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STEM CELLS

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STEM CELLS

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ABSTRACT

The use of stem cells is a relatively new technological advancement in medicine, and is a heavily debated topic world-wide. The purpose of this project was to investigate this topic, especially key debated points to make recommendations and opinions. The findings and discussions of this project are based on a variety of sources, and help clarify some common misperceptions.

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PROJECT OBJECTIVES

The purpose of this project is to investigate the topic of stem cells, focusing especially on key debated points. Sufficient background was obtained to allow the authors to make general recommendations and opinions.

Chapter 1- STEM CELL TYPES AND SOURCES

Chapter 1 is an overview of what stem cells are and discusses the different types of stem cells that are used in medical research and applications. It also explains how each type of these cells is obtained. The outcome of this chapter allows the reader to understand that not all stem cells are alike, each has its own properties and ethical issues.

Chapter 2- STEM CELL APPLICATIONS

In this chapter, specific examples of stem cell applications are described. Some of the applications are treatments that have been proven safe and effective while others are in the development stage and are still being researched in animal models or in early human trials. Chapter 2 demonstrates the potential uses for these stem cells, as a beginning point for subsequent ethical discussions.

Chapter 3- STEM CELL ETHICS

Chapter 3 explains the moral issues that are involved with using various types of stem cells. There is a wide spectrum of positions taken on the use of stem cells, and this chapter summarizes different opinions from religious groups, to political views concerning different types of stem cells and their uses.

Chapter 4- STEM CELL LEGALITIES

Chapter 4 discusses the legal issues that regulate the use of stems cells for medical treatments and research. Similar to chapter 3, there are many different opinions on stem cells and therefore many different federal and state laws have been passed on the use of stem cells, including laws that support the use of the cells through funding, or laws that completely prohibit the use of specific types of stem cells.

CHAPTER-1: STEM CELL TYPES AND SOURCES

What Are Stem Cells?

Stem cells are often termed the "master" cells of the body because they are unspecialized cells with the ability to renew themselves for many years through cellular division. They can differentiate into different types of cells with specialized functions if proper conditions are available; in particular, factors that control cell structure and function can produce these conditions that lead to differentiation (National Institute of Health, 2005). One type of "master cell," the human embryonic stem cell (hESC), possesses unique properties including a normal karyotype, high telomerase activity, and long-term proliferation, a process which provides for unlimited growth. These cells can amazingly differentiate into the three embryonic germ layers if they are transferred to an *in vivo* environment (Odorico et al., 2001). Stem cell division is asymmetric (Figure-1), producing either daughter cells of the same biological potential, or producing cells of lesser more specialized potential.

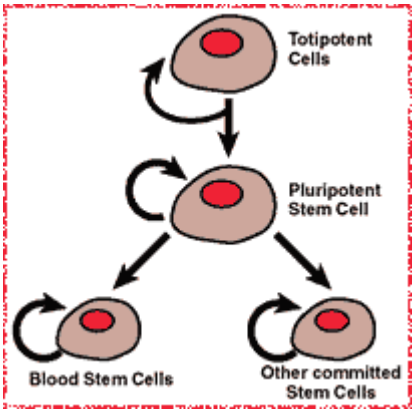

Figure 1: Asymmetric Stem Cell Division. Totipotent cells (upper center) such as a newly fertilized egg, have the greatest biological potential. Pluripotent stem cells (center) such as ES cells, have excellent but slightly lesser potential. Multipotent stem cells (lower left) such as hematopoietic stem cells, are able to differentiate into several related cell types. Unipotent stem cells (lower right) can usually only differentiate into one type of tissue (Why Files Guide to Stem Cells, 2008).

When people think about stem cells, many tend to think only of destroyed embryos. And it is this notion that embryos are destroyed that makes many in the public uncomfortable. And this discomfort has led to a lot of controversy. When some people hear the expression "stem cells," they think of destroyed fertilized human eggs which are, in their minds anyway, tiny, little humans. However, adult stem cells (ASCs), and in particular hematopoietic stem cells (HSCs) isolated from bone marrow, have been used for more than 40 years for people who underwent bone marrow transplantation. And these cells raise far fewer ethical debates. This means that not all stem cells are the same, which many people do not realize. In fact, stem cells can be obtained from sources other than embryos, including some adult organs, fetal tissues, umbilical cords, and placentas (Godandscience, 2004). Recently, scientists have discovered that even cells isolated from a baby's tooth or amniotic fluids may have the possibility of forming different cell types (Frequently Asked Questions on Stem Cell Research, 2006). In this chapter, stem cells types and sources are explored in more detail. Some sources and types are less controversial than (ESCs) because no embryo destruction is involved, yet such cells still have some potential to cure debilitating diseases.

Stem Cells Potencies

Not all stem cells have the same potency to give rise to all body cells (Figure-2). Totipotent stem cells (diagram upper part) are represented by the fertilized egg, the zygote. These types of cells can differentiate into any type of cells, including the three germ layers (ectoderm, mesoderm, and endoderm) and the placenta (Adult Stem Cells, 2006). Pluripotent stem cells (purple in the figure) are less specialized than totipotent stem cells, where they only give rise to the cells derived from the three germ layers. Pluripotent stem cells are derived from the inner cell

mass (ICM) of a blastocyst (Adult Stem Cells, 2006) and are represented by embryonic stem (ES) cells. Multipotent stem cells (diagram right center) are limited to differentiating into specific types of cells, and they are found in adult tissues (MedIndia.com, 2006). Examples of multipotent stem cells are hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs). Unipotent stem cells are usually capable of forming only one type of cell (National Institute of Health, 2005). An example of a unipotent stem cell is neuronal stem cells (NSCs) (diagram lower center). Some stem cells are more powerful than others, but future research may help equalize their potentials, allowing the use of less controversial types for a variety of medical applications.

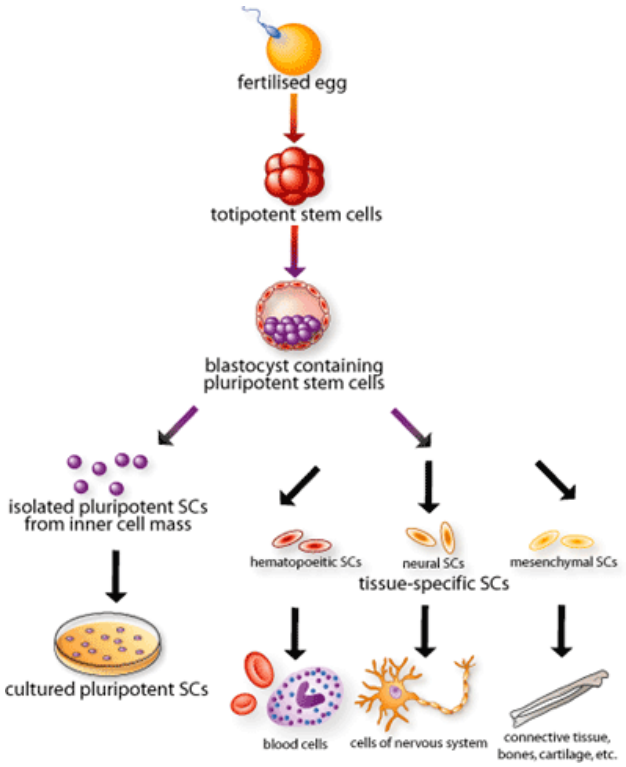

Figure 2: Origin, Isolation, and Specialization of Stem Cells. This diagram shows various types of stem cells. Those with the greatest biological potencies (i.e. able to differentiate into the largest number of different tissues) are shown at the top. Potency decreases with lower positions on the diagram. (Chaudry, 2004).

Embryonic Stem (ES) Cells

Scientists have been able to obtain ESCs from mice as long as 20 years ago (National Institute of Health, 2005). ESCs are derived from a 5 to 6 old-day embryos (Embryonic Germ Cells, 2007). This type of stem cell has the potential to virtually become any cell type, except for placenta. After ovum fertilization by a sperm, a zygote is formed and embryonic development begins (National Academy Press, 2001). The zygote divides, then after 3 to 4 days, the embryo is composed of 12 or more cells known as a morula (National Academy Press, 2001). After 5 to 6 days, the embryo is termed a blastocyst, a hollow sphere 150 microns in diameter (National Academy Press, 2001). Blastocysts form an outer layer called the trophoblast, and an inner layer composed of a cluster of cells called the inner cell mass (ICM). By this time, 70 cells constitute the trophoblast layer, while 30 cells make up the inner cell mass or ES cells (National Academy Press, 2001).

Isolating and Culturing ESCs

Human embryonic stem cells are isolated through the removal of the ICM into a plastic laboratory culture dish containing a nutrient broth known as a culture medium (National Institute of Health, 2005). Then the cells start to divide and coat the surface of the dish. Usually, the inner surface of the dish is also covered with mouse embryonic skin cells which are designed so they will not be able to divide (National Institute of Health, 2005). This layer is called the feeder layer, which provides a sticky surface where ESCs can attach (National Institute of Health, 2005). The purpose of using the feeder layer is to supply the medium with the essential nutrients and growth factors.

Efforts are being made to develop new ways to maintain ESCs without using a mouse feeder layer (National Institute of Health, 2005) to avoid exposing the ES cells to animal proteins that might affect the transplant compatibility of the ES cells. The medium includes bovine serum. However, adding a cytokine, leukemia inhibitory factor (LIF), to the bovine serum containing medium permits the mouse ES cells to proliferate without using a feeder layer (Thomson, 2006). To prevent stem cell differentiation and specialization, scientists are studying internal and external cell signals (National Institute of Health, 2005) that help maintain an undifferentiated state. Internal signals are controlled by a cell's genes, while external signals are chemicals produced via physical contact with nearby cells (National Institute of Health, 2005).

Since 1998, around 200 embryonic stem cell lines have at some point been in use nationally (Blow, 2008). However, ethical issues concerning ESCs led the US government to allow federal money to support only cell lines established prior to August 2001 (discussed in Chapter-4), and to establish a list of 21 embryonic stem lines which can be utilized for research goals (Blow, 2008). Since then, huge efforts were put forth to improve techniques for stem cells culturing.

Induced Pluripotent Stem Cells (iPS)

In June 2006, Shinya Yamanka, of Kyoto University in Japan, created a method in which stem cells can be produced without cloning or destroying embryos (Holden and Vogel, 2008). Yamanka's idea was based on reprogramming adult mouse fibroblast cells to ESCs, instead of eggs. Four genes - Oct3/4, Sox2, c-Myc, and Klf4 (Cyranoski, 2008) -which encode transcription factors, were transferred into the fibroblast cells using retroviruses (Cyranoski, 2007). These factors stimulate the expression of other genes which make cells convert into pluripotent stem

cells with the ability to produce any type of cells in the human body (Cyranoski, 2007) except placenta.

After Yamanka produced iPS cells in mice, researchers were able to create iPS cells in humans. They found that four-transcription factors, known as Oct4, Sox2, Nanog, and Lin28, were able to reprogram human fibroblast to ESCs. The iPS cells were found to possess normal karyotypes, express telomerase activity, and to display other traits characteristic of hESCs. These human iPS lines were shown to be useful for research purposes (Yu et al., 2007) yet do not have the strong ethical concerns of ES cells.

Embryonic Stem Cell Sources

a. *In vitro fertilization*

Currently, there are about 400,000 fertilized human embryos in frozen storage in the United States that are used to treat infertile couples, but roughly 2.8% are predetermined to be discarded (Thomson, 2006). *In vitro* fertilization (IVF) clinics are considered to be a big reservoir of ESCs. Fertilization normally occurs in a woman's body, but in some cases when a woman has difficulties conceiving, IVF is a solution (The National Academy of Science, 2008). IVF requires a surgeon to take a woman's egg through an operation. In this surgery, the doctor uses hormones to stimulate a woman's ovary to produce several mature eggs. Doctors usually fertilize all the donated eggs to maximize the probability that one egg will produce a viable blastocyst that can be re-embedded in a woman's womb. Since not all the attempted fertilized eggs are implanted again, any excess of blastocyts are kept in freezers serving as a bank for ESCs (The National Academy of Science, 2008).

