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STEM CELLS

An Interactive Qualifying Project Report

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PROJECT ABSTRACT

Stem cells are able to regenerate specific tissues and provide immense potential medicinal benefits. Adult stem cells have already been used to save innumerable lives while embryonic stem cells obtained from embryos have encountered many ethical constraints and have not entered clinical trials yet. The purpose of this IQP was to investigate this controversial topic, describe the types, functions, and clinical applications of stem cells, as well as focusing on their impact on society through ethical and legal issues.

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EXECUTIVE SUMMARY

In this IQP, the primary objective was to cover and expound upon the whirlwind of controversy that current stem cell research is stirring up. To do this, the project was divided into different chapters to present these aspects in a logical manner. Firstly, each type of stem cell and its biological source was accounted for. With the information to differentiate between these categories, future and current applications were covered in Chapter-2. Next, the reader is presented with both pro and anti stem cell arguments in accordance with religious, moral, and ethical guidelines in Chapter-3. Lastly, the legality of stem cell research was compared in different countries and between states of the US. Together all this information presented was used to draw a knowledgeable conclusion on stem cells, on which types should have a continuing place in medicine to benefit human kind and society.

The first chapter describes what stem cells are and where they come from. Stem cells are immortal, non-specific cells that have the ability to become many specialized cell types. These cells are classified into 3 categories: embryonic, adult, and umbilical. The earlier in development a stem cell is harvested the more potency it has. A newly fertilized egg is considered totipotent. If the egg is allowed to grow to a morula (6-8) cells the cells remain totipotent. Such cells are able to regenerate virtually any tissue in the body. If the cells grow for 5-6 more days to blastocyst stage, the embryonic stem (ES) cells of the inner cell mass become pluripotent. The majority of cells in the body can be regenerated by these cells. Hematopoietic stem cells (HSCs) are present in umbilical cord and bone marrow, but are only multipotent, able to develop into a limited type of cells (i.e various kinds of blood cells). Adult stem cells can be pluripotent (i.e. bone marrow HSCs) or unipotent (i.e. neuronal stem cells). The later in biological development a

stem cell is found, the fewer kinds of cells it can become. In the lab an artificially produced blastocyst (produced by treating unfertilized eggs with chemicals) has served as a new source of primate ES cells, but not human cells yet. Mammailan parthenotes can not divide past the blastocyst stage, but their ES cells can be harvested providing a less controversial source of ES cells.

The next chapter explains the difference between already successful human and animal stem cell treatments. Additionally, it clarifies what is currently applicable versus what remains pie in the sky. Embryonic stem cells do have the most medical potential, but many have moral hang-ups in their use. Human trials will inevitably occur though. Animal studies with ES cells have shown stunning results, but this is still a far cry from actual human application. Although human ES clinical trials await results, stunning successes have already been achieved with adult stem cells. Parthenote-derived ES cells will eventually become a viable option, when the technology is perfected. Each stem cell type will contribute to healing a myriad of human illnesses.

In the third chapter, the ethical use of stem cell use in regenerative medicine is documented. The problem comes with ES cells that are taken from a blastocyst, and usually results in an embryo's destruction. Whether it is murder is quite murky. A majority of the world's major religions allow ES stem cell research, as long as the embryo has not developed past the point where it has a 'soul'. Religious law is up to interpretation and is sometimes not supported by all believers. All four of the world's major religions support the use of umbilical, adult and parthenote stem cells, so long as they are used to support the "common good". These stem cells are isolated from tissues that can not become a human being, so their use is not seen as possible infanticide. It's also notable that animal sacrifice/suffering and abortion are allowed, but

using ES cells (that can't feel pain) in humans isn't. Who will foot the bill for stem cell treatments and what are acceptable applications was considered. The author is against stem cell use for cosmetic purposes, especially if paid by taxpayer money. The author also agrees that frozen IVF embryos slated for discard by the parents should be the preferred method of obtaining embryos if parthenotes are not available.

Lastly, the laws related to world wide stem cell permissiveness are addressed. Since ES cells are highly controversial, laws regulating their use vary substantially. In the United States federal money for human ES cell research on any cells derived from blastocysts after 9:00pm on 9 August 2001 was banned (Holden and Vogel, 2002). Only embryos that had already been destroyed to create a cell line, could be used for research. California, Connecticut, New Jersey, Massachusetts and Pennsylvania have either lessened restrictions or provided state money for their own ES cell research. This has not been enough, so due to the restrictions in the United States many scientists have fled to England, Sweden, Singapore, Germany, Japan, or China to research ES cells. South Korea has been pioneering new stem cell work, which raises the bar for countries with more strict polices to relax them. In some countries the science and technology, culture, ethics, and government are all compatible to further research. These countries still affect the world of science and don't remain controversy free in the global context though. In others, government or culture only imposes a minimal interference, while others put large blockage to progress. Prudence is a good thing with new technology, but common sense needs to be observed as well.

The ability to understand what stem cells are, their medical potential, ethical issues and world wide legality demystifies much of the controversy surrounding stem cells. Ultimately, stem cells do not feel pain, and have shown to be tremendous miracle cures. ES cells are on the

forefront of stem cell technology, and they will be utilized, if not in the US, in another willing country. As long as stem cells are used for human benefit, there is little real controversy to this author over their use in regenerative treatment. Another era of medicine has begun.

PROJECT OBJECTIVE

The main goal of this IQP was to explain and present the highly debated issues involving stem cell research, and to explore their effects on society. A detailed background is given on the types and sources of stem cells in order to help the reader understand where the controversy originates. With this framework in place, the limitless applications of stem cells for use in regenerative medicine are described. In view of stem cell healing potentials; religious, moral, ethical and legal concerns have been detailed. Finally, based on this research, an informed decision was made on which stem cell types will have a place in society to change human kind for the better.

CHAPTER-1: STEM CELL TYPES AND SOURCES

What are ***stem cells***? Where do they come from? How can we use them? What do we use/hope to use them for? What's the controversy surrounding them all about? What are the current laws regulating their use, and will those laws hinder stem cell researchers?

All of these questions will be addressed in this IQP, but before we can get to the controversial stances on the obtaining of the cells, uses and applications, and the current laws in place regarding their use in research, we must first understand what stem cells are, and where they come from. Stem cells are essentially immortal, undifferentiated cells that have the potential to develop into specialized cells, such as cartilage, blood, and bone. Since they are immortal, they can be used to generate cell lines that can be amplified to generate large amounts of cells for therapy. Also, due to their capability of differentiation, they can generate heart cells for someone possessing a damaged heart, brain cells for a Parkinson's or Alzheimer's patient, liver cells for a hepatitis patient, or nerve cells for spinal cord injuries.

Yet look in any dictionary, and you are bound to find several different definitions for these cells which can easily confuse the layperson. They are hard to explain and do not have one mspecific meaning or explanation, as such some dictionaries give more details about what they are and/or what they do than others. Look up "stem cells" in Taber's Cyclopedic Medical Dictionary and you will get a definition of "a cell which gives rise to a specific type of cell as in hematopoiesis". In this case they are referring to an adult hematopoietic stem cell (HSC). This type of stem cell has been used in bone marrow transplants for 30 years now to recreate a patient's blood system following radiation or chemotherapy. Cross reference it with Webster's New World Medical Dictionary and you get:

> One of the human body's master cells, with the ability to grow into any one of the body's 200 cell types. Stem cells are unspecialized (undifferentiated) cells that are characteristically of the same family type (lineage). They retain the ability to divide throughout life and give rise to cells that can become highly specialized and take the place of cells that die or are lost. Stem cells contribute to the body's ability to renew and repair its tissues. Unlike mature cells, which are permanently committed to their fate, stem cells can both renew themselves and create new cells of whatever tissue they belong to (and other tissues). Bone marrow stem cells, for example, are the most primitive cells in the marrow. From them all the various types of blood cells are descended. Bone marrow stem cell transfusions (or transplants) were originally given to replace various types of blood cells.

