

STEM CELLS

An Interactive Qualifying Project Report

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ABSTRACT

The purpose of this IQP was to investigate stem cell technology, examining a variety of stem cell types, as well as the ethics and legalities surrounding their research. This report investigated various stem cell types and sources, current medical applications, ethical issues associated with each type, and legal stances the world has on this research. We conclude that embryonic stem (ES) cells have the greatest medical potential, and the greatest ethical and legal concerns. Adult stem cells are more difficult to grow, and have less differentiation potential. New alternative technologies have been developed to avoid the destruction of embryos to obtain ES cells, and we support these efforts. We conclude that of the five major world religions, Christianity (especially Catholics) and Buddhism oppose ES cell research, while the 3 others are somewhat supportive of it. All five support adult stem cell research. Legal restrictions placed on stem cell research by countries such as the U.S. and Germany have hindered research into ES cells relative to other more progressive countries.

TABLE OF CONTENTS

Signature Page	1
Abstract	2
Table of Contents	3
Project Objective	4
Chapter-1: Stem Cell Types and Sources.....	5
Chapter-2: Stem Cell Applications	19
Chapter-3: Stem Cell Ethics	30
Chapter-4: Stem Cell Legalities	40
Conclusions	49

PROJECT OBJECTIVES

The purpose of this project was to explore the breadth of the topic of stem cells and go beyond a discussion of the technology to include the effect of the technology on society. The purpose of Chapter-1 was to describe properties of stem cells and note that there are more types of stem cells than just embryonic stem cells. The purpose of Chapter-2 was to go in depth on which experiments stem cells have been successfully used for, to illuminate their potential as a prelude to discussing their ethics. The purpose of Chapter-3 was to explore the ethics surrounding this controversial topic to assess their effect on society. The purpose of Chapter-4 was to determine the extent of stem cell use as governed by current Federal, state, and international laws.

CHAPTER-1: STEM CELL TYPES AND SOURCES

Stem cells have become a hot topic among many in the field of biology due to the wonderful properties they possess, compared to most other types of cells that constitute the human body. A stem cell is a type of cell that is characterized as being undifferentiated, meaning that depending on the conditions it encounters, it can be programmed to develop into another specialized tissue or organ of the body. Ever since decades ago, stem cells have been used in extensive studies. Through various experiments, stem cells have been used as simple tools for understanding critical molecular mechanisms behind human development. In the field of medicine they have been used to treat various diseases. Interestingly enough, stem cells do not just come from five-day old blastocyst-stage embryos, which are associated with serious ethical concerns, as we will see later. They are in turn obtained from two general sources: adults as well as embryos. In turn, based on how well the cells differentiate, they are characterized by levels of potency: totipotent, pluripotent, multipotent, and unipotent.

Overview of Stem Cell Types

It is necessary at this point to note that not all stem cells are alike, to contrast the common notion that all stem cells are alike or similar. Thus, when it comes to someone saying that he or she is against stem cell research, it is necessary to greatly distinguish what kind of stem cell research one is against. As mentioned before, stem cells are classified into two major categories: embryonic and adult, and further into levels of potency: totipotent, pluripotent, multipotent, and unipotent. Newly fertilized eggs through about the 8-cell stage of development are totipotent, meaning they are capable of forming any cell in the body, or the placenta. Embryonic stem cells, or ES cells, are pluripotent, able to form almost any cell in the body. Hematopoietic

stem cells (HSCs) are multipotent, able to form several types of related cells (i.e. white blood cells, red blood cells, platelets, etc). Mesenchymal stem cells (MSCs) are also multipotent. Cells such as skin stem cells are usually regarded as unipotent, able to generate only other skin cells.

Embryonic Stem Cells

Embryonic stem cells originate from the inner cell mass of a blastocyst, or an embryo in its very early stage of development of only five days. At this time, the fertilized zygote exists as an approximately 150-celled organism. Here, the blastocyst's basic structure consists of two layers of distinctive cells: the outer layer of trophoblastic cells, and the inner cell layer, where the stem cells exist (see Figure-1).

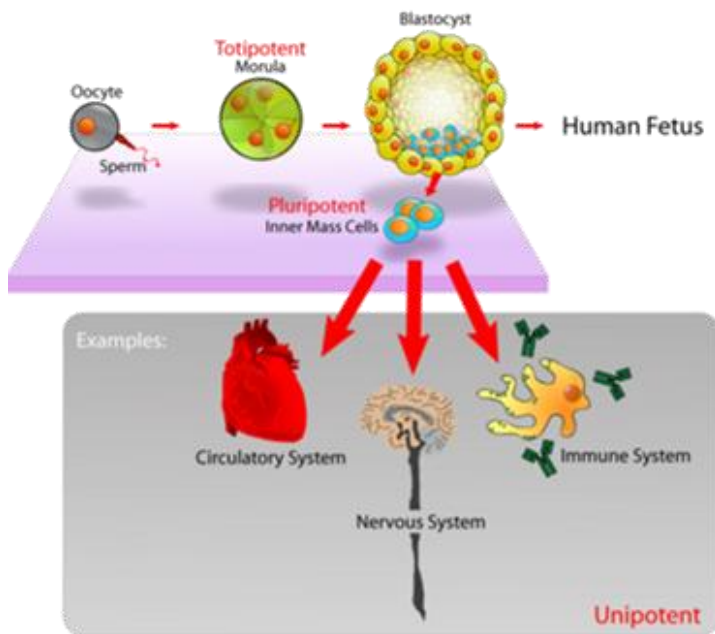


Figure-1: Formation of a Human Blastocyst with Differential Potentials. Egg and sperm are united during *in vitro* fertilization (upper left) and grow to the 4-8 cell stage (morula, green), and continue growing for about 5-6 days to make a blastocyst (upper right, yellow). Within the blastocyst is the inner cell mass (blue) that contains ES cells, which can differentiate into a variety of tissues (lower portion of diagram). (Stem Cells, 2008).

ES cells are pluripotent, meaning they have the potential to differentiate into almost any cell of the human body (Frequently Asked Questions, 2006). The process of cultivating ES cells requires extraction of cells from the inner cell mass, and this extraction causes the embryo to cease to exist. Thus, one can argue that taking cells from the inner cell mass is immorally destroying a potential human's right to live, which is quite a debate as will be discussed later in Chapter 3. However, scientists have recently devised alternate methods of ES cell production, including parthenogenesis, somatic cell nuclear transfer, and induced pluripotent ES cells, as will be discussed later in this chapter. And adult stem cells can sometimes be used in lieu of ES cells, for certain medical applications as an alternative to ES cells.

Adult Stem Cells

In comparison, adult stem cells, or ASCs, are undifferentiated cells found in several parts of the human body, especially in certain organs and tissues (Frequently Asked Questions, 2006). Recent research has shown that they also come from fetal cord blood, baby dental pulp, and amniotic fluid. The main purpose of ASCs is to repair damaged tissue, and help organs replenish themselves. Thus in theory, ASCs exist with a lower level of potency than ES cells, and have a limit as to which types of cells they can become. However, this is not completely true, as a handful of certain types of adult stem cells, including MSCs and HSCs, have some evidence for plasticity (ability to differentiate into a type of tissue different than the one from which they were isolated) (Kirschstein, 2001).

ASCs prove a valuable source of stem cells to work with, because no embryo is destroyed to obtain them, yet they are associated with some inconvenient disadvantages. They are rare, they do not exist in numerous quantities in the organs they originate from, and scientists must

rely on a handful of extraction, analytical, and purification methods to capture the light of these cells, that are considerably tedious. They are also less potent than ES cells, however, some studies have shown hints that such cells may have the potential to trans-differentiate into multiple cell types (Kirschstein, 2001). It has not been proven, however, that this can occur *in vivo*, but many in the scientific community do embrace the possibility, and argue such cells would help replace ES cells.

Hematopoietic Stem Cells (HSCs)

These are stem cells that are isolated mainly from the bone marrow, fetal umbilical cord blood, or from the peripheral blood of a person, say, who has undergone hormonal therapy to encourage the release of such cells into the blood from the bone marrow. Such stem cells, when exposed to their associated typical conditions, give rise to all the types of blood cells, including those associated with the immune system. These cells include not just red blood cells, but also B and T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, macrophages, and platelets. This property dubs hematopoietic stem cells as multipotent stem cells, as they can differentiate into many cell types, and in turn they continue to be used especially in immunological-related treatments (see Figure-2 for the typical differentiation pathways of a hemato- poietic stem cell). It has been recently known that HSCs from cord blood have been used to treat over forty life-threatening diseases, including blood-related cancers, certain genetic diseases, immune system deficiencies, and blood diseases (Viacord, 2008).