Excess blastocysts obtained via IVF and not used for reproduction are sometimes used for medical research purposes, with the donor's consent. However, IVF embryos not created for reproductive purposes have raised some ethical concerns since these purposely made blastocyts would be made knowing they would never develop into a human being (The National Academy of Science, 2008). In order for researchers to use frozen embryos, they have to obtain consent of the couple who originally donated the fertilized eggs for reproductive purposes (The National Academy of Science, 2008). One disadvantage of ES cells derived from IVF embryos is that such cells will be genetically rejected without the continual application of immunosuppressive drugs in the host since they are not genetically engineered to match a patient; rejection occurs when the recipient's body recognizes these cells as a foreign body (Byrne et al., 2007).

b. *Somatic Cell Nuclear Transfer*

Somatic cell nuclear transfer (SCNT) is another method for obtaining ESCs. This technique involves placing a nucleus from an already differentiated somatic adult cell, such as a skin fibroblast cell, into a donated egg that is free of its nucleus (Frequently Asked Questions on Stem Cell Research, 2006). In this case, the egg will contain the genetic material that is specific to the host the nucleus was obtained from. Then the egg is cultured to form a blastocyst from which ESCs are derived (Figure-3). The nuclear DNA is the same as the host so the ES cell graft would not be rejected (The National Academy of Science, 2008). However this SCNT process has only successfully been done in mice and primates, not in humans yet.

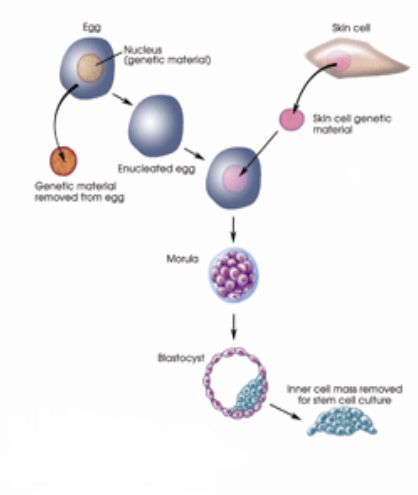

Figure-3: Obtaining ES Cells Through Somatic Cell Nuclear Transfer. This process involves taking a nucleus from an adult somatic cell (upper right) and injecting it into an enucleated egg (diagram center). The egg is then cultured to make a blastocyst (lower center) from which ES cells are obtained that are genetically identical to the donor of the adult nucleus. (The National Academy of Science, 2008).

In addition to providing patient-specific ES cells, preparing ES cell lines from patients with specific genetic diseases would create ES lines in which to study the process by which a particular disease develops. As is the case for IVF, SCNT requires the egg donor's consent. And as with any ES cell preparation process involving blastocysts, SCNT has ethical issues because it involves the destruction of a blastocyst (The National Academy of Science, 2008). But what is to come may eventually nullify any arguments against these present ethical concerns.

Once SCNT has been achieved for humans, in the future, scientists can possibly create "personalized" stem cells containing the DNA from a specific patient (The National Academy of Science, 2008). A big advantage of this technique, as opposed to stem cells obtained from non-enucleated eggs, is that the patient's body will not reject the stem cell transplants. Since stem cells generated via SCNT are purposely genetically engineered to match that patient, this it is referred to as therapeutic cloning (The National Academy of Science, 2008), or oocyte-assisted reprogramming (Baker, 2007). Therapeutic cloning differs from reproductive cloning (i.e. Dolly the world's first cloned mammal), in which a cloned embryo is implanted into a womb and allowed to develop into a complete individual (The National Academy of Science, 2008).

Therapeutic cloning aims to use stem cells to help individuals stricken with devastating diseases which have no cure or effective therapies otherwise.

Nature reported the accomplishment of producing ES cell lines by SCNT using the nuclei from adult rhesus monkey cells (Baker, 2007), and scientists are now trying to achieve the same in humans. A team led by Shoukhart Mitalipov at the Oregon Health & Science University in Portland successfully obtained primate ES cell lines using the method of SCNT. The team took nuclei from skin cells of an adult monkey and inserted those into an enucleated egg from fertile monkeys. After blastocyst formation, the cells in the ICM were taken and cultured on laboratory dishes forming embryonic stem lines (Baker, 2007). A South Korean group reported the first derivation of human ESC line (SCNT-hES-1) using the technique of SCNT (Yu and Thomson, 2006) however this report was subsequently retracted due to fraud, so to date no reliable report exists for SCNT success in humans.

c. *Parthenotes*

The process of parthenogenesis, known since the 1900s (Henahan, 2002), is defined as a process by which a single egg can develop in the absence of a male counterpart (Brevini and Gandolfi, 2008). This mechanism of reproduction is found in some animals including ants, bees, flies, lizards, and snakes, which can reproduce without the contribution of a male's genetic material. Mammalian oocytes can undergo artificial parthenogenesis *in vitro* by mimicking the calcium wave induced by a sperm at usual fertilization (Brevini and Gandolfi, 2008). Parthenogenetic stimulation can be accomplished at different stages along occyte meiosis, which result in parthenotes with different chromosome complementation (Brevini and Gandolfi, 2008). Since both parental genomes are needed for generating a functional mammalian genome

parthenogenetic blastocysts lack a functional genome. Usually parthenotes cannot develop further than a few cell divisions (Brevini and Gandolfi, 2008).

A team led by Dr. Daley obtained ESCs through the process of parthenogenesis in mice (Macintyre, 2007). Another group composed of Yan-Ling Feng and Jerry Hall of the Institute for Reproductive Medicine and Genetics in Los Angeles was able to show that it could obtain stem cells, which would later have the ability to develop into neurons from mouse parthenotes (Holden, 2002). David Wininger, a fertility specialist from Maryland, was able to grow human pES (parthenogenetic ES) cells to the blastocyst stage (Westphal, 2003), however the stem cells taken were alive only for a few days. Mammalian parthenotes usually die before implantation in the womb, but they can survive long enough to be sources of ES cells.

One disadvantage to obtaining stem cells by parthenogenesis is that this process cannot be used to make genetically compatible ES cells for men, or for women after menopause. On the other hand, cells made via parthenogenesis have two identical sets of chromosomes; therefore, they have less variation in the surface proteins on the cells that can stimulate an immune response (Westphal, 2003).

d. *Single-Cell Biopsy*

The discovery of a new way to obtain ESCs through single cell removal from an embryo without any destruction has rooted hope for stem cell research with fewer ethical concerns (Gearhart and Moreno, 2006). Generating ESCs using single-cell biopsy is similar to the one used in preimplantation genetic diagnosis that does not hinder embryonic development (Klimanskayza et al., 2006), thus an embryo can potentially serve as a source of ES cells while still retaining complete competence for reproduction.

Germ Embryonic Stem Cells

Germ embryonic stem cells (GECs), also known as embryonic germ cells (EGCs), are derived from a part of the embryo known as the "gonadal ridge". Usually, these germ cells have the ability develop into eggs or sperm. Such cells are isolated from fetuses older than 8 weeks of development. As opposed to ESCs, GECs do not form tumors upon transferring to the body, thus making them a reliable source for transplant tissue and cell-based therapies. However, EGCs raise some ethical challenges for researchers because they are derived from embryos older than blastocysts or from aborted fetuses (Embryonic Germ Cells, 2007).

Adult Stem Cells (ASCs)

ASCs help to maintain homeostasis by renewing or replacing the dead or injured cells in an adult organism. Some scientists describe ASCs as somatic stem cells whose origin is not defined (Adult Stem Cells, 2006). They have less differentiation potential than ES cells, but they can usually be differentiated to obtain the major specialized cell type of the tissue or organ in which they reside (National Institute of Health, 2005). ASCs are found most often in the organs that need a continuous supply of cells and that are undergoing constant cell division, such as the blood, the skin, the lining of the gut, and the brain (although the brain is not widely known to renew its cells) (The National Academy of Science, 2008). ASCs raise fewer controversial issues than ES cells. However, ASCs are difficult to identify, isolate, maintain, and grow in the lab (The National Academy of Science, 2008). Also, they are less flexible compared to ESCs

because they usually only differentiate to certain types of cells. Though experiments have shown some evidence for ASC flexibility or transdifferentiation in mice, they have not shown the same thing in humans (The National Academy of Science, 2008).

Adult stem cells can be found in several places, including the bone marrow, umbilical cord blood, pancreas and brain. Currently, there are about 70 identified diseases that have been treated using non-ESCs, including breast cancer and sickle cell anemia (Earll, 2005) some of which will be discussed in Chapter-2.

a. Adult Hematopoietic Stem Cells

Hematopoietic stem cells (HSCs) are the blood-forming stem cells. They form white blood cells, red blood cells, and platelets (National Institute of Health, 2005). Recently, researchers have found through animal experimentation that HSCs exhibit some plasticity. Also, HSCs have the ability to undergo a process known as apoptosis, or programmed cell death, in which unneeded cells undergo self-destruction. Unfortunately, HSCs are hard to identify (National Institute of Health, 2005). They can be isolated from several sources such as bone marrow, cord blood cells, and the blood stream.

The Bone marrow is a spongy tissue most often found in the breast bone (sternum), ribs, hip bone, skull, and spine. It is a big reservoir of white blood cells, red blood cells, and platelets (Abbott, 2003). Bone marrow transplantation can be used to treat various debilitating diseases of the blood and immune systems (Abbott, 2003). In this process, bone marrow is taken from living donors. There are three types of bone marrow donors. They can be autologous (the bone marrow is from the same person), syngeneic (from an identical twin donor), or allogeneic (from another

person who is genetically not identical to the recipient, but has a sufficient HLA match) (Abbott, 2003).

Peripheral stem cells are stem cells found in the arteries and veins. Growth of peripheral stem cells is stimulated via hormones. A process called apheresis can be used to collect the stem cells from the blood (Figure-4). A needle inserted into both arms of the donor. Then, the blood is taken from one arm and circulated through the machine to obtain the stem cells. The remainder of the blood is returned through a needle into the opposite arm. The process takes five hours and is painless (Abbott, 2003).

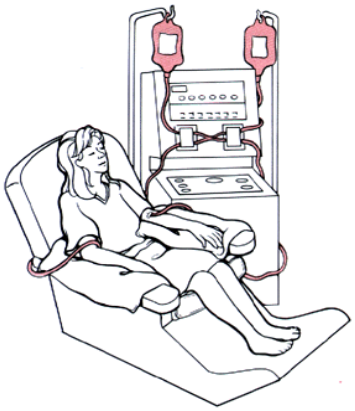

Figure-4: Peripheral Blood Hematopoietic Stem Cell Harvest by Apheresis (Przepiorka, 1996).

Cord Blood Stem Cells are another source for HSCs. Cord blood stem cells are derived from umbilical cords or a placenta after a baby's birth. Usually, the cord and placenta are discarded at birth, however is increasingly common to ask the parents permission to freeze the cord blood in case the baby develops medical problems and needs a HSC infusion (*Cord Blood Registry - Client Stories*, 2004).

There are two ways to store cord blood from newborn babies; one is public and the other is private family banking. (A) Family cord blood bank is exclusively used for family members, and

is not avalible to the public. There is a 75% chance that a baby's cord blood stem cells are an acceptable match for his siblings. Usually, cord blood stem cells are twice as sucessful if used to treat a family member. (B) Public cord blood bank is used by any member of the public who may be in need of a transplant. If the family who donated the cord blood needs it, they are not guaranteed it will be available for them. Also, this approach is limited to certain hospitals in the United States (Viacord, 2007).

b. Adult Neuronal Stem Cells

Recently, neuronal stem cells (NSCs) were obtained from adult mice (Cassidy and Frisen, 2001). Previously, it was thought that our nerve cells were incapable of forming new neurons, but in the 1960s experiments showed that nerve cells can replenish themselves in specific parts of an adult's brain. Neurons and supporting cells (the glial and oligodendrocytes) were derived from NSCs. These cells have the potential to cure neurodegenerative diseases such as Parkinson's disease or Alzheimer's (Cassidy and Frisen, 2001). Neural stem cells are found in the wall of ventricles, which are lined by a single layer of cells known as ependymal cells, and beneath it is a narrow zone of tissue, known as the subventricular zone (Figure-5). Two types of neural stem cells were identified as ependymal cells and astrocytes. Unfortunately, within this region of the brain only 0.3% of the cells are stem cells, therefore NSCs are hard to isolate (Cassidy and Frisen, 2001).