This New World Medical Dictionary explanation is considerably more detailed and precise than the one from Taber's, but look online and you might get something like:

> An unspecialized cell that gives rise to a specific specialized cell, such as a blood cell. (dictionary.com); Stem cells are primal, undifferentiated cells which have the unique potential to produce any kind of cell in the body. Medical researchers believe stem cells have the potential to change the face of human disease by being used to repair specific tissues or to grow organs. (wikipedia.org); Stem cells have the remarkable potential to develop into many different cell types in the body. Serving as a sort of repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. (nih.gov)

Stem Cell Potentials

One way to classify stem cells is on the basis of their potential to form other kinds of cells. These classifications include: the totipotent egg, the pleuripotent embryonic stem (ES) cell, multipotent stem cells, and unipotent stem cells. The totipotent egg (top of the diagram in Figure-1) is the newly fertilized egg that can develop into a complete embryo and therefore eventually a person. The pleuripotent ES cells (located in the middle of Figure-1) have the

ability to differentiate into a variety of tissues (i.e. blood, neurons, liver, pancreas) but cannot become an entire organism. These ES cells are obtained from the inner cell mass of a blastocyst about 5-6 days post-fertilization, thus their use often destroys a blastocyst possessing the potential to develop into a fetus. These are the cells scientists are most interested in because they hold the greatest potential for medicinal purposes (E-mail to the author from Dave Adams).

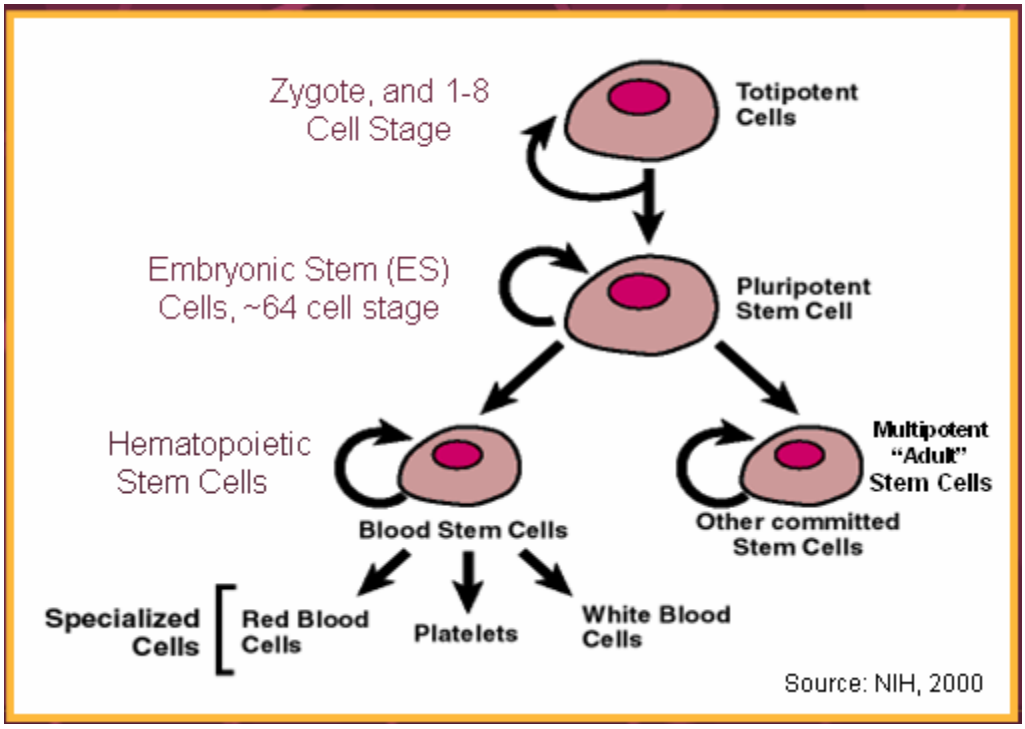


Figure-1: Stem Cell Potentials. This diagram shows the four main levels of stem cells based on their potential to make other kinds of cells (NIH, 2000).

Multipotent stem cells are found in adults (lower right of Figure-1), and can only generate a few different cell types (E-mail to Hillary Perkins from Dave Adams).
The hematopoietic stem cell (HSC) is one such cell. Since these cells exist in adults (HSCs are frequently obtained from bone marrow donors), there are relatively few ethical considerations than with ES cells. Lastly there are the unipotent stem cells (not shown in Figure-1) that primarily only possess the ability to generate a single type of cell. Neuronal stem cells are an

example of this category of cell, which have the ability to make neurons for treating neurodegenerative diseases like Parkinson's or Alzheimer's.

Adult Stem Cells

Another mode of classification for stem cells is through their source- whether they are obtained from adults or embryos. Adult stem cells are currently in use in humans for procedures such as bone marrow HSC transplants and umbilical cord HSC transplants. Although the cord cells are derived from the fetus, post-birth, the baby no longer needs it and it is usually discarded, so cord is frequently classified as an "adult" tissue. As a result, these HSCs are isolated from "adult" donors, meaning that no embryos are destroyed in the process, and there is generally very little controversy surrounding this type of stem cell. Figure-2 shows a picture of HSCs.

Multipotent and unipotent stem cells are the only two types of stem cells that are found in adults. Scientific evidence demonstrates the existence of hematopoietic, neuronal, and mesenchymal adult stem cells in mice and humans, but to date only the HSCs have been used for therapy in humans.

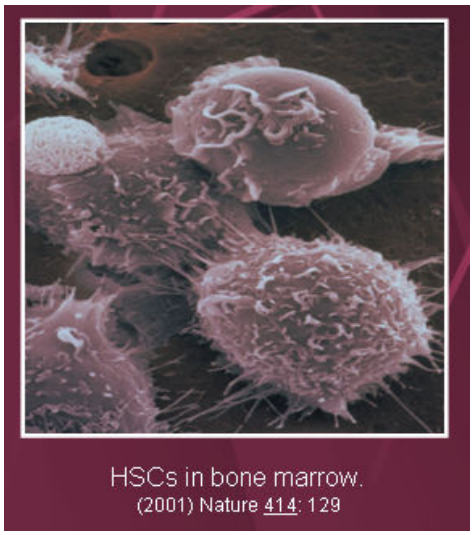


Figure-2: Picture of Hematopoietic Stem Cells in Bone Marrow.

Most adult stem cells are classified under the unipotent category of stem cells, with the exception of the multipotent hematopoietic stem cells. This is because they are already somewhat differentiated, and specialized for a given tissue type. Hematopoietic stem cells are harvested from adult bone marrow or umbilical cord, and produce all the different types of blood cells which is the reasoning for their multipotent stem cell classification. Neuronal stem cells produce neurons and glia, and form the fetal brain. Mesenchymal stem cells form into adult bone marrow and produce bone, muscle, tendons, and cartilage (Billiar et al, 2004).

The first adult stem cells to be found and identified were the HSCs. They were eventually discovered as a result of the testing done by Henri Becquerel and Marie Curie who discovered radiation. It has also been found, again through testing, that stem cells are abundant in both the developing brain and in two areas of the adult central nervous system (CNS): the hippocampus and the olfactory bulb. These stem cells do not replace themselves as efficiently as HSCs do, and therefore cannot be defined in the same manner, but these CNS stem cells can be grown easily in the lab (under the proper conditions) and differentiate into the neurons and non-neuronal cells of the CNS. The mesenchymal stem cells we know exist since the first bone marrow transplants proved to be successful.

