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STEM CELLS AND SOCIETY

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ABSTRACT

One of the most controversial issues in the scientific community is that of stem cell research. The conflict comes from the ethical questions brought to light by this field of exploration and its effect on society. There are numerous types of stem cells and sources, and each has its own set of properties. The clinical use of stem cells has shown promise for many suffering from disease or injury. However, research is being restrained by the inability of legislators to come to an agreement on what should be permissible. Many reservations are founded in the ethical beliefs of those involved. We conclude that while some branches of stem cell research are indeed ethically questionable, there are facets that should be explored further, and more tolerant legislation should be passed to allow researchers to do so.

TABLE OF CONTENTS

PROJECT OBJECTIVE

The objective of this IQP project was to explore the many facets of the topic of stem cell research and its effect on society, and to provide a resource for those in nonscientific fields looking to become more knowledgeable about the subject. Chapter-1 was designed to present the different types of stem cells and their various sources to help dispel the commnon myth that all stem cells are alike. The purpose of chapter-2 was to provide an account of past, present, and future uses of stem cells, including some actual success stories. Chapter-3 viewed the ethics behind the research and clinical use of stem cells, including the views of major religions. The purpose of chapter-4 was to document former and current legislation regarding the use of stem cells both in the United States and abroad. Finally a conclusion was 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 TYPES AND SOURCES

Stem Cell History

Hematopoietic stem cells (HSCs) were the first type of stem cell discovered. The existence of these cells was shown in the mid 1940's following World War II. Observations of Japanese survivors of Hiroshima showed the impact of strong radiation on blood cell formation hematopoiesis. Concurrent experiments with mice showed that protecting a long bone (such as a leg) from the strong radiation allowed the blood cells to reform, saving the animal's life. The long bones were subsequently shown to harbor bone marrow, and HSCs.

The study of embryonic stem (ES) cells came about with the examination of cells removed from embryos created by *in vitro* fertilization (IVF) before they had been implanted. Researchers noticed that these special cells maintained their unique characteristics through many cell divisions. Richard Gardner, a graduate student at Cambridge University, inserted these cells into an early mouse embryo, producing the first mouse chimaera. A chimaera is an organism with tissues from two distinct genetic lines, that is, the DNA in one tissue of the animal is different than the DNA in another tissue. From there, work with stem cells continued in the Department of Genetics at Cambridge University (Edwards, 2001).

Stem Cell Classification

In spite of common public misperceptions, not all stem cells are alike. Stem cells can be classified into four groups based on potency, or their potential to differentiate. Ranging from most to least versatile, they are: totipotent, pluripotent, multipotent, and unipotent. Totipotent cells are capable of becoming absolutely any type of cell. The only true totipotent cells are

newly fertilized eggs. Pluripotent cells, such as ES cells, can differentiate into any tissue, except placenta. The differentiation of multipotent cells is limited to a specific tissue, e.g. hematopoietic cells can become red blood cells and white blood cells, but normally not liver or kidney cells. The most limited variety of stem cells is unipotent cells, which are capable of becoming only one type of cell.

Stem Cell Sources

The different potencies of stem cells originate from their different sources. Since the only true totipotent cells are fertilized eggs before they begin to divide, the only method to obtain one is to fertilize an egg. For research purposes, this fertilization is performed *in vitro*, and the needed embryos are provided by consenting donors from IVF clinics. Pluripotent cells are collected from the inner cell mass of a blastocyst, an embryo about five days after fertilization, containing around 150 cells ("Frequently Asked Questions," 2006) (Figure 1). Both multipotent and unipotent cells are collected from adult organisms from already-formed tissues, such as the brain or the liver. Stem cells from different sources are lumped into two main categories: embryonic stem cells (ESCs) and adult stem cells. This latter category also includes HSCs obtained from umbilical cord blood, even though such cells are not isolated from adult tissue.

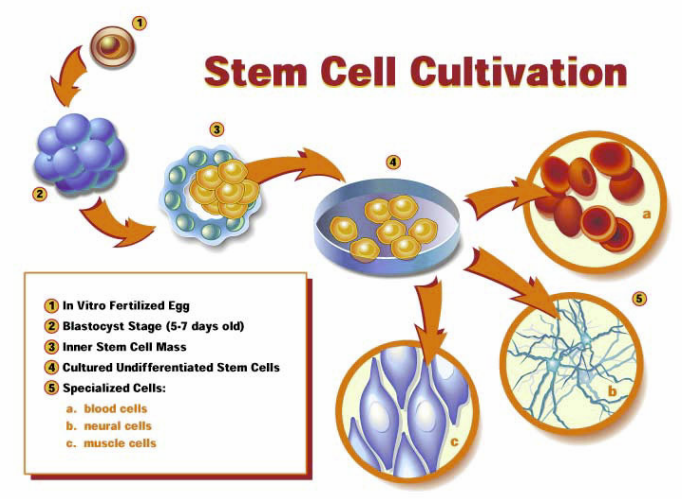

Figure 1. The cultivation of ES cells, from fertilized egg to specialized cells ("Stem Cells", 2002).

Embryonic Stem Cells

As the name would suggest, embryonic stem cells (Figure 2) are collected from embryos. Although first cultured from humans in 1998 (Shamblott, *et al.*, 1999; Thomson, *et al.,* 1998) using mouse feeder layer cells to provide growth factors, it was not until 2006 that the minimum nutritional requirements for growing human ESCs in a laboratory setting without contact with animal cells were established. The growth medium, called HESCO, contains cholesterol, transferrin (a molecule used for transportation), albumin (a blood protein), Wnt3, basic fibroblast growth factors, and April/BAFF (a B-cell activator) (Emanuel, 2006). That same year it was discovered that ESCs can be cultivated from a single cell removed from a human embryo, instead of removing the entire inner cell mass (Klimanskayza, *et al.,* 2006) raising the possibility of eventually deriving ES cell lines without destroying an embryo (although the embryo was destroyed in the 2006 experiment to obtain the single cell). Mouse ESCs are able to become dopamine neurons in Parkinson's disease applications (Bjorklund, *et al.,* 2002; Kim, *et al.*,

2002), while human ESCs have been shown to produce neuronal, cardiac, and hematopoietic cells (Itskovitz-Eldor, *et al*., 2000).