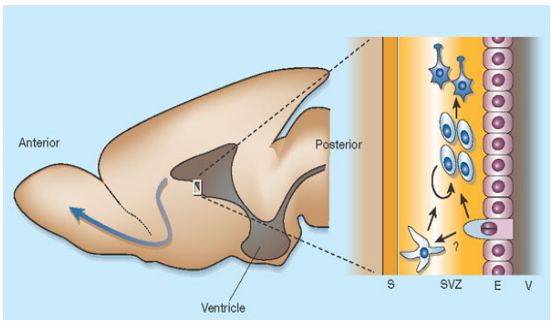

Figure 5: A Section of a Mouse Brain Showing the Ventricle Wall From Which Neural Stem Cells Are Isolated. (Cassidy and Frisen, 2001).

Neural stem cells exhibit some plasticity, meaning they can generate different types of non-neural cell types if proper experimental conditions are met (Cassidy and Frisen, 2001). It was shown that multipotent stem cells can be induced to differentiate into nerve cells *in vitro* by using retinoic acid (Huettner, 2006).

c. Adult Cardiac Stem Cells

As is the case with the brain, the heart is formed of terminally differentiated cells, but it is not a terminally differentiated organ. The heart also contains stem cells which help in cell regeneration. This is a promising opportunity for curing myocardial infarction. Lin-negative, c-kit-positive cells have cardiac stem cell properties, including a self-renewing, clonogenic, and multipotent properties, which is utilized within myocytes, smooth muscles, and endothelial cells. Upon cardiac stem cell injection to ischemic heart, these cells have the ability to reconstitute a well-differentiated myocardium (Beltrami et al., 2003). Researchers suggest that the heart sustains a reservoir of stem cells that have the ability to make new cells in case of damage. Piero Anversa and his colleagues have discovered pockets of cardiac stem cells in the spaces between muscle cells in the heart of rats (Figure-6). After maintaining and growing these cells in cell-

culture medium, the cells were injected into rats with damaged heart tissues. 70% of the damaged tissues were repaired within 20 days. Also, previous studies conducted by Anversa have shown that cells from the bone marrow also have the potential to restore damaged heart muscle (Touchette, 2004).

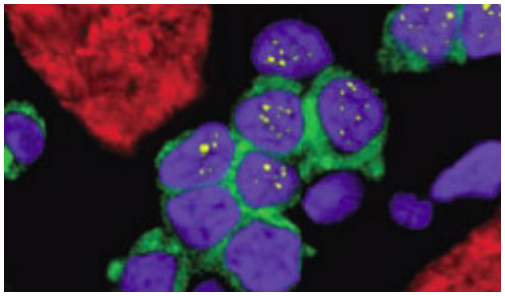

Figure 6: Picture of a Cluster of Cardiac Stem Cells (blue) Found Between Heart Muscle Cells (red) in Human Heart Tissue (Touchette, 2004).

One of the paramount cardiac cells, the cardiomyocyte, is heart muscle which contracts to eject the blood out of the heart's main pumping chamber (National Institute of Health, 2005). Two other types of cardiac cells are the vascular endothelial cell, which forms the inner lining of the blood vessel, and the smooth muscle cell, which forms the wall of a blood vessel. Under specific growth conditions, stem cells on culture dishes can develop into cardiomyocytes and vascular endothelial cells (National Institute of Health, 2005).

Recently, *Nature* reported the existence of cardiac progenitor stem cells that were formally thought to be absent after birth. Those cells were found in the heart of newborn rats, mice, and humans, and have the potential of differentiating into fully mature cardiac tissue (Augs, 2005). Researchers identified cells called *isl1*+ progenitor cells in the tissues of newborn rats, mice, and human infants who were undergoing surgery for congenital heart defect. If *isl1*+ cells were given the proper conditions, they have the ability to renew themselves and become a mature

cardiac muscle tissue. These cells, which are found in the atrium, are normally discarded during cardiac surgery, but can now be stored frozen. Thus, infants can now use their own cardiac stem cells to correct a wide range of heart diseases (Augs, 2005).

d. Adult Epithelial Stem Cells

Epithelial stem cells are found in the lining of the digestive tract, and exist in deep crypts, the epidermis, and in hair follicles. Stratified squamous epithelia, such as the epidermis contains layers of cells known as keratinocytes, which migrate to the surface of the skin and form a protective layer. The basal layer, the one next to dermis, is the only place which contains cells that have the ability to divide. A number of these cells are identified to be stem cells, but the others are called transit amplifying cells. Keratinocytes move slowly outward through the epidermis as they mature (Encyclopedia Britannica 2008).

Experimental evidence has also suggested that mammary cells exist, and their differentiation is the result of a sequence of a hierarchical process originating in a stem cell with the capacity of self-renewal. But the lack of methods for mammary stem cell isolation has restricted the analysis of their properties and regulation. Mammary stem cells are continuously cycling population in normal adults, and they exhibit molecular characteristics suggesting a basal position in the mammary epithelium (Sting et al., 2006).

e. *Adult Mesenchymal Stem Cells*

Adult mesenchymal stem cells (MSCs) are multipotent, and are found in the stromal fraction of the bone marrow. In fresh bone marrow, MSCs account for only 0.01-0.0001% of

nucleated marrow cells. Mesenchymal cell types include osteoblasts, chondrocytes and adipocytes. Some studies show that MSCs—easily collected and isolated-- possess some plasticity in which some MSCs form neural stem cells *in vitro*. Cells, which exhibit MSCs structures and cellular characteristics, were isolated from several sources including adult peripheral blood, adipose tissue, skin tissue, trabecular bone, fetal blood, and liver. In addition, umbilical cord blood and the chorionic villi of the placenta were shown to have MSC-like populations (Jackson *et al.*, 2007)

The transplantation of mesenchymal progenitor cells can possibly cure any genetic disorder of bone, cartilage and muscle; unfortunately clinical evidence for this transplantation is lacking. Allogeneic bone marrow transplantation is a way of engrafting functional mesenchymal progenitor cells, which has had a big impact on treating a disease known as osteogenesis imperfecta (Horwitz *et al.*, 1999). Researchers have also used a 6-hydroxydopamine (6-OHDA) animal model of Parkinson disease to determine the capability of the transplanted MSC to migrate and differentiate. Results showed that rodents which underwent MSCs transplantation survive better in the 6-OHDA-induced damaged hemisphere compared to the un-lesioned side. This shows that 6-OHDA damage raises the viability of transplanted MSCs and attracts these cells from the other hemisphere (Hellmann et al., 2006).

f. *Adult Intestinal Stem Cells*

The surface of the gastrointestinal tract is lined by a simple columnar epithelium which is folded to form invaginations called crypts. Each crypt has about 250 cells, depending on the species. The size and the organization of crypts are uniform within the gastrointestinal tract. All major gut epithelial cells move towards the lumen of the gut as they mature, except Paneth's

cells. The functional and differentiated cells are found on the vili or toward the top of the colonic crypt. Different experiments proposed that the number of stem cells per crypt is highly regulated; therefore, each stem cell can detect each other's presence and respond properly (Booth and Potten, 2000).

The intestinal epithelium is considered to be one of the most rapidly self-renewing tissues in adult mammals. Currently, researchers believe that there are 4-6 stem cells per crypt, and they are found at the +4-position immediately above the Paneth cells in the small intestine. Unfortunately, intestinal stem cells have not been isolated and purified due to their lack of unique markers and stem-cell assays. There are three types of differentiated intestinal cells, including enterocytes, goblet cells and enteroendocrine cells. These cells form from the transit-amplifying cells at the crypt–villus junction. Paneth cells, are the fourth type of cells which resides at the crypt bottom. Until now, no stem cells have yet been discovered in the colon (Barker et al, 2007).

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CHAPTER 2: STEM CELL APPLICATIONS

Stem cells hold promise for the treatment of many diseases because they are capable of dividing endlessly and developing into many different types of cells in the human body, thus they have many applications in the areas of scientific research and cell therapy. During cell therapy, stem cells are used to produce cells and tissues that are required to repair body organs that have been damaged by disease or accidents. Stem cells can be used to treat diseases such as cancer, spinal cord injuries, and Parkinson's disease. Whether from embryonic, adult, or umbilical cord stem cells, studies have demonstrated great potential for treating these diseases in animals, and even humans.

In the most far reaching applications, pluripotent embryonic stem (ES) stem cells with wide differentiation potential could be used to create an unlimited supply of cells, tissues, or even organs to restore function without the use of toxic immunosuppression drugs and without the necessity of tissue matching compatibility, if the ES cells are genetically derived from the nucleus of the patient's skin fibroblast cells (Chapman, 1999). Such cells, when used in transplantation therapies would not be immune-rejected. In more traditional applications, bone marrow transplantation, when the transplant is not compatible, is associated with potential adverse effects, and it could become safe, cost effective, and be available for treating a wider range of clinical disorders like aplastic anemia and certain blood disorders, when the hematopoietic stem cells are derived from the same patient. This would be especially helpful to people who have lost bone marrow function from radiation or exposure to toxic agents. Growth and transplant of other tissues lost to disease or injury, for example, skin, heart, nervous system

components, and other major organs, are becoming a possibility (Applications of Stem Cells, 2005).

Stem Cell Treatment of Diabetes

Type I diabetes is a disease characterized by the destruction of insulin producing cells in the pancreas. Some treatments for these patients include human islet transplantation in an effort to restore insulin secretion. But as with most transplants, a common problem occurs from complications from the immunosuppressive treatments required to prevent graft rejection. The chance of graft rejection in a diabetic patient is increased because the immune system helped destroy this tissue in the first place. And pancreatic tissue transplants are limited by the small numbers of donated pancreas available (Assady et al., 2001). Stem cells potentially could be used to effectively resist immune attack as well as graft rejection. The discovery of methods to isolate and grow human ES cells raises hopes of doctors, researchers, and patients that a cure for type I diabetes, and perhaps type II diabetes, is within reach. In theory, ES cells could be cultivated and coaxed into developing into the insulin-producing islet cells of the pancreas. With a ready supply of cultured stem cells at hand, the theory is that a line of ES stem cells could be produced for anyone requiring a transplant. Before transplantation, the cells could be engineered to avoid immune rejection by maturing them into non-immunogenic cells so that they would not be rejected, and the patient would avoid the negative effects of immunosuppressant drugs. Although this technique has been successful in animals, having a sufficient supply of insulin-producing cells for transplant into humans could be a long way off, but researchers have been making remarkable progress in their quest for it. While some researchers have pursued the

research on ES stem cells, others have focused on isolating insulin-producing precursor cells that develop naturally in adult and fetal tissues (Stem Cells and Diabetes, 2007).

Nervous System Diseases

Nervous system diseases result from a loss or damaging of nerve cells. Scientists previously thought that mature nerve cells do not divide, and so there is no way to replace those neurons that are destroyed. In Parkinson's disease, nerve cells that make the chemical dopamine die. In Alzheimer's disease, cells produce highly neurotoxic beta-amyloid protein that kills nerve cells. In amyotrophic lateral sclerosis, the motor nerve cells that activate muscles die. In multiple sclerosis, the cells that protect nerve fibers are lost. In spinal cord injury, brain trauma, and even stroke, many different types of central nervous system cells are lost or die.