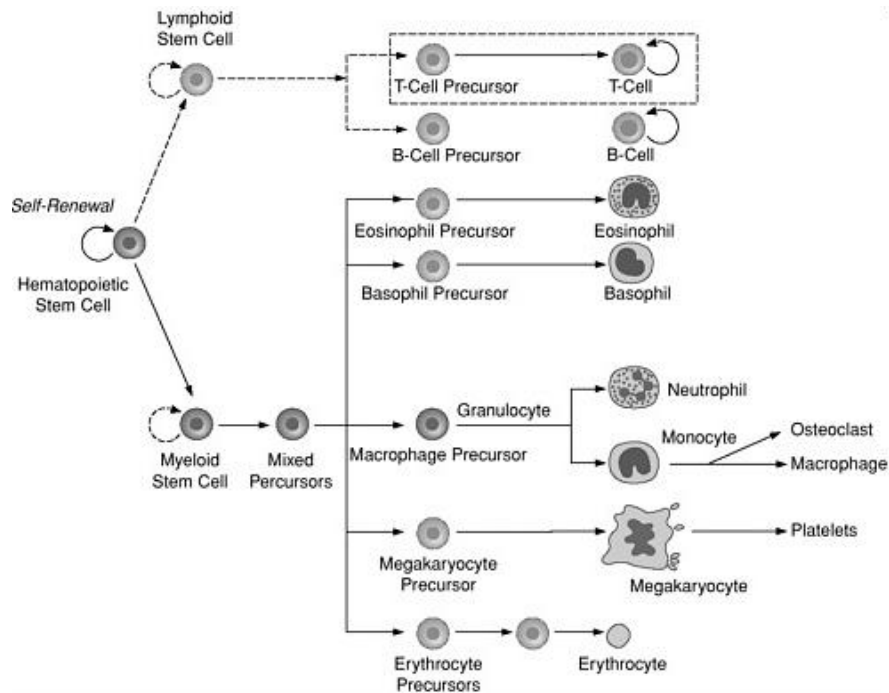


Figure-2: Diagram of Hematopoiesis. Hematopoietic stem cells (left, center) differentiate into lymphoid (upper) or myeloid (lower) lineages that form all the cellular components of blood. (National Academy Press, 2001).

Mesenchymal Stem Cells (MSCs)

Also known as bone marrow stromal stem cells, these cells, like hematopoietic cells, also originate typically from the bone marrow. When grown under specified conditions in vitro in the laboratory, however, they differentiate into osteocytes, chondrocytes, adipocytes, and connective tissue cells, which in turn work together to form tissues such as bone, cartilage, fat, tendons, and ligaments (Kirschstein, 2001). Mesenchymal stem cells have even been found to differentiate into some muscle components. Such an ability of MSCs differentiating into a wide array of cells gives them the greatest variety of specialization among all other types of adult stem cells. Thus, they will increasingly be relied on in the medical community.

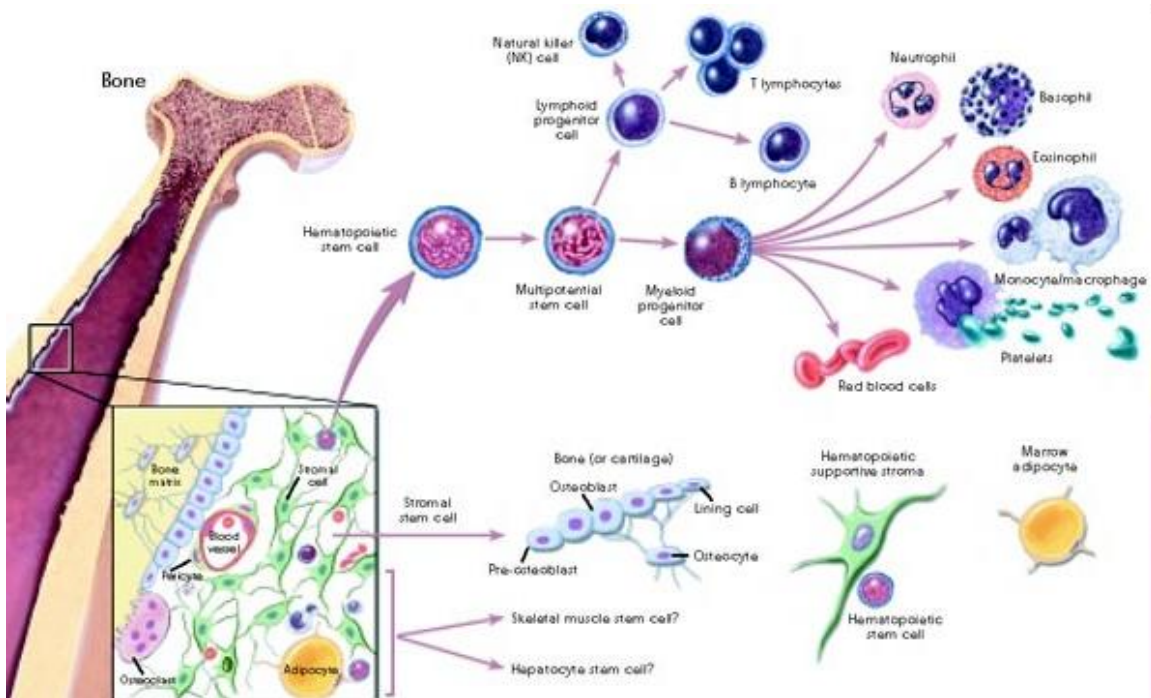


Figure-3: Differentiation of Bone Marrow Hematopoietic and Stromal Stem Cells. The bottom half of this diagram shows the differentiation of mesenchymal stem cells into their components (Kirschstein, 2001).

Neural Stem Cells (NSCs)

These cells are found mainly in the human brain (especially in the hippocampus and the olfactory bulb), and in the spinal cord in the central nervous system. Typically they differentiate into three major cell types: nerve cells, or neurons; and two major categories of “non-neuronal” cells: astrocytes and oligodendrocytes (Frequently Asked Questions, 2006). Astrocytes and oligodendrocytes serve to support and nourish precious nerve tissue. Neural stem cells are currently under extensive research to treat critical disorders such as Alzheimer’s Disease or Parkinson’s, and experiments involving such studies have been done in mice so far, as will be discussed in Chapter-2.

Epithelial, Skin, and Cardiac Stem Cells

Epithelial stem cells, or ESCs, are unique adult stem cells that originate from continuously self-rejuvenating linings of epithelial tissue, including the gastrointestinal digestive tract, some parts of the skin, and the adult eye. ESCs appear to be more unipotent than multipotent compared to the other adult stem cell types, as they form a number of tissues only dependent on where they originally came from. For instance, those produced in the deep crypts of the digestive tract's lining differentiate only into such cells including absorptive cells, goblet cells, Paneth cells, and enteroendocrine cells (Kirschstein, 2001).

In comparison, skin stem cells are absolutely unipotent. In such a case, these stem cells are classified as having the highest degree of specificity and can just give rise to only one other cell type. Skin stem cells are born from only two places in the skin: the epidermis' basal layer, and at the base of hair follicles. From these areas, skin stem cells give rise to keratinocytes which migrate to form a protective layer at the surface of the skin, and they also form parts of the hair follicle and the epidermis (Kirschstein, 2001). Although epidermal stem cells are unipotent, they actually have advantages that make them reliable in transplantation therapy and molecular research. One of these great advantages is that since they can only differentiate into one kind of body cell, they are easier to study in molecular terms. Other advantages include that skin stem cells are easy to extract and have a great ability to self-renew, and they can be used to form skin grafts in effectively treating burns and other injuries on a patient's body, without any risk of immunorejection since the cells would come straight from the patient's own body.

Cardiac stem cells (CSCs), compared to epidermal stem cells, are unipotent stem cells that rise from the heart muscle and give rise to only one type of tissue: the cardiac tissue. So far,

CSCs have been used in case studies involving humans as well as laboratory mice in healing and repairing damaged heart tissue.

Current Alternative Strategies to Embryo Destruction

Recently cell and molecular biologists have been developing promising strategies for obtaining ES cells without destroying an embryo. These alternatives include parthenotes, iPS cells, and single cell micromanipulation.

Parthenotes

An alternative strategy that researchers have developed within the past few years that can give rise to pluripotent ES-like cells is known as parthenogenesis. Under this method, a non-fertilized egg is stimulated through chemical treatment such as strontium chloride to divide, as if it was a fertilized egg, until it has reached the blastocyst stage. At this point, ES cells can be obtained, but no further division occurs by the egg. As the original egg was not fertilized and the resulting “embryos” have no potential to develop into human beings, their place in the field of stem cell research is taken much more lightly than ES cells by ethicists. So far, primate parthenote ES cells were successfully derived in 2001 (Cibelli et al., 2002), and human parthenote ES cells in 2007 (Kim et al., 2007). Thus, parthenotes may serve as an alternate source of ES cells in the years to come. However, this technique would only work for the derivation of ES cells from a female patient, since only females can donate the original egg.