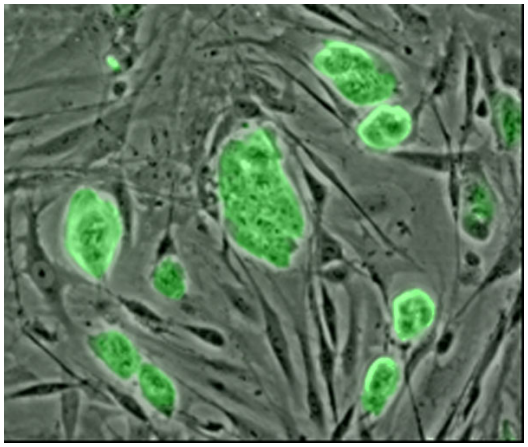

Figure 2. Picture of Mouse Embryonic Stem Cells ("Derivation," 2003).

Adult Stem Cells

Adult stem cells, however, are not only collected from adults, but from any tissue that has already differentiated. These cells are named after the tissue in which they are found and/or the tissue(s) which they form (Figure 3), for example cardiac stem cells, skin stem cells, and neural stem cells. Other types of adult stem cells include hematopoietic stem cells (HSCs), from which different types of blood cells are made; mesenchymal stem cells (MSCs), from which blood vessels and connective tissues are made; and epithelial stem cells, which become the lining of organs, tissues, and cavities throughout the body.

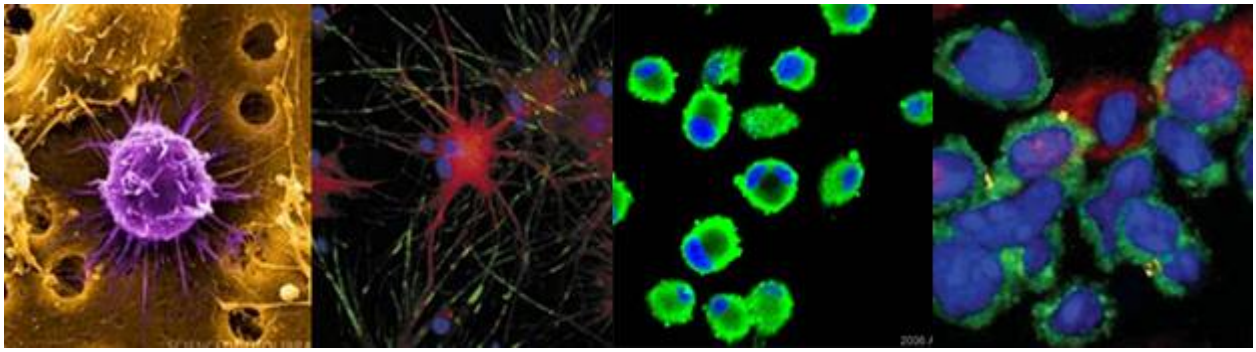

Figure 3. Pictures of Adult Stem Cells. Cells are (from left to right) bone marrow stem cells ("Stem Cell Heart Trial Begins," 2005), neural stem cells from a rat ("Stem Cells Special," 2006), mouse mesenchymal stem cells ("β-Galactosidase Antibody"), and cardiac stem cells (in yellow) ("Medicine", 2006).

Originally it was thought that the brain did not have the same ability to regenerate missing or damaged cells as the skin and liver can, and that the formation of neurons occurred in only a few locations in the brain. However, it was observed in monkeys that further neogenesis can occur, but the resulting cells were short lived. Mouse neural cells also displayed further development, however the products were not true neurons (Bjorklund and Lindvall, 2000). These studies showed that the brain may have unlocked regenerative capabilities. Then in 1992 and 1993, neurons were created from cells isolated from the central nervous system of a mouse (Reynolds and Weiss, 1992; Lois and Alvarez-Buylla, 1993). Three years later in 1996, neuronal stem cells were found in the spinal chord of a mouse (Weiss, *et al.*, 1996), but it wasn't until 2001 that these NSCs were purely isolated (Cassidy and Frisen, 2001). For humans, a major step was taken in 1998 when what had been known as ependymal cells were identified as human NSCs (Johansson, *et al.*, 1999).

As with the brain, it was once believed that the heart was also unable to regenerate needed cells. In 2000 multipotent cells that were able to differentiate into three different types of heart tissue were found in rats (Beltrami, *et al.*, 2003). Cardiac cells in mice were shown to

express a stem cell antigen in 2003 (Oh, *et al.,* 2003), and another type of cardiac precursor cell was found in rats, mice, and humans in 2005 (Laugwitz, *et al.*, 2005). Even more remarkably, last year it was demonstrated in zebrafish that cells with "precardiac markers" were able to regenerate damaged tissue after trauma (Lepilina, *et al.*, 2006).

Less is known about adult epithelial stem cells. There was once thought to be two types of cells that differentiated to become the lining of many parts of the body. However, a study conducted earlier this year demonstrated that it was a single variety of cell that was responsible for preserving the integrity of the epidermis of mouse tails (Clayton, *et al.*, 2007). Also known is that the mammary epithelium is maintained through the use of stem cells, as was demonstrated along with a new isolation method last year (Sting, *et al.,* 2006).

Much is being done in the area of hematopoietic stem cell cultivation and research. Hematopoietic stem cells are found in the blood stream, bone marrow, and umbilical cord blood. It is believed that the earlier in development HSCs are isolated, the heartier and more successful they will be ("Hematopoietic Stem Cells," 2005). For example, stem cells collected from umbilical cord blood would be preferred over those from the bone marrow of a full-grown adult. While some sources suggest the plasticity of HSCs (their ability to change into non-blood cells) (Couzin, 2006), others believe they do not possess this capability (Wagers, *et al.*, 2002).