Figure-3 shows the different cell types that stem cells can develop into and the paths that they take in their transitions into different cell types.

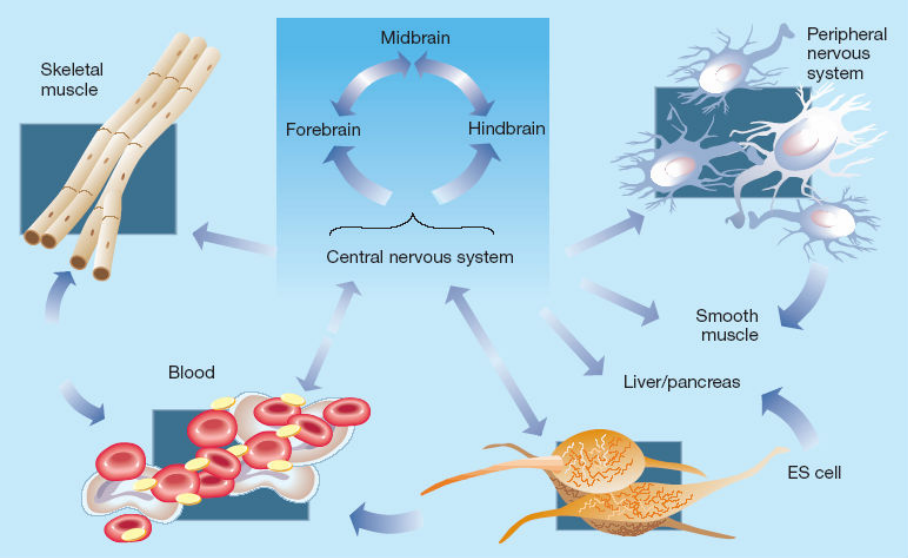


Figure 1 **Stem-cell transitions. At least in the lab, stem cells are not always restricted to one particular pathway of differentiation. For example, central nervous system (CNS) stem cells form the different cell types of the CNS, but can also differentiate into haematopoietic (blood) stem cells. Blood stem cells in turn form the different cell types found in blood, as shown here, but can also differentiate into skeletal muscle stem cells (which differentiate into skeletal muscle cells, pictured) and central nervous system cells. Embryonic stem (ES) cells are pluripotent, and contribute to all of the tissues of developing mammals. For simplicity, only a few of the stem-cell types that ES cells can produce are shown here.**

Figure 3- Diagram of Stem Cell Transitions (McKay, 2000).

Transdifferentation or Plasticity of Adult Stem Cells-

Another area that is currently being looked into with adult stem cells is whether or not they are capable of transdifferentiation which is also referred to as the plasticity of stem cells. Transdifferentiation is the process which "takes place when a non-stem cell transforms into a different type of cell, or when an already differentiated stem cell creates cells outside its already established differentiation" (Google, 2005). Transdifferentiation does occur in nature in special circumstances however, both natural and artificial transdifferentiation is a very rare occurrence.

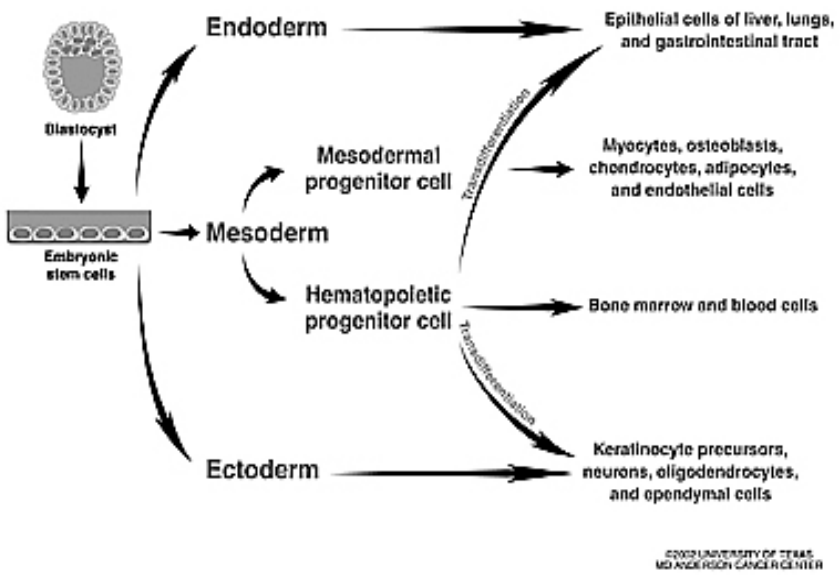


Figure 4- Diagram showing differentiation pathways from Blastocyst stage to end product. Galloway, 2003.

We know that ES cells are capable of differentiating into any of the three germ-layer cells. However, adult stem cells were believed to be able to differentiate only along a certain pathway, yet some recent studies have suggested that hematopoietic stem cells can actually cross germ-layer boundaries to form endodermal or ectodermal cells (Galloway, 2003). In 2001, the biologist Philippe Collas published results that showed that some cells were capable of being transformed into other types of cells. Scientists at Nucleotech were able to demonstrate in vitro reprogramming of fibroblasts by creating tiny pores in the cells through reversible permabilization and then exposing the permeabilized cells to an extract derived from immune cells that contained a mixture of regulatory factors, but were free of genetic material. The reprogrammed cells ended up being able to express molecules and functions characteristic of immune cells. However, since these cells only switched on some of the genes characteristic to the cells that they had been transformed into, and did not completely switch off all of the genes that were native to the original cells, some biologists are still skeptical of the transdifferentiation

demonstrated by Collas. Currently it is still unknown whether transdifferentiation could cause a complete change of a cell-type, and whether the change would be able to be maintained after reimplantation in the body.

It has been found that in mice, stem cells from their central nervous system (CNS) can differentiate to form cells of other organs including muscle, blood, intestine, liver, and heart and that blood cells can differentiate into brain cells. So, it is with information like this that researchers are trying to find out just how this is possible to manipulate a cell to cross barriers and differentiate into a different type of cell from what it would normally be. Unfortunately, unlike the murine cells which have shown this remarkable ability, human adult stem cells have not shown such potential (McKay, 2000).

Embryonic Stem Cells

In the case of embryonic stem (ES) cells (Figure-4), the cells are obtained from the inner cell mass of the blastocyst stage which occurs about 5-6 days after fertilization. Regarding stem cell ethics discussed in Chapter-3, it is important to note here that the blastocyst used to obtain ES cells does not possess the ability to feel pain as it has no nervous system, no sight, no brain, and no heart, and is essentially a cell mass about the size of the period at the end of this sentence. However, the blastocyst stage occurs near the time of embryo implantation into the uterine wall which is important to traditional Catholics as they believe that conception is the starting point of life.

These ES cells possess the ability to develop into a fetus and therefore possess the ability to develop into any part of the body from the blood and bone to the neurons and muscles. However, at the time which they possess these remarkable abilities, it is still too early in the

fertilized egg's development for it to be considered more than just a mass of rapidly dividing cells, the stage referred to as the blastocyst stage.

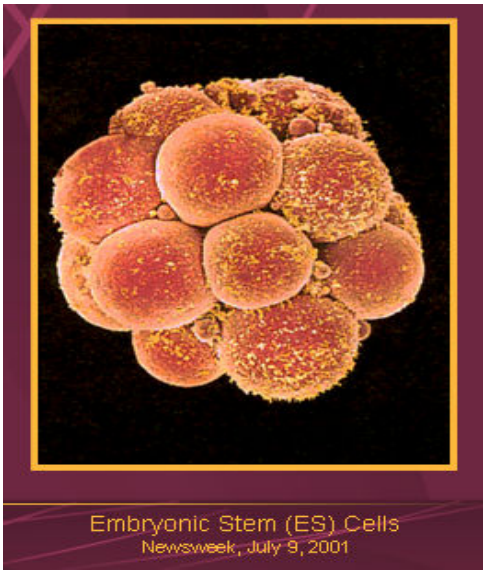


Figure-4: Picture of Human ES Cells.