Scientists have now shown that neurons can be induced to regrow using either ES cells to differentiate into neurons, or using adult neural stem cells (NSCs) to divide into more neurons. The most effective treatment for these health issues comes from the possibility to create new nerve tissues from pluripotent ES cells (Applications of Stem Cells, 2005). Numerous animal studies have shown that ES cells have the ability to differentiate into dopaminergic neurons in animal models for Parkinson's disease. Scientists have established various procedures to "coax" the cells to differentiate into neurons. Some procedures include the treatment of cells with specific growth factors, the introduction of specific genes into the cells that cause differentiation, or the growth of ES cells in co-culture with other feeder cells to prompt differentiation. Methods have also been established to identify specific markers within the transplanted cells to confirm that dopaminergic neurons have indeed been produced and are able to survive. When the differentiated cells are transplanted into animals, the cells have been shown to survive for weeks,

and significant behavioral improvement has been recorded. However the survival and function of these transplanted neurons after grafting needs to be assessed. It is unknown how effective these procedures will be using human ES cells (Stem Cell Treatment Succeeds, 2006).

In addition to ES therapies, adult stem cells, which come from already developed nervous system tissue, have also been studied as a source of replacement cells for these types of problems. Depending on the region of the nervous system that the cells are isolated, the adult stem cells can have slightly different properties, and scientists are working to establish the conditions for efficiently growing these stem cells and differentiating them into dopaminergic neurons. Many different techniques have been studied; however, after transplantation of ASCs into animals, the survival of these cells is relatively low. Scientists are attempting to determine the signals in the nervous system environment that are required to allow the transplanted cells to survive, integrate, and function correctly (Study Establishes, 2006).

Adult stem cells from bone marrow also surprisingly have the potential to be useful for the treatment of nervous system disorders due to their apparent ability to trans-differentiate into non-blood tissues. Studies have shown that these bone marrow-derived cells are capable of changing into neuronal cells that can integrate in the brain. However, other studies have suggested that the cells may actually fuse with cells already existing in the brain, so more studies are needed to determine the effectiveness these HSCs for neural therapies.

Neural Stem Cells to Treat Spinal Cord Injuries

An injured spinal cord loses its ability to regenerate myelin cells, an insulating layer around nerve fibers that transmits signals from the brain, leading to paralysis. Each year, over 11,000 Americans suffer from spinal cord injury, most commonly in traffic accidents. Costs of

aid for the condition are approaching ten billion dollars per year. Spinal cord injuries often have permanent effects since the myelin cells cannot regenerate on their own. However, according to many animal studies, stem cells can repair damaged spinal tissue and help restore function in rodents with spinal cord injuries. The treatments being given to the test subjects may eventually lead to new treatments for humans with spinal cord injuries (Stem Cell Treatment Succeeds, 2006).

One study showed that in cases where stem cells restored myelin in the injured spine, rats showed some recovery and walked with more coordination. Cells from the brains of adult mice were labeled with a fluorescent marker, enabling researchers to trace those cells after they were transplanted into rats whose spines had been crushed. Adult NSCs transplanted into those rats only two weeks after the initial injury survived due to specific growth factors and immune-suppressing drugs the researchers used. More than one-third of the transplanted NSCs traveled along the spinal cord, fused with the damaged tissue, developed into the type of cells that were destroyed at the injured site, and produced myelin. One important finding demonstrated by the study is that "the maximal effect of transplanting these cells is early after injury," says New York University School of Medicine professor Moses Chao, PhD. "The timing of NSC application therefore is critical to successful therapy in the injured spinal cord" (Stem Cell Treatment Succeeds, 2005).

In a similar study, Hans Keirstead and his colleagues from Reeve-Irvine Research Center at UC Irvine, found that a human ES stem cell treatment was successful in restoring the insulation tissue for neurons in rodents treated within seven days after the initial injury. The treatment led to a moderate recovery of motor skills, but the same treatment did not work for rats that had been injured for more than ten months (Study Establishes, 2006).

Both of these key studies show the potential of using NSC and ES cell-derived therapies for the treatment of spinal cord damage, and show the treatment is most effective during early stages of the injury. One focus of future research will be to determine why stem cells transplanted late after the injury fail to develop functioning tissues or survive (Vasich, 2005).

Neural Stem Cells to Treat Parkinson's Disease

Stem cells also offer hope to patients with Parkinson's disease, which is caused by the loss of dopamine-producing nerve cells in the brain. If stem cells can be cultivated to become these dopamine-producing nerve cells, researchers believe that they could replace the lost cells (Garfinkel, 2005). Stem cell based therapies for Parkinson's disease are not yet a common clinical procedure, but success has been achieved in animal models of the disease. Scientists agree that more information and research is needed about the causes of Parkinson's disease and the biology of stem cells before safe, effective and long-lasting therapies can be developed and practiced in humans. Because a single, well-identified type of cell is affected in Parkinson's disease (the substantia nigra) stem cells offer great potential for treatment. The basis for such treatment would be to replace the cells that have died with other identical dopaminergic nerve cells, developed from stem cells (The Promise of Stem Cells, 2004). Studies have shown that human stem cells transplanted into rats led to significant improvements in Parkinson's like systems. Post-mortem examinations showed that the stem cells had successfully developed into dopamine-producing cells (Ryan, 2004).

In recent human clinical trials, fetal brain tissues were transplanted into the brains of Parkinson's disease patients, and the results showed major and long-lasting improvements in

some of the patients (What is Parkinson's disease, 2008). The trials also emphasized problems with these treatments, like the need to produce large amounts of uniform cells for transplantation into patients. Stem cells provide the greatest hope for treatment since dopaminergic-like cells have already been obtained from both ES and fetal brain stem cells (What is Parkinson's disease, 2008).

Neural Stem Cells to Treat Alzheimer's Disease

A research team led by a University of Central Florida professor Kiminobu Sugaya, found that treating bone marrow cells in with bromodeoxyuridine, a compound that incorporates into replicating DNA, made adult human stem cells more likely to develop as brain cells after they were implanted in adult rat brains. Sugaya and his colleagues hope to eventually show that stem cells transplanted from a patient's blood or bone marrow will be an effective treatment for Alzheimer's and other neurological diseases because they can replace cells that die from those ailments. The researchers are working with a $1.4 million grant from the National Institutes of Health (Binette, 2005). "By using a patient's own stem cells instead of embryonic stem cells, we're able to avoid the ethical concerns many people have about stem cell research," Sugaya said. "We also don't have to worry about the immune system rejecting the new cells, because they come from the same patient." In the same experiments, they reported successes in culturing stem cells from bone marrow to become neural cells after they were implanted in rats. Improving the chances of implanted cells functioning as neural cells is demonstrating possibilities for the treatment of Alzheimer's disease (Binette, 2005).

Neural Stem Cells to Treat Stroke

Strokes cause temporary loss of blood supply to the brain which results in areas of brain tissue dying, causing the loss of certain bodily functions such as speech and motor skills. Neural stem cells offer new possibilities for brain tissue regeneration which could help stroke victims. However, there are still major limitations in delivering these cells to the brain. While NSC transplantation has been proven to improve conditions in rats with stroke damage, little reduction in lesion volume has been observed (Stem Cell Therapy Studies For Stroke, 2008). In one study a neurobiologist from the Institute of Psychiatry, Dr Modo, explains: "We propose that using scaffold particles could support NSCs in the cavity to re-form the lost tissue and provide a more complete functional repair. The ultimate aim is to establish if this approach can provide a more efficient and effective repair process in stroke" (Brain Tissue,2008). Thus when using neural stem cells to treat brain disorders, the future of the field may involve using scaffolds to provide a substrate for the transplanted cells to grow on.

Stem Cell Treatment of Damaged Heart Muscle

New studies have shown that stem cells might be used to treat patients who have suffered from a heart attack. By injecting bone marrow stem cells into damaged tissues of the heart, new vascular endothelium, cardiomyocytes, and smooth muscle cells can be formed.

One animal study performed on mice treated with bone marrow stem cells showed that the newly formed tissues occupied sixty eight percent of the damaged area only nine days after treatment, and treated mice survived in much greater numbers than the mice that did not receive any treatment (Can Stem Cells Repair a Damaged Heart, 2006).

A human study performed at the American College of Cardiology Innovation in New Orleans showed that heart attack patients who received a new intravenous mesenchymal stem cell therapy called Provacel, experienced a lower number of adverse effects such as cardiac arrhythmias, and showed signs of significant improvements in heart, lung and global function, compared to those patients who received a placebo. Provacel is a treatment containing adult mesenchymal stem cells pre-formulated for intravenous delivery. Patients were administered a dose of either Provacel or placebo within ten days of having a heart attack. Mesenchymal stem cells are found in adult bone marrow, and have the potential to develop into mature heart cells or new blood vessels. The "MSCs" are obtained from healthy adult volunteer bone marrow donors and are not derived from a fetus, embryo, or animal. Because the cells are in such an early stage of development, it is believed that they do not cause an immune rejection when transplanted in a patient. Similar to type O blood, MSCs can be donated without tissue type matching to a specific patient. Another benefit of this type of stem cell therapy is that it can be given to patients through a simple intravenous injection. Other therapies require delivery of stem cells directly to the site of the damaged tissue through catheterization or open surgical procedures (Heart Attack Patients, 2007).

Dutch researchers at the University Medical Center Utrecht and the Hubrecht Institute have developed a procedure to grow large numbers of adult stem cells from human hearts and have them create new heart muscle cells. The stem cells are derived from material left over from open-heart surgeries. The researchers used a method to isolate the stem cells from this material and culture them in the laboratory, which are then allowed to develop. The cells grow into fully developed heart muscle cells that are able to contract rhythmically, respond to electrical activity, and even react to adrenaline (Heart Derived Stem Cells, 2008).

Stem Cell Treatment of Primary Immunodeficiency Diseases

Pluripotent stem cells could potentially be used in the treatment of virtually all primary immunodeficiency diseases. Presently, more than 70 different forms of deficiencies of the immune system have been recognized. These are among the most complicated diseases to treat. Diseases such as severe combined immunodeficiency disease, Wiskott-Aldrich Syndrome, lupus, and the immune deficiencies suffered as a result of acquired immune deficiency syndrome (AIDS) are just a few of these forms. These diseases are characterized by a high susceptibility to infection and are often associated with anemia, arthritis, and diarrhea.

However, the transplantation of stem cells engineered with the normal gene could result in recovery of the immune function. Successful transplantation could increase the life span and quality of life for these people (Applications of Stem Cells, 2005). Researchers from the UCLA AIDS Institute and the Institute for Stem Cell Biology and Medicine have demonstrated that human embryonic stem cells can be genetically manipulated and "coaxed" to develop into mature T-cells. T-cells are one of the body's main defenses against infection and disease, and are lowered in patients infected with HIV. The new T-cells create possibilities for a gene therapy to combat AIDS. The study suggests that it is possible to convert human embryonic stem cells into blood-forming stem cells that can differentiate into the helper T-cells that HIV specifically targets. The results mark the first time that scientists have been able to derive T-cells out of human embryonic stem cells. In their study, the researchers cultured human embryonic stem cells grown on mouse bone marrow support cells, which in turn converted them into blood-forming cells. Those cells were then injected into a human thymus gland that had been implanted in a mouse, and the thymus then changed those blood-forming cells into T-cells (Researchers Develop T-cells, 2005).

Stem Cell Treatment of Cancer

Since stem cells can be damaged in certain cancer treatments, CTCA hospitals developed techniques to add healthy stem cells back into your body after damaging cancer-fighting chemotherapy treatments take place. At the present time, adult bone marrow stem cells are used to treat patients following high doses chemotherapy. These treatments using stem cells may also be used for patients who have had radiation treatment for their cancer. Unfortunately, bone marrow cells are somewhat limited in their capacity to restore immune function completely, so researchers are working to develop injections of properly-differentiated stem cells that would return the complete functionality of the immune system to patients undergoing bone marrow transplantation. More successful stem cell recovery would enable the use of very toxic, and effective chemotherapeutic procedures that can not currently be utilized due lack of an ability to restore bone marrow and immune function following their use (Stem Cells Used in Cancer Therapies, 2008).