Despite the number of sources from which HSCs are derived, they are extremely difficult to isolate. In mice, HSCs only occur about one in every ten to fifteen thousand cells in bone marrow, and one in every hundred thousand peripheral blood cells. In addition to their rarity, HSCs are also challenging to identify based on shape and size because they resemble white blood cells in culture. Steps have been taken to use proteins on the surface of cells to distinguish HSCs from other blood cells. Approximately six proteins have been identified as potential HSC

markers. These markers can be tagged with fluorescent antibodies to make the cells glow under certain conditions, as can be seen in parts of Figure 3. Another hurdle that must be overcome in the research of HSCs is the fact that they are difficult to grow in culture ("Hematopoietic Stem Cells," 2005).

There are two types of hematopoietic stem cells: short-term HSCs and long-term HSCs. Short-term HSCs are able to quickly differentiate into many cell types, but are fairly unstable and do not proliferate undifferentiated for extended periods of time. Long-term HSCs are self-renewing and have the ability to divide without differentiating much longer. Long-term HSCs are seen as the more important of the two, but are much rarer. Unfortunately, it is impossible in a lab at this time to distinguish between these two types ("Hematopoietic Stem Cells," 2005).

Research is being done to determine better ways to identify, isolate, and culture HSCs. Mice whose ability to create blood cells has been destroyed by radiation or chemotherapy are injected with a sample of cells from another source. If the mice recover and regenerate their blood systems, the sample must have contained HSCs. Other experiments with mice have been able to increase the concentration of HSCs 500- to 1000-fold. Nearly all procedures being used currently use mice. Human research in this field is still extremely rare ("Hematopoietic Stem Cells," 2005), although human bone marrow transplants have been in existence for 35 years already.

Until recent years, embryonic stem cells have been thought to be infinitely more useful than adult stem cells, owing to their seemingly unlimited potential. However, some studies suggest that adult stem cells may possess a trait known as plasticity, meaning that even though a stem cell is linked to a particular tissue, it may still have the ability to become another type of cell (Holden and Vogel, "Plasticity," 2002). This property has been demonstrated in mice, with

blood cells becoming brain cells, and neuronal cells becoming heart, liver, blood, intestine, and muscle cells, but has yet to be shown in any of the approximately twenty varieties of adult stem cells present in humans (McKay, 2000).

Parthenotes

"When is an embryo not an embryo?" asks Rick Weiss, staff writer for the *Washington Post*. The answer: when it's a parthenote. Another promising source of stem cells is the product of an unfertilized egg stimulated to divide. Some insect species use parthenotes to prepare genetically identical clones, for example worker bees, or worker ants. However mammalian parthenotes do not normally make an adult organism. Early parthenotes had been created from small mammals, but they never developed fully (Weiss, 2001). More recently, parthenotes have been created from mice that have developed into fertile adult females (Figure 4) (Kono, *et al*., 2004). Scientists have begun studying parthenogenesis in humans, but the first human parthenotes created contained no ESCs (Weiss, 2001). After successfully obtaining ESCs that differentiated into more than eight different cell types from monkeys (Weiss, 2001; Cibelli, *et al.*, 2002; Holden, 2002; Vrana, *et al.*, 2003), ESC-containing human parthenotes have been created (Weiss, 2001). In Milan, two ESC lines have been established from human parthenotes (Marchant, 2006). Despite the creation of ESC-containing human parthenotes, none have the capability of becoming a live human. It is unknown whether or not the genetic defect preventing the parthenotes from developing fully into babies will have an impact on the success of any therapy involving the resulting ESCs (Cheshire, 2003).

Figure 4. Adult Female Mouse Parthenote With Offspring (Kono, *et al.*, 2004).

As promising as culturing ESCs from human parthenotes may be as an alternative to deriving ES cells from fertilized embryos, some obstacles still stand in the way of complete success. Usable eggs are hard to obtain from older women, who would be most likely to benefit from this type of therapy. Using a woman's own eggs would virtually eliminate the chance of transplant rejection (Weiss, 2001).

Another method of obtaining embryonic stem cells is through somatic cell nuclear transfer (SCNT), or therapeutic cloning. This is the process by which an embryo is created by inserting the nucleus from the patient's skin cell for example into an enucleated egg. This provides ESCs that are a genetic match for the patient, thereby removing the possibility of rejection ("Somatic Cell Nuclear Transfer", 2007). Although this SCNT process has worked in mice, it has not yet been achieved for humans.

CHAPTER 2: STEM CELL APPLICATIONS

The purpose of this chapter is to document some of the work that has already been done with stem cells, paying particular attention to distinguishing hype from factual medical studies, and distinguishing animal experiments from human clinical trials.

Neural Stem Cells

As one would imagine for a cell capable of regenerating neural tissue, neural stem cells have the potential to treat a variety of neurological disorders and injuries, such as Parkinson's disease and amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) or Huntington's disease (Levesque, 2005; "Rebuilding," 2005). Most of the pioneering work with neural stem cells has been done with rodents, while human clinical trials are only recently underway for some of these diseases. The use of NSCs is more effective than neural tissue replacement, another form of treatment for neurodegenerative disease. Rats experiencing some of the symptoms of Huntington's were given human NSCs, resulting in a decrease in the uncontrolled movements associated with the disease, thus in the future, patients with ALS may also see relief from similar use of NSCs. Some success has been seen with the transplantation of neurons derived from these cells in rats. Neurogenesis, or the formation of new neurons, has been seen with the use of NSCs in the damaged tissue of rats, providing some light at the end of the tunnel for so many people who have had strokes (Lindvall and Kokaia, 2006).

Neural stem cells have also shown promise to those with spinal injuries. Laura Dominguez is just one of many people that have benefited from the use of NSCs. When she was sixteen, a car accident left her paralyzed from the neck down. She underwent experimental NSC

transplant surgery in Portugal, and has shown major improvements toward walking again (Hughes, 2005).