ES cells can be obtained from the embryo and grown in the laboratory to make ES cell lines that are used for medical treatments. So far, most of the research with ES cells has been done with mice in labs, since it is much easier to obtain their cells for culture due to the legal restrictions on human ES (hES) cells. Some of this research will be discussed in Chapter-2. Clinical trials with hES cells are only recently underway in the U.S. These are the cells that researchers hold the most hope for as they have the potential to develop into any type of tissue found in the human body.

hES cells are much harder to obtain, especially in the U.S. because of the fact that an embryo has to be destroyed in order for the stem cells to be used for the research (see Chapter- 4 for an explanation of the current legal issues regarding stem cell use). As a result, many arguments have been raised from those opposed to the experimentation. Most of the embryos used for this type of research are obtained from in vitro fertilization (IVF) clinics. These

embryos are the ones that are slated for destruction since they are no longer able to produce human life, or simply no longer wanted, yet since they still possess the potential to develop into a human life, they are still argued over.

The ethical debate about these cells discussed in Chapter-3 will focus on the issue of when life begins, and whether the blastocyst is alive. Some devout Catholics consider life to begin at conception, while other groups argue life begins at embryo implantation, and others when the heart begins beating.

Parthenotes as an Alternative Source for ES Cells

Since there is so much controversy surrounding the use of ES cells (refer to Chapters 3 and 4 to find out more about the controversy), in particular from humans, scientists have started to look to parthenotes as a possible source of ES cells. In nature Parthenotes are eggs which have not been fertilized by a sperm but that can still develop into embryos and offspring. Only arthropods (insects, crustacean, chelicerates, etc.) as well as some female reptiles, aphids, and turkeys are capable of this process naturally. For example, bees and ants produce "workers" via parthenogenesis.

In the lab, parthenotes are chemically treated eggs that have the ability to divide to the blastocyst stage, but can not develop to any later stage. Due to the fact that these are not fertilized eggs that can develop into adults, most religions argue they have lower moral status than a normal embryo, and may serve as an alternative source of blastocysts for ES cells (Weiss, 2001). In the lab, parthenotes have been derived for primates and humans and rabbits and mice. In 2001, scientists were able to successfully create a human parthenote blastocyst. They did this at Worcester's Advanced Cell Technology. Michael West and colleagues were able to

chemically stimulate human eggs to grow into an embryo-like state consisting of about 100 cells. Unfortunately however, these parthenotes did not contain any stem cells although they do believe it is possible, yet when tests like this were performed on primate eggs, they were able to retrieve what appeared to be stem cells from one of the parthenotes. However, since this research is fairly new, it remains to be seen if these cells will be completely normal or if they will end up metatisizing like a tumor cell would since all the genetic information would come from one parent (Weiss, 2001).

CHAPTER-2: STEM CELL APPLICATIONS

If there is any biological advance in heavy focus as of late, it's stem cells. These microscopic bodies hold the inherent ability to treat many diseases. But what is the true potential of these cells to cure disease? Do stem cell cures remain "pie in the sky" or have lives actually been saved? Is everything based only on animal research, or have human clinical trials actually begun?

Embryonic stem (ES) cells are those which are from an embryo only a few days old. The ES cells from the inner cell mass of this ball of cells becomes every tissue in the body. The cells must divide very rapidly to produce distinctive types of organized cells. When any cell multiplies quickly the chance for mistakes increases dramatically. Indeed other problems also happen, because of genetic defects or other external influences of embryo maturation. Early stem cells often correct mistakes by releasing chemical signals that help defective cells become the cell type. If there was no error correction mechanism, there would be an exponentially higher amount of miscarriages and severely deformed infants. If a problem occurs in very early development, it could have grave consequences such as the malformation of limb, or a defective heart. A problem in later development may only result in a deformed finger or toe. At that point stem cells have already become more specialized and committed themselves to becoming specific types of cells (blood, eye, muscle etc.). With increased differentiation, stem cells lose some potential to correct mistakes. Embryonic stem cells are sought after due to their lack of differentiation to help cure adult ailments. While much research has extensively been done with animal stem cells, clinical studies have only just begun with humans.

The only drawback of using embryonic stem cells is some ethical concerns on whether the embryo used to obtain them is a life, and whether using it would be considered murder. This topic will be discussed in detail in Chapter-3. Regardless, research has continued using ES cell lines derived from already existing frozen embryos left over from fertility clinics.

Animal ES Studies

Most of what we know about stem cells comes from animal studies. Even though human trials with ES cells are still on the ground floor, much progress has been made in animals, where ethical restrictions are more lax. Much of this research used rats, as they are easy to acquire and provide a decent model for many diseases/injuries. "Hans Keirstead and his colleagues… at UC Irvine have found that a human embryonic stem cell-derived treatment they developed was successful in restoring the insulation tissue for neurons in rats treated seven days after the initial spinal cord injury, which led to a recovery of motor skills" (UC Irvine, 2005). Thus, ES cells are able to be chemically prodded to become motor neurons and help at the site of injury.

Interestingly though, the animals whose spinal injury was older than 10 months did not show any recovery, thus scar tissue formed during healing can hinder reinnervation. If after an accident, one could stabilize the spine, and start stem cell treatments within the 10 month period, recovery would be more likely. Patients like the late Christopher Reeve would have the potential to walk again, if the same technology was applied to paralyzed human subjects.

Another seemingly radical use of embryonic stem cells is their use as biological catalysts. A research group led by Fraidenrach and colleagues have been studying this effect on mouse embryos (Fraidenraich, 2004). They created three genetic errors in the mouse embryos and implanted them in pseudo-pregnant mice. The genetic mutations purposely caused the Id genes

to interfere with cells' ability to differentiate into other cells. In fact, the embryos' hearts have a thin lining (thin myocardial wall syndrome) and die during the pregnancy. Since the embryos' cells do not end up as heart cells, the lining is very thin. It was "found that injection of mutant blastocyst embryos with as few as 15-wild-type ES cells rescued a subset of the cardiac defects and prevented death of the embryos" (Chien et al., 2004). By injecting healthy ES cells into the defective embryos, the mice did develop and survive to birth. This experiment proves that ES cells have the potential to rescue mutations causing diseases. Also, the embryos even benefited when the ES cells were injected into the mother rat not the embryos themselves, indicating the ES cells could target the embryo remotely! Though this is amazing, only half of these mice survived to birth. It was theorized that the embryonic stem cells must be secreting something that is rescuing the defective cells in the embryos. Since the stem cells in the mother were not in direct contact with the embryos they had to be communicating in such a way. Among the factors being secreted was found to be IGF-1 (insulin-like growth factor 1) and Wnt5a. Both of these proteins have been shown to promote the division and growth of early heart cells. Although IGF-1 injected into pregnant mice with mutant embryos (see Figure 1) helped the mutant mice, it was not as effective as the injection of normal embryonic stem cells, thus, the full cocktail of chemicals secreted by the ES cells is still somewhat of a mystery. If the exact content of it could be determined, the ES cells themselves would not be needed for therapy (this would be ethically beneficial). In humans, testing is often done on embryos with a high risk for a certain genetic defect. Using this technology, someday it may be possible to inject a mixture of helpful chemicals to ensure healthy baby development.