There are 3 types of stem cell transplants: Autologous stem cell transplants, allogeneic stem cell transplants, and syngeneic stem cell transplants. In autologous stem cell transplants, the patient serves as their own donor. Bone marrow or peripheral blood stem cells are taken from the patient, frozen until needed, then given transplanted back into the patient after they have received high doses of chemotherapy, radiation or both to destroy cancer cells. An allogeneic stem cell transplant occurs when bone marrow is replaced with new, healthy bone marrow or peripheral blood stem cells from another tissue matched donor. Most allogeneic stem cell transplants have been performed using stem cells from the bone marrow, but the use of peripheral blood stem cells is increasing. In a syngeneic stem cell transplant, a patient receives

stem cells from their identical twin. Since identical twins aren't very common, syngeneic transplantations are rare. Because identical twins have the same genes, they also possess the same human leukocyte associated antigens which help dictate histocompatibility, so there is less chance of the transplant being rejected (Stem Cell Transplantation, 2008).

Stem cells have provided new hope for many patients who suffer from a large range of diseases that currently have little or no therapeutic treatments. Advancements in this particular medical field have shown the potential of many different types of stem cells. Some procedures like bone marrow transplant have already been a proven to be a safe and effective method of treating cancer patients, while new studies strive to develop treatments for spinal cord injuries, Parkinson's disease and many other health issues. Due to the ability to produce an unlimited amount of these cells from single lines of stem cells, researchers believe that many of the new procedures will become feasible and cost efficient methods for treating patients. Even though many of the hopeful applications of stem cells have not been perfected of proven safe, the potential of these cells appear to be limitless.

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CHAPTER-3: STEM CELL ETHICS

Just because we can work with stem cells, should we? In this chapter, the stances of the world's five major religions (Christianity, Islam, Judaism, Hinduism, and Buddhism) towards stem cell ethics will be analyzed and discussed in more detail. During human history, so-called scientific progress has given rise to controversy for scientific and religious communities, but society has to balance religion and science to determine the ethics and morality of new advancements within their context (Mannoia, 2004). And another question arises whether society is fully knowledgeable of the stem cell controversy. For this, we will investigate media coverage of this issue.

Not until the summer of 2001 did the media pay large amounts of attention to the stem cell issue; therefore, it was not surprising when surveyed in the fall of 2000, only 20% of Americans reported following the issue either "very closely" or "fairly closely." This percentage increased to 38 % in July 2001 before US President Bush's August 9, 2001, decision to limit federal funding for embryo stem-cell research. In September 2002, a year after Bush's decision, 13% of respondents reported having seen, read, or heard "a lot" about the issue, whereas 46% of respondents reported knowing "not much" or "nothing at all," showing that overall public attention had declined from 2001 levels, parallel to a drop in media attention (Nisbet, 2004). "Polls show that the public doesn't know much about the science or the policy surrounding stem-cell research, and that means they really haven't solidified their opinions," said Matthew Nisbet, an assistant professor of journalism and communication at Ohio State University (Grabmeier, 2004).

Politics and religion play a central role in influencing the public's ethics of stem cell research. Major religious authorities in the U.S. have influenced politicians on their decisions regarding the stem cell debate. In the United States, the major stem cells ethics dilemma started back in 1998 when the first *human* stem cells were extracted from an embryo. Since then, several questions have been raised, including:

- When does human life begin? (Bhikkhu, 2007)
- Is it morally allowable to use living human embryos for the preparation of embryonic stem cells (ESCs)?
- Is it morally acceptable to engage in "therapeutic cloning" for the purpose of producing human embryos and then destroying these embryos to obtain their stem cells?
- Is it morally permissible to use ES cells, and the differentiated cells obtained from them, which are supplied by researchers or are commercially accessible? (Correa and Sgreccia, 2000)
- Is it morally licit to sacrifice an embryo for its stem cells that can save, or treat people afflicted with debilitating diseases, or is the cost of doing this too high?
- Is it permitted to fertilize ova to create an embryo solely to use its stem cells?
- Is it ethical to use the tissues from aborted fetuses for medical treatments? (Eisenberg, 2006)

It is obvious from media reports and their effects on political discourse that religious beliefs have a big influence on the stem cells issue. Furthermore, this debate demonstrates the connection between science and religion (Mannoia, 2004). Everything "new" that appears in a modern and high-tech society has to make peace with everything "old" that already exists. While science cares about answering the question of how everything works, religion on the other hand

tries deals with what is right and acceptable (Tyagananda, 2002). Generally, religious traditions refer to sacred texts and theological teachings to express their thoughts on a matter. This leads to the presence of a wide-spectrum of opinions and ideas even within one tradition, since the current issues were not dealt with before in the sacred ancient texts of religious traditions. Therefore, giving a religious perspective on a matter now includes interpretations and diverse viewpoints (Tyagananda, 2002).

Where should the red-line be drawn in this complex matter between our desire as scientists to discover new advancements to cure different diseases, and as human being with our ethics and values? What about our moral commitment to heal the sick and relieve suffering due to an injury or illness (Chapman et al., 1999)? The answers for these questions in this chapter will be based on what each major religion believes, including disagreements within a religion (Chapman et al., 1999).

Embryonic Stem Cells Ethics

Research involving embryonic stem cells (ESCs) is the most debatable aspect of the entire stem cell issue. It has caused huge controversies among religious leaders and politicians, so in this section the view of the five-major religions on ESCs will be analyzed in more detail. ESCs, as mentioned in earlier chapters, are derived from the inner cell mass of a 5-6 day old blastocyst, so a key question to be answered is: should we equate hESCs to human embryos (de Wert and Mummery , 2003)? Some religions believe that life begins at conception. Others believe life begins when the primitive streak, the precursor of the spinal cord in embryos,

develops, while others believe life begins after birth (Derbyshire, 2001). In *Nature Reviews: Genetics*, John Robertson divides the ethical objectors to embryonic research into three main groups:

A. Those who consider the embryo as a person with full rights and interests, thus any destruction of an embryo would be considered as murder.
B. Those who believe that although an embryo lacks the capacity to be considered a "person," it still has the *potential* to become a person; therefore, it has a special representative value and needs to be protected in respect of human life.
C. Those who believe the embryo is just a group of cells (Derbyshire, 2001). Such individuals might be considered as scientific materialists. This group will not associate an embryo with personhood or religious significance, but rather will consider it as a beneficial resource (Mannoia, 2004).

Christian Stance on Embryonic Stem Cells

Christianity has the largest number of followers in the world, around 2.1 billion people (Major Religions of the World Ranked by Number of Adherents, 2005). Christianity has many denominations and schools of thought, so no one speaks for all teachings of its traditions (Bhikkhu, 2007). In general, however, Christianity teaches that life begins at conception, when an egg is fertilized by a sperm. The Roman Catholics, Eastern Orthodoxers, and Southern Baptists believe that from conception onward, the embryo has a soul and thus needs to be treated as a human being (KohsL, 2008). This belief is confirmed by the Catholic Pope and his bishops: The human embryo is precious and is treated as a person from the time of fertilization; it should not be destroyed or seen as a disposable tissue that might be used for research, and no

embryos should be created for research purposes (Shannon, 2006). Therefore, by many Christian jurists, using embryonic stem cells in research is morally unacceptable. In his statement to the National Bioethics Advisory Commission (NBAC), the Roman Catholic layman Edmund Pellegrino explains: "In the Roman Catholic view, human life is a continuum from the one-cell stage to death. At every stage, human life has dignity and merits protection. Upon conception, the biological and ontological individuality of a human being is established" (KohsL, 2008). The U.S. Roman Catholic Bishops are against ESC research, and described it as "immoral, illegal, and unnecessary" (Religious Views on Stem Cell Research, 2001).

The Anglican-Episcopal tradition has argued that embryos do not have the capacity to become a distinct *individual* with the ability to develop into a human being until the fourteenth-day of gestation, when the primitive streak forms and the embryo can no longer split into several individuals (KohsL, 2008). Eastern Orthodoxy states that the embryo and the adult are both humans, regardless the different stages of development. However, Eastern Orthodoxy allows research only on existing human ESC lines and not on human embryos for therapeutic purposes (Walters, 2004).

The main Christian Catholic objection to ESC research is demonstrated by the reaction of U.S. Catholic bishops towards President Bush's August 9, 2001 law when he decided to allow a limited federal funding for ESC research. Bishop Joseph A. Fiorenza, President of the U.S. Catholic Conference of Bishops, issued a statement on August 10 calling the decision as morally unacceptable: "The federal government, for the first time in history, will support research that relies on the destruction of some defenseless human beings for possible benefit to others. However, such a decision is hedged with qualifications, it allows our nation's research

enterprise to cultivate a disrespect for human life" (American Catholic Organization, 2006). While the Roman Catholic Church is against embryo research, the Unitarian-Universalists, the Episcopal Church, the Evangelical Lutheran Church, the United Methodist Church, and the Church of Jesus Christ of Latter Day Saints have no official position (Derbyshire, 2001).

In summary, Christianity can be divided into three categories with respect to its stance on ESCs:

A. Those who are opposed to human ESCs research (Catholic).
B. Those who limit the use of embryos until the fourteenth-day, but include the use of blastocysts to provide ES cells (Anglican-Episcopal).
C. Those who accept the use excess embryos from infertility treatments for ES research (Anglican-Episcopal, Unitarian, Lutheran, Methodist, and Latter Day Saints) (KohsL, 2008). This topic will be discussed later in the chapter in the section on IVF ethics.

Islamic Stance on Embryonic Stem Cells

Islam, as opposed to Christianity, is more flexible when it comes to human ESCs because the status of the embryo (when life begins) is different in Islam than it is in Christianity. Islam has the second largest number of followers after Christianity, with about 1.5 billion people. The main sub-groups within Islam are Sunni and Shi'a (Major Religions of the World Ranked by Number of Adherents, 2005). Islam bases its laws on two sources, the Qur'an (the Islamic religious text) and the Shari'ah (Islamic law which teaches Muslims how to worship God according to the Qur'an and the Prophet Muhammad). Islamic laws are flexible and are supposed to be analyzed under current times to deal with new issues (Weckerly, 2002).

Among Muslims, one cannot speak in consensus on the question of embryonic moral status. As a result, various scholars and religious leaders present their opinions, but no single individual or group exercises a high authority in matters of practice (Walters, 2004). Many Islamic scholars designate that "ensoulment" of the fetus does not occur until the fourth month of pregnancy (Weckerly, 2006). In both Sunni and Shi'a tradition, ESC research is permitted, as Abdulaziz Sachedina testifies, "It is correct to suggest that a majority of the Sunni and Shi'ite jurists will have little problem in endorsing ethically regulated research on stem cells that promises potential therapeutic value" (KohsL, 2008).

The Shari'ah laws make a distinction between *actual* and *potential* life, thus the embryo as a *potential* human being is not a human being until ensolument occurs under Islamic law. So destroying an embryo is not murder, and the use of human ESCs for research will not violate Islamic laws (Weckerly, 2006). ESC research is taking place in Iran, where a big population of Shi'a Muslims exists (Bhikkhu, 2007). In both Sunni and Shi'a traditions, human ESC research is encouraged if it is being done to produce tissues, valves, and new organs ultimately for treatment purposes (Bhikkhu, 2007).