Hematopoietic Stem Cells

The use of stem cells for healing human patients is not a new science. The clinical use of hematopoietic stem cells has shown to a promising treatment for a number of ailments for over 35 years. For decades, bone fragment and marrow transplants from both humans and mice have been effective in rebuilding the marrow and blood systems of immunosuppressed mice (Verfaillie, 2002). These new systems were active and functional for several months following treatment (Kyoizumi, *et al*., 1992; Nolta, *et al*., 1997). Bone marrow transplants in humans are responsible for treating several types of cancer, including leukemia (Bordignon, 2006; "Hematopoietic Stem Cells," 2005; Earll, 2005) and lymphoma. Hematopoietic stem cells from umbilical cord blood have even been shown to exhibit anti-tumor activity in mice against kidney and breast cancer ("Hematopoietic Stem Cells," 2005).

In addition to treating diseases of the blood, stem cells from blood and bone marrow are giving hope to those whose hearts have been damaged by heart attacks (Britten, *et al*., 2003) or other injury. Studies in mice show that HSCs injected into the wall of the heart can repair damage done to heart tissue. Also shown to be effective is a dose of stem cells into the bone marrow of the mice before the heart attack occurs. Human HSCs transplanted in rats have become vascular tissue, demonstrating the plasticity of HSCs ("Can Stem Cells," 2005). Although not definitively conclusive, studies in Germany and Norway show that injecting bone marrow directly into the heart of a patient may aid in recovery after a heart attack (Couzin, 2006).

A heart attack is not the only sort of damage one's heart can encounter. Sixteen-year-old Dimitri Bonnville's heart was shot through by a nail gun. Instead of a heart transplant, his doctors suggested a new treatment involving stem cells. Bonnville's body was stimulated by hormone treatments to produce more HSCs, which were then collected and transplanted into his heart. According to his doctors, his recovery was amazing (Philipkoski, 2003).

Also demonstrating the plasticity of HSCs is the use of bone marrow in the treatment of victims of Parkinson's disease and strokes to rebuild damaged portions of the central nervous system (Lindvall and Kokaia, 2006).

Embryonic Stem Cells

One of the most promising uses of ESCs is in the treatment of type 1 and possibly type 2 diabetes (Chapman *et al.*, 1999; "Embryonic Stem Cells," 2005). Currently, one method of treating diabetes is with pancreatic islet transplants from cadavers. These transplants have been shown to be effective for more than three years, but donors can be difficult to find (Roche, *et al*., 2003) and the patient must use immune-suppressants to prevent rejection of the transplant. In mice, ESCs have been shown to form structures that mimic the islets of the pancreas and secrete insulin in the presence of glucose (Lumelsky, *et al*., 2001). If this technology could be applied to humans, patients would not have to worry about finding pancreatic donors. Murine ES cells have also been stimulated to differentiate into insulin-secreting β-cells, opening the door for possible cell replacement therapy (Assady, *et al*., 2005). Treated diabetic animals have shown improvement in just one week (Soria, *et al*., 2000).

Murine ES cells have also been shown to reverse hemophilia when injected into the liver of mice ("Embryonic Stem Cells," 2005) and provide an alternate for HSCs in repairing heart damage (Klug, *et al*., 1996; Srivastava and Ivey, 2006).

Others who may benefit from the use of ESCs are those suffering from neurological disorders. In addition to the use of NSCs, the use of ESCs may provide some promising treatments. In animal studies, dopamine-producing ESCs (both animal and human) have shown to be somewhat beneficial to animal models with Parkinson's disease (Bjorklund, *et al*., 2002; Kim, *et al*., 2002; Ryan, 2004; Lindvall and Kokaia, 2006). ESCs from monkeys transplanted into rats have produced new neural tissue, similar to the results obtained using NSCs, a treatment that may be useful in treating patients who have suffered from strokes. When injected into the spinal fluid of rats with ALS, ESCs were able to produce some improvement, which may be even more successful with the use of genetic modification (Lindvall and Kokaia, 2006). Researchers have also seen improvement in mice with ALS through treatment with ESCs ("Rebuilding," 2005). One study successfully produced motor neurons, like those destroyed with ALS, from ESCs (Wichterle, *et al*., 2002). Oligodendrocyte progenitor cells derived from ESCs are capable of reforming the protective coating (myelin) on mouse neurons, giving hope to those suffering the demyelination of multiple sclerosis (Lindvall and Kokaia, 2006). Patients who have suffered spinal cord injuries may also benefit from treatment based on ESCs ("Stem Cell Treatment," 2005).

Other diseases that could benefit from therapy with ESCs include immunodeficiencies, such as AIDS, severe combined immunodeficiency disease, lupus, and Wiskott-Aldrich syndrome (Chapman *et al.*, 1999). Heart defects have been fixed in mice using these pluripotent

cells (Chien, 2004). Research is also being done using ESCs as treatment for osteoarthritis and osteoporosis ("Human Embryonic Stem Cell Programs," 2004).

Other Stem Cells

Hope for patients with diabetes may not come only from treatments with ESCs. Researchers have found that pancreatic stem cells could also help this disease (Earll, 2005). In addition, as recently as 2003, stem cells have been found in the outer ring of the iris of the eye that have the potential to differentiate into any of the types of cells that make up the eye. According to one study, each eye contains enough stem cells to give rise to 150 million progenitor cells ("Dead Could Help," 2003). The use of these cells is known as limbal stem cell transplantation (Hughes, 2005). Although still recent, this discovery gives hope to those who suffer from visual impairments and eye injuries.

CHAPTER 3: STEM CELL ETHICS

Perhaps the most significant roadblock standing in the way of stem cell research is that of the ethical dilemma surrounding the topic. There is much disagreement among the major world religions as to the morality of destroying an embryo in the name of science. Because different religions have different beliefs as to when life actually begins, there is no general consensus on stem cell research among those who form their opinions based on religious beliefs. There is even dissent within individual religions regarding the ethics of pursuing this field of research.