Figure-4: Digital Photograph of a Human Parthenote. Photo of a human ovum fifteen hours after chemical parthenogenetic activation (An Alternative to Cloning, 2005).

Single-Cell Micromanipulation

Some very recent studies document techniques that allow single cells to be extracted from an early stage embryo (usually the 8-cell stage) or from a blastocyst without destroying the embryo (Chamany, 2004). These techniques are termed single-cell biopsy or micromanipulation, which involve the extraction of only a very small quantity of ES cells without affecting subsequent development of the embryo. Because such an embryo could in theory still be used for reproductive purposes, it may have less ethical concerns than destroying a viable embryo. In June 2006 a team of researchers headed by M.D. Robert Lanza of Advanced Cell Technology in Worcester, MA carried out a single-cell biopsy on an eight-cell human embryo, to produce four ES cell lines (Markwith, 2006). The biopsied embryo was then placed in cryogenic containment, and later was found to still be a viable embryo. The ACT team especially made note that this technique is very much similar to preimplantation genetic diagnosis, in which a single cell extraction does not interfere with the embryo's developmental potential (Lanza et al., 2006). So

far, these techniques are only at their early stages of development, and it may actually take awhile until it they are proven to work effectively.

Induced ES (iES) Cells

A lesser controversial strategy for obtaining ES cells is the creation of induced ES (iES) cells. More commonly known as induced pluripotent (iPS) cells, these are initially non-pluripotent adult cells (usually skin fibroblast cells which are convenient to obtain) that are genetically engineered to behave like pluripotent ES cells. iES cells are produced by inserting copies of combinations of three to four genes [encoding transcription factors known to induce a de-differentiated state (Takahashi et al., 2007)] into fibroblast cells using retroviruses (Frequently Asked Questions, 2006).

The technique was originally devised in June 2006 in Japan by the molecular biologist Shinya Yamanaka of Kyoto University. He collected skin fibroblast cells from mice and reprogrammed the cells to an ES-like state by transferring four genes encoding four transcription factor proteins with the aid of retroviruses. Retroviruses are commonly used in genetic engineering to incorporate bits of molecular information into genomes. Because no embryos are destroyed in this process, such iES cells have far fewer ethical considerations than traditional ES cells. This technique (like SCNT) might also be used to create ES cells compatible with a specific patient; it could be applied to a patient's fibroblast cell. So far, the technique has been achieved with mouse cells (Cyranski, 2007), and human cells (Takahashi et al., 2007; Yu et al., 2007; Park et al., 2008). It is, however, unknown how safe iPS cells will be to treat human disease without causing cancer, for example.

Somatic Cell Nuclear Transfer (SCNT)

Recently, researchers have attempted to devise a protocol for preparing ES cells genetically identical to a specific patient. Such patient-compatible stem cells would presumably not be rejected by the host during engraftment. In this technique, known as somatic cell nuclear transfer (SCNT) procedure, an enucleated egg whose nucleus has been removed is microinjected with the nucleus of any typical cell from a specific patient. As when producing iPS cells, skin fibroblast cells are usually used since such cells are convenient to obtain. Once the oocyte is treated with the genetic material of an adult somatic cell, it is then stimulated to undergo cell division as if it had had been fertilized by a sperm cell, just as in parthenogenesis (Chamany, 2004). Once the dividing egg reaches the blastocyst stage, ES cells can be isolated genetically identical to the patient. As this is so, SCNT is particularly thought of as a way to obtain ES-like cells to treat patients without running the risk of immunological rejection upon tissue transplantations. Thus, it can be referred to at times as a therapeutic cloning. So far, SCNT has been used to clone primate ES cells (Byrne et al., 2007), however, the original claim of SCNT success in humans (Hwang et al., 2005) was later retracted, so this technique has not yet been achieved in humans.

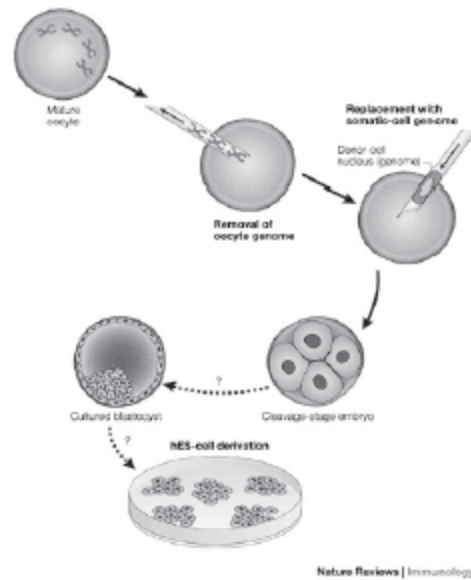


Figure-5: Diagram of the SCNT Technique. A mature oocyte (upper left) is obtained and its genome is removed (upper center), and is replaced (upper right) with the nucleus of an individual's fibroblast skin cell (upper right). The embryo is grown to the 8-cells stage (center), then grown to the blastocyst stage (lower left), from which ES cells are obtained (bottom) that are genetically identical to the patient (Embryonic Stem Cells, 2007).

Research in this area indicates caution is necessary, as mouse models have revealed that SCNT clones often have aberrant genomic imprinting patterns, or chemical modifications of DNA (Chamany, 2004). The efficacy of producing viable offspring is very low, and a majority of embryos produced by this method experience developmental abnormalities and/or the offspring die shortly after birth (Chamany, 2004). It has yet to be determined whether ES cells derived by SCNT will show similar abnormalities.

Chapter-1 Conclusion

To date, with so many different types of stem cells isolated, each with their own benefits, it can be well inferred that stem cell research has come a very long way since their discovery in mice in the 1960's. The purpose of this chapter was to document the different types of stem

cells, paying special attention to which ones require the destruction of an embryo, and which ones do not, as a lead into the ethics discussion in Chapter-3. We shall now move on to discuss in the next chapter the myriad of invaluable applications of specific stem cells in detail.

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Chapter 2: Stem Cell Applications

Although the previous chapter described the existence of many different types of stem cells, not all of them have been proven to have medical applications at this time. The purpose of this chapter is to outline some stem cell applications that have successfully been done with several types of diseases.

Treatment of Diabetes with Stem Cells

Embryonic stem (ES) cells have the most medical potential of all types of stem cells due to their ability to differentiate into almost any type of tissue. ES cells have been used for a variety of applications, but are best documented for the treatment of diabetes. This autoimmune disease causes the destruction of pancreatic islet beta cells, which in turn affects the amount of insulin the body produces. One early study done *in vitro* utilized pluripotent undifferentiated human embryonic stem (hES) cells in adherent and in suspension cultures, to demonstrate their differentiation into beta cells with the ability to produce insulin. The release of insulin by these differentiated cells in culture was documented using beta cell markers. This study demonstrated the ES cell potential for treating this disease, and gives a positive outlook on future use of such cell lines to be used in cell replacement therapy for diabetic patients. When obtaining such results, hES's are grown as undifferentiated colonies in culture. These cells are usually placed on a feeder layer of mouse fibroblasts. In some cases, embryoid bodies (EB's) form, comprised of all three embryonic layers, ectoderm, mesoderm, and endoderm. Through the use of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) performed on RNA isolated from the hES cells, differentiated cell lines were detected that produced mRNA encoding insulin protein.

In addition, immunostaining was also performed to demonstrate insulin production (Figure-1). After embryoid bodies “EB’s” were seen in culture, cells were isolated every 3 days for a total of 19 days. After about the 14th day, insulin producing cells were evident, as tested by immuno-histochemical staining, and these positive cells became progressively more evident at day 19 where approximately 60-70% of the cells stained positive for insulin (Figure-1). These findings validate the hES cell model as a potential system for producing insulin during cell replacement therapy for diabetes.