Judaic Stance on Embryonic Stem Cells

Jewish traditions teach that human bodies belong to God, and that they are on loan for a life-duration on earth. God, as the owner of human bodies, is able to, and does impose, conditions on the use of human bodies. As a result, there is a duty to seek new cures for human diseases (Dorff, 2001). Judaism accepts artificial ways to overcome illnesses. Judaism considers physicians as agents of God in the continuing act of healing (Dorff, 2001). The task of healing in Judaism is not only permitted, it is mandated (Walters, 2004). According to Orthodox Judaism,

embryonic stem cell research is not debatable at all, as indicated by Rabbi Yosil Rosenzweig of Beth Jacob Congregation synagogue in Kitchener. Stem cell research in Judaism is acceptable for two reasons:

A. Based on the Talmud, rabbinic interpretations of the Scriptures and how to apply commandments in the contemporary world, the embryo is not considered a human being at conception.
B. Judaism does not count the embryo as a human being until it is 41 days-old; before that time the embryo is just a living tissue (Bhikkhu, 2007).

Therefore, within the Jewish tradition, the embryo is owed protection after 40 days of gestation, but not before. Rabbi Moshe Dovid Tendler states that: "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" (KohsL, 2008). At the same time, Judaism is against creating human embryos specifically for scientific research purposes (Bhikkhu, 2007). However, the Jewish religious tradition focuses on not just research, but saving lives, and strongly supports human ESCs. Several commentators from this tradition have emphasized the ultimate goal of human ESCs to save lives (Walters, 2004).

As described in Jewish tradition, the embryo is not considered as human at the time of fertilization; instead, the virtually-unanimous view is that the human embryo is "like water" during the first 40 days of its development, in the words of Moshe Tendler, an Orthodox scholar. The Judeo-Biblical tradition does not hold any moral status to an embryo before the 40-days of gestation. Some look at the moral status of early embryos as male and female gametes, and the

destruction prior to implantation as being the same moral significance as the "wasting of human seed" (Walters, 2004).

Hindu and Buddhist Stances on Embryonic Stem Cells

Hinduism and Buddhism (the so-called Eastern religions) have a lot in common. Unlike other religions, Hinduism and Buddhism have no central authority (like a Church) to speak on ethical dilemmas. Therefore, there is no clear-cut answer from Hinduism and Buddhism on ESCs ethics (Keown, 2004).

Hindus believe that life starts at conception. As a result, the fetus is considered as a person at that moment (Castillo, 2006). In the Hindu tradition, conception is the beginning of a soul's rebirth from a previous life. Some Hindu traditions place the start of personhood between three and five months of gestation, while a few believe that incarnation can occur as late as the seventh month, both of which allow using embryos to derive ES cells (General Positions on Stem Cell Research and When Personhood Begins, 2006), however it is difficult to come up with an exact answer since there is no single authoritative voice that can speak for the entire tradition or community (Tyagananda, 2002).

In an article he wrote, Tyagananda (a Hindu monk), presents “a” Hindu perspective rather than “*the*” perspective on issues related to stem cell research (Tyagananda, 2002). Based on Hinduism, the human soul is the spiritual component of the personality, and it is different from the mind and body. Hindus also understand that life and death come together, and cannot be separated from each other. Thus, Tyagananda came up with the food-chain analogy; the survival of one living organism is often at the expense of another living creature (Tyagananda, 2002). For example, if a hungry lion eats a deer, it is not considered an un-ethical act or bad karma.

Therefore, destroying life, one's own or somebody else's, is bad karma unless it was done in an unavoidable circumstance and for the greater good (Tyagananda, 2002). Tyagananda questions: Is the destruction of embryos for stem cell research considered an "unavoidable circumstance" and an act "done for greater good"? If so, then Hindus will accept ES research as ethically justified (Tyagananda, 2002).

Also, there can be other concerns that might test the restrictions of an ethical consideration. For example, what would be the source of stem cells? From the Hindu perspective, it will be acceptable if the embryo donation is charitable and for scientific purposes, but not for commercial purposes (Tyagananda, 2002). Another question is: Who would be the beneficiaries from such research? In the Hindu tradition, if the benefits of the stem cell research were distributed equally, not only for wealthy who could afford the high price of advanced stem cell medicine, then the stem cell research would not be considered un-ethical (Tyagananda, 2002).

Another source that also helped to clarify the stance of Hinduism on stem cell research is The Hindu Endowments Board of Singapore, which indicated its acceptance of stem cell research within certain time limits (Walters, 2004), using embryos no more than 14 days old.

Buddhism looks at the *intentions* behind human ESC research to determine its morality. For example, if the intention is to cure ill people, then the use of ESCs is considered ethical. On the other hand, if the research on ESCs was performed for the sake of money, then it is unethical (Walters, 2004). The Buddhist religion is based on the principle of "ahimsa" (non-harming); therefore, Buddhism has serious worries about any scientific technique that might involve the destruction of life. Such acts are prohibited by the First Precept of Buddhism which prohibits causing death or injury to living creatures (Walters, 2004). Buddhism believes in the central

virtues of knowledge “prajña”, compassion “karua”, and its long tradition of practicing medicine (Keown, 2004). Buddhism believes that life starts at conception and agrees with Hinduism on the re-birth theory (General Positions on Stem Cell Research and When Personhood Begins, 2006). Since Buddhism believes in the re-birth in which the new being bearing the karmic identity of a recently deceased individual, the embryo has the same moral respect as an adult (Keown, 2004) so Buddhism considers any intentional destruction of embryos to obtain human ESCs as morally not permitted (Keown, 2001).

In Vitro Fertilization Ethics

Currently, the main source of ESCs is the surplus of embryos created *in vitro* fertilization (IVF). In the process of IVF, egg and sperm donated by a couple are united in a test tube, and the embryo is cultured for 5-6 days to the blastocyst stage, then is usually implated into the uterus of a woman for reproductive purposes. Because the process is not always successful, extra embryos are created for the couple. Once the couple has enough children, the excess embryos are either destroyed or are donated to another couple (Siddiqi, 2002). The remaining embryos could be either been frozen or destroyed. Usually, the couple is given four options for their “spare embryos”:

A. Have the excess embryos discarded.
B. Donate the excess embryos to infertile couples (embryo adoption).
C. Donate the excess embryos for research.
D. Preserve the excess embryos under very low temperature for possible use in the future (Robinson, 2005).

Few parents are willing to give their embryos to another couple for various emotional reasons, and few couples are willing to receive them for emotional reasons (Robinson, 2005). Preserving embryos at a very low temperature (in liquid nitrogen) can be very expensive, so most couples choose to discard them (Robinson, 2005).

The Muslim stance on IVF is clear. As mentioned before, according to the Shari'ah laws a distinction should be made for the embryo between actual and *potential* life. And at the same time, there has to be some differences between a fertilized egg in a dish and a fertilized egg in a womb (Siddiqi, 2002). No embryo will survive to adulthood unless placed in its natural environment, the womb, so research using these embryos, surplus embryos from IVF, is permitted by Muslims especially if the goal is to cure disease. Islamic scholars observe that if these embryos were treated as a full human, it would have been forbidden to produce them in surplus and destroy them later (Siddiqi, 2002). Islam prohibits surrogate parenting or human embryo adoption due to the significance of determining a child's true parentage and inheritance rights. Therefore, the Qur'an encourages using excess embryos for research purposes, since under Islamic law surplus embryos can only be used by the couple that created them (Weckerly, 2002). The Washington-based Islamic Institute stated, "Under [the] Islamic principle of the 'purposes and higher causes of the Shari'ah,' we believe it is a societal obligation to perform research on these extra embryos instead of discarding them" (Weckerly, 2002). The Jewish stance is also clear. In Judaism, using IVF embryos is permitted prior to forty-days of gestation, because as discussed earlier, at this stage, the fetus lacks "humanity" (Eisenberg, 2006).

As to the Catholic stance, stem cells produced via IVF are condemned. In his 1995 encyclical *The Gospel of Life*, Pope John Paul II wrote: "Human embryos obtained *in vitro* are human beings with rights; their dignity and right to life must be respected from the first moment

of their existence. It is immoral to produce human embryos destined to be exploited as disposable 'biological material'" (Filteau, 2007). On the other hand, the Presbyterian Church (U.S) and the Methodist Church have no objections on conducting research or using excess embryos produced by IVF. In his address to the UN Mission Ambassadors on the cloning concerns, Jim Winkler, an official of the United Methodist Church, states that "The Church supports embryonic stem cell research using embryos leftover from in-vitro fertilization procedures, but NOT cloning" (KohsL, 2008).

As indicated before, the Hindu Endowments Board of Singapore indicated its acceptance of stem cell research within certain time limits, using embryos no more than 14 days old. Hindus will most likely support the use of surplus IVF embryos that are no longer needed for reproduction purposes so long as the embryos are younger than 14 days. Also, ESCs derived from 5 day old frozen embryos can be used to establish ES cell lines (Walters, 2004). But according to Buddhism, it is immoral to use the excess embryos or frozen embryos created via IVF regardless of the fact that they will be destroyed anyway (Keown, 2004).

Somatic Cell Nuclear Transfer Ethics

Somatic cell nuclear transfer (SCNT), otherwise known as “therapeutic cloning,” as discussed in Chapter-1 is a process where a nucleus is removed from an adult skin fibroblast cell and injected into an enucleated egg for purposes of deriving embryos and ES cells genetically identical to the original patient. SCNT could be performed for therapeutic purposes (using ES cells for treating a disease) or for “reproductive cloning” in which the new embryo is implanted into a surrogate mother and would give birth to a child genetically identical to the donor of the nucleus. Many Islamic scholars consider cloning embryos for the *therapeutic* purposes to be

acceptable (Weckerly, 2006). But most Christian leaders strongly oppose *therapeutic* cloning (Frazzetto, 2004).

The stance of Judaism on therapeutic cloning is similar to Islam. According to the Torah, Jews have an obligation to search for knowledge, and scientific knowledge is granted high value. "Our theological predisposition is not only to welcome, but to aggressively pursue new technologies that improve our lives and our world" (Frazzetto, 2004). There is no clear position on therapeutic cloning from the Hindu perspective. However, Dr. Muthuswamy said the general opinion was in favor of allowing "therapeutic cloning" (The Hindu, 2006). Also, Hinduism makes a distinction between the destruction of a preimplantation embryo (permitted) and abortion (condemned), by accepting the research on preimplantation embryos if the goal was to save lives (Walters, 2004). In Buddhism, it is immoral to use stem cells obtained from cloned embryos (Keown, 2004).

When discussing therapeutic cloning, the ethics behind donating the eggs to perform research has to be discussed. Stem cell researchers need eggs to perform SCNT, with the goal of producing stem cells that match patients' DNA (Pearson, 2006). So far, scientists have relied on women undergoing fertility treatment to obtain their extra eggs after the women's agreement for surplus egg donation. Unfortunately, researchers are facing some difficulty in obtaining eggs. To increase availability of human eggs, several labs have persuaded some women by offering them financial rewards. This leads to a debate about how such women should be compensated (Pearson, 2006). Some argue that women have to be compensated for the distress and effort involved in the process. Others are concerned that this will trigger poor women to give up their eggs for money (Pearson, 2006). Is this process mostly for "therapeutic" or "commercial" purposes?

Parthenotes Ethics

As mentioned in Chapter-1, parthenogenesis is defined as the process by which a single egg can develop in the absence of a male counterpart (Brevini and Gandolfi, 2008). In nature, this process of asexual reproduction is commonly used to create worker bees and ants. In primates and humans, an unfertilized egg is treated with chemicals such as strontium chloride to induce cell division. The embryo can divide to the blastocyst stage from which ES cells are obtained, but the embryo cannot produce a child. When dealing with the ethics of parthenogenesis, we have to ask ourselves: Are we dealing with a human being? Are they "lesser humans," "diseased humans," or "not humans at all" (Jones, 2003)?

Not much has been written by Catholic bioethicists on the specific question of the parthenote personhood (Latkovic, 2006). Parthenote advocates propose that destruction of a parthenote embryo raises fewer ethical problems, because the created embryos are unable to complete gestation, hence such an embryo is considered non human. Dr. William Cheshire retorts that "careful examination of all the medical evidence, however, fails to demonstrate conclusively that the living human parthenote embryo can not be a human being," therefore, designating a parthenote as “ambiguous humanity” is premature (Family Research Council, 2008).