Catholic Church and Stem Cells

The Catholic Church, believing that life begins at conception, is outspokenly again ESC research (Derbyshire, 2001). The Medieval Church believed that a fetus only received a soul when it began resembling a human, but in 1869 Pope Pius IX declared that ensoulment occurred at conception (Frazzetto, 2004). Nearly 140 years later, Pope John Paul II, in a statement to the diplomatic corps accredited to the Holy See, declared, "Whatever violates the integrity and dignity of the embryo is ethically inadmissible. Similarly, any form of scientific research which treats the embryo merely as a laboratory specimen is unworthy of man (Pope John Paul II, 2005)." The following year, current Pope Benedict XVI echoed the sentiments of his predecessor, "In fact, this research advances through the suppression of human lives that are equal in dignity to the lives of other human individuals and the lives of the researchers themselves (Pope Benedict XVI, 2006)." Despite their condemnation of ESC research, both Popes have publicly supported and praised continuing research with adult stem cells (ASCs) (Pope John Paul II, 2005; Pope Benedict XVI, 2006). Others at the Vatican also agree that while

ESC research may be immoral, research with stem cells from adult sources may prove to be acceptable in the eyes of the church (de Dios Vial Correa, 2000). In the United States, Bishop Joseph A. Fiorenza, President of the U.S. Catholic Conference of Bishops, has been outspoken against President George W. Bush's decision to allow government funding to be provided for the continuing research on pre-established ESC lines ("U.S. Bishops," 2006). Some Catholics believe that, even with the question of when life begins aside, it would be more ethical to spend that money on providing healthcare to those who currently cannot afford it, rather than pursuing technology that will only be available to those who can afford it (Shannon, 2006).

Hindu and Buddhist Stance on Stem Cells

Another religious group generally known to be against embryonic stem cell research is the Hindu and Buddhist community. Traditional Hinduism believes life begins at conception, while other Hindu groups believe a fetus becomes a person later on, three to five months after conception. In Buddhism, life begins at conception ("General Positions," 2006). Many leaders of Hinduism have spoken out against ESC research as having dire consequences, and it will cause more harm than good. Mahanandaleshwar Paramhaus Swami Maheshwarandanda believes that, "when mixed breeds come, purity is lost and destruction is the result," in response to genetic modification. However, not everyone shares this extreme view. According to Swami Karshini Gurusharnananda, "Nothing is wrong. The only issue is how it's being used ("Dharma Discussions," 2004)." This last statement leads one to believe that research may be supported under certain circumstances, perhaps where human lives are being saved. There is also uncertainty among Buddhists, where ESC research is seen as a form of disrespecting life, but the

definition of life itself is being challenged owing to its nontraditional beginning in a laboratory (Frazzetto, 2004).

Islam and Stem Cells

One religion that seems to be mostly in favor of ESC research is Islam. Their beliefs state that life begins when an embryo is implanted into the womb (Derbyshire, 2001), which occurs about ten days after fertilization, and ensoulment occurs on the 120th day (Frazzetto, 2004). Other sources claim that the critical point is at forty days of gestation ("General Position," 2006). Whichever way Islamic law is interpreted, these views all allow for the use of five-day-old blastocysts for research. Although there is still some division in the Muslim community (Holmes, 2004), Shari'ah, or the method of obtaining laws from the teaching of the Qur'an, dictates that there is a difference between life and potential life. An embryo of less than forty days is less human than one of more than forty days, which, in turn, is less human than a child after birth. According to this way of thinking, an embryo outside the womb is not a person at all, and therefore there is nothing unethical about ESC research. However, Islam is against the misuse of such technology, such as the trading of embryos for monetary gain or creating more than the standard number of embryos for IVF with the intent of having excess for experimentation (Siddiqi, 2002). Some interpretations of Islamic law even believe that ESC research is the will of Allah (Weckerly, 2006).

Stem Cells and Judaism

One religious community that is much less decisive with its position on ESC research is the Jewish community. According to Rabbi Moshe Dovid Tendler:

Jewish law consists of biblical and rabbinic legislation. A good deal of rabbinic law consists of erecting fences to protect biblical law. Surely our tradition respects the effort of the Vatican and fundamentalist Christian faiths to erect fences that will protect the biblical prohibition against abortion. But a fence that prevents the cure of fatal diseases must not be erected, for then the loss is greater than the benefit. In the Judeo-biblical legislative tradition, a fence that causes pain and suffering is dismantled. Even biblical law is superseded by the duty to save lives, except for the three cardinal sins of adultery, idolatry, and murder.

Life saving abortion is a categorical imperative in Jewish biblical law. Mastery of nature for the benefit of those suffering from vital organ failure is an obligation. Human embryonic stem cell research holds that promise. (Eisenberg, 2006) Rabbi Elliot Dorff is also of this view, believing that ESC research is permissible because it is for the common good (Derbyshire, 2001). Many Jews believe that they have an obligation to G-d to seek knowledge, and are therefore obligated to pursue any research that can help save lives. It would be considered a mitzvah (a good deed or act of kindness) to use leftover embryos from IVF for research, rather than discarding them (Yearwood, 2006). This coincides with their belief that the preservation of human life should outrank any sin that may be involved, with the exception of murder, adultery, and idolatry (Frazzetto, 2004; Yearwood, 2006). Yoel Jakobovits, of Torah.org, reports that Jews believe that scientists may play G-d, as long as they play by His rules (2006). The National Council of Jewish Women and the Women's Zionist Organization of America are known supporters of stem cell research (Yearwood, 2006).

According to Judaism, life begins at birth, although abortion is condemned as destroying the potential for life. Like Islamic culture, Jewish culture recognizes a change in status at forty days post-fertilization ("General Positions," 2006; Eisenberg, 2006; Yearwood, 2006; Ayon, 2002). Also as with Islamic culture, a portion of the Torah would lead one to believe that there is a distinction between a fetus and an infant. One such passage states, "If in the course of an altercation with a third party, a person causes a woman to miscarry, he pays only monetary

damages, while if the woman herself were to die of her injuries, the aggressor would receive a death sentence (Eisenberg, 2006)." The ambiguity of this passage lies with intent. What would the penalty be if the aggressor's intent was to harm the unborn child and the miscarriage was the goal instead of unintentional consequence?