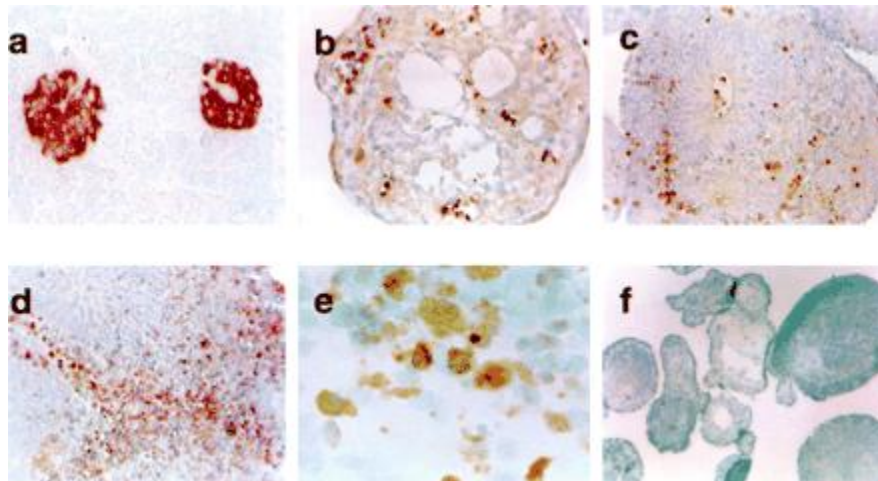


Figure-1: Picture of Human ES Cells Differentiated to Embryoid Bodies That Produce Insulin. The reddish brown color denotes positive immunostaining for insulin protein. Panel-A, normal human pancreas (40X) (positive control); B-D, differentiated embryoid bodies at day-19 (40X); E, EB at day-19 (100X); F, EB at day-19, nonimmune negative control. (Assady et al., 2005)

Recently, James Shapiro and his colleagues (Edmonton, Canada) developed a means of transplanting large amounts of pancreatic islet cells into patients using immuno-suppressant therapy, allowing the cells to easily adapt and thrive in the patient’s body (Stem Cells and Diabetes, 2005). All seven patients undergoing this procedure progressed to the point that about

a year after surgery they no longer needed insulin injections. This technique is now being tested in 10 of the world's most prestigious research centers. However, the drawback of this procedure is the limited amount of islet cells available for transplant. Currently, these cells are taken from cadavers, so this is where hES cells comes into play. If scientists can culture hES cells and differentiate them successfully into islet cells producing sufficient amounts of insulin, the need for cadavers and the low quantity of such cells will be a thing of the past.

One key question in ES diabetes research is how to optimize the production of insulin. A recent finding indicates cells surrounding the beta cells help this production. Through research it has been discovered that beta cells that are surrounded by other types of islet cells are more efficient and responsive to changes in glucose levels than those found in solidarity, such as beta islet cells on their own. Scientists have discovered that differentiated isolated beta cells sometimes release insulin in an all or nothing sequence, which could have detrimental effects on a patient. Culturing a cluster of all the islet cells together allows them to work in harmony producing the appropriate amount of insulin at the right time.

Recently, researchers are trying to develop methods for avoiding immuno-rejection of the beta cell transplants. This can be done by placing the cultured cells into a nonimmunogenic material before transplantation allowing less chance of rejection. Researchers are also trying to utilize the technique of somatic cell nuclear transfer (SCNT) for making ES cell lines specific for one patient. In this technique, a nucleus is isolated from a skin fibroblast cell from a patient, and then is microinjected into an enucleated ES cell, so the ES cell line is genetically compatible with the patient. However this procedure has only been done with mice and primates, and has not yet been done with humans (Stem Cells and Diabetes, 2005).

Researchers in Spain have recently discovered a way to select ES cells while they are differentiating, making it easier to select for the insulin producing cells (Stem Cells and Diabetes, 2005). The cells are grown in an antibiotic rich media where only the insulin producing cells survive. These cells were then cloned and transplanted into diabetic mice eventually reversing the effects of the disease. When transplanting these cells into the mice, great care was taken to avoid transplanting outlying cells that could give rise to tumors that could be life threatening. Figure 2 shows embryoid bodies made up of all three embryonic germ layers. The cells that contained the beta cell marker insulin were then extracted and utilized in a five step culturing system to produce clusters of islet performing cells (Stem Cells and Diabetes, 2005) (Figure-2).

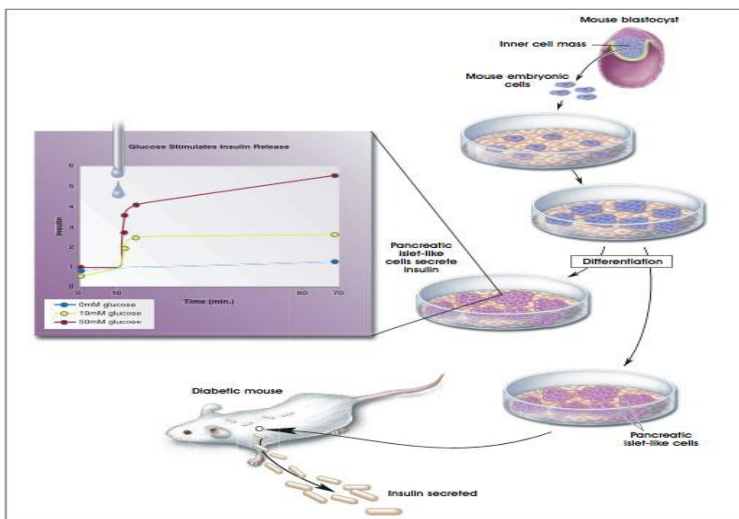


Figure-2: Diagram of the Culture of Mouse ES Cells Used to Treat a Diabetic Mouse. Mouse ES cells were isolated from in IVF blastocyst (upper right), then cultured on a feeder layer and differentiated (center right). The cells were screened for insulin producing cells (lower right) then transplanted into a diabetic mouse (lower center). Inset shows the lowering of blood glucose in the transplant mice. (Stem Cells and Diabetes, 2005).

Treatment of Damaged Heart Muscle Using Stem Cells

The damage of heart muscle cells (cardiomyocytes) results in health problems such as heart attacks, coronary artery disease, hypertension, and other debilitating symptoms, that can negatively affect the heart and its surrounding organs. Through use of stem cells, doctors are trying to transplant new differentiated cardiomyocytes into the heart itself which will take the place of the damaged cells, and which will allow the heart to repair itself. Cardiomyocytes contract allowing blood to flow throughout the body. Researchers have discovered that under specific growth conditions, mouse and human ES and hematopoietic stem cells can be differentiated into both cardiomyocytes, as well as vascular endothelial cells, both of which help conduct blood throughout the body. Transplanting cultured, working heart tissue into a patient's damaged heart instead of transplanting an entire heart from another person would be much easier and more effective long term.

One example of this stem cell procedure involves hematopoietic stem cells (HSCs) taken from adult mouse bone marrow (NIH Stem Cell Information, 2001). After a heart attack was surgically induced in a mouse by tying off a major blood vessel, HSCs were injected into the damaged area of the heart. The mice that received these HSC injections showed a much greater rate of recovery from the induced heart attacks than those that did not. The injected stem cells eventually formed new cardiomyocytes, as well as vascular endothelium and smooth muscle cells, all of which are needed to successfully create new heart and blood vessel tissue. The study concluded that the transplanted HSCs were triggered by the injured myocardium to migrate and differentiate leading to a healthy working heart.

Another study showed that *human* adult HSCs can be taken from a donor's bone marrow and injected into a rat model for heart attacks where they differentiated into vascular endothelial cells (Figure-3) (NIH Stem Cell Information, 2001). Similar to the mouse study, this rat study was also performed by inducing a heart attack by tying off the main coronary artery. The human HSCs were injected into the blood vessels of the rat, and the damaged area was then repaired.

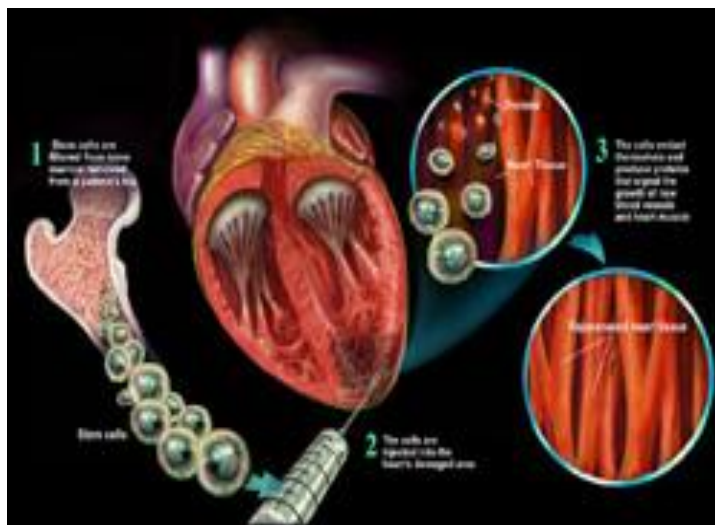


Figure 3: Diagram of the Injection of Human HSCs into a Rat Heart. HSCs isolated from bone marrow (left side) are injected into the heart ventricle (diagram center), and subsequently differentiate into cardiac muscle (right side) (New Stem Cell, 2005).

In these experiments, specific HSC markers were used to identify and purify HSCs from other cells, which increased the therapeutic potential of the graft. Their purification was aided by the use of antibodies that tagged proteins on the surface of HSCs specific for this cell type. Once the HSCs had been tagged with the antibodies containing a fluorescent label, those fluorescing cells were purified by fluorescent activated cell sorting (FACS).

In addition to using HSCs, ES cells have also been used to treat heart attacks in animal models (NIH Stem Cell Information, 2001). In one study, hES cells were first differentiated in culture into embryoid bodies containing all the three embryonic germ layers, and the final data was promising.

Some recent work has also been done with autologous transplants using a patient's own HSCs. The University of Pittsburgh Medical Center is testing the use of a patient's own bone marrow derived stem cells and injecting them directly into the heart muscle. This treatment is being researched as a potential cure for congestive heart failure. This research will be the first time that scientists will be able to observe the results of such a procedure in a human heart. All patients in this study must have a ventricle assist device (VAD) implanted, which will be utilized as a bridge for stem cell attachment. The patient's bone marrow is harvested from the hip bone where it is then directly injected into the site during the (VAD) surgical procedure. Once the patient has been equipped with the VAD leading to the heart, 20 to 40 different injections will be conducted into the heart depending on the patient's weight, each containing 30-40 million stem cells mixed with blood plasma. A negative control containing only blood plasma is used to allow the researchers to observe what effects the stem cells actually have on the cellular structures surrounding the heart (Kormos, 2005).

Use of Stem Cells to Treat Parkinson's Disease

A group of doctors in Israel have discovered a way to differentiate ES cells into the brain neuronal cells that Parkinson's patients have lost (Ben-Hur et al., 2004). Parkinson's patients lose cells in an area of the brain termed the substantia nigra that is involved in dopamine production. Without the production of this key dopamine neurotransmitter, patients show diminished neuroskeletal coordination, and a difficulty initiating movement. The scientists utilized human ES cells to treat a rat model for this disease. This was actually the first time that these types of stem cells had been used effectively to treat an animal with this disease. The human ES cells transplanted into the rodent brains allowed them to show behavioral improvements. They stopped turning continuously in circles, and when dragged across a surface they began to be able to side step, where before treatment these rats lacked these specific motor skills. When the rats were tested at autopsy, results showed that the transplanted ES cells had differentiated into neuronal cells producing dopamine.

One problem that arose in this (Ben-Hur et al., 2004) study was that some of the transplanted ES cells did not fully proliferate and differentiate into dopamine-producing cells. This can be very dangerous to the patient, possibly causing death and or brain damage to that region. Dr. Benjamin Reubinoff who is the leader of the Israeli group of doctors says that such results are very promising for future use in human patients, yet there are still too many questions about the treatment that need to be answered before this type of treatment can be conducted in humans. This type of treatment in humans may also be more difficult than in rats because of difficulties that accompany the production of clinical grade stem cells which must be free from

viruses, and also to conduct longer trials to make sure that cancerous tumors do not form from treatment (Ryan, 2004).

Patients with Parkinson's disease have also received treatment through receiving their own adult neural stem cells (NSCs), which were cultured into dopamine producing neurons. These modified NSCs were then injected into patient's the left side of the brain which controls the right side of the body affected most strongly in this patient. The patient in this study is known as Dr. Dennis Turner who was treated by Dr. Levesque. Dr. Turner testified in front of the US senate committee on his progress and recovery from surgery which showed positive results. He states that soon after the cells were injected into his brain, his Parkinson's symptoms gradually began to decline until the point where normal function was recovered on the right side. The patient was able to do all the activities of a normal healthy human being whom never acquired Parkinson's (Stem Cell Therapy, 2004). Dr. Turner indicated during his testimony to the U.S. Senate Committee, "Since being diagnosed with Parkinson's disease my condition had slowly, but continuously worsened. I can't say with certainty what my condition would have become if Dr. Levesque had not used my own adult stem cells to treat me. But I have no doubt that because of this treatment I've enjoyed five years of quality life that I feared had passed me by" (Dr. Turner, 2004).

In a similar study with Parkinson's, instead of the patients receiving adult stem cells, they received an injection of a protein known as glial cell line derived neurotrophic factor (GDNF). This protein is known to stimulate the patient's own adult stem cells in the areas of the brain affected by Parkinson's. The study was closely observed for about a year, and all five of the patients that had this procedure showed about a 60% increase in movement and coordination,

as well as a lessened severity of the symptoms they were exhibiting one year before (Stem Cell Therapy, 2004).

A similar study to Dr. Turner's was performed on monkeys in Japan at Kyoto University. Researchers used adult monkey stem cells that generated dopamine releasing neurons. These neurons were then transplanted into the brains of monkeys suffering from Parkinson's. The results showed a full recovery from the symptoms. Instead of injection at numerous sites like in Dr. Turner's case, transplantation of these cells was performed directly to the areas of the brain that were affected. This study shows that under certain conditions, adult stem cells can be differentiated into healthy neuronal cells, eventually reversing the effects of the disease (Stem Cell Therapy, 2004).

Use of Stem Cells for Spinal Cord Injuries

Human embryonic stem cells (hES cells) were recently used on the campus of UC Irvine to improve the mobility of rats suffering spinal cord injuries. Researchers found hES cells to be adequate substitutes to older or damaged spinal cord tissue through differentiation. Hans Keirstead and his colleagues discovered a way to use hES cells to restore neuron insulation in rats treated one week after a spinal injury was induced. The UC Irvine team created a way for hES cells to differentiate into oligodendrocytes which form myelin sheaths that coat the neurons and insulate them. The treatment led to a full recovery of the rat's motor skills. The oligodendrocytes wrapped around the damaged neurons and slowly formed the myelin sheath that originally protected the area, eventually leading to healthy neuronal activity and increased motor skills from the rats.

This same procedure was tested on rat's injured for approximately 10 months, however the results were the opposite showing the technique only works if it is administered shortly after injury (Stem Cell Treatment, 2005). The myelin never formed because of the presence of scar tissue that had formed (Stem Cell Treatment, 2005).

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CHAPTER-3: STEM CELL ETHICS

So far we have discussed the various types of stem cells, ranging from pluripotent ES cells, to ES cells derived from parthenote eggs, to ASCs, to stem cells produced by somatic cell nuclear transfer, to stem cells derived from adult fibroblasts induced to de-differentiate into iPS cells. We have also discussed the incredible potentials they have to treat various diseases and make breakthroughs in the field of molecular science. Although these cells could be of very high value to society, some types come with strong ethical concerns, particularly those that involve the destruction of an embryo, or that involve cloning. The purpose of this chapter is to discuss some of the ethical concerns surrounding this controversial topic.

The major ethical conflict with stem cells comes primarily from the use of ES cells, because many people believe the embryo used to obtain the valuable cells is a precursor to a human being. Thus the discussion of ES cells revolves around the definition of human life, the status of the human embryo, and especially when personhood begins and ends. For most people, their own religions teach them important values in life, and it is notable that each religion emphasizes its own beliefs of how valuable human life is at different stages, and how far one must go to protect it. Most people have faith and trust in their own religion, and they rely on it to help them decide about stem cell research. The ethical debate on the use of ES cells is relatively complex, and even leaders within one religion disagree on the topic.

From the outset it should be stated that none of the five major world religions as discussed below are against working with adult stem cells. These ASCs do not destroy an embryo to obtain them, and are provided with adult donor consent. Thus, most of this chapter will focus on the ethics of ES cells, parthenotes, SCNT cells, and iES cells.

Christianity and Embryonic Stem Cells

Christianity is one of the most followed major world religions. Approximately 33% of the world population follows Christian beliefs, making it a widespread and well-followed religion (Major Religions...2005). In turn, the Christian religion has a diverse level of complexity; it is divided up into the major sects [Roman] Catholic and Protestant, with the Protestant sect further divided into separate churches such as South Baptist Convention and American Presbyterian Church. Despite the various denominations, most sects follow a form of general Christian belief, and believe life is defined as beginning at conception, when the sperm cell fertilizes the egg cell. Thus, most Christians firmly support the preservation of life.

The Roman Catholic Church has had quite a varied historical past. In past traditions, by order of the disciples Augustine of Hippo and Thomas Aquinas, the church maintained for centuries the adopted Aristotelian view that life begins 40 days after conception, the time of ensoulment. Such a view would have allowed 5-6 day old embryos to be used to derive ES cells. But after 1869, the Catholic Church discredited this doctrine, and established a newer view requiring that human life be protected at the earliest possible time, which is taken to be at conception” (National Academy Press, 2001). This view was based on a supplanting notion that “we cannot know with certainty when human life has really become established” (National Academy Press, 2001). As Roman Catholic Christianity is a conservative sect compared to most others, most Catholics are against ES cell research, and the Vatican who is charge of leading the beliefs of the Catholic Church defines life as beginning at conception, and has issued a strong statement condemning ES cell research for any purpose (Chamany, 2004). In addition, Roman Catholics consider contraception and abortion before the 40th day of gestation as a sinful but

nonhomicidal act, and due to the belief that early embryos should be given dignity, theologians find it an immoral act to buy or sell embryos that are used in research (Chamany, 2004).

In contrast, within Protestant Christian sects, there actually exist diverse views on ESC research, and a majority does not support the strict Catholic stance that human life must be protected at all times. Some conservative protestant groups reject the use of embryos for research as the Roman Catholic Church, but most Protestants accept ESC research (National Academy Press, 2001), to a limited extent. For instance, the Eastern Orthodox Church defines life as beginning at conception, yet it supports therapeutic applications using only existing stem cell lines without deriving any new additional embryos (National Academy Press, 2001). Those who follow the American Presbyterian Church approve of ES cell research if the goals are to use them for medicinal purposes, and so long as a cure cannot be reached in any other manner. A majority of nonconservative Protestants approve of research on embryos within a limited fifteen-day window from initial fertilization, and that cannot be used for reproductive purposes (General Positions...2006).

Judaism and Embryonic Stem Cells

Judaism, one of the oldest known religions, is currently practiced among fourteen million people worldwide, or a surprisingly 0.22% of the world population (Major Religions...2005). Like Christianity and Islam (the latter of which will be discussed later), Judaism is an Abrahamic religion following by adhering monotheism, but its own beliefs on moral and ethical statuses on life differ with other conservative religions. Followers of Judaism follow the way of the Torah, or the holy manuscript of the Jewish community. Rabbis Elliot Dorff and Moshe Dovid Tendler explained that in Jewish law and tradition, the embryo has no moral status until 40 days after

implantation, which would allow 5-6 day old blastocysts to be researched. Yet, once the embryo has implanted in its mother's womb, the child is viewed as a part of its mother's body and is considered to be alive, although its *own* life is believed to begin only when the child is born. In terms of ES cell research and Judaism, eggs and sperm mixed together in a petri dish have no legal status, because they will never implant in a woman's womb and become part of a true human being (National Academy Press, 2001).

Furthermore, Jews are responsible to make the best out of the life they gain from God, and must abide by the task of healing through their duty to save life (National Academy Press, 2001). Thus Jews believe they must rely on ways they feel would be righteous with respect to their moral beliefs, to fight disease and create cures. Although some laws within Judaism prevent researchers from going overboard experimenting with too many embryos, Jewish sects do support ES cell research to a more liberal extent than Christianity. It can be inferred that Jews mandate the use of only excess IVF embryos in stem cell research (Chamany, 2004).

Islam and Embryonic Stem Cells

Islam is the world's second most followed major religion, with about 1.5 billion people, or 21% of the world population, following Islamic culture and beliefs. Sunni and Shi'ite Muslims constitute the two major sects, with a third minor sect constituting small groups such as the Sufis, Druze, and Ahmadiyya (Major Religions...2005). Muslim faith is based on the teachings of the holy Islamic book the Koran and the ways of the Prophet Mohammad, interpreted by way of the Shari'ah (Chamany, 2004). According to Muslim tradition, and emphasized by legal literature, a human embryo has no legal or moral status until it has developed into a fetus at the end of the fourth month of pregnancy, or about 120 days. Muslim religious leaders believe that

this is the time when ensoulment, or the time when the embryo has become a person, has officially taken place. Thus, it can be inferred that Muslims support ES cell research, as long as the embryo is made and sustained in an environment different from the mother's womb, like the laboratory, in which case the embryo does not gain the status of a human being.

Similar to Judaism, the holy book of Islam does teach its disciples to control themselves and embrace values important in life. For instance, Islamic law strongly emphasizes spousal love and lineage, as well as spiritual connections. It also emphasizes the importance of establishing a child's true lineage and inheritance rights, with no immoral action taken to disrupt gene flow. Thus by way of Muslim religious law, ES cell research is carefully regulated and limited for the convenience and consideration of especially donors. And therapeutic cloning is tolerated more, compared to reproductive cloning.

Buddhism, Hinduism, and Embryonic Stem Cells

About 376 million people, or about 6% of the world's population, follow Buddhism, another of the world's major religions (Major Religions...2005). Compared to the monotheistic religions (Christianity, Judaism, and Islam), Buddhism is a polytheistic religion, where there is a belief in many gods. The philosophy Buddhists follow is based on the teachings of Siddhartha Gautama, the founder of this religion. Those who follow Buddhism emphasize the power of healing, as well as the central virtues of knowledge and compassion, so they welcome the great development of curing agents which help alleviate human suffering (Keown, 2001). However, Buddhists believe in the philosophical concept of *ahimsa*, or nonviolence, which in turn leads them to the belief in the prohibition of death and injury to living organisms. In addition, they

believe, like Hinduism, that individual life begins at conception and is entitled to the same moral respect as an adult human being (Keown, 2001).

As a result, most Buddhists are against using ES cells created from surplus unwanted or IVF embryos, or even from SCNT human embryos created for research purposes, as this involves the intentional destruction of human life, which they find as an immoral act. As for adult stem cells, Buddhists encourage their use, since through the process of obtaining them, no human being is significantly harmed. Followers of Buddhism encourage the gathering and research of stem cells obtained from aborted fetuses, provided the fetuses were already deceased by some developmental failure or they had to be removed if the mother was in some sort of danger at the same. This they would consider moral, but they would consider it immoral to harvest stem cells from a fetus or embryo, if it was aborted intentionally. For now there really exists a teetering diversity of Buddhist opinion on how ES cells should be regarded, as Buddhists do not rely on a central authority to pronounce on these ethical dilemmas (Keown, 2001), and it is obvious that Buddhists find it hard to really deal with ES technology.

Hinduism is another major religion, practiced by about 14% of the world population. Much like in Buddhist philosophy, traditional Hindu beliefs believe that conception is the beginning of a soul's rebirth from a previous life (when personhood may begin). Hindus, like Buddhists, find abortion a denouncing procedure, as they believe that the fetus has a right to live. They also believe by way of Hindu doctrine that it is not immoral to perform stem cell research on embryos created in an IVF clinic, so long as the embryos are not implanted.

Non-Religious Viewpoints of Stem Cell Ethics

It is evident from our discussion so far, that in view of religion, human life is greatly valued and different moral guidelines based on thoughtful belief are in effect for each religion. Although religion certainly has a major say in individual beliefs, some people have their own views on what they feel would be just and appropriate to society. For instance, some individuals would find (based on their own non-religious beliefs) that it is permissible to derive new ES cell lines from “excess” IVF embryos produced for reproductive purposes, so long as they are really no longer needed for reproductive purposes, and so long as the donors consent. In the case of embryo discard, some individuals might even consider it immoral to discard them without trying to save human lives by extracting ES cells. With current ES cell technology, obtaining good quality ES cell lines is a tough process, so having a larger numbers of IVF embryo donors would help improve the overall quality of ES cells for therapy.

The debate behind using excess 5-6 day old IVF embryos for research, that have no developed nervous system, no brain, no eyes, no limbs, no heart, etc., pales in view of the debate to use much older fetal tissue donations where some claim “unborn human beings are harvested for cells they might provide to another human being” (Wright, 1999). Here the debate focuses on using aborted fetuses to provide tissue, and which types of abortion are allowed (elective abortions, spontaneous abortions, or abortions to save the life of the mother)?

Parthenote and Somatic Cell Nuclear Transfer Ethics

As discussed in Chapter-1, parthenogenesis is a possible alternative to obtaining ES cells from a fertilized embryo. This process involves the self-fertilization and stimulation of a haploid ovum *in vitro* to reach a blastocyst stage where pluripotent-like stem cells can be obtained, but

the embryo is not capable of any further division. Although parthenotes cannot become human beings, to most religions parthenogenesis comes with impractical problems. Based on recent experiments conducted on parthenotes, only a few ES cell lines have been established through the use of large quantities of eggs. As a result, parthenotes do not yet provide a reasonably efficient means to obtain ES cells. In addition, since the eggs required for this procedure come from women, moral dilemmas arise concerning collecting eggs from women's ovaries for therapeutic purposes (Kiessling, 2005).

Somatic Cell Nuclear Transfer, or SCNT, has been described as a technique used to create a line of ES cell-like cells that are genetically identical to the original donor. It involves the transfer of a donor's somatic cell's genetic material into an enucleated egg, which is then stimulated to divide to the blastocyst stage from which ES-celllike cells are obtained. So far it has been shown that this procedure works in mice, but not yet in humans. The ES cells carry the same genome as those of the original donor; thus a patient could in theory be treated with his own ES cells. SCNT is a type of therapeutic cloning. Despite the valuable practicality that may come with SCNT, SCNT has strong ethical opposition. Some people find the termination of the blastocyst after removal of the ICM cell mass a morally and ethically objectionable matter. SCNT could also be applied to reproductive cloning, where the blastocyst formed from SCNT would be implanted in the womb to develop to full term to become a clone instead of being destroyed. Thus, most religious groups and governments find this process worthy to take a stand against, and especially find it immoral and unnatural for a person to be created without two parents. Because of these major probable concerns, most governments have laws in effect banning [human] SCNT technology, which shall be further discussed in Chapter-4.

Ethics Behind iPS Cells

As discussed in Chapter-1, induced pluripotent (iPS) stem cells represent another possible alternative to obtaining ES-like cells without having to destroy an embryo. The process involves obtaining a number of convenient adult somatic cells, such as skin cells, and reprogramming them so that they are induced to an ES cell-like state. This reprogramming is done by means of inserting copies of combinations of three or four genes encoding transcription factor proteins into the cells' nuclei, with the aid of pragmatic retroviruses. It can be noted that no embryo is formed or destroyed through this procedure, and no [donor] eggs are required to obtain pluripotent cells, thus the production of iPS cells does not raise as many critical concerns as ES cells, parthenotes, or SCNT. The production of iPS cells is actually an inefficient procedure, only 5% of the treated cells are fully reprogrammed (Cyranoski, 2008), but the reprogrammed cells can be amplified.

Although iPS cells in theory can be created genetically identical to a patient to avoid immunorejection, for now it is impractical to produce large numbers of patient-specific stem cell lines for everyone, so for now iPS therapies would focus on providing iPS cells with as close an immunological match as possible. The genetic engineering technique (transfection) used to make iPS cells is considered relatively easy according to Dr. Shinya Yamanaka, "...many people can do this – and without telling anybody" (Cyranoski, 2008). But it is expensive, so the rich could pay to have an iPS line generated specific to them (Cyranoski, 2008), raising a different type of ethical concern. In addition, some might use iPS cells to derive gametes, which may be used in an *in vitro* fertilization procedure; this to most people would be considered strange and potentially dangerous, allowing human reproductive cloning, a currently illegal procedure.

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Chapter 4: Stem Cell Legalities

Stem cell research is a very young experimental field where many questions arise pertaining to the ethics of where these cells originate from. As is typical for most controversial technologies, regulations have been laid down by federal and state legislatures to govern this emerging field. However, questions arise as to whether these regulations hinder stem cell research from achieving its true potential as a life saving treatment for injuries and diseases.

U.S. Federal Funding for ES Cells

Federally funded research involving the use of human embryonic stem cells (hES's) has been hindered in the U.S. because of philosophical and political views surrounding where these cells are obtained. As mentioned in earlier chapters, ES cells are obtained from the inner cell mass of a 5-6 day old blastocyst created by *in vitro* fertilization. Harvesting the ES cells destroys the blastocyst which if implanted into a uterus had the potential to become a human being, thus creating the ethical quagmire. U.S. scientists are finding it hard to continue such research due to so many uncertainties and laws surrounding the field. Many of the scientists that propose ES research on different diseases or injury are either shut down due to lack of funds, or their research is declared illegal and unethical. Keith Yamamoto who is Vice Dean for Research at the University of California School of Medicine states that “ It’s too much work to put together a research proposal only to find out it’s going to be made illegal, or that there will be a four year moratorium proposed” (Agnew, 2003).

In 1993, while Bill Clinton was in office, an act called the National Institutes of Health Revitalization Act was constructed by Clinton and Congress approving the funding for human

embryo research. NIH gathered a group of advisors, including scientists, ethicists, public policy experts, and patient advocates, whose purpose was to make recommendations. One of the NIH's recommendations was to allow spare human embryos to be used to obtain ES cells. In 1995, congress found that federal funding for the creation and/or destruction of human embryos was unethical and so it was banned in the Dickey-Wicker Amendment. This amendment was named after the congressmen who developed the amendment, Jay Dickey a republican from Arkansas, and Roger Wicker a republican from Mississippi (Dunn, 2005).

In early January of 1999, Harriet Rabb concluded that since human embryonic stem cells are not actually a human embryo, the Dickey-Wicker amendment does not include these types, so it is possible to utilize ES cells. The then new Clinton administration guidelines implemented during August of 2000 allowed research with ES cells that privately funded scientists had already taken from spare embryos that were set up for destruction at fertility clinics. The Clinton administration truly opened the door for federal funding of such research, until it was shut down by President Bush in 2001 (Dunn, 2005).

In 2001, a law was passed by President George Bush stating that scientists receiving federal funding for research may only use ES cells that existed before August 9, 2001 (Agnew, 2003). Although initially there appeared to be approximately 60 ES cell lines meeting this pre-2001 criterion, further testing revealed in actuality there is only about 9 unique ES cell lines left. This is apparently also scaring scientists away from performing research since not enough of these stem cells are available.

President Bush also feels strongly against the idea of human cloning, and he urges congress to ban such ideas and research. Legislation to ban the use of somatic cell nuclear transfer (SCNT) (the technique utilized to clone Dolly the sheep) was introduced to the U.S.

senate and the House of Representatives. Nearly one hundred co-sponsors were attracted to this house bill within only a few days of its circulation (Agnew, 2003). However, another bill was also introduced to the senate for debate that would allow SCNT for therapeutic purposes only, and would ban human reproductive cloning (Agnew, 2003). In this therapeutic process, the nucleus from a patient's fibroblast skin cell would be introduced into an enucleated egg, then the egg is grown *in vitro* to the blastocyst stage from which ES cells can be derived that are genetically identical to the patient. Therapeutic cloning would allow ES cells to be created that are specific for a patient (not immuno-rejected). Essentially, the person whom needs treatment would allow the researcher to utilize his or her own somatic cells from which ES cells could be grown. Transplanting such cells would lead to no immunological problems since the cells were their own from the beginning. SCNT has been successfully achieved with some animal species, but not yet with humans. It is important to note that both types of SCNT (therapeutic and reproductive) involve embryo destruction.

Proponents for both sides of the argument have currently created a stalemate in the Senate where neither side can officially overrule the other. However, even if a stem cell bill passed the Senate, the House would more than likely disagree. And even if the bill made it through Congress, President Bush would likely veto the bill (Agnew, 2003). The House of Representatives has twice prohibited all forms of cloning in 2001 and again in 2003 (Dunn, 2005). U.S. Senator Hatch argued for the use of SCNT saying, "Even those who believe that life begins at conception, even if the union of sperm and egg takes place in the lab, need to consider carefully whether the joinder of an enucleated egg with a somatic cell nucleus, accompanied by chemical or electrical stimulation, should fairly be thought of as the same process as conception" (Agnew, 2003).

During June 2004, 58 US senators delivered a letter to President Bush urging him to allow more of the available ES cell lines to be federally funded for research. This group included 14 republicans as well as two well known abortion opponents. In March 2005, the House of Representatives drafted a bill which would allow federal funding of research on ES cells, however Bush vetoed the legislation (Dunn, 2005).

Individual States and Stem Cells

Numerous states, including New Jersey, Massachusetts, and California have passed laws allowing state funds to be used to support ES cell research. Some of the larger educational institutions have created stem cell institutes that use money received from state bonds. These institutions include Stanford, UCSF, and the University of Massachusetts Medical Center (Worcester) (Agnew, 2003).

One of the most prominent stem cell states in the US is California, where the people have approved a \$3 billion dollar bond funding stem cell research to be utilized over a 10 year period. The California legislation also passed proposition 71 where California became the first state to appropriate money for this type of research. Approximately 11% of the US's biotech scientists are currently employed in research facilities in California (Stem Cell Legislation, 2005). The California law allows the use of human ES cells and SCNT embryos for research, but the cloned embryos cannot be used reproductively. California was the first state in the US to pass such a law.

In 2004, New Jersey established a state funded stem cell research facility (Stem Cell Legislation, 2005). Later on that year, proposition 71 was passed which allowed \$3 billion

dollars to be dispersed over a 10 year period to the stem cell research facilities in California (Stem Cell Legislation, 2005).

In Massachusetts, legislation was introduced in 2005 to allow state funds to support ES research, but then governor Mitt Romney vetoed the bill twice (Dunn, 2005). Under Governor Patrick, the Massachusetts legislature approved a Bio-initiatives bill for about one billion dollars to fund stem cell research, which passed both the state senate and house in 2007, and the funds were released in 2008 (Dunn, 2005).

In Maine, the law prohibits the use of *in vitro* fertilized embryos post implantation for research. In New Hampshire, it is prohibited to use unfrozen fertilized embryos after 14 days (although this allows the use of 5-6 day old blastocysts for obtaining ES cells). On the other hand, in New York stem cell research is greatly encouraged. In January of 2006, the state decided to fund the New York State Institute for Stem Cell Research and Regenerative Medicine. A total of about \$300 million will be dispersed to the research center, some of it going towards ES cell research (Stem Cell Legislation, 2005).

International Stem Cell Legislation

The stem cell legislation in different countries (see Figure-1) can be loosely divided into conservative (yellow), moderate (light brown), or flexible (dark brown). Examples of conservative countries include the U.S., Argentina, Africa, Italy, and Germany. Moderate countries include Canada, Brazil, and Spain. Countries with flexible stem cell policies include England, Sweden, Finland, India, China, and Australia.

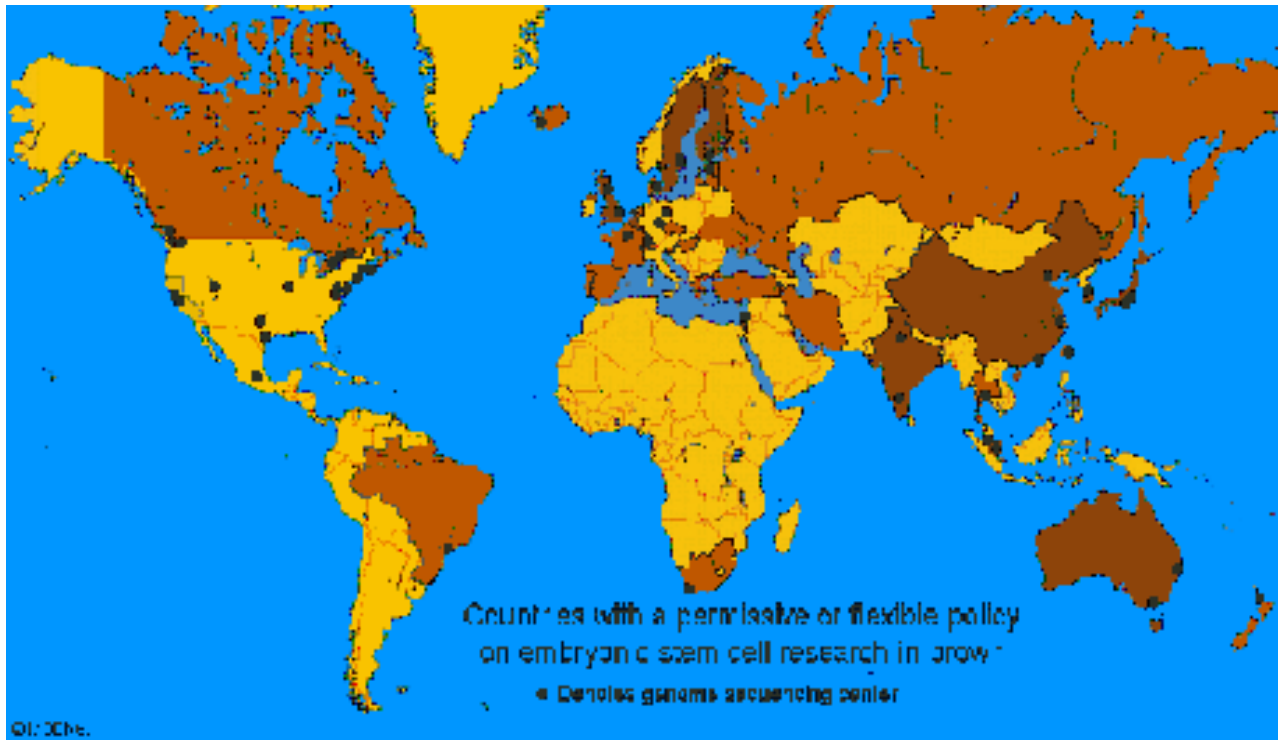


Figure 1: World Diagram Showing Stem Cell Legislations. This diagram shows various countries labeled for their stem cell laws as being conservative (yellow), moderate (light brown), or flexible (dark brown) (Hoffman, 2005).

In South Korea, a corporation known as the World Stem Cell Foundation, led by the south Korean researcher who claimed to be the first to clone a human embryo for the creation of stem cells (and who later admitted to fraud) has begun producing approximately 100 new cell lines annually and to make them available to scientists, mainly those in the US that are struggling because of limited federal funding. This is a way to go around the policies laid down by President Bush and to acquire these new stem cell lines from overseas (Kaplan, 2005).

In February of 2002, the German parliament voted to allowing the import of human ES cells into the country. This would be allowed only under close government supervision. The current German law bans all research on human embryos, allowing IVF only for reproductive purposes. The German parliament also passed a law that stated that researchers can only use

stem cells that have already been created and new cell lines cannot be created within this country (Kim, 2002).

The French are also fighting through ethical issues on whether to allow the use of imported stem cells. A 1994 French law states that research on human embryos is prohibited. Sweden on the other hand, one of the world leaders in stem cell research, recently received support by two governmental ministers urging the cloning of human embryos for therapeutic purposes. Dr. Jochen Taupitz who is a member of Germany's National Ethics Council states, "In a European comparison, Germany has some of the strictest laws, so even with this resolution we are pretty isolated in Europe. In all countries there's a fierce debate. There's no country in Europe where there is a unanimous opinion on this issue" (Kim, 2002).

Germany is such a large European player when it comes to stem cell research that as long as the regulations for such experimentation hold strong, the rest of the surrounding countries will more than likely continue to follow suit. Only time will tell what affect this power will have on other smaller countries might have, such as Austria, Portugal, and Ireland (Davies, 2003).

Sweden, as stated earlier, is one of the leading countries currently performing research on ES cells. Sweden's stem cell community is backed by strong moral support from it's occupants, as well as reliable government funding and a great bioethical environment. There are approximately 30 plus research groups found in Sweden, and approximately 300 scientists working at numerous institutions around the country. Sweden is the only country that allows stem cells to be extracted from embryos that are no longer being utilized. With such freedoms, Sweden is one of the most successful biomedical science and research locations in the world. In March of 2002, Sweden joined with the US to create additional funding in the ballpark of about \$7.5 million dollars to benefit stem cell research on Swedish grounds. The Secretary General of

the Medicine section at the Swedish Research Council states, “The entire stem cell field is on the threshold of development. These grants are extremely important for advancing research so that we can identify areas with the greatest potential. Today, we hope that stem cells will eventually be able to cure a number of diseases, but before we can say if and when this will be possible, much intensive research is needed” (Sweden Stem Cell Success, 2002).

Chapter Conclusion

As one can see, a great deal of ethical/moral decisions must be made by many people on the topic of stem cell research, and these decisions affect state and federal laws. The key to this situation is that people must begin to understand the benefits of such research and the medical advances that await, as well as the ongoing research to create alternative sources for ES cells. We have the key to the future of regenerative medicine, but we must cautiously use this gift and not abuse it. People must understand that in some situations, using adult stem cells does not involve the killing of a baby fetus or the destruction of a life. And even for ES cells, the extra IVF embryos are already slated for destruction, so perhaps they could be used instead to try to save lives. In the end, this research is pro life, and can only benefit our chances at long, disease free, healthy lives. Before one makes a judgment on the subject I urge them to think carefully and to understand what stem cell research can do to modern medicine and the positive changes it can have on many people’s lives that are suffering and need these medical breakthroughs.

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CONCLUSIONS

The purpose of this IQP was to investigate stem cell technology, examining a variety of stem cell types, as well as the ethics and legalities surrounding their research. We conclude that different from what is commonly thought, not all stem cells are alike, and not all of them require the destruction of an embryo. Embryonic stem (ES) cells have the greatest medical potentials, but the greatest ethical and legal concerns. Adult stem cells (ASCs) are more difficult to grow, and have less differentiation potential, usually restricted to forming the main tissue from which they were obtained. We support the development of new alternative technologies, such as iPS cells, that avoid the destruction of embryos to obtain ES cells. We conclude that of the five major world religions, Christianity (especially Catholics) and Buddhism oppose ES cell research, while the 3 others are somewhat supportive of it. All five support adult stem cell research. Legal restrictions placed on stem cell research by countries such as the U.S. and Germany have hindered research into ES cells relative to other more progressive countries.