Unlike the clearly negative Catholic stance on therapeutic cloning and using surplus IVF embryos, the Catholic stance on parthenogenesis is not clear, but it has accepted a “wait-and-see” approach, says Tadeusz Pacholczyk, a neurologist and priest at the National Catholic Bioethics Center in Philadelphia (Barry, 2007). Therefore, the Catholic Church will not have an official conclusion until the scientific research establishes whether blastocyst parthenotes are non-viable balls of cells or viable human embryos that happened to be defective. Pacholczyk states: "Until we have really clear and convincing evidence whether [of what] makes a true human embryo, the

church is not going to step into these parthenogenesis waters" (Jones, 2003). In general however, the Catholic Church sees parthenogenesis contrary to moral law because it contradicts the dignity of human procreation and conjugal union (Statement of the Catholic Leadership Conference on Human Cloning, 2001). So in summary, the religious stance on parthenotes can be divided to two groups: A) Those who argue that the parthenote is not a viable true embryo since it can never develop, and B) those who hold that a parthenote embryo should be treated like a normal embryo unless it can be proven otherwise (McConchie, 2005).

Embryonic Germ Cells Ethics

When discussing the ethics of embryonic germ cells (EGCs), the topic of abortion is correlated since EGCs are derived from aborted fetuses not 5-day old embryos (Embryonic Germ Cells, 2007). In Judaism, abortion is permitted only if there is a direct danger to the life of the mother carrying the fetus, while abortion to prevent abnormalities in a fetus is forbidden (Eisenberg, 2006). Although abortion in Judaism is a severe offense, it is hard to justify the use of tissues from EGCs to save lives fearing from encouraging abortion. This is a case where the charge of preventative endorsement could be the avoidable death of human beings (Eisenberg, 2006). In Islam, abortion is allowed if performed before the fourth month of pregnancy (Weckerly, 2006). Muslim jurists have made a distinction between the early stages of pregnancy and its later stages. For example, if a woman was attacked by someone and aborts her baby in the early pregnancy, that person's penalty will be less than if he attacked a pregnant woman during her full pregnancy (Siddiqi, 2002).

For many Hindus, abortion is a terrible act (Castillo, 2006), however there are some exceptions when saving the life of the mother (Castillo, 2006). EGCs as mentioned are obtained

from aborted fetuses, so the question that rises is: Where does this generally negative position on abortion leave Hindus on the subject of EGC stem cell research? Dr. Valavandan Manickavel of www.hinduismtoday.com states that this is one of the major ethical questions for Hindus. Hindus follow other the religions in supporting the saving of lives, but how far people should go to save lives it is difficult to judge and define (Castillo, 2006). The Singapore Hindu Endowment Board in their written response on this issue for the Singapore Bioethics Advisory Committee recently offered a typically ambiguous statement: "There is no non-acceptance to the use of these [EGCs] to protect human life, and to advance life by curing disease." Later they added: "Killing a fetus is a sinful act" (Manickavel, 2004). Although there is no Hindu rejection of EGCs themselves (Walters, 2004), the Hindu Endowments Board of Singapore went on to designate its rejection of EGCs research because the rest of the fetus would be killed (Walters, 2004).

In Buddhism, some believe EGCs are permissible because the main fetal donor is already deceased. The case might be similar to cadaveric organ donation for transplantation (Keown, 2004). The Catholic Church allows the use of germ cells if they came from non-deliberate miscarriages (Pacholczyk, 2008).

Induced Pluripotent Stem Cells Ethics

As was indicated in chapter-1, upon the insertion of four genes into a human skin fibroblast cell, these genes are able to re-program or *induce* the cell into ES-like cells (iESCs) (Humphrey, 2008). Some scientists claim iES cells have the same potential as ESCs that can be grown and differentiated into any kind of human tissues to cure different diseases (Humphrey, 2008). Recently two research teams successfully reprogrammed human skin cell to behave like ESCs. This finding was welcomed by Catholic leaders as being a moral landmark with widely

enormous clinical promise. Dr. Marie Hilliard, RN, director of bioethics and public policy for the National Catholic Bioethics Center in Philadelphia said, "From both a practical and moral perspective, this advance represents a significant benefit over embryonic stem cell research" (Doyle, 2007). However only time will tell whether iESCs truly have the same full medical capabilities as ESCs.

Adult Stem Cells Ethics

Adult stem cells (ASCs) are considered to be the most ethically reasonable source of obtaining stem cells. ASCs such as hematopoietic stem cells (HSCs) have been used for over 35 years, saving hundreds of lives. ASCs as opposed to ESCs pose far fewer ethical problems for any major world religion since no embryos destruction is involved (Shannon, 2006). Marvelous discoveries continue to show that ASCs carry many of the benefits of ESCs but without the negative ethics of embryo destruction (Shannon, 2006). So far, the five major religions of the world do not present any objections towards ASCs. Pope Benedict XVI approved ASCs research (Catholic Online, 2008). As stated by Jakki Jeffs of *Alliance for Life Ontario*: 2001-JUL: "Adult stem cell research provides a legitimate, moral and ethical alternative area of research. Adult stem cell research has already been used successfully for therapeutic benefit in human beings" (Robinson, 2007).

Chapter-3 Conclusion

In this chapter (3), the stances on ESCs were viewed based on the five major religions in the world. The negative Catholic Christian view on human ESCs is contrasted with the positive view of Judaism and Islam. In Christianity, the embryo is a human being at conception, whereas in Judaism 40 days after conception, and in Islam after 120 days. Based on how each religion

answers the question of when life begins, its stance on ESCs was determined, although the Hinduism stance on ESCs is inexact. All five major religions permit and support the use of ASCs. Surplus embryos taken from IVF clinics are permitted to be used for research in Islam, Hinduism, and Judaism, as opposed to Christianity (though not by all groups) and Buddhism. Islam, Judaism, and Hinduism (most likely) support therapeutic cloning, contrasted with Christians and Buddhism. The use of EGCs from aborted fetuses was allowed under certain circumstances by each religion as discussed above, especially if the fetus is already dead. Since parthenogenesis and induced pluripotent stem cells are new methods of obtaining stem cells, little is mentioned about them, but they do seem to provide promising sources for stem cells that have the same or similar properties as ESCs.

Author's Perspective (For Chapters-1 & 3)

The author for this section of the IQP strongly supports the use of embryonic stem cells obtained from IVF. These embryos would be discarded anyways, so if these embryos were used to derive immortal ES cell lines that can be expanded to create large numbers of cells, it would potentially benefit millions of people and improve the health standards and quality of nations. New methods of obtaining adult stem cells have to be researched, as these cells provide a feasible alternative to embryonic stem cells without all of the controversial ethical issues. Induced pluripotent stem cells are a clear indication of advanced scientific technology, and exemplify a worthy effort to avoid using embryos.

As seen in Chapter-3, religious bodies and their representatives have various reactions towards ESCs research. The responses were based on their faith, religious text, and theological teachings. Being a Muslim, it was surprising and interesting to this author to know that Islam is

among the most permissible religions regarding using embryonic stem cells for research purposes. In fact, Islam is one the religions that has rigid traditions of legal laws. As a Muslim I believe in the sense of viewing the embryo as a human being through "process" or "stages" of development, and not from the "moment" of conception. Though as mentioned in this chapter, in Islam stem cells can be obtained from an embryo before the fourth month, before ensolument occurs. It seems that Islamic and Christian stances on ESCs are totally different; maybe if the two stances were balanced, a compromised solution would be achieved! Sometimes, it is hard to judge in this complex argument because in the end we are humans, when most of the time we judge situations based or on our feelings and emotions before our facts and common sense. For example, if my parents or any member in my family were afflicted with any debilitating disease, am I going to do anything to save their lives even if the cost was obtaining stem cells from human embryos? As a scientist, the most important question to me is as following: If I am given the chance to work with ESCs, do I still want to conduct the research, knowing morally it is condemned by some religions, but acknowledging the huge benefits from such research? If nobody executes the research, who is going to do it? The situation is like going to a war knowing for sure the cost is losing civilian-lives! In turn, as a scientist, my obligation is to develop and design new ways to achieve a compromised solution of obtaining stem cells, such as iPS cells, which satisfy most religious groups, since as seen in this section, religion and science have to intersect. This way, we will not sacrifice scientific advances for the expense of our moral values. It is important to relate theology to the problems of the modern world and the new bio-advancements. Also, as new technologies are evolved for the sake of mankind, (i.e. IVF to assist reproduction), there has to be some sort of limitation, or a red-line that has to be drawn so these technologies will not be misused solely for commercial purposes. The stem cell debate,

especially for ESCs, is very complicated and has to be taken seriously. There should be published guidelines based on one-and-only-one dynamic religious-scientific organization considering and respecting each religion's views and implications.

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CHAPTER 4: STEM CELL LEGALITIES

Research on stem cells has become one of the most controversial topics of the 21st century. Many people support stem cell research and use, while others strongly oppose it. Stem cells are such a heavily debated issue that laws and regulations have been implemented to support, fund, or even prohibit stem cell research in various countries. Stems cells isolated from human embryos stir the most commotion, and therefore have the most laws and regulations. Legal issues concerning stem cells have had an impact on the progress made in this particular field of medical research. Due to personal beliefs and moral standings on stem cells, many limitations have been implemented, and have possibly restrained potential breakthroughs in treatments for many diseases.

U.S. Federal Stem Cell Legislation

In the United States, research involving human ES cells has slowed because of moral debates, political opposition, and confusion about the science. In August 2001, President Bush declared that scientists who receive federal research funds, which is the most common source of research funding, could only work with a handful of stem cell lines that were in developed before August 9, 2001. He said research on these stem cell lines was permissible because the embryo had already been destroyed (Kruse, 2008). Since Bush's address, the public has debated the current federal policy. Supporters of stem cell research find the policy far too restrictive, while critics say no research of this type should take place under any circumstances, much less federally funded research.

The White House initially said that more than sixty usable ES cell lines were available for use, but after tests were performed to certify uniqueness, in reality the number was closer to nine, most of which are now considered outdated. To intensify the problem, Congress has proposed bills that would make it illegal to use cloning to create new stem cell lines for biomedical research. The process of cloning would be required to create ES cell lines specific to a given patient that would be less likely to be rejected. The possibility that Congress might outlaw the use of cloning technology to derive new cell lines is discouraging researchers. Even if the Senate passed a pro-research bill, the House of Representatives would be unlikely to agree. And even if such a bill made it through Congress, President Bush would likely veto it, since he strongly opposes most stem cell research.

In June of 2004, 58 U.S. Senators sent a letter to President Bush urging him to change his policy and expand the number of stem cell lines eligible for federally funded research. Surprisingly among the signatories were abortion opponents Trent Lott and Orrin Hatch. In April of 2004, 206 members of the U.S. House of Representatives signed a similar letter to try to persuade the President. To date the President has not changed his opinion about research on human embryonic stem cells (Kruse, 2008).

U.S. States and Stem Cells

Individual states have the authority to pass laws to permit human embryonic stem cell research using state funds. Unless Congress passes a law that bans it, states may pay for research using human embryonic stem cell lines that are not eligible for federal funding (Palca, 2007). However not all states agree on this issue either. State laws may restrict the use of ES cells from some or all sources, or specifically permit certain activities. While some states have passed

legislations that ban all forms of cloning or human ES cell research, others strongly support research and provide significant funding (Stem Cell Research, 2008).

In 2002, California became the first state to officially endorse human ES cell research, including experiments that involve cloned embryos. In 2004, New Jersey established the nation's first state-supported stem cell research facility. Later in 2004, California voters approved Proposition 71, a bond measure that will provide three billion dollars over ten years to aid stem cell research, including work with cloned human embryos and the stem cells they produce. Stem cell research policies in California, Connecticut, Illinois, Iowa, Maryland, Massachusetts, New Jersey, and New York, encourage ES cell research, while other states like South Dakota strictly prohibits research on embryos regardless of the source. States that permit and fund ES cell research have specific guidelines for researchers, such as consent requirements, and approval and review processes for projects (Dunn, 2005).

Thus, due to the strict federal stance on funding ES cell research, state governments have taken the unusual step of funding biomedical research, which is typically done with federal grants. Stem cell scientists in favorable states are pursuing private and state bond avenues of support, however there could be complications if scientists in different states want to collaborate. Embryonic stem cells have come to represent potential treatments for many people suffering from incurable diseases. "This is why we are not waiting for anyone to do it for us," California Governor Arnold Schwarzenegger has said. "We are creating the action right here in California." California is leading the way by passing a bill that provides three hundred million dollars a year for stem-cell research. But California isn't alone in its support of embryonic stem cells. Connecticut Governor Jodi Rell said the goal of her state's ten million dollar annual funding was to find stem cell therapies for a wide range of diseases (Palca, 2007).

"Some states current standing on the issue of stem cells are described below:

- In November 2004 voters in California passed of Proposition 71 to fund adult and embryonic stem cell research. The measure authorized the issuance of bonds in the amount of $3 billion beginning in 2005 not to exceed sale of over $350 million per year. Training grants have been awarded, but the award of research grants has been slowed by litigation. As a result, the Governor decided to loan the institute $150 million in August 2006, and the institute is currently seeking proposals. The California Institute of Regenerative Medicine (CIRM), which administers the state stem cell research program, has developed a Scientific Strategic Plan approved by its governing board in December 2006. The plan projects that CIRM will spend over $622 million through FY 2008-09.

- In 2005 the Connecticut legislature passed Senate Bill 934, which created a fund to provide ten million dollars in grants a year over ten years to do the same. Applications for the first round of grant awards were due in July 2006.

- Illinois Governor Blagojevich signed an executive order to create the Illinois Regenerative Medicine Institute (IRMI) and provide for grants to medical research facilities for adult and embryonic stem cell research. At the same time, the Governor transferred $10 million to this new program, and grants were awarded in April 2006. In August 2006 an additional $5 million in FY 07 funds appropriated to the health department was allocated to the stem cell program and grants were awarded. The Illinois legislature passed a bill in August 2007 permitting IRMI to conduct stem cell research on cells from any source.

- Indiana legislators created an adult stem cell research center at Indiana University. $50,000 dollars has been appropriated to establish the center.

- In 2006 the Maryland legislature created the Maryland Stem Cell Research Fund, which will provide grants for adult and embryonic stem cell research. Unused donated materials under this program may not include oocytes. The Maryland budget for FY 2007 included $15 million for the fund.

- After overriding the Governor's veto, Massachusetts legislators added two new sections to the statutes on stem cell research. The first creates an institute for stem cell research and regenerative medicine at the University of Massachusetts with an appropriation of $1,000,000 to be spent on the stem cell biology core. The second establishes a life sciences center to promote life sciences research in advanced and applied sciences, including but not limited to stem cell research, regenerative medicine, biotechnology, and nanotechnology and creates the Life Sciences Investment Fund to make appropriations, allocations, grants or loans to leverage development and investments in stem cell research and other areas. $10,000,000 was appropriated to the fund.

- In early 2004 New Jersey became the first state to appropriate funds specifically for adult and embryonic stem cell research. State funding for adult stem cell research was already occurring in at least one state, Ohio. In FY05 and FY 06 a total of $23 million in general revenues were allocated to the New Jersey Stem Cell Institute, according to New Jersey's Commission on Science and Technology. The state of New Jersey awarded its first grants in December 2005. Grants were awarded to 17 institutions for research on stem cells from embryos and other sources. In 2007, voters rejected a ballot measure to allow the sale of bonds to fund stem cell research.

- In 2007 New York legislators created The Empire State Stem Cell Trust to support stem cell research on cells from any source. $100 million was earmarked for FY2007-2008, and $500 million was earmarked at $50 million per year for ten years beginning in FY 2008-2009. Applications for the first grant awards are due January 4, 2008.

- The Center for Stem Cell and Regenerative Medicine was established in 2003 with $19.4 million in state funding to support research on adult stem cells. The center also received $8 million from the state in 2006.

- The Washington legislature created the Life Sciences Discovery Fund, which may result in grants for stem cell research in the future. Planning for the fund is still in process.

- On October 10, 2006 the Wisconsin Governor announced $100 million funding for Stem Cell Products, Inc., which creates blood products from embryonic stem cells.

- The Virginia legislature has created a fund to support adult stem cell research only. Money was not appropriated at the time the fund was established.

- Nebraska statutes limit the use of state funds for embryonic stem cell research. Restrictions only apply to state healthcare cash funds provided by tobacco settlement dollars.

- Arizona law prohibits the use of public monies for reproductive or therapeutic cloning.“ (Eligibility Criteria, 2008)

The Current Situation in the U.S.

Arguments are currently being made for removing the Bush restrictions. The President's policy limits federal funding to research to only about twenty cell lines that existed over three years ago. Scientists argue that dozens of other stem cell lines have since been created through private funds, some of which are easier to access, easier to maintain in the lab, easier to turn into

desired cell types, and more likely to contribute to actual human cell therapies (Ford, 2006). Since the new ES lines have not been in contact with mouse co-feeder cells, unlike all of the approved lines, the cells can be used for many new procedures. In February 2005 a poll taken by Results for America, a project of the Civil Society Institute, demonstrated that 70 percent of Americans favored loosening the Bush restrictions on stem cell funding. Those in favor included more than half of conservatives (56 percent), 80 percent of moderates, and 84 percent of liberals. However, not everyone agrees that there should be more federal funding for stem cell research. Especially those who, like President Bush, believe life begins with the very early human embryo (Dunn, 2005).

The U.S. is still considered a leader in stem cell research, but there is concern that it is slipping behind countries such as the U.K., Korea, Singapore, Sweden, Israel, Australia and China. Private funding for stem cell research in the U.S. currently provides more funding than the federal Government, which bans funding for research on new ES cells (Agnew, 2003). This restrictive U.S. policy makes collaboration with foreign scientists more difficult, and leads to a large amount of worldwide funding for stem cell research on less useful lines.

International Stem Cell Policies

In the U.K., studies in ES cell research are subject to the oversight of the Human Fertilization and Embryology Authority (Moreno, 2006). Clinical studies in adult stem research are subject to review from an independent body as well. In Canada, the largest source of stem cell research funding is the Canadian Institutes of Health, followed by government and health charities (Cook, 2004). As restrictions have tightened, the US has seen more scientists move to

the UK, which allows research on ES cells derived from human embryos up to 14 days of development.

Governments around the world are closing the gap, and a number of countries are emerging as powerhouses in the field. In Australia, the government is funding research and helping to set up a national stem cell research center. In the Czech Republic, Dvorak's lab at the Mendel University of Agriculture and Forestry is part of a Centre for Cell Therapy and Tissue Repair, and is supported and fully funded by the government. South Korea has derived almost as many new ES lines as the United States, according to the Globe survey, and researchers there were the first to claim to create stem cells from a cloned human embryo, a scientific milestone that American researchers initially grumbled should have happened in the United States (Ebbin, 2007), although this initial South Korean claim has since been withdrawn for data fabrication.

Future Stem Cell Policies in the U.S.

Despite the current restrictive policies on stem cell research under President Bush, drastic changes could be implemented in the near future with a presidential election in 2008. Depending on who wins, the federal laws restricting research funds could be lifted. The two leading candidates have very different positions on the subject and whoever is elected will have a large impact on advancements made in stem cell research. Barack Obama supports all stem cell research, while John McCain opposes human embryonic research. Their official positions on the matter are:

Barack Obama

"I stand in full support of the Stem Cell Research Enhancement Act as I did when this bill was introduced and sent to the President's desk in the 109th Congress. I am proud to be an original cosponsor of this bill. I am frustrated by the opposition this bill has generated, and saddened that we are preventing the advancement of important science that could potentially impact millions of suffering Americans. The study of stem cells holds enormous promise for the treatment of debilitating and life-threatening diseases. However, in order to reach this level of medical achievement, much more research is necessary to understand, and eventually harness, the amazing potential of stem cells. Instead of creating roadblocks, we must all work together to expand federal funding of stem cell research and continue moving forward in our fight against disease by advancing our knowledge through science and medicine. Two of my constituents, Mary Schneider and her son Ryan, are well aware of the potential of cord blood treatments. Her son, diagnosed with cerebral palsy at 2 years of age, has made what appears to be a full recovery after treatment with his own cord blood. Despite the compelling results witnessed by the Schneider family, they also firmly believe and support expanded research of embryonic stem cells to combat disease. The President's veto of the stem cell bill proposed in the last Congress prevents government funding beyond 78 previously established stem cell lines. However, recent estimates on the number of viable cell lines bring the numbers down closer to 20. Clearly, we are moving backwards in our efforts with these current restrictions. Stymieing embryonic stem cell research is a step in the wrong direction. It closes the door on many Americans awaiting new treatments that could potentially provide a better quality of life, or, perhaps, even save their life. My hope, and the hope of so many in this country, is to provide our researchers with the means

to explore the uses of embryonic stem cells so that we can begin to turn the tide on the devastating diseases affecting our nation and the world" (LaBolt, 2007).

John McCain

"Stem cell research offers tremendous hope for those suffering from a variety of deadly diseases - hope for both cures and life-extending treatments. However, the compassion to relieve suffering and to cure deadly disease cannot erode moral and ethical principles. For this reason, John McCain opposes the intentional creation of human embryos for research purposes. To that end, Senator McCain voted to ban the practice of "fetal farming," making it a federal crime for researchers to use cells or fetal tissue from an embryo created for research purposes. Furthermore, he voted to ban attempts to use or obtain human cells gestated in animals. Finally, John McCain strongly opposes human cloning, and voted to ban the practice, and any related experimentation, under federal law. As President, John McCain will strongly support funding for promising research programs, including amniotic fluid and adult stem cell research and other types of scientific study that do not involve the use of human embryos. Where federal funds are used for stem cell research, Senator McCain believes clear lines should be drawn that reflect a refusal to sacrifice moral values and ethical principles for the sake of scientific progress, and that any such research should be subject to strict federal guidelines" (Addressing. 2008).

Due to the moral debate on stem cells, especially human embryonic stem cells, many laws and regulations have been placed on the use of these cells. Positions on stem cells range from supporting and promoting research through alternative funding to completely prohibiting any use of particular lines of stem cells. Legalities on stem cells have directly effected the

advancements in this field, and have limited the potential of developing new procedures for many diseases. Even though our federal government does not support stem cell research at this time, many other sources of funding have supported research and other countries continue to make breakthroughs. Stem cells hold great potential in treating many diseases, but procedures are relatively new and more research is needed for prove them safe and effective. Funding for this research is critical, but is not easily obtained. The legal issues on stem cells greatly impact the level of advancement and will continue to restrict new discoveries as long as there are limitations on research.

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CONCLUSIONS

The author for Chapters 1 and 3 of this IQP strongly supports the use of excess embryos obtained for the purpose of reproduction via IVF to derive new ES cell lines. This author also supports all efforts to develop new methods for obtaining alternative sources of ESCs such as ASCs and iPS cells. The results of such alternative methods would be an excellent compromise solution for using ES cells without destroying an embryo that should satisfy most religious groups. The author believes in viewing the embryo as a human being through various "stages" of development, not from the "moment" of conception where no ensolument has occurred yet, hence using embryos to derive ESCs within 5-6 days to obtain the blastocyst is acceptable. The author also feels the current federal stance against ES cells is too strict, and believes the US Federal government must fund and encourage research on ESCs because of the enormous potential that these cells have in curing afflicted people with debilitating diseases. At the same time the author also agrees with individual states that have taken the initiative to privately fund ESCs research.

The author for chapters 2 and 4 believes that all types of stem cells should be utilized in research and medical procedures. This author disagrees with current US federal laws that do not allow national government funding to derive new ES cell lines, and believes more could be done and should be done by the government to support the use of stem cells.