While some sources report overwhelming support (Holmes, 2004), not everyone of Jewish faith is leaning in favor of embryonic stem cell research. Some see it as a form of "wasting male seed (Eisenberg, 2006)," since the embryos are not being used for procreation. Others are comfortable with the use of stem cells from the umbilical cord and adult sources, but are unsure about the treatment of leftover embryos from IVF (Jakobovits, 2006). The belief of the preservation of life is interpreted by some to mean that even the potential for life should be preserved, making it unethical in their eyes to destroy embryos (Yearwood, 2006). With so many interpretations and opinions, the Jewish community appears far from a consensus on embryonic stem cell research.

Other Religions and Stem Cells

Other smaller religious groups are just as much at odds about this issue as the major religions. According to one source, Unitarian-Universalists, the United Methodist Church, the Church of Jesus Christ of Latter Day Saints, the Episcopalian Church, and the Evangelical Lutheran Church are not officially for or against ESC research (Derbyshire, 2001), although the National Association of Evangelicals was known to support President Bush's policy (Holmes, 2004). In general it seems that most Protestant churches support ESC research, although there are exceptions. Among these are the Southern Baptist Church, which is opposed, and the American Presbyterian Church, which supports ESC research if there are no other options

("General Positions," 2006). Some Christians are afraid that allowing ESC research will cause a slippery slope effect, leading ultimately to the cloning of humans ("Why Christians Should," 2005).

Religious groups are not the only ones weighing in on the ethics of stem cell research. Some people support ESC research because it is a way of immortalizing an embryo, rather than destroying it (de Wert and Mummery, 2003). Certain polls show American support of ESC research to be as high as eighty percent (Holmes, 2004). However, this estimate may be high. According to their web site, the Concerned Women for America are against stem cell research (Vick, 2000).

Despite the varying views on embryonic stem cell research, it seems that most do not object to research with adult stem cells. Some religions, such as the Catholic Church and members of the Jewish community, have been vocal about their support of ASC research as an alternative to the use of ESCs. It can safely be assumed that those groups that have no ethical qualms with ESC research would have no issue with the use of ASCs since embryos are not destroyed to obtain ACSs. As for those who are opposed to working with ESCs, the majority of their concerns are based on destroying a life or the potential for life. With ASC research, nothing is being destroyed. Cells from inside the body are cultured outside the body and reintroduced to rebuild damaged or diseased tissues. Therefore, it follows that many of the ethical issues surrounding stem cell research lie with the use of embryos.

Parthenote Ethics

Unfortunately, the discussion of ethics does not end here. With the development of new technology come even more questions. The development of human parthenotes is not without

controversy. Some feel that since parthenotes lack the ability to grow into people, there should be no problem using them as a source of stem cells (Weiss, 2001). Those against the use of parthenotes as a source of stem cells include the Center for Bioethics and Human Dignity, who believe that the treatment of parthenotes would be equivalent to the treatment of embryos containing a genetic defect, such as Down Syndrome or any other number of genetic abnormalities that are considered abnormal (Jones, 2003). Since mouse parthenotes have survived into adulthood, maybe these fears are well-founded. If it's possible with mice, who's to say it won't someday be possible with humans? After all, through the use of cloning technology, we have the ability to produce an entire human being from a single cell. Says Jerry Hall, Laboratory Director at the Institute for Reproductive Medicine and Genetic Testing, "If you look at it that way, then a body cell may have more rights or more moral basis than a parthenote (Weiss, 2001)."

CHAPTER 4: STEM CELL LEGALITIES

U.S. Federal Stem Cell Legislation

In addition to the ethical questions, the legalities of stem cell research are also standing in the way of advancements. On August 9, 2001, President George W. Bush passed legislation that prohibited federal funding to be used for embryonic stem cell research using lines that had not already been created (Abbott, *et al*., 2006). Researchers would be allowed to continue using "existing stem cell lines where the life and death decision has already been made ("Stem Cell Laws," 2005)." This bill came with a few provisos: (1) the embryos must have been created for IVF; (2) the embryos must no longer be needed for reproductive purposes; (3) the embryos must have been obtained with the consent of the parents; and (4) the embryos must have been donated and not bought ("Information on Eligibility," 2006).

At the time, there were sixty-four established ESC lines available worldwide that met Bush's restrictions (Abbott, *et al*., 2006; Agnew, 2003; Holden and Vogel, "Show Us," 2002). However, the number of available, useful lines has been estimated anywhere between nine (Agnew, 2003; Garfinkel, 2004; NIH Registry, 2005) to sixteen ("Information on Eligibility," 2006; Holden and Vogel, "Show Us," 2002). Some even estimate the number to be in the low twenties (Abbot, *et al*., 2006; Dunn, 2005). Whatever the number, it is significantly less than the sixty-four Bush had intended. Of the original number of lines, many were too old, contained genetic mutations, grew too slowly, had become diseased, or exhibited unpredictable behavior. Also, many of the cell lines had been grown using animal products, such as mouse feeder cell layer, and were therefore unusable for human research (Abbott, *et al*., 2006).

Bush's legislation came only one month after the House introduced a bill banning human cloning, but allowing somatic cell nuclear transfer (SCNT) that could not make it past a Senate filibuster. Among this bill's supporters were Dianne Feinstein (D-CA), Ted Kennedy (D-MA), Zell Miller (D-GA), and Orrin Hatch (R-UT) (Agnew, 2003), all four of whom are from different religious backgrounds: Jewish ("Dianne Feinstein," 2007), Roman Catholic ("Ted Kennedy," 2007), Methodist ("Zell Miller," 2007), and Mormon ("Orrin Hatch," 2007), respectively. Bush's stance remained firm, "Because no human life should be started or ended as the object of an experiment (Agnew, 2003)."