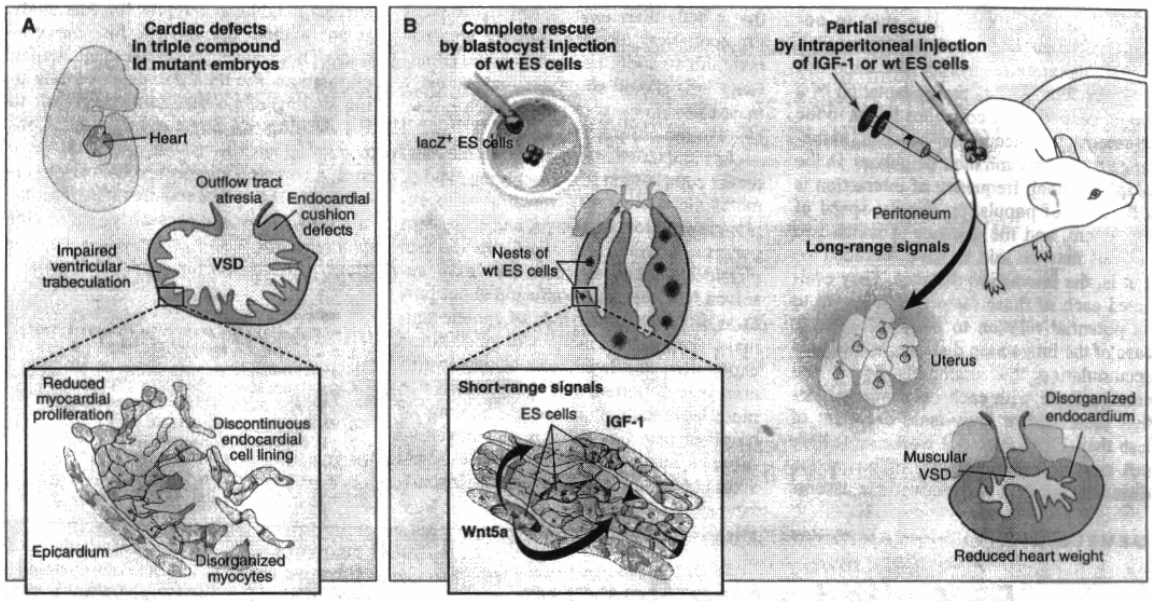


Figure 1. Rescue of mutant mouse embryos. Notice the close up in Panel A of thin heart wall in the mutant embryos. In the left part of B, an injection of normal ES cells completely cures the heart. In the right part of B, IGF-1 or ES cells injected in the mother do help restore some heart wall thickness (Chien et al., 2004).

Rats have also been used as a model for Parkinson's disease, and ES cell therapy has shown some promise with this model. While the actual cause of Parkinson's disease is unknown, low levels of dopamine is a symptom. Dopamine is a neurotransmitter (chemical in the brain) that is involved with movement. An Israeli group transplanted human ES cells into the Parkinson's rat model. Before implantation the rat would be "unable to make side steps while they were being dragged across a surface" (Ryan, 2004). After treatment, the symptoms decreased, and "when post-mortem examinations were carried out on the rats, it was found that the stem cells had developed into dopamine-producing cells" (Ryan, 2004). This example provides proof that embryonic stem cells do have the potential to alleviate the symptoms of some diseases that plague humans.

Upcoming Human ES Cell & Adult Therapy Examples

With the initiation of human clinical trials, the reality of how beneficial embryonic stem cells are will soon become apparent. ES cells can be grown into certain tissue types, and the drugs tested on them instead. If a new heart medication was developed, it could be directly applied to heart tissue derived from ES cells to judge its effectiveness. While this may prove a helpful addition/alternative to animal testing, actual human trials are where the cutting edge is.

Due to the ethical quagmire that exists, no confirmed clinical trials have yet been performed with ES cells in humans. Stem cell lines that were previously derived have been studied and categorized, but not used in human treatments. Despite the relatively new status of ES cell research in human trials, quite a few amazing applications have only been proposed. A company called Geron plans to change this soon, starting with treating spinal cord injuries. "Even enthusiasts agree that Geron's goal- to testing human embryonic (hES) cell therapy in patients within a year--is a long shot" (Vogel, 2005). It may not happen this year, but once FDA approval is granted (they have applied), and safety protocols are in place, the testing will occur.

Geron believes its “first clinical trial will focus on treatment for acute spinal cord injury” (Geron, 2005). This pending trial will be crucial in substantiating the utility of ES stem cells in human patients. While treatments such as these have been fruitful in other mammals, human application has yet to be achieved. At the same time, Geron is improving the production of liver, insulin producing, muscle, bone, cartilage, and neuronal cell progenitors derived from human ES cells. After spinal cord treatments are approved and applied, clinical studies will move to the alignments seen in Figure 2 below.

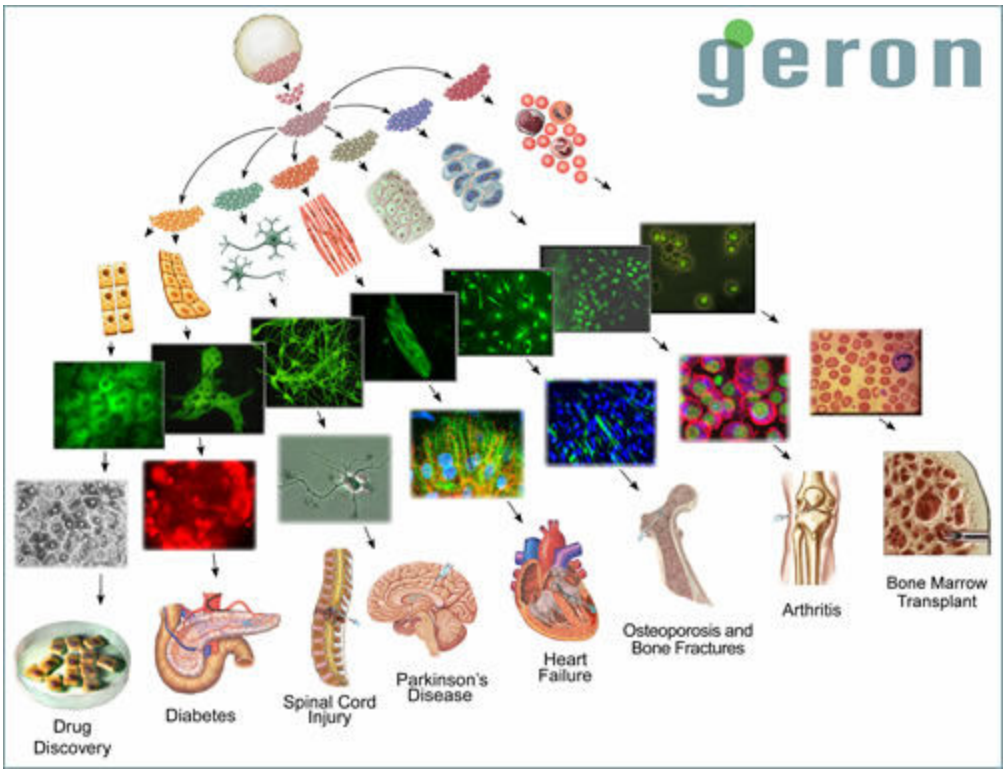


Figure 2. ES derived stem cells which Geron wishes to use in human trials to treat many illnesses and aid drug disovery (Geron, 2005). "Geron is developing treatments for Parkinson's disease and spinal cord injury using hESC-derived neural cells, treatments for heart disease using hESC-derived cardiomyocytes, and treatments for diabetes using hESC-derived pancreatic islet cells" (Geron, 2002).

Such diseases as amyotrophic lateral sclerosis, Parkinson's, multiple sclerosis, and diabetes are seen as prime candidates for study in humans. The crucial factor is the FDA approval of ES stem cell treatments, and a loosening of U.S. laws on ES cell uses. Adult stem cell treatments have been approved and have succeeded in the same areas that will get eventual approval for ES stem cell treatments. The amount of time this will take is subject to much speculation. Biotech-companies such as ViaCell have successfully amplified adult HSCs for use in human trials. When harvesting adult stem cells, a large amount must be taken. ViaCell is pioneering a technique to "selectively amplify" just the desired adult stem cells, so only a small amount of stem cells are taken (ViaCell, 2005). This same technology is planned to be used to amplify embryonic stem cells, which will then be used in treatments.

In an upcoming trial, the company Osiris Therapeutics is targeting arthritis. The "trial squirts adult stem cells into damaged knees after surgery to regrow meniscus, restoring the tissue that acts as a shock absorber and preventing onset of arthritis" (Henderson, 2005). As the study has already been FDA approved, they expect to have three marketable treatments by 2007. Additionally, studies will be done to prevent tissue rejection with bone marrow transplants. At John Hopkins Hospital, another approved clinical trial is beginning where cardiac heart cells are being injected to repair heart attack damaged hearts. "The process uses adult stem cells taken from the bone marrow. These cells, called mesenchymal cells, have been shown to give rise to a variety of cell types" (CNN, 2005). So far two of an initial 48 patients have signed up for the treatment.

Without any concrete proof ES stem cell treatment works in humans, some may write off human applications as pie in the sky. This technology is on the verge of being approved in the same way adult stem cells have been. New adult and umbilical stem cells trials are continuing to develop in the interim. These non-ES cells are continually being applied to more diseases, and the techniques being refined to a marketable standpoint so that much more individuals can benefit safely. It remains to be seen how long it will take ES stem cell research to catch up to the current adult stem cells in clinical applications.

Success Stories for Adult Stem Cell Treatments in Animals

Because of their reduced ethical concerns, much effort has also been placed in exploring the applications of adult stem cells. Adult stem cells reside in baby teeth, bone marrow, brain, skin, and several other areas in the body. While they have a diminished capability to become other cell types, they at least have the potential to regenerate the same tissue they were isolated

from, and many successes have been achieved in humans and animals. First we will talk about what has been done in animals.

Regeneration of Heart Muscle

"It may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease" (National Institute of Health, 2004). Heart muscle stem cells (Figure 3, left side) or bone marrow stem cells (Figure 3, right side) have been implanted into damaged heart tissue and these cells differentiated into new heart cells. When a patient has a heart attack, oxygenated blood flow to the heart stops, and causes some heart cells to die. The heart only has a few cardiac stem cells, and never is able to fully repair the heart. Scar tissue often forms and other heart cells expand to fill the gaps. The end result is a weaker heart beat, and a less healthy individual. By implanting adult stem cells, heart function can be greatly improved.

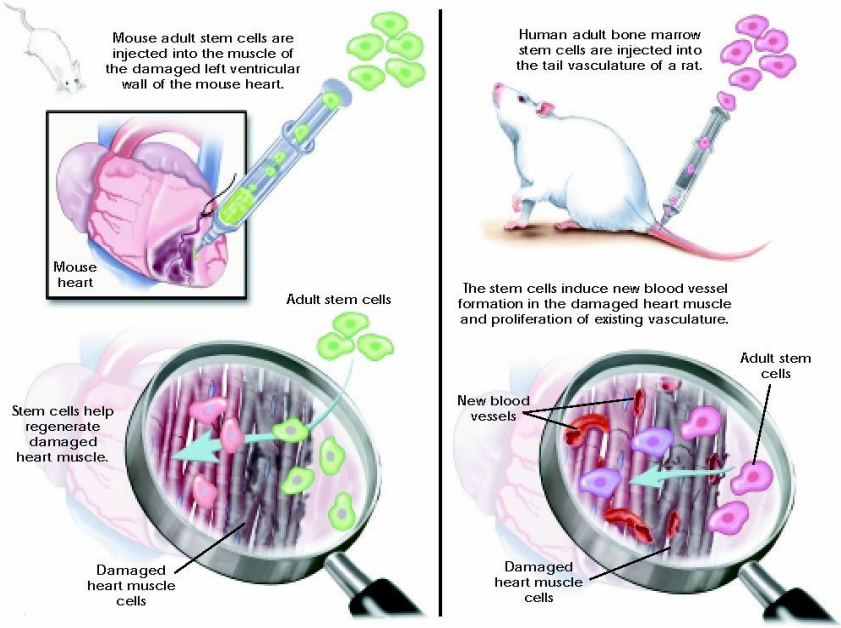


Figure 3. Heart Damage Repair with Stem Cells (National Institute Of Health, 2004).

Muscular Dystrophy

Adult mesoangioblast stem cells have shown promise in treating muscular dystrophy. Patients with muscular dystrophy suffer from a genetic defect that causes weakness throughout the body. In Italy, "researchers injected stem cells from the blood vessels of healthy mice into leg arteries of mice with muscular dystrophy. The stem cells... accumulated in the diseased muscle within hours and eventually gave rise to healthy muscle tissue" (Touchette, 2003). It's amazing how stem cells have the attribute of being able to search out and find damaged tissue. If it was discovered how stem cells hone in on injured tissues, perhaps other non-stem cell treatments could one day be developed. The stem cells that were isolated are "mesoangioblasts", and they are able to leave the blood stream and enter muscle. Specifically they find the injured tissue (see Figure 4) and start repair.

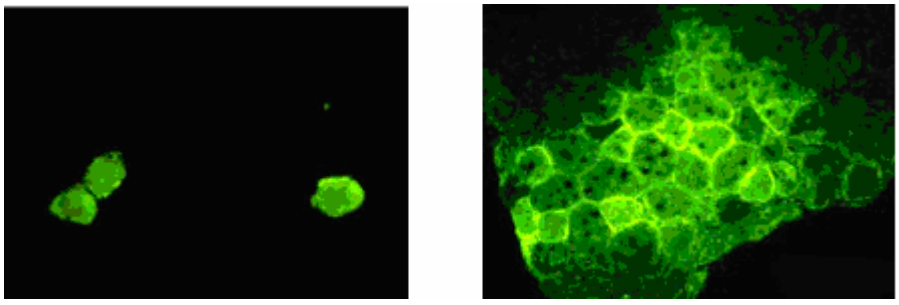


Figure 4. The leg of a untreated dystrophic mouse (left) has much less muscle growth (green) than a leg injected with mesoangioblast stem cells (right) (Touchette, 2003).

Diabetes Treatment

For individuals with type I diabetes, insulin producing cells are destroyed by the body's own immune system. "New studies indicate that it may be possible to direct the differentiation of human embryonic stem cells in cell culture to form insulin-producing cells that eventually could be used in transplantation therapy for diabetics" (National Health Institute, 2004). Although

most studies in this category focus on injecting pancreatic adult stem cells, in rats it has been shown that rat liver cells can become insulin producing. Isolated adult rat liver stem cells were placed in a medium containing high amounts of sugar. In response, the cells began to produce insulin, a function normal liver cells never do. "Researchers subsequently implanted the cells into a small number of diabetic mice. Blood-sugar levels dropped to normal within 10 days in one mouse that had been given a high number of insulin-producing cells." Two other mice had smaller amounts of cells implanted and still had high blood sugar levels associated with diabetes (Ross, 2002). If this procedure could be applied to humans as with heart muscle repair, more than 15 million people worldwide could benefit. Vitro Diagnostics (a biotech company located in Aurora, Colorado) is currently in the process of getting a patent for "a new process to generate immortal cell lines that can be induced to form beta islet cells by exposure to certain environmental conditions, … [they] are not derived from human embryonic stem cells but rather from partially differentiated human pancreatic cell lines" (Business Wire, 2005). Beta-islets are the cells naturally present in the pancreas that produce insulin. If this technology becomes effective, transplantation of these cells may well be the cure for type I diabetes, especially if they are protected via encapsulation from the autoimmune response that is already present in the patient.

Success Stories for Adult Stem Cell Treatments in Humans

"Currently, more than 70 identified diseases and disabilities are treatable using non-embryonic stem cells, including breast cancer, leukemia and sickle cell anemia" (Earll, 2005). The best way to fully explain these treatments is through some actual cases. Adult stem cells have proven to be a virtual dynamo in medicinal value. Despite the lack of human trials for

embryonic stem cells, there has been a lot of success with some of the diseases mentioned above with adult human stem cells.

Hematopoietic Stem Cell Treatments

Without a doubt, the strongest successes performed in humans to date with stem cells use hematopoietic stem cells (HSCs), which are the "active" component of bone marrow transplants and umbilical cord transplants. For over three decades bone marrow transplants have been performed, and well over 15,000 are performed annually in the United States alone (Beckestein, 2004). They are performed "mainly for the treatment of leukemias, lymphomas Hodgkin's disease and multiple myeloma" (Beckestein, 2004). All blood cells in the body are made in the bone marrow by HSCs. Radiation and chemotherapy poison used to kill off the cancerous/diseased cells in a sick patient also kill the HSCs affecting the patient's ability to manufacture their own blood cells. Thus the infusion of HSCs in the bone marrow treatment restores this capability.

Two types of bone marrow transplants can occur, allogenic or autologous. Allogenic transplants come from an individual with very similar genetic backgrounds. Autologous are from the same individual, normally taken from a specimen frozen much earlier (Meadows, 2000). A healthy individual donates bone marrow (normally from the pelvis) and the marrow is injected into a compatible individual. Healthy HSC's are then able to regenerate healthy blood cells in the afflicted individual. The National Marrow Donor Program is currently "the world's largest and most diverse registry of more than 5.5 millions potential volunteer marrow and blood cell donors, and more than 40,000 cord blood units" (NMDP, 2004). Also 3.8 million more donors are available thru other registries. Every year the NMDP gains 300,000 more volunteers and the

total possible donors available increases (NMDP, 2004). The success rate varies depending on what disease is being treated, the patient's condition, the donor's age, and other factors. "Success can range from 80 to 90 percent for children with inherited abnormalities of the immune system, to as low as 10 percent for patients with aggressive, resistant diseases" (Meadows, 2000). Overall, around 80% of all patients do survive in the long term, compared to 25% who undergo chemotherapy alone (London Sciences Centre, 2003). Without a doubt, bone marrow transplants and their accompanying HSCs have and continue to give sick patients a new lease on life.

Umbilical stem cells are obtained not from the body, but from the blood of the umbilical cord and placenta at birth. This blood is a rich source of HSCs , which many parents opt to freeze for later use. If the child is stricken with any serious sickness, the stem cells could be thawed and applied to the area in need. Umbilical cord stem cells have the benefit of having the same antigenic profile as any other cell in the person they are taken from, so they will not produce an immune response in that individual (just like adult stem cells). But unlike adult stem cells, there is no need to harvest them from the body, which can be difficult depending where they come from (i.e the heart).

Umbilical cord stem cells are being seen more and more as a viable alternative to bone marrow HSC's. Especially considering "more than 106,000 people in the U.S. each year are diagnosed with [blood cancer diseases treatable by HSC transplant]" (Swanson, 2004). 15,000 bone marrow transplants per year is just not enough to cure all the suffering patients. One advantage of cord HSCs over bone marrow HScs, the harvesting of umbilical stem cells is completely pain free, which is not the case in bone marrow transplants. Plus matching a donor and recipient is a lot easier, since the umbilical stem cells produce much less of an antigenic response. The patient is able to accept the umbilical cells, and rejection is less likely (Schiavone,

1998). Also, blood cord banks store frozen samples, and it only takes a few days to produce a sample for transplant. In contrast, bone marrow transplants have to be taken for a specific recipient, and often take months to acquire (Swanson, 2004). The range of treatable diseases appears to be broader than bone marrow HSC's as well.

Many of the same problems treated with adult stem cells have also had great success with umbilical cord stem cells. In Korea, a paralyzed woman was unable to walk for over 19 years, due to a lower spinal cord injury. She believed she would be condemned to a wheelchair for the entirety of her life. "Using stem cells isolated from umbilical cord blood, succeeded in reversing the paralysis of the lower limbs caused by spinal cord injury, of a 37-year-old female patient" (Tae-gyu, 2004) (see Figure 5).

Figure 5. Taking her first steps in 19 years following treatment with umbilical cord stem cells (Tae-gyu, 2004).

This example not only shows that adult stem cells prove useful in paralysis treatment, it demonstrates that even old injuries can be healed. This is in conflict with the aforementioned paralysis treatments that did not work after 10 weeks on rats treated with embryonic stem cells. Maybe this is because embryonic stem cells are best at repairing embryonic injuries, as it has been documented if an embryo gets a severed spine it will be reattached and healed in the uterus. Adult and umbilical stem cells are left over guardians prepared to help a more mature body, and replenish its cells. Thus, reimplantion in the right area yields triumphant results even on old damage.

Leukemia is a blood cancer where white blood cells (lymphocytes) are produced in abnormally high amounts. Nathan Salley was diagnosed with acute myeloid leukemia. After treatment with cord HSCs, his health took a complete turn around. He told a congressional committee; “I am living proof that there are promising and useful alternatives to embryonic stem cell research. . . . Embryonic stem cell research did not save me – cord blood research did" (Earll, 2005). Hundreds of thousands of other patients with leukemia have been cured the same way using HSCs from either bone marrow or cord. Umbilical stem cells also can prove an acceptable replacement for those who need a bone marrow transplant, but cannot find a match. Mark Fulford was such an individual suffering from non-Hodgkin's lymphoma was cured with cord stem cells (Hughes Jr., 2005).

Sickle cell anemia is another application for umbilical stem cell treatment. Keone Penn was afflicted with sickle cell until he was eleven years old. He lived with extreme joint pain and had to undergo several blood transfusions. Soon after receiving umbilical cord HSCs his body ceased to produce the defective blood cells, and he now has no symptoms whatsoever. “More than two hundred sickle cell patients have undergone hematopoietic stem cell transplantation

with an 80 to 85 percent success rate"(Hughes Jr., 2005). So what do all these real examples of non-embryo stem cell therapies tell us? Those who have serious illness may have a cure inside a miraculous stem cell. Those who suffer in incredible pain may have salvation in biology. Stem cell technology does work in humans, and should be pursued to the nth degree.

Repair of Heart Muscle

Recently, the same heart damage repair discussed above for animals has also been achieved in humans! Four of five Brazilian heart-failure patients, "no longer needed a heart transplant after being treated with their own stem cells" (Reuters, 2003). The four were part of a group of 14 patients whom all showed better heart function after stem cell treatment. Stem cells from their bone marrow were harvested and then injected into the left ventricle of the heart. In skeletal muscle, stem cells from a patient with heart disease were re-implanted to the heart. This was the first time any heart degeneration was restored (Huges Jr., 2005). "German heart specialist Bodo Eckehard Strauer successfully treated a heart patient using stem cells from the man's bone marrow" (Earll, 2005). The patient's condition improved dramatically. Again, the adult stem cell proves quite versatile. Thus, stem cells (even adult) have the ability to repair damaged tissues.

Diabetes Treatment

Fifteen type 1 diabetes patients received adult pancreatic ß-cell transplants, after which eleven no longer need insulin (Medical Post, 2001). In a similar experiment, 250 diabetics were given injections of "islet cells from the pancreases of deceased human donors, and more than 80 percent were able to stop their insulin shots for more than a year" (Fagan, 2003). These

treatments did not use adult stem cells, but rather mature insulin producing cells (ß-cells). ß-cells do not come from an adult stem cell precursor, but rather from already existing ß-cells (Melton et al., 2004). Evidence shows only ES cells are inducible to become ß-cells. Vitro Diagnostics, Inc. recently applied for a patent "regarding a procedure for the generation of beta islets from stem cells [via environmental control]" (Genetic Engineering News, 2004). Therefore, ES stem cells could be a valuable tool in curing diabetic suffers. Also, as noted earlier rat liver adult stem cells could be induced to produce insulin (they did not become islet cells). So actual pancreatic cells may not have to be used if another adult stem type can also be coerced into making insulin (and then implanted).

Multiple Sclerosis Treatment

Multiple Sclerosis has also been treated by an adult stem cell transplant. "Susan Stross is one of more than 20 MS patients whose conditions have remained steady or improved" after treatment (Earll, 2005).

Nasal Stem Cell Treatments

Strangely enough, there are stem cells that live in your nose. The nasal cavity contains some adult stem cells. Laura Dominguez was sixteen years old when she was in a car accident and was paralyzed from the neck down, as she fractured her C6 vertebrae. There seemed little hope she would ever walk again. After failed therapy, see underwent "olfactory mucosa transplantation, that involved transplantation of stem cells found in the nasal region into the injured area" (Hughes Jr., 2005). After therapy and healing, she improved greatly. After only six months, sensation came back to her abdomen. "An MRI was conducted; physicians informed her

that her spinal cord had begun healing and that 70 percent of the lesion had recovered into normal spinal tissue" (Hughes Jr., 2005). She has regained upper body movement, and can walk with a walker. Susan Fajt, another spinal cord injured patient as the result of a car accident, had the same procedure, and in 2004 could also walk with braces. As this technology advances, hope for those with spinal cord injuries grows.

Parkinson's Treatments

Dennis Turner, a man with Parkinson's disease had an "80 percent reduction in his symptoms after he received an injection of his own neuronal (brain) stem cells" (Earll, 2005). He now even brags he is able put his contact lenses in, something he would never be able to do before the treatment. Four years after treatment, improvement continues. "He also affirmed that he would pursue another treatment involving his own stem cells to further improve his condition. The procedure would involve a second extraction of stem cells from his brain and implantation into the right side" (Hughes Jr., 2005). Additionally, Turner has been to Africa on a safari and has been swimming in the Atlantic Ocean.

Stroke Treatments

Stem cells seemingly are able to cure other brain problems as well. Strokes cut off the blood flow the brain (as does a heart attack to the heart), and can cause paralysis, speech, and sight issues. The brain is an incredibly complex organ, in which an unimaginable amount of chemical reactions occur every second. A lack of oxygen disrupts the careful balance that exists. The Catholic University of Korea transplanted bone marrow stem cells into five stroke patients,

three of whom had “great improvement in the paralysis symptoms and speech disorders” (Earll, 2005).

Eye Stem Cells

Adult stem cells are of great value in treating eye diseases as well. “Limbal stem cell transplantation offers hope to those suffering from corneal degeneration, blindness, and other ocular diseases.” The eye provides yet another source for stem cells, in particular the limbus. The limbus is between the cornea and sclera (outer layer). Stem cells are extracted from a healthy part of the eye or the eye of a cadaver. Extracted stem cells can then be put into the defective part of the eye (see Figure 6). These cells then differentiate into corneal cells (Hughes Jr., 2005).

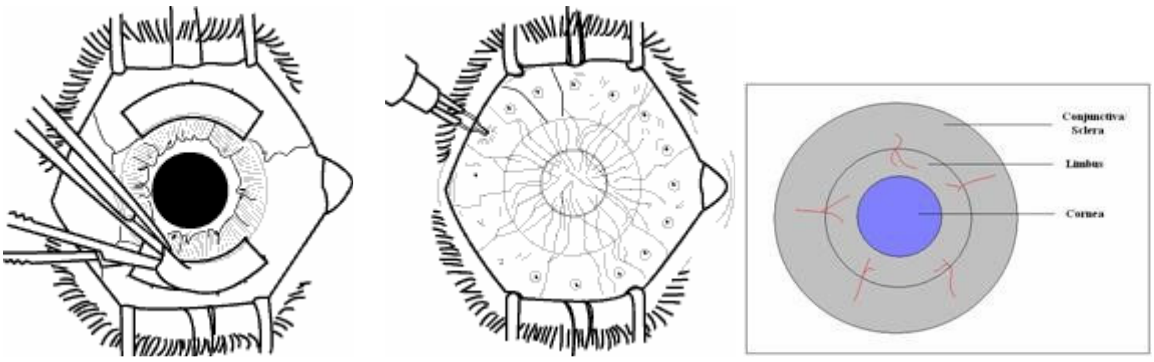


Figure 6. Extraction of limbal stem cells (left), reimplantation of limbal stem cells (middle), and a diagram of the human eye (right) (Health link, 2002).

Michael May lost the vision in his right eye due to a chemical explosion. After receiving a limbal stem cell transplant and cornea transplant 43 years later, he was able to see again. It only took two years for his vision to be fully restored (Hughes Jr., 2005).

Lupus Treatment

Systemic lupus erythematosus (lupus) is a type of auto-immune disorder when organs no longer perform their required function. Adult blood stem cells were also used to treat an 18 year old girl with this condition. "She had experienced pneumonia, lung weakness, and blood deficiency, among other ailments" (Hughes Jr., 2005). Fifteen months after a transplant of blood stem cells, she returned to full health with no ill effects. Similarly, Crohn's disease is a treatable autoimmunity disorder in which the digestive system is attacked by the body. A 22 year old female was given her own blood cells and three months later was free from digestive discomfort after eating. (Hughes Jr., 2005). Even a severe incidence of Behcet's disease was treated in a four year old girl with her own blood (hematopoitetic) stem cells. Behcet's is a nasty condition where inflammation "creates oral ulcers, genital ulcers, and skin lesions" (Hughes Jr. 2005). Only two years later she was on the road to recovery. Without a doubt, adult stem cells have a tremendous value in treating a multitude of health problems. In the future, the range of treatable diseases should increase further.

Future Applications

One of the newer stem cell types to provoke interest are Parthenotes. Parthenotes are derived by electrically stimulating egg cells to divide to the blastocyst stage where the inner mass cells are then taken and an ES cell line is established. Because parthenote embryos can not divide past the blastocyst stage, they can not become a fetus, thus they have less moral status than a blastocyst from a fertilized egg. Currently, parthenote blastocysts have been derived from both primates (Cibelli et al, 2002) and humans (Cibelli et al, 2001), but parthonote ES cell lines have only been established from primates (Cibelli et al, 2002). Monkey parthenote stem cells

have successfully been used to treat Parkinson's diseased monkeys (Bedford Stem Cell Research Foundation, 2004). They may eventually become as useful as adult and umbilical stem cells have proved to be.

Perhaps it's a bit far reaching, but total organ replacement has long been a dream of science. An undifferentiated stem cell is like a blank page, it can become a page of notes, a colorful crayon artwork, or origami swan. The challenge is finding the key to make the cells transform into what we want them to be. So far, stem cells have been induced to become certain type of cells, but this is far from a complete tissue or organ. Sometimes, an organ is irreparably damaged and is beyond stem cell treatment, even embryonic. One day a complete heart may be able to grown in culture, but getting there is an incredibly long fought battle, starting with animals of course.

The British biotech company Odontis has pioneered a procedure in which they used rat stem cells to produce new teeth. Harvested stem cells are induced and grown into a ball of cells, called a bud. "Tests reveal what type of tooth - for example, a molar or an incisor - the bud will form. Using a local anesthetic, the tooth bud is inserted through a small