2005). However the Public Health Council under Romney changed the word "donating" to the word "using" the embryo for research (Massachusetts Law Updates, 2006) . The wording change alarmed many researchers because it could possibly subjugate them to criminal acts for "using" these types of embryos. The change essentially prohibited fertilized eggs for the purpose of research rather than the original statement which prohibited donating these. For scientists, this was an added limit that was uncalled for and made research more difficult in Massachusetts. By the change, Romney sought to imply in the bill that life begins at fertilization, and thus a fertilized egg that is "used" for ES cells is prohibited. But the law when drafted and passed, explicitly mentioned that life for an embryo begins when it is implanted into the womb of the mother. Thus, the change worried and frustrated both proponents of stem cell research and scientists because it created a gray zone that could be litigated as breaking the law. The change by Romney, which was taken into effect in August of 2006 had a real impact on the confidence and progress that Massachusetts might offer for stem cell research (Kaiser Network, 2006). Romney's rationale for changing the bill was that the section had a loophole for researchers allowing them to create their own embryos for their research and this would not be considered donation because it was making the embryo for themselves. However, his change of wording to "using" would make it unlawful for the researcher to use these embryos thus preventing them

from creating these embryos in the first place. Thus, if they cannot use them the scientists would not create embryos for their own use in the first place. Romney claimed that this change would close this loophole and discourage researchers from pursuing the creation of embryos for the purpose of research. The Massachusetts Public Health commissioner endorsed Romney's change saying, "[The changes made to the bill will provide a] *bright line to guide the researchers in the future as to what they can do and what they can't*." (Cote, 2006). Although he claimed that it clears up the law and rids the bill of the loophole, scientists saw the change as murky since they were not sure if their work is illegal or not, and fear that it could hamper efforts to speed up research and keep scientists from leaving the state.

Starting in 2007 a new Governor, Deval Patrick, won the heated state elections defeating Romney's Lieutenant Governor Kerry Healy. Patrick a democrat, had supported stem cell research throughout his campaign and expressed his frustration of Romney's reluctance to accept the stem cell bill and his controversial change in the law. Once Deval Patrick took control, he promised that he would change any damage that Romney had done to stem cell research (USA Today, 2007). Governor Patrick however, has pushed further than just fixing the changes made by Romney and has proposed a more robust plan including allocating state funding to keep Massachusetts at the top of stem cell research and help to bring to life the medical promises that stem cells have. Patrick expressed his desire to continue at a biotechnology convention saying, "*We want Massachusetts to provide the global platform for bringing your innovations from the drawing board to the market, from inspiration to commercialization, from ideas to cures*" (Patrick, 2007).

In May 8, 2007 Patrick unveiled his much anticipated plan to boost stem cell research in Massachusetts. Keeping in competition with other states such as California and New Jersey, the

governor pledged to provide funding from the state to life science research especially stem cell research. His plan which will be created into the form of a bill and sent to the state legislature, will pledge 1.25 billion dollars for stem cell research and other cutting edge life science research. 1 billion dollars will be from state tax monies and will be distributed in the form of bonds and grants over 10 years (Belluck, 2007). The money will help go to research hospitals such as Massachusetts General Hospital, The Harvard Stem Cell Institute and other research teams. The other 250 million dollars will come from private business who have pledged to contribute to stem cell research. The initiative by Patrick lays out even more ambitious plans that will keep Massachusetts ahead. One is to create a stem cell bank that leading institutions and companies in Massachusetts will contribute their lines to the bank (Mass. Governor's Office, 2007). This bank is significant because it would become the first stem cell repository (bank) in the United States. Patrick has set aside over 500 million dollars from the funding plan of 1.25 billion and has said the University of Massachusetts will house the bank. Also, he has added state life sciences centers that will help coordinate and contribute to stem cell research and serve similar to California's Institute for Regenerative Medicine except his plan would be the culmination of many research areas in the life sciences.

The significance of this entire plan by Governor Patrick is tremendous for the scientific community especially after Romney's opposition. Scientists from the Harvard Stem Cell Institute and other stem cell research centers have been ecstatic that not only is there state support from the 2005 bill, but also Patrick's funding initiative that will provide a springboard for their research and would help attract scientists to pursue stem cell research, and make Massachusetts a hub for new and experienced researchers. For example, the executive director of the Harvard Stem Cell institute said, "*the state's investment would help scientists who have had to delay*

research because of limited federal financing and would attract the new junior faculty, the rising stars." (Reeve, 2007). State legislators have also been supportive of Patrick's plan and say it significantly adds to the previous 2005 legislation encouraging stem cell research. Sal DiMasi the speaker of the state House of Representatives for example responded to Patrick's bill saying, "*We're to help. It is our future. It is for the benefit of mankind and society.*" (DiMasi, 2007). DiMasi's comments highlights the two main purposes of Patrick's action. One, the plan would help maintain Massachusetts prowess in science and keep a mainstay of it's economy that is education and technology ahead. Second, the promise of tangible medical breakthroughs with stem cells is irresistible and would be foolish to turn away from.

Although Patrick's plan is still only on paper and must be passed by the legislature to make it law, it has really impacted the behavior of scientists in this area of research from hesitation and frustration (during Romney's reign) to hope and anticipation that will be an important driving force in making stem cell research a success in Massachusetts and as a whole. Patrick noted this sentiment saying accurately in his speech unveiling his plan, "*In many ways the health of this industry* [life sciences and stem cell research] *and the health of our society are very closely linked. That's why we will not rest on our laurels.*" (Patrick, 2007). Both the 2005 law and Patrick's plan will make Massachusetts another show of defiance against Bush's federal restrictions and underscores again the tremendous will to bring stem cell research for many diseases such as Parkinson's, Alzheimer's and Heart Disease to the clinic.

Other States

Other state support for ES stem cell research has been growing. Other states have come out with their own legislations and funding proposals based on the economy and support the

stem cell research has. States such as Illinois, Connecticut, New York, and Maryland have all passed legislation supporting and/or funding stem cell research in their states. Illinois Governor Blagojavich has used his executive order to provide 10 million dollars to stem cell research and did not need the state legislature's approval (CBS News, 2006). Connecticut Governor Jodi Rell along with the Connecticut legislature passed a bill that would give 100 million dollars of state money in 10 years to stem cell research (Connecticut Governor's Office, 2006). New York has also passed legislation in 2006 supporting stem cell research and establishing The New York Institute for Stem Cell Research and Regenerative Medicine providing 300 million dollars for the years 2007 and 2008 in state funding to the Institute. Maryland has also signed a law in 2006 supporting stem cell research by providing over 15 million dollars of state money for 2007.

Although the list of states supporting and funding stem cell research is growing, these states remain in the minority. Most states have no legislation or policy towards stem cell research or have tightened restrictions. But fortunately, states such as California and Massachusetts—states supporting stem cell research, are home to many of the key research facilities and top researchers and have attracted companies and researchers from other states. Another positive result of state sponsorship of stem cell research is that it has created healthy competition among these states and has pushed other states to join the competition. Although, the NIH which is a federal agency has been limited to only federal funds and must abide by Bush's 2001 restrictions, state institutions have filled in many cases research that has been limited by the Bush restrictions. In general, states that have supported stem cell research has given a legal back door where researchers can receive the funding they need to discover more on stem cell's medical benefits. It will not be a substitute for federal money, but state support will make a difference in the way and the speed that such research will progress.

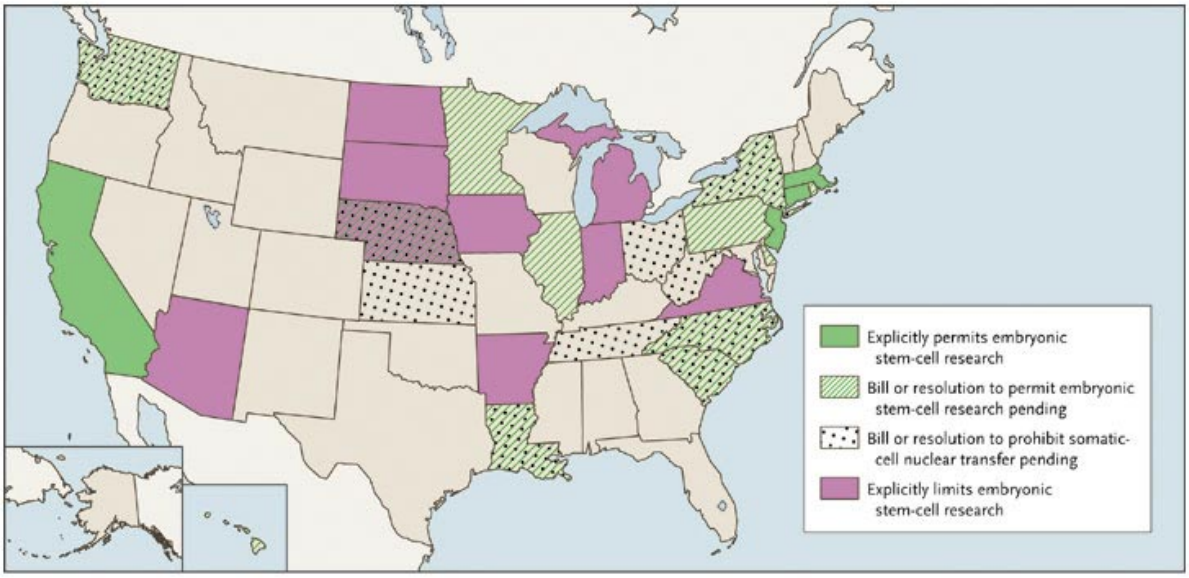

Figure 19. Map of US state legislation as of 2005 on stem cell research. *The map shows which states approve of stem cell techniques. Solid green indicates those states that have supported hES cell research. Diagonal green lines indicates legislation supporting hES cell research is still awaiting approval by the legislature or in process. The black dots indicates prohibition of SCNT (therapeutic cloning) that is pending. The Solid purple indicates states that have explicitly have put restrictions to hES cell research. The light gray indicates states that have not passed any legislation as of 2005* (New England Journal of Medicine, 2005).

International Stem Cell Policies and Regulations

Countries around the world have also had to grapple with the ethical ramifications of stem cell research. Many countries have drafted legislation that has differed from Bush's national restrictions, and some have been harsher. However, many countries have quickly become top research centers on stem cells that have rivaled US stem cell research. More and more fascinating findings on stem cells have come from countries that have welcomed ES cell research, therapeutic cloning, and adult stem cells research. Many in the United States have criticized Bush's stem cell policies for allowing foreign researchers to start to take the upper hand in many areas of stem cell research. Other countries have also dealt with heated debates.

Those countries that support stem cell research, including hES cell research have seen the economic, scientific, and medical opportunities that stem cells bring. Although policies vary from country to country, religious and political beliefs have played a major role in shaping legislation that dictates stem cell research. In this section, I will discuss the policies of various countries on stem cell research and which country has the best stem cell policy based on my own criteria and understanding.

The European Union (EU)

The European Union (EU) which is comprised of 27 European member states countries) has also been split on whether hES cell research should be encouraged and funded by the union. The EU has its own legislative body that makes decisions on key issues within the member states. The EU also pools money that can be used for approved legislation. Although nations in the EU have their own political independence, unlike the states in US, and do not necessarily have to follow legislation made by the EU. The stem cell debate has been heated within the EU and legislation has struggled to take hold. The EU also has no official religion and the moral stance is based on the ethical beliefs of the member states. The first legislative policy that was adopted by the EU was in 2003. Although it stopped short of a specific legislative move, the EU commission (the executive branch of EU) provided a glimpse at the deep division in Europe. The Commission said that the EU should fund hES cell research but limited funding to only already frozen IVF spare embryos for fertility purposes (BBC, 2003). Also, the EU commission laid down another regulation in order for researchers to receive EU funding. This regulation allows funding for only embryos created for IVF up to June 27, 2002. However, funding would not be provided to member nations that have already passed legislation restricting hES cell research.

Also, nations could refuse funding if they wish. Even though, this policy was not clear, new legislation by the EU in 2006 laid down clearer regulation and funding capabilities. It also further revealed the divisions that exist in Europe and also shows the moral cloud that has also developed in Europe.

In July of 2006 the legislative and executive body passed legislation that allowed the funding of hES cell research. Although there was strong opposition by countries such as Germany, Poland, and Italy among other members, the legislation was approved and laid out clearer policies for EU members who wish to receive EU money for hES cell research. The first significant policy was the amount of funding that would be given. They decided to provide 65 billion US dollars for hES cell research for those countries that favored the legislation (Sliva, 2006). Those members who did not approve, do not have to contribute to the funding. The funding was set to start in 2007 and expire in 2013. However, the legislation laid down strict guidelines for how and when this funding would be allowed. The first rule is that EU funding will not be provided to the actual process of destroying the embryo but funding will be provided to hES cell research after the destruction of the embryo (Sliva, 2006). Also, it banned reproductive cloning and genetic manipulation of the embryo and those researching this would not receive any of the EU funding. The EU policies do not discuss adult stem cell research because most of the member nations have not ethical problem with adult stem cell research. Consequently, virtually no legislation has been formed discussing adult stem cell research. It is important to note that the EU does not regulate what the countries can or cannot do, but it does provide policies that are nonbinding and popular within the membership. Thus, countries in the EU can still have their own policies while also choosing to adopt or deny EU recommendations.

United Kingdom (UK)

Being part of the EU, the UK has taken a repeatedly supportive stance on stem cell research. This support stems from their own polices that have been very lenient towards stem cell research. The UK has had a long tradition of being the center for biological research and innovation. The UK's legislation has been among the oldest for dealing with embryos and their ethical nature. The first law that was passed involving embryos was in 1990 called the Human Fertilisation and Embryology Act. This act allowed research on unused embryos from IVF clinics to be conducted for the purpose of researching genetic defects and human development (Human Fertilisation and Embryology Act 1990 c.37, 1990). Although it did not discuss stem cells, it laid down the ethical ground work for whether embryos could be used for research. This law made it clear that embryos could be used for research purposes. However, later when human ES cells were isolated and SCNT was discovered, newer laws that set clearer regulations were needed. In 2001 an amendment to the 1990 Human Fertilisation and Embryology Act was passed which set new guidelines on using embryos for stem cell research. The amendment allowed the destruction of embryos if it meets one of three criteria: 1. Increases knowledge about the development of embryos, 2. Increases knowledge of serious diseases, 3. Enables any such knowledge to be applied in developing treatments for serious diseases. Thus because hES cell research has great potential to help treat diseases, destruction of the embryo is allowed and encouraged under this amendment. The amendment also created a framework for stem cell research. It allows the usage of IVF spare embryos to be used for creating ES cell lines. Also, it allows the creation of a human embryo for research purposes. Further, the use of SCNT for therapeutic purposes (therapeutic cloning) was also permitted but reproduce cloning became explicitly illegal. The legislation in 2001 also set that researchers who wanted to research on

human embryos need a license from the Human Fertilisation and Embryology Authority which was established in 1990 (Human Fertilisation and Embryology Authority, 2007). The agency is responsible for coordinating and funding research on stem cells (from embryos) and regulating research based on the 1990 and 2001 legislation. In 2004 as more stem cell research started revealing the medical potential of this research, the UK government allocated public money to be given for stem cell research. They provided 25 million pounds for research including adult, embryonic from IVF clinics, embryonic for research and therapeutic cloning research for the year 2004-2005. The rationale was because the government had allowed these research techniques, funding would help UK scientists to continue to make more breakthroughs and keep the UK on the map as a respectable research center. In 2005 a new funding plan by the UK government was initiated. The plan formally called the UK Stem Cell Initiative (UKSCI) was a long term 10 year initiative to provide public and private funding to various types of stem cell research. The initiative entitled over 100 million pounds of public funds for a two year term starting from the year 2005 to 2008. The money would help go to the UK Stem Cell Bank which has become a growing repository of different lines, private researchers, biotech companies, and institutions (UK Department of Health, 2005). The funding would also go to those studying adult stem cells, hES cells, and therapeutic cloning. The money would be mainly regulated by the Human Fertilisation and Embryology Authority. The support in the UK public is strong as well and one poll in 2003 found that 70% of the British public supported using human embryos for medical research (Ipsos-MORI, 2003). Both the public and the government in the UK support using the most controversial hES cell research for it's medical potential. The House of Commons Chairman of the science and technology committee Ian Gibson expressed the national interest and importance of stem cell research saying, "*We must be ready to move fast. Too often scientific*

discoveries have been exploited elsewhere - this time they must be developed in this country [UK].” (Gibson, 2005). Here he is referring to the US dominance of many of other scientific advancements in the past, and sees stem cell research as a way to possibly steal back scientific glory after Bush announced his 2001 restrictions. It is easy to see that even among other nations stem cell research has become highly competitive but an ethically daunting task. In general, the United Kingdom supports and funds stem cell research and even has stood behind controversial methods including hES cell research both from spare embryos and ones created in the lab for research purposes.

Germany

Like the UK, Germany is also a member of the EU, but has mainly been on the other side of the debate. Germany has shared a similar stance as Bush’s restrictions. In June of 2002, the German Legislature passed a law that put specific restrictions on hES cell research. The legislation called the German Stem Cell Act of 2002 banned the destruction of human embryos for research purposes (UK Department of Health, 2005). The act further banned research of both reproductive and therapeutic cloning. The law claimed that only hES cell lines already isolated before January 1, 2002 could be used for research and these had to come from consented donors of spare IVF embryos that did not receive money for them (ISCCR, 2005). However, other lines may be imported from other countries but it must be proven that they are a necessity. These rules are quite similar to the current US policy. The German government seems to follow a conservative Christian ethical belief like that of Bush. However, unlike Bush’s restrictions Germany’s law not only restricts funding but researcher public or private may face criminal charges including jail time and steep fines if this law (German Stem Cell Act of 2002) is violated. Thus, even private companies in Germany cannot with their own funds destroy a human

embryo for stem cell research. However, Germany does not restrict adult stem research and in fact have claimed this as a moral way to conduct research. Germans have become leaders in adult stem research and has been a source for many publications on adult stem cells applications and advantages over embryonic stem cells. However, scientists and ethicists in Germany have been battling on whether the ban on hES cell research has effected the image of Germany. For example, an official for German government's medical advisory committee 'The National Ethics Council' made an assessment of the strict legislation saying, "*If the current rules remain, German science will be hopelessly sidelined*." (Dreier, 2007). However, the government has sided with powerful Catholic and Protestant churches that reside in Germany and are fervently opposed to the destruction of "living" embryos. Thus, in Germany religious ethical concerns has become the moral force behind the restrictive legislation and has undermined ES cell research.

Israel

Israel which is a small country embedded in the middle east, has long been involved hES cell research and adult stem cell research. Although Israel has not set specific rules on the research that can be done, it has been supportive of embryonic stem cell research and adult stem cell research. In 1998 laws were passed that banned research on human reproductive for five years and was renewed for another fives until 2009 (ISCCR, 2005). The Israeli government also does not have a funding plan for stem cell research and relies on mostly private or cooperate monies for its research. However, despite little government funding, Israel has produced some of the brightest stem cell researchers and landmark publications. For example, in 1998 James Thomson along with Itskovitz Eldor at the University of Wisconsin were the first to successful

isolate hES cells (Thomson et al., 1998). Eldor is an Israeli scientist who has been noted for numerous achievements in stem cell research. Even more remarkable is Israeli researchers have isolated four of the five original stem cell lines (ISCCR, 2005). Stem cell research in Israel is supported by the government but is a corporate entity funded mainly by investors. The Israeli public overwhelmingly supports both hES cell research and adult stem cell research. Because the population is mainly Jewish and Muslim, and both have little ethical issues with using human embryos, there has been little debate on whether to use embryos, and has let researchers freely do their research without a constant tug of war of ethical legislation. However, Israel's lack of legislative funding has made stem cell research a risky venture because if investors do not see results they may pull their money out and it may compromise the progress of research (UK Department of Health, 2005). Thus, in Israel, stem cell researchers are allowed to freely research both embryonic and adult stem cells, but research is mainly governed by private investors who see its economic and medical potential.

Singapore

Like Israel, Singapore is a small country that has become a hub for stem cell research. Because many stem cell research companies and researchers including hES cell research have moved to Singapore, the Singapore government passed legislation that weighed the ethical nature of this research in their country. The first action taken in 2000, was the Singaporean Cabinet passed legislation that created the Bioethics Advisory Committee (BAC) which would report to the Singapore government on their investigation regarding stem cell research and other biological research (ISCCR, 2005). In 2002 the BAC issued a report that concluded that hES cell

research and adult stem cell research are both ethically moral, and should be pursued in Singapore. The Parliament responded to the committee's findings, and in 2004 passed the 'Human Cloning and Other Prohibited Practices Act' (BAC Singapore, 2002). This act outlined ethical boundaries for stem cells. The act first outlawed human reproductive cloning. It also prohibited the exchange of already cloned human embryos. The act however, allowed hES cell research but the embryo must be within 14 days old. After 14 days researching on the embryo would be prohibited. Because hES cell research is done with a 5 day blastocyst, hES cell research would not break the law and is permitted. The Act also allowed therapeutic cloning but again it could not be grown to more that 14 days old (UK Department of Health, 2005). Thus, Singapore allows working with hES cells creating and destroying 5 day blastocysts, as well as using SCNT for therapeutic purposes.

Singapore has also set up organizations that helps pool resources and talent within the country. In 2005 Singapore established The Stem Cell Consortium which was responsible for coordinating and funding research across Singapore (ISCCR, 2005). The consortium also allowed new and experienced researchers to cooperate and share ideas and creating avenues for researchers to team with clinical personnel such as doctors. Despite stem cell research being a largely foreign corporate entity, Singapore has provided over 40 million dollars in public money each year to the Consortium which then distributes the money to companies or researchers. Singapore has found it's niche as a thriving biotechnology country. Although the vast majority of scientists researching in Singapore are western, it's acceptance of hES cell research has made it a magnet for those coming from countries that have put stricter legislation, which has made Singapore's economy strong and a world class stem cell research center.

South Korea

South Korea has become another Asian country that has had to deal with the explosion of controversial research involving hES stem cells. The first major legislative policy in South Korea explicitly for stem cell research took effect in 2005. The policy called the Bioethics and Biosafety Act determined what research on embryos was legal or illegal. The first provision in the Act declared that spare embryos created from IVF clinics could be used for research (The Hinxton Group, 2006). However, the law banned researchers from creating embryos for the sole purpose of research. Furthermore, it made it clear that human reproductive cloning is illegal and punishable, but therapeutic cloning research would be allowed. However, the political climate was shifted after an embarrassing event that shook up the entire scientific community. A top and respected researcher at the Seoul National University, Woo-suk Hwang, claimed that he had successfully created the first cloned human embryo. This finding initially was a landmark finding and he became an instant celebrity. Initially the government was highly supportive and he became a national symbol of proof of the advanced science it was able to perfom. But it was later discovered in 2006 that his claim was proven false, and the Korean government changed it's view from confidence to skepticism (Bhattacharya, 2006). However, despite this debacle, the government did not change its policy and still holds the Bioethics and Biosafety Act as a rational and ethical law for Korean researchers. When it comes to funding, the South Korean government has been generous in supporting both university and private researchers. In 2004 while the Bioethics and Biosafety Act was being debated in the Korean Parliament, The South Korean government appropriated 5 billion US dollars for stem cell research. The money was given to the Ministry of Science and Technology which would oversee and coordinate research and give

money to researchers (UK Department of Health, 2005). Although the controversy with Dr. Hwang greatly affected South Korea's world image, it still remains one of the countries with the finest stem cell research facilities and researchers in the world. When it comes to policy, South Korea supports and funds adult, embryonic, and therapeutic cloning stem cell research.

China

Some of the brightest and talented stem cell researchers have been Chinese. However, most of these researchers have done their research in western countries where research facilities are top notch and funding is available. China has also seen the economic, scientific, medical benefit that the other countries have seen. However, unlike many other countries, the government has had to deal with little debate on even the most controversial stem cell research. China's policy on stem cell research was explicitly presented in 2003 when the Chinese government released the 'Ethical Guidelines for Human Embryonic Stem Cells' (The Hinxton Group, 2006). The regulation made human reproductive cloning illegal but allowed SCNT for therapeutic cloning. It also allowed the use of spare IVF embryos for deriving ES cell lines. Further, it authorized using human parthenogenic embryos for isolating ES cells. Thus, in China, researchers are allowed to work with a wide variety of hES cell research techniques. China has seen stem cell research as way to reclaim its researchers and join the competition to find medical treatments. When it comes to funding, China has been on the low end, giving only 4 to 10 million dollars a year for Chinese stem cell research (UK Department of Health, 2006). In terms of leniency, China's policy is known to be the most liberal and unrestrictive. In fact, China has very little oversight for research and rarely enforces regulations. Also, there has been no government agency that coordinates and distributes funds. Despite having the most lenient

embryonic stem cell policy in the world, many Chinese scientists have been more interested in using adult stem cells on human trials for treating heart disease, brain disorders etc. The Chinese public which is mostly either Chinese Confucian, a traditional culture, or lack a religion totally and have had little ethical problems with the policies allowing the use of human embryos for research. The Confucian tradition holds that life comes into being at birth (Murray and Spar, 2006). Thus, morally, most of the public would not have objections to ES cell research which only uses a 5 day old embryo. Thus, the policies implemented by the Chinese government on stem cells reflects the traditional cultural views. Many in the US after Bush's 2001 restrictions have voiced concern that China, a natural competitor of the US, could make significant advances in the area of hES cell research because of China's lax research laws and the vast public support it has.

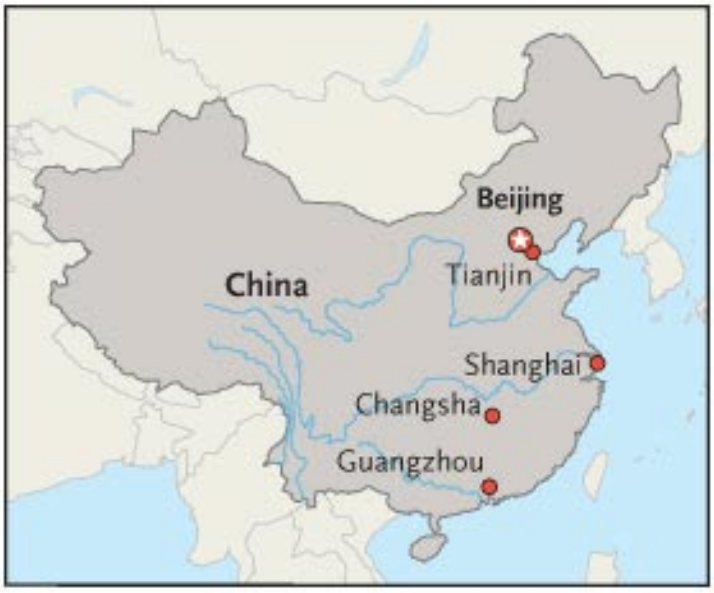

Figure 20. Map of China Showing Cities that have established stem cell research centers.
The Map shows five major Chinese cities harboring stem cell research centers. As stem cell research continues to grow the number research centers will likely rise in china and face little political pressure. There are also researchers working on adult stem cells in clinics and research hospitals that are not shown in this map. China is hoping that stem cell research may be the stepping stone for it's lagging scientific industry (Murray and Spar, 2006).

Australia

The first policy in Australia regarding stem cell research was in 2002 when the Australian Legislature passed the 'Research Involving Human Embryo Act of 2002' (The Hinxton Group, 2006). Although it did not discuss adult stem cells, they were clearly ethical and required little clarification. The Act allowed the use of spare embryos from fertility clinics with the donors consent. However, it banned the creation of embryos for the sake of research and only those from IVF clinics could be used to isolate hES cells. The law thus allowed researchers to continue to destroy (IVF clinic) embryos and create new ES cell lines. The Act also, outlawed using therapeutic cloning on human embryos. The 2002 laws left two options for researchers; one was to use spare IVF embryos for extracting and studying hES cells, and two, use adult stem cells such as hematopoietic stem cells as their main research. Consequently, many Australian researchers have done brilliant work on hematopoietic stem cells, and have experimented their use on heart disease or enhancing hematopoietic transplants for blood disorders.

In terms of government organizations, Australia in 2002 in conjunction with it's 'Research Involving Human Embryo Act of 2002' created the Australian Stem Cell Centre (ASCC) which opened in 2003 (ASCC, 2006). The idea of government run research center was to coordinate and manage research within the country and to oversee and express the guidelines set by the government. It's is to unify institution, corporate and government stem cell research and communicate with international organizations and teams. Based in Monash University in Melbourne, the Stem Cell Centre would also help distribute and fund researchers across Australia with public monies (ISCCR, 2005). The Australian government in 2002 awarded the ASCC with 43.55 million US dollars for two years both for starting the center and for allocating

federal funding for researchers abiding by the 2002 law. The government in 2004 further awarded the ASCC with 55 million US dollars of a five year term starting from 2006 running to 2011(UK Department of Health, 2006).

Despite the establishment of the ASCC and government funding, the 2002 legislation by many was viewed as still too restrictive. The law required those who wished to pursue ES cell research to apply for a license. Also, the law was seen as complicated and unclear on certain issues. In light of these concerns, the government issued a review on the 2002 Act in 2005. The reviewed law was passed through both chambers of the legislature where it could be adjusted (ISCCR, 2006). One of the most significant changes made was that therapeutic cloning originally illegal by the 2002 law became legal under the examination from the legislature. The new amendment was passed and became in November of 2006 and took affect in May of 2007. The amendment also loosened restraints on obtaining licensing for embryonic stem cell research and therapeutic cloning. This law is the current regulation for stem cell research. In general, Australian legislation permits isolating hES cells from spare embryos made for fertility purposes, therapeutic cloning, and adult stem cell research. However, Australia still bans creating embryos for research purposes as well as reproductive cloning. The Australian public seems to be supportive of hES cell research. In one poll conducted by the ASCC, it found that 82% of Australians approved of using spare IVF embryos for medical research (Roy Morgan Research, 2006).

Other Countries

Other countries have also dealt with the stem cell ethical concerns and have drafted legislation. Countries such as Brazil, Canada, Finland, France, Iran, India, Japan, Russia, Spain,

Sweden and South Africa have also crafted policies that allow hES cell research (MBBNet, 2007). Although they vary widely, all have proactive legislative policies that have taken careful measure of the economic, scientific and ethical dynamics in different countries. Other countries such as Italy, Austria, Poland, and Lithuania have had policies similar to Germany's and the United States. Most other countries not discussed have had no policy towards stem cells or lack the infrastructure and resources to carry out stem cell research. The United Nations which is the largest and most prominent organization for international accord has had a tough time passing any legislation for or against stem cell research. The only resolution passed was a non-binding call to all 191 member nations not to use cloning techniques on humans and the inference was made also to therapeutic cloning (Transplant News, 2005). Although the topic of stem cell research is ethically sensitive, most (industrialized) countries have taken a nonrestrictive approach unlike the United States. The acceptance by many countries of hES cell research indicates that the ethical status of the embryo is not universal as some in the United States say it should be. To those countries investing in stem cell research it has become a competitive area of research with each country hoping to make their country the promise of stem cells a reality.

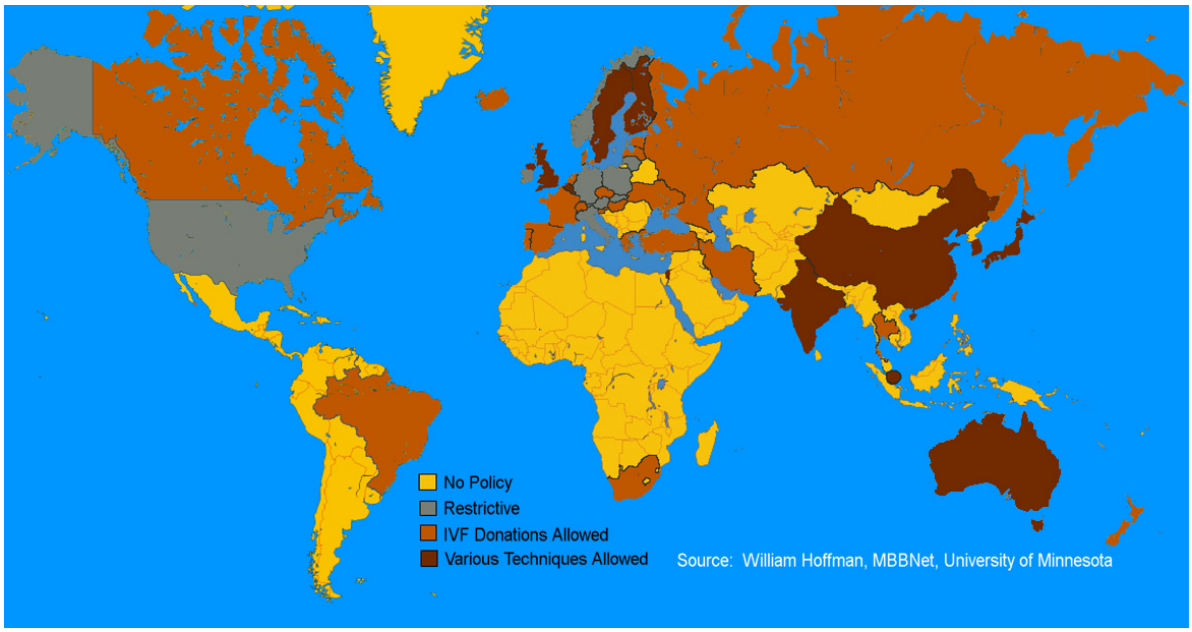

Figure 21. World Map showing stem cell policies of various countries. *This world map is color coded to show the different policies that countries have. Light brown or tan means that the country has no set policy regarding stem cells. Gray means the country has a restrictive policy towards stem cells. Notice the US is in gray meaning it has a restrictive policy stemming from Bush's 2001 legislation. Medium brown means hES cell research is allowed but only through donated spare IVF embryos. Dark brown means those countries have numerous ways to use or obtain ES cells including therapeutic cloning or creating embryos for only research* (Hoffman, 2006).

Chapter Conclusions

When assessing international policies, and making a decision on which policy I would best agree with, there are several questions that need to asked that would allow me to make a fair and unbiased conclusion based on stem cell policies residing in highly diverse societies. The first important question is whether or not the policy respects the ethical concerns of the cultural or religious beliefs of that country? The second question is whether the policy allows researchers to conduct the necessary stem cell research including, hES cell research and therapeutic (not reproductive) cloning? And third, does the country's policy include important government funding at the highest levels? These are questions that I believe if all can be positively answered would make the best standing policy regarding stem cells in the world.

After looking at the various policies, I believe the United Kingdom (UK) has the most comprehensive and well tailored polices to date for stem cell research. Although, I discussed the UK's policy previous in detail, answering these questions requires a revisit of some what has been already said. My first question asked whether the policy respects religious or cultural beliefs of that country. In the UK most mark themselves as Christians but many distance themselves from any actual religion. However, the important thing is whether the public making up different religions and cultures agrees with the policy. In the section on the UK I mentioned that 70% of UK citizens agree with using human embryos for medical research. So strong

approval from the public is critical in sustaining any policy including stem cells policies. The second question dealt with whether the policy drafted by the government is adequate for keeping pace with research. The UK has been one of the first countries in the world to establish laws describing the legality of the embryo. The 'Human Fertilisation and Embryology Act of 1990' allowed research on embryos for studying congenital diseases and human development even before human embryo were being used to isolate stem cells. When amended in 2001, the law accepted the use of human embryos for stem cells and also gave approval for therapeutic cloning, and creating embryos for the sake of research. The policy gave plenty of room for researchers to carry out research but safeguarded against abuse by using the Fertilisation and Embryology Authority to issue licenses to scientists who wish to pursue all forms of hES cell research. The third question I had was whether the policies would not only support stem cell research but would also fund it. I believe that funding is the most crucial part in science and even with support if there is no money research will come to a grinding halt. Government money to me is vital because it allows researchers to receive a stable amount of money to continue research. Also governments are the only ones usually able or willing to provide hundreds of millions or billions of dollars needed for meaningful research. The UK has invested over 125 million pounds (over 250 million US dollars) to its own stem cell bank and home grown research institutes involved in stem cell research. Although it is not the highest figure that has been given, it has been used to fund a stem cell bank that has become international repository. Therefore, the UK has the best policy towards stem cell research and also has word class research centers that combined makes UK one of the leaders if not the leader in stem cell research. In my view UK's stem cell policy is ethical, positive, and a fruitful alternative to the US's restrictive federal policy.

CONCLUSIONS

In order that research on stem cells progresses, it is essential that both adult and embryonic stem cells continue to be researched. I believe that using spare IVF embryos for research, as well as creating embryo for research purposes should be allowed. Both therapeutic cloning and parthenogenesis research are also key to understanding the potential of stem cells and must be permitted. The United Kingdom's laws have set in place regulations and funding that encourage ES and adult stem cell research, embracing therapeutic cloning and creating human embryos for experimentation. Thus, the UK's current laws best fit with the conclusions I have reached, and allow ample opportunity for all forms of stem cell research to flourish and hopefully benefit society.

BIBLIOGRAPHY

Abbott, Cate (2003) "Bone Marrow Transplantation". London Health Sciences Centre. http://www.lhsc.on.ca/transplant/bnmarrow.htm.

ABC News/Washington Post Poll. Jan. 16-19, 2007. "Science and Nature, Stem Cell Research." http://www.pollingreport.com/science.htm?

ABC News/Washington Post Poll (2001) Stem Cell Research. http://www.pollingreport.com/science.htm?

Advanced Fertility Center of Chicago (2007) "Photo: Human Blastocyst at 5 days" http://www.advancedfertility.com

Alzheimer's Association (2007) " What is Alzheimer's?" http://www.alz.org/alzheimers_disease_what_is_alzheimers.asp

American Association for the Advancement of Science (2003) "GOP Moderates Questions Bush Stem Cell Policy" http://www.aaas.org/spp/cstc/news/articles2003/030630_stemcells.shtml

American Association of Medical Colleges (2007) Somatic Cell Nuclear Transfer (Therapeutic Cloning), http://www.aamc.org/advocacy/library/research/res0003.htm

American Catholic (2001) "U.S. Bishops Protest Embryo Stem-cell Research". http://www.americancatholic.org/News/StemCell/bishops_stemcell.asp

American Diabetes Association (2007) Type 1 Diabetes. http://www.diabetes.org/type-1-diabetes.jsp

American Federation for Aging Research (2003) What Are Stem Cells? http://www.infoaging.org/toti

Australian Stem Cell Centre (2006) "Research in Australia" http://www.stemcellcentre.edu.au/public-education_research.aspx

Bash, Dana (2006) "Bush Vetoes embryonic stem cell bill" CNN Politics. http://www.cnn.com/2006/POLITICS/07/19/stemcells.veto/index.html

Basu, Paroma (2005) "Scientists Rid Stem Cell Culture of Key Animal Cells" University of Wisconsin—Madison News. http://www.news.wisc.edu/10720.html

BBC News (2003) "EU Split Over Stem Cell Research" http://news.bbc.co.uk/1/hi/health/3055103.stm

Belluck, Pam (2007) Massachusetts Proposes Stem Cell Research Grant" The New York Times. http://query.nytimes.com/gst/fullpage.html?sec=health&res=9E00E1DB1731F93AA35756C0A9619C8B63

Beltrami AP, Barlucchi L, Torella D, Baker M, Limana F, et al (2003) Adult Cardiac Stem Cells Are Multipotent and Support Myocardial Regeneration. *Cell* **114**: 763-776.

Ben-Hur T, Idelson M, Khaner H, Pera M, Reinhartz E, Itzik A, Reubinoff BE (2004) Transplantation of Human Embryonic Stem Cell–Derived Neural Progenitors Improves Behavioral Deficit in Parkinsonian Rats. *Stem Cells* **22**: 1246-1255.

Bhattacharya, Shaoni (2006) "Hwang Faked all Research on Human Stem Cells" New Scientist. http://www.newscientist.com/article.ns?id=dn8557
Murray, Fiona, Deborah Spar (2006) "Bit Player or Powerhouse? China and Stem Cell Research" *The New England Journal of Medicine* **355**: 1191-1194

Bhikkhu, Deba Mitra (2007) "Stem Cells and the Meaning of Life" The Record. http://www.therecord.com/NASApp/cs/ContentServer?pagename=record/Layout/Article_Type1&c=Article&cid=1185002166331&call_pageid=1024322088745&col=1024322217916

Bioethics Advisory Committee of Singapore (2002) "Ethical, Legal, and Social Issues in Stem Cell Research, Reproductive and Therapeutic Cloning" http://www.bioethics-singapore.org/resources/reports1.html

Bjorklund A, Lindvall O (2000) Self Repair in the Brain. *Nature* **405**: 892-895.

Bjorklund LM, Sanchez-Pernaute R, Chung S, Andersson T, Chen IYC, McNaught KSP, Brownell AL, Jenkins BG, Wahlestedt C, Kim KS, Isacson O (2002) "Embryonic stem cells develop into functional dopaminergic neurons after transplantation in a Parkinson rat model." *Proceedings of the National Academy of Sciences USA* **99**(4): 2344-2349.

Braiker, Brian (2007) "God's Numbers" MSNBC: Beliefs. http://www.msnbc.msn.com/id/17879317/site/newsweek/
Bush, George W. (2001) "President Bush Discusses Stem Cell Research" The Whitehouse. http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html

Bush, George W. (2006) "President Bush Delivers on Stem Cell Research Policy" Washington Post. http://www.washingtonpost.com/wp-dyn/content/article/2006/07/19/AR2006071901223.html

Bush, George W. (2006) "Bush Vetoes embryonic stem cell bill" CNN Politics. http://www.cnn.com/2006/POLITICS/07/19/stemcells.veto/index.html

Cancer Research UK (2002) "Types of Cells and Cancer" http://www.cancerhelp.org.uk/help/default.asp?page=98

California Institute for Regenerative Medicine (2007) "About CIRM" http://www.cirm.ca.gov/

Cassidy R, Frisen J (2001) Stem Cells on the Brain. *Nature* **412**: 690-691.

Cavazzana-Calvo Marina, Salima Hacein-Bey,Geneviève de Saint Basile, Fabian Gross, Eric Yvon, Patrick Nusbaum, Françoise Selz, Christophe Hue, Stéphanie Certain, Jean-Laurent Casanova, Philippe Bousso, Françoise Le Deist, Alain Fischer (2000) "Gene Therapy of Human Severe Combined Immunodeficiency (SCID)-X1 Disease" *Science* 288: 669-672

CBS News (2006) "Two Governors Fund Stem Cell Research" http://www.cbsnews.com/stories/2006/07/19/politics/main1818040.shtml

Center for Genetics and Society (2006) "Reproductive Cloning Basic Science: Parthenogenesis" http://geneticsandsociety.org/article.php?id=281

Childs R, Chernoff A, Contentin N, Bahceci E, Schrump D, Leitman S, Read EJ, Tisdale J, Dunbar C, Linehan WM, Young NS, and Barrett AJ (2000) Regression of metastatic renal-cell carcinoma after nonmyeloablative allogeneic peripheral-blood stem-cell transplantation. *New England Journal of Medicine* **343**: 750-758.

Cibelli JB, Kiessling AA, Cunniff K, Richards C, Lanza RP, West MD (2001) Somatic Cell Nuclear Transfer in Humans: Pronuclear and Early Embryonic Development. *Journal of Regenerative Medicine* **2**: 25-31.

Clayton E, Doupe DP, Klein AM, Winton DJ, Simons BD, Jones PH (2007) A Single Type of Progenitor Cell Maintains Normal Epidermis. *Nature* 446: 185-189.
CNN/Opinion Research Corporation Poll (2007) "Science and Nature: Stem Cell Research" http://www.pollingreport.com/science.htm?

CNN Politics (2005) "House Passes Embryonic Stem Cell Bill" http://www.cnn.com/2005/POLITICS/05/24/stem.cells/

CNN/USA Today Poll (2001) "Science and Nature: Stem Cell Research" http://www.pollingreport.com/science.htm?

Connecticut's Governor's Office (2006) "Governor Rell Urges Senate Approval For Stem Cell Research Funding" State of Connecticut Executive Chamber. http://www.ct.gov/governorrell/cwp/view.asp?A=2425&Q=317678

Correa, Prof. Juan de Dios Vial, S.E. Mons. Elio Sgreccia (2000) "Declaration on the production and the scientific and therapeutic use of human embryonic stem cells." The Vatican. http://www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20000824_cellule-staminali_en.html

Cote, Paul (2006) “State Politics and Policy: Massachusetts Council's New Regulations on Embryonic Stem Cell Research Spark Controversy Among State Legislators” Kaiser Network. http://kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=39550

Cross WR, Thomas DFM, Southgate J (2003) Tissue engineering and stem cell research in urology. *The British Journal of Urology* **92**: 165-171.

Cyranoski, David (2007) Simple Switch Turns on Cells Embryonic. *Nature* **447**: 618-619.

Daily News Central (2005) “Massachusetts Stem-Cell Bill Becomes Law Despite Veto” Daily News Central: Health News. http://health.dailynewscentral.com/content/view/929/62

Deacon T, Dinsmore J, Constantini, L, Ratliff J, and Isacson O (1998) Blastula-stage stem cells can differentiate into dopanimergic and serotonergic neurons after transplantation. *Experimental Neurology* **149**: 28-41.

DiMasi, Salvatore (2007) “Massachusetts Governor Proposes $1 billion for Stem Cell Research.” Associated Press. http://sfgate.com/cgi-bin/article.cgi?f=/n/a/2007/05/08/state/n130518D95.DTL&hw=biotech&sn=002&sc=184

Dorff, Elliot (2000) “Stem Cell Research”. *Ethical Issues in Human Stem Cell Research*, Volume 3: Religious Perspectives.

Elliot, Emma, Stephanie Porowski (2005) “Adult Stem Cell Treatment: A Better Way” Concerned Women for America. http://www.cwfa.org/articledisplay.asp?id=4805&department=CWA&categoryid=life

Fenn, Jennifer (2005) “Poll: Voters Back Stem Cells” Spinal Cord Information Pages News. http://www.sci-info-pages.com/2005/03/poll-voters-back-stem-cell-research.html

Finer, Jonathan (2005) “Mass. Senate Passes Stem Cell Bill That May Face Governor’s Veto” The Washington Post. http://www.washingtonpost.com/wp-dyn/articles/A13970-2005Mar30.html

Freudenrich, Craig C. How Cloning Works, (2004) http://www.howstuffworks.com/cloning.htm

Frist, Bill (2006) “Bush Vetoes embryonic stem cell bill” CNN Politics. http://www.cnn.com/2006/POLITICS/07/19/stemcells.veto/index.html

Gage FH (2000) Mammalian Neural Stem Cells. *Science* **287**: 1433-1438.

Garfinkel, Michele (2004) “Stem Cells: Policies and Players” Genome News Network. http://www.genomenewsnetwork.org/resources/policiesandplayers/

Gatti RA, Meuwissen HJ, Allen HD, et al. (1968) “Immunological reconstitution of sex-linked lymphopenic immunological deficiency.” *Lancet* **2**: 580-585.

Gene Therapy (2000) “Bursting the Bubble on Severe Combined Immunodeficiency Syndrome (SCID)” http://student.biology.arizona.edu/honors2000/group08/main.html

Genome News Network (2004) “ Stem Cell Policies and Players” http://www.genomenewsnetwork.org/resources/policiesandplayers/

Gibson, Ian (2005) “Effort begun in UK to establish a 100 million pound Stem Cell Research Fund” Transplant News. http://findarticles.com/p/articles/mi_m0YUG/is_1_15/ai_n17208385

Glaser Vicki, (2003) Regenerative Medicine R&D Come of Age. *Genetic Engineering News* **23**: 24-26.

Glaser Vicki, (2004) Medicines to Repair & Restore the Body. *Genetic Engineering News* **24**: 12-18.

Gluckman, E. Broxmeyer HE, Auerbach ADD, et al.(1989) "Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbelical from HLA-identical sibiling. *New England Journal of Medicine* **321**: 1174-1178

Hess D, Li L, Martin M, Sakano S, Hill D, Strutt B, Thyssen S, Gray DA, Bhatia M (2003) Bone marrow-derived stem cells initiate pancreatic regeneration. *Nature Biotechnology* **7**: 763-770.

Hidemasa Oh, Bradfute SB, Gallardo TD, Nakanura T, Gaussin V, et al (2003) Cardiac Progenitor Cells From Adult Myocardium: Homing, Differentiation, and Fusion after Infarction. *PNAS* **100**: 12313-12318.

Hoffman, William (2006) “Map of World Stem Cell Policies” The University of Minnesota. http://mbbnet.umn.edu/scmap/senatemap.jpg

Holden, Constance (2005) “Stem Cells Hit Snag in Massachusetts” *Science* http://sciencenow.sciencemag.org/cgi/content/full/2005/211/1

Hug, Kristina (2006) “Therapeutic perspectives of human embryonic stem cell research versus the status of human embryo—does one have to be compromised for the other” *Medicina* 42(2): 107-114.

Human Fertilisation and Embryology Act 1990 c.37 (1990) http://www.opsi.gov.uk/acts/acts1990/Ukpga_19900037_en_1.htm

Human Fertilisation and Embryology Authority (2007) “How We Regulate” http://www.hfea.gov.uk/en/275.html

Illinois Family Institute (2007) “Figure: Cartoon Showing Ethical Controversy of Embryonic Stem Cell Research” http://www.illinoisfamily.org/

Institute of Developmental Genetics (2007) "Adult Neural Stem Cells and Neurogenisis" www.gsf.de/.../adult_neurogenesis/start.html

International Society of Stem Cell Research (2005). "Frequently Asked Questions on Stem Cell Research." http://isscr.org/science/faq.htm.

Ipsos-MORI (2003) "Seven In Ten Members of the Public Support the Use of Embryos for Medical Research." http://www.ipsos-mori.com/polls/2003/amrc.shtml

Jakobovits, Yoel (2006) "Judaism and Stem Cell Research." Torah.org. Project Genesis, Inc. http://www.torah.org/features/secondlook/stemcell.html

Johns Hopkins (2007) Method Developed to Replicate Stem Cells from the Heart. http://www.hopkinsmedicine.org/Press_releases/2004/11_08a_04.html

Jyoti, Chaitanya (2007) "Stem Cells and the Meaning of Life" The Record. http://www.therecord.com/NASApp/cs/ContentServer?pagename=record/Layout/Article_Type1&c=Article&cid=1185002166331&call_pageid=1024322088745&col=1024322217916

Kaiser Network (2006) "State Politics and Policy: Massachusetts Council's New Regulations on Embryonic Stem Cell Research Spark Controversy Among State Legislators" http://kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=39550

Keefe, Michael (2004) "Nancy Reagan Political Cartoon" The Denver Post.

Kehat, I, Kenyagin-Karsenti, D, Druckmann, M, Segev, H, Amit, M, Gepstein, A, Livne, E, Binah, O, Itskovitz-Eldor, J, and Gepstein, L (2001) Human embryonic stem cells can differentiate into myocytes portraying cardiomyocytic structural and functional properties. *Journal of Clinical Investigation* **108**: 407-414.

Keirstead Hans S, Nistor G, Bernal G, Totoiu M, Cloutier F, Sharp K, and Steward O (2005) Human Embryonic Stem Cell-Derived Oligodendrocyte Progenitor Cell Transplants Remyelinate and Restore Locomotion after Spinal Cord Injury. *The Journal of Neuroscience* **25**(19): 4694-4705.

Keown, Damien (2001) "Cellular Division" Science and Spirit. http://www.science-spirit.org/webextras/keown.html

Keown, Damien (2004) "'No Harm' Applies to Stem Cell Embryos: One Bhuddist's Perspective" Belief Net. http://www.beliefnet.com/story/143/story_14399_1.html

Kiessling Ann (2005) Human Parthenotes: An Ethical Source of Stem Cells for Therapies? *Nature* **434**: 145.

Kim JH, Auerbach JM, Rodriguez-Gomez JA, Velasco I, Gavin D, Lumelsky N, Lee SH, Nguyen J, Sanchez-Pernaute R, Bankiewicz K, McKay R (2002) Dopamine Neurons Derived

From Embryonic Stem Cells Function in an Animal Model of Parkinson's Disease. *Nature* **418:** 50-56.

Kirschstein R and Skirboll LR (2001) "Stem Cells: Scientific Progress and Future Research Directions". National Institutes of Health, Department of Health and Human Services. http://stemcells.nih.gov/info/basics/

Klug MG, Soonpaa MH, Koh GV, and Field LJ (1996) Genetically Selected Cardiomyocytes from Differentiating Embryonic Stem Cells Form Stable Intracardiac Grafts. *Journal of Clinical Investigation* **98**: 216-224.

Kocher, AA, Schuster, MD, Szabolcs, MJ, Takuma, S, Burkhoff, D, Wang, J, Homma, S, Edwards, NM, and Itescu, S (2001) Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function. *Nature Medicine* **7:** 430–436.

Kunkel, Dennis (2001) "SEM: Human Egg and Sperm" Kunkel Microscopy Inc. http://www.sp.uconn.edu/%7Ebi107vc/images/cell/sperm%2Begg.JPG

Latkovic, Mark S (2006) "The Science and Ethics of Parthenogenesis: Are We Dealing with a Human Being? A Catholic Perspective" http://www.aodonline.org/AODonline-sqlimages/SHMS/Faculty/LatkovicMark/Bioethics/TheEthicsofParth.pdf

Lepilina A, Coon AN, Kikuchi K, Holdway JE, Roberts RW, Burns CG, Poss KD (2006) A Dynamic Epicardial Injury Response Supports Progenitor Cell Activity During Zebrafish Heart Regeneration. *Cell* **127**(3): 607-619.

Lindvall O, and Kokaia Z (2006) Stem Cells for the Treatment of Neurological Disorders. *Nature* **441**: 1094-1096.

Lumelsky N, Blondel 0, Laeng P, Velasco I, Ravin R, and McKay R (2001) Differentiation of Embryonic Stem Cells to Insulin-Secreting Structures Similar to Pancreatic Islets. *Science* **292**: 1389-1394.

Lunde Ketil, Svein Solheim, Svend Aakhus, Harald Arnesen, Michael Abdelnoor, Torstein Egeland, Knut Endresen, Arnfinn Ilebekk, Arild Mangschau, Jan G. Fjeld, Hans Jørgen Smith, Eli Taraldsrud, Haakon Kiil Grøgaard, Reidar Bjørnerheim, Magne Brekke, Carl Müller, Einar Hopp, Asgrimur Ragnarsson, Jan E. Brinchmann, and Kolbjørn Forfang, (2006) Intracoronary Injection of Mononuclear Bone Marrow Cells in Acute Myocardial Infarction. *The New England Journal of Medicine* **355**: 1199-1209.

Mansnerus, Laura (2005) "New Jersey Faces Tough Competition for Stem Cell Scientists" The New York Times. http://www.nytimes.com/2005/01/17/nyregion/17cell.html?ex=1186891200&en=5b018b9b7fd3312c&ei=5070

March, David (2004) “Method Developed to Replicate Stem Cells from the Heart” Johns Hopkins Medicine. http://www.hopkinsmedicine.org/Press_releases/2004/11_08a_04.html

Marchant J (2006) Human Eggs Supply Ethical Stem Cells. *Nature* **441**: 1038.

Massachusetts Governor’s Office (2007) “Governor Patrick Massachusetts’s New Life Sciences Initiative” The Commonwealth of Massachusetts Executive Department. http://www.mass.gov/?pageID=pressreleases&agId=Agov3&prModName=gov3pressrelease&prFile=agov3_pr_070508_life_science_initiative.xml

McDonald JW, Liu XZ, Qu V, Liu S, Mickey SK, Turetsky D, Gottlieb DI, and Choi DW (1999) Transplanted Embryonic Stem Cells Survive, Differentiate, and Promote Recovery in Injured Rat Spinal Cord. *Nature Medicine* **5**: 1410-1412.

National Institute of Health (2006) “Stem Cell Basics.” Stem Cell Information. http://stemcells.nih.gov/info/basics/basics2.asp.

National Institute of Health (2007) “NIH Human Embryonic Stem Cell Registry” Stem Cell Information. http://stemcells.nih.gov/research/registry/

Newsweek Poll conducted by Princeton Survey Research Associates International. Aug. 24-25, 2006 “Science and Nature, Stem Cell Research” http://www.pollingreport.com/science.htm

Newton DE (2007) Stem Cell Research, New York: Facts on File, 2007.

Okarma, Thomas B (2001) Human Embryonic Stem Cells: A Primer on the Technology and Its Medical Applications, Boston: MIT Press, 2001.

O'Mathúna, Dónal P. (1999) “Stem Cell Research and the Moral Status of the Human Embryo” American Bioethics Advisory Commission. http://www.all.org/abac/dpo001.htm

Orlic D, Kajstura J, Chimenti S, Jakoniuk I, Anderson SM, Li B, Pickel J, McKay R, Nadal-Ginard B, Bodine DM, Leri A, and Anversa P (2001) Bone marrow cells regenerate infarcted myocardium. *Nature*. **410***:* 701–705.

Panno, Joseph (2005). Stem Cell Research: Medical Applications and Ethical Controversy, New York: Facts on File.

Patrick, Deval (2007) “Massachusetts Governor proposes $1 billion for stem cell research” Associated Press. http://sfgate.com/cgi-bin/article.cgi?f=/n/a/2007/05/08/state/n130518D95.DTL&hw=biotech&sn=002&sc=184

Patrick, Deval (2007) “Massachusetts Proposes Stem Cell Research Grants” The New York Times. http://query.nytimes.com/gst/fullpage.html?sec=health&res=9E00E1DB1731F93AA35756C0A9619C8B63

Pelligrino, ED (2000) Testimony to the NBAC. Ethical Issues in Human Stem Cell Research. Volume 3: Religious Perspectives.

Pope Benedict XVI (2007) "Benedict endorses adult stem-cell research as respecting human life" Catholic Online. http://www.catholic.org/international/international_story.php?id=21301

Pope John Paul II (2005) "Address of his holiness Pope John Paul II to the diplomatic corps accredited to the holy see for the traditional exchange of new year greetings." The Vatican. 10 Jan. 2005 http://www.vatican.va/holy_father/john_paul_ii/speeches/2005/january/documents/hf_jp-ii_spe_20050110_diplomatic-corps_en.html

Reeve, Brock C. (2007) "Massachusetts Proposes Stem Cell Research Grants" The New York Times. http://query.nytimes.com/gst/fullpage.html?sec=health&res=9E00E1DB1731F93AA35756C0A9619C8B63

Reichenbach, Bruce R. (2004) "Miracle Cure or Moral Quagmire?" The Evangelical Covenant Church. http://www.covchurch.org/companion/articles/2004-october-miracle-cure-or-moral-quagmire

Romney, Mitt (2005) "Stem Cells Hit Snag in Massachusetts" *Science* http://sciencenow.sciencemag.org/cgi/content/full/2005/211/1

Sachedina, Abdulaziz (2000) Islamic Perspectives on Research with Human Embryonic Stem Cells. Ethical Issues in Human Stem Cell Research, Vol. 3: Religious Perspectives.

Saraswati, Acharya Mahamandaleshwar Swami Samvidanand (2003) "Dharma Discussions, Mela 2003" Hinduism Today: Himalayan Academy. http://www.hinduismtoday.com/archives/2004/1-3/28-35_discussion.shtml

SB 253 (2002) "California Senate Bill 253" http://info.sen.ca.gov/pub/01-02/bill/sen/sb_0251-0300/sb_253_bill_20020922_chaptered.html

Schächinger Volker, Sandra Erbs, Albrecht Elsässer, Werner Haberbosch, Rainer Hambrecht, Hans Hölschermann, Jiangtao Yu, Roberto Corti, Detlef G. Mathey, Christian W. Hamm, Tim Süselbeck, Birgit Assmus, Torsten Tonn, Stefanie Dimmeler, Andreas M. Zeiher, (2006) Intracoronary Bone Marrow–Derived Progenitor Cells in Acute Myocardial Infarction. *The New England Journal of Medicine* **355:** 1210-1221.

Section 8 b. (2005) "Stem Cell Research Regulation Controversy" Massachusetts Law Updates. http://www.lawlib.state.ma.us/2006/09/stem-cell-research-regulation.html
Massachusetts Law Updates (2005) "Stem Cell Research Regulation Controversy" Massachusetts Trial Court Law Libraries. http://www.lawlib.state.ma.us/2006/09/stem-cell-research-regulation.html

Senate Bill No. 25 (2005) "The Commonwealth of Massachusetts: An Act Promoting Stem Cell Research" http://www.mass.gov/legis/bills/senate/st00/st00025.htm

Severe Combined Immunodeficiency (2006) "SCID Information" http://www.scid.net/

Shannon, Thomas (2001) Human Embryonic Stem Cell Therapy. Theological Studies **62**: 811-824.

Siddiqi, Muzammil (2002) "An Islamic Perspective on Stem Cell Research." IslamiCity http://www.islamicity.com/articles/Articles.asp?ref=IC0202-404

Sinha Gujan (2005) Human Embryonic Stem Cells May Be Toxicology's New Best Friends. *Science* 308: 5728-1538.

Slack JMW, (2000) Stem Cells in Epithelial Tissues. *Science* **287**: 1431–1433.

Sliva, Jan (2006) "EU to Continue Stem-Cell Research Funding" CBS News. http://www.cbsnews.com/stories/2006/07/24/ap/health/mainD8J2ETVG0.shtml

Smart Voter (2004) "Proposition 71: Stem Cell Research, Funding, Bonds in the State of California" http://www.smartvoter.org/2004/11/02/ca/state/prop/71/

Snow, Tony (2006) "White House Softens Tone on Embryo Use" Washington Post. http://www.washingtonpost.com/wp-dyn/content/article/2006/07/24/AR2006072400990.html

Soria B, Roche E, Berna G, Leon-Quinto T, Reig JA, Martin F (2000) Insulin-Secreting Cells Derived From Embryonic Stem Cells Normalize Glycemia in Streptozotocin-Induced Diabetic Mice. *Diabetes* **49**: 157-162.

Srivastava, Deepak, Katherine Ivey (2006) "Potential of Stem Cell Based Therapies for Heart Disease" *Nature* **441**: 1097-1099

Sting J, Eirew P, Ricketson I, Shackleton M, Vaillant F, Choi S, Li H, and Eaves CJ (2006) Purification and Unique Properties of Mammary Epithelial Stem Cells. *Nature* **439**: 993-997.

Tendler, Rabbi Moshe Dovid (2000) "Stem Cell Research and Therapy: A Judeo-Biblical Perspective" *Ethical Issues in Human Stem Cell Research,* Volume 3: Religious Perspectives.

Texas Children's Hospital (2004) "Photo: Reflections of Texas Children's: David Vetter in Plastic Bubble" http://www.texaschildrenshospital.org/Web/50Years/history_70s.htm

The Hinxton Group (2006) "World Stem Cell Policies" http://www.hinxtongroup.org/wp.html

The National Institute of Health (2001) "Chapter 5:Hematopoietic Stem Cells" Stem Cell Information. http://stemcells.nih.gov/info/scireport/chapter5.asp#Thomas

The National Institute for Neurological Disorders and Stroke (2007) Parkinson's Disease. http://www.ninds.nih.gov/disorders/parkinsons disease/parkinsons disease.htm

The National Institute of Health (2001) "Chapter 7: Stem Cells and Diabetes." Stem Cell Information. http://stemcells.nih.gov/info/scireport/chapter7.asp

The National Institute of Health (2001) Chapter 8: Rebuilding the Nervous System with Stem Cells. http://stemcells.nih.gov/info/scireport/chapter8.asp

The National Institute of Health (2001) "Chapter 9: Can Stem Cells Repair a Damaged Heart?". Stem Cell Information. http://stemcells.nih.gov/info/scireport/chapter9.asp

The New England Journal of Medicine (2005) " Map: State Laws and Proposed Legislation Governing Embryonic Stem Cell Research" http://content.nejm.org/cgi/content/full/353/1/1/F1

The President's Council on Bioethics. Human Cloning and Human Dignity: Chapter Four. July 2002. June 20, 2007 < www.bioethics.gov/.../background.html> .

The President's Council on Bioethics (2002) "About the Council" http://www.bioethics.gov/about/

Thomas, E Donnall (2000) "Bone Marrow Transplantation: A Historical Review" *Medicina* **33**: 209-218.

Thomas ED, Lochte HL, Lu WC, et al. (1957) "Intravenous infusion of bone marrow in patients recieving radiation and chemotherapy." *New England Journal of Medicine* **257**: 496-496.

Thomson, James A., Joseph Itskoviz-Eldor, Sander S. Shapiro, Michelle A. Waknitz, Jennifer J. Swiergiel, Vivienne S. Marshall, Jeffery M. Jones, (1998) "Embryonic Stem Cell Lines Derived From Human Blastocysts" *Science* **282**: 1145-1147

Transplant of Hematopoietic Stem Cells (2006) Diagram: Autologous Bone Marrow Transplant, http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/M/MarrowTransplants.html

Tuszynski MH, et al. (2005) "A phase 1 clinical trial of nerve growth factor gene therapy for Alzheimer's Disease" *Nature Medicine* **11**: 551-555.

UK Department of Health (2005) "UK Stem Cell Initiative" http://www.advisorybodies.doh.gov.uk/uksci/index.htm

UK Department of Health (2005) "Stem Cell Initiative: Global Positions on Stem Cell Research" http://www.advisorybodies.doh.gov.uk/uksci/global/index.htm

United States Senate Science, Technology and Space Subcommittee Hearing Testimony of Mr. Turner, July 14, 2004. http://commerce.senate.gov/hearings/testimony.cfm?id=1268&wit_id=3676

United States Senate Science, Technology and Space Subcommittee Hearing Testimony of Ms. Fajt, July 14, 2004.
http://commerce.senate.gov/hearings/testimony.cfm?id=1268&wit_id=3674

USA Today/Gallup Poll (2007) "Science and Nature: Stem Cell Research"
http://www.pollingreport.com/science.htm?

USA Today (2007) "Gov. Aims to Reverse Romney' Stem Cell Rule's"
http://www.usatoday.com/news/nation/2007-03-30-stem-cells_N.htm

van Rood JJ, Eernisse JG, van Leeuwen A. (1958) "Leukocyte antibodies in sera from pregnant women." *Nature* **181**: 1735-1736.

Viacord, a Viacell Company (2007) Why Cord Blood is the Premier Source of Stem Cells. The Bone Marrow Foundation. http://www.viacord.com

Vick, Hannah (2000) Embryonic Stem Cell Research: Ethically Wrong Treatment of the Tiniest of Humans. Concerned Women for America Library.
http://www.cwfa.org/articledisplay.asp?id=1423&department=CWA&categoryid=life

Viegas, Jennifer. The Library of Future Medicine: Stem Cell Research. New York: The Rosen Publishing Group, 2003.

Vogel, Gretchen (2002) Studies Cast Doubt on Plasticity of Adult Cells. *Science* **295**: 1989-1991.

Vogel, Gretchen (2003) Same Results, Different Interpretations. *Science* **299**: 324.

Voltarelli JC, Carlos EB, Couri AB, PL Stracieri, MC Oliveira, DA Moraes, F Pieroni, M Coutinho, KCR Malmegrim, MC Foss-Freitas, BP Simões, MC Foss, E Squiers, RK Burt (2007) "Autologous Nonmyeloablative Hematopoietic Stem Cell Transplantation in Newly Diagnosed Type 1 Diabetes Mellitus." *The Journal of the American Medical Association* **297**: 1568-1576.

Wagers AJ, Sherwood RI, Christensen JL, Weissman IL (2002) Little Evidence for Developmental Plasticity of Adult Hematopoietic Stem Cells. *Science* **297**: 2256-2259.

Weckerly M (2006) "The Islamic View on Stem Cell Research*"* People of Faith for Stem Cell Research. http://www.pfaith.org/islam.htm

Weiss, Rick (2001) "'Parthenotes' Expand the Debate on Stem Cells".
http://www.washingtonpost.com/ac2/wp-dyn/A18046-2001Dec9?language=printer

Wilmut I, Schnieke AE, McWhir J, Kind AJ, Campbell KHS (1997) Viable Offspring Derived From Fetal and Adult Mammalian Cells. *Nature* **385**: 810-813.

Wong, Alex (2006) “Photo: First Bush Veto Maintains Limits on Stem Cell Use” The New York Times.
http://www.nytimes.com/2006/07/20/washington/20bush.html?ex=1311048000&en=706eb16610c12416&ei=5088&partner=rssnyt&emc=rss

Zoloth, Laurie (2000) “The Ethics of the Eighth Day: Jewish Bioethics and Genetic Medicine. A Jewish Contribution to the Discourse.” *Ethical Issues in Human Stem Cell Research*, Volume 3: Religious Perspectives.