President Bush is not the first to enact legislation against stem cell research. In 1996, two years before the first ESCs were isolated, the Dickey Amendment was passed, which prohibited federal funding for any research that involved destroying embryos. However, some ambiguity in the exact wording of the legislation may provide a loophole that permits ESC research (LAO, 2004).

Despite the already existing American Society for Bioethics and Humanities and the National Institute of Health, President Bush established the President's Council on Bioethics in 2001 ("the President's Council," 2007). Less than three years later, Bush replaced two members on the Council who supported stem cell research with three who did not. Leon Kass, Chairman of the Council, even frowns upon IVF ("Stem Cell Laws," 2005) and is against SCNT. He is in favor of a four-year moratorium on legislation amending Bush's 2001 decision (Agnew, 2003). In both 2005 and 2006, Congress attempted to pass legislation relaxing the restrictions on ESC research in the United States, only to be vetoed by President Bush. Unfortunately, both times, the House and the Senate were unable to gather enough votes to override a veto (Baker, 2005; Babington, 2006; Holden, 2006). Said Bush, "I made my position very clear on embryonic stem

cells (Baker, 2005)." Early this year, Congress tried to pass the Stem Cell Research Enhancement Act of 2007 (SCREA), which would allow research to include new embryos left over from IVF, and the Hope Act, which would permit research to take place with "naturally dead" embryos. The act defines "naturally dead" embryos as those "having naturally and irreversibly lost the capacity for integrated cellular division, growth, and differentiation (Wadman, 2007)." Presidential hopefuls for the 2008 election had mixed feelings on the SCREA. While republican candidates Sam Brownbeck (KA) and Mitt Romney (MA) do not support the legislation, fellow republican John McCain (AZ) does. Other proponents of SCREA included democrats John Edward (NC), Hilary Clinton (NY), and Barack Obama (IL), with Clinton and Obama cosponsoring the bill. Republican candidate Rudy Giuliani (NY) has yet to take a definitive stand on this issue (Wadman, 2007). Bush, maintaining his position that his 2001 legislation is "encouraging – not banning ("White House Press Release," 2001)," promised to veto both the SCREA (Wadman, 2007) and the Hope Act, claiming, "If it advances all the way through Congress to my desk, I will veto it ("White House Press Release," 2001)."

Not everyone shares the views of the current president. Back in1993, President Clinton allowed the NIH to fund ESC research (Dunn, 2005). Senator Tom Harkin (D-IA) believe it is hypocritical of Bush do allow excess embryos from IVF to be frozen or discarded, but not donated for research purposes (Babington, 2006). One poll shows that seventy percent of Americans are in favor of loosening restrictions placed on ESC research, citing fifty-six percent of conservatives, eighty percent of moderates, and eighty-four percent of liberals (Dunn, 2005). Another poll shows the percentage of Americans supporting stem cell research at about sixty-seven percent (Langer, 2005), rising seven percent from 2001 to 2005 ("Public Support," 2005). Some believe that Bush's ban is responsible for keeping people ignorant about stem cell research

(Rowley, *et al*., 2002). Bruce Agnew of the Genome News Network says, "The most likely outcome now seems to be a continuing standoff unless members of Congress can learn the difference between using stem cells for research and using them for human reproduction (2003)."

Institution and State Funding of Stem Cells

Without the support of government funding, researchers must rely on private backers to financially support their projects. Some states have taken funding such projects into their own hands (Figure-5). In 2002, California became the first state to have a university with privately-funded ESC research at Stanford. Later that year, the University of California San Francisco and Johns Hopkins University followed (Check, 2002). Two years later, New Jersey funded the first state-supported research facility for ESCs. Also in 2004, California granted $3 billion over ten years for research (Dunn, 2005). The following year, Governor M. Jodi Rell (R-CT) proposed $100 million over ten years (Johnson and Williams, 2006) under the conditions that the embryos could not be grown more than fourteen days, could never be implanted, and could not be paid for ("Rell Signs 10 Year," 2005). Massachusetts Governor Mitt Romney attempted to veto a stem cell bill because it included funding for cloning, but his veto was overridden (Johnson and Williams, 2006). Also in Massachusetts, Harvard University, which had been reluctant to oppose Bush's ruling (Check, 2002), received $6 million for research from Stowers Medical Institute in Cambridge (Holden, 2006). Four years after Bush's restrictions, Governor Bob Taft of Ohio overturned a state ban on ESC funding (Ertelt, 2005). In California in 2006, the $150 million California Institute of Regenerative Medicine was established. That year also saw a $50,000 research grant at the University of Michigan Ann Arbor and $15 million for research in

Illinois (Holden, 2006). Other states that also saw funding for various stem cell projects included Indiana, Maryland, Missouri, Virginia, and Wisconsin (Johnson and Williams, 2006).

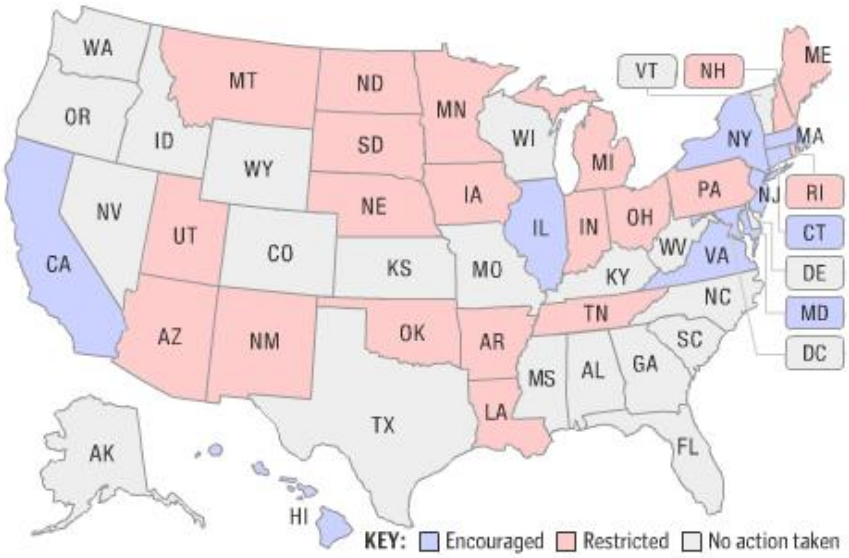

Figure 5. Legislation on Stem Cell Research by State as of 2005 ("Stem Cell Legislation," 2005).

Other Countries and Stem Cells

The United States is not the only country in the world dealing with the issue of stem cell research. Hot spots for stem cell research around the world include China, Korea, and the United Kingdom (Weiss, 2005). Table I shows the number of ESC lines available in various countries. China has six labs and anywhere from ten to seventy stem cell lines available for research (Abbott, *et al*., 2006). Korea can produce upwards of one hundred ESC lines per year and is home to the World Stem Cell Foundation, aiding other countries with branches in San Francisco and Oxford (Kaplan, 2005). Scientists were allowed to create new ESC lines for one year

beginning in 2004 in the United Kingdom, which objected to a ban proposed to the United Nations by the United States (Garfinkel, 2004).

Country	Lines	Country	Lines
United States	>100	Iran	6
China	>10	Spain	6
Sweden	55	Finland	4
Australia	30	Israel	3
Great Britain	24	Japan	3
S. Korea	18	Canada	2
Turkey	11	India	1
Belgium	7	Singapore	1
Czech Rep.	7	Switzerland	1
Denmark	6		

Table I. ESC lines established by country as of July 27, 2006 (Abbott, *et al*., 2006).

Perhaps one country on the front lines of stem cell research is Sweden. Owing to its long tradition of support for scientific research, Sweden provides government funding to thirty groups and three hundred people who partake in stem cell research. With its National Stem Cell Bank and embryos left over from IVF ("Sweden's Stem Cell Success," 2002), Sweden has been able to derive over fifty ESC lines.

Funded by the European Union, the Sixth Framework Programme (FP6) has given €12 million ($15 million) to twenty labs in ten countries, which have been able to derive fifty-two ESC lines (Abbott, *et al*., 2006). Despite the amount of support in Europe, stem cell research is

not without opposition there, either. Figure-6 shows a world map and the various stem cell policies for each country. Germany is among those countries against the European Union funding such research. Also sharing this view are Austria, Poland, Slovakia, Slovenia, Lithuania, Luxemburg, and Malta ("Germany Calls," 2006).

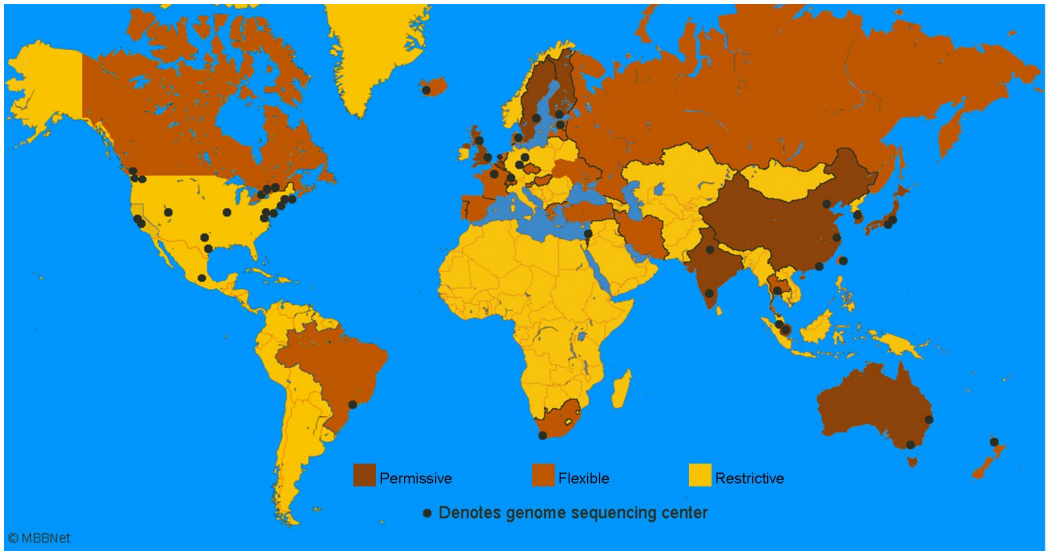

Figure 6. Map of Stem Cell Policies Around the World. Dark Brown, Permissive: allow research including SCNT; Orange, Flexible: allow research with excess from IVF only, no SCNT; Yellow, Restrictive: limited research allowed or no legislation (Hoffman, 2005).

CONCLUSIONS

The use of stem cells in the treatment of numerous conditions and diseases gives hope where there was none before. It can hardly be denied that at least some facets of stem cell research are worth pursuing. Ethical qualms regarding the use of parthenotes are minimal, and those regarding the use of adult stem cells are virtually nonexistent. These seem to be the two paths of least resistance and therefore should be researched more aggressively than the highly controversial use of embryonic stem cells. However, the importance of ESCs should not be discounted altogether. While the act of creating embryos solely for harvesting ESCs is reprehensible, collecting the precious cells from embryos already created for IVF and slated to be discarded is a strong alternative.

It is imperative for legislature dealing with stem cell research, whether restrictive or permissive, to remain contemporary with the ever-evolving technology. Because of the dwindling number of usable, established ESC lines, researchers in the United States must be allowed to create new cell lines in order to use these new technologies to the furthest extent of their abilities. Although more permissive laws are required for the continued success of stem cell research, new laws must ensure a focus on saving lives. There is a fine line between using technology to help cure and prevent disease and using it for egoistical purposes. If that line becomes blurry for even an instant, all advances in the name of fighting disease and healing injury may come to a screeching halt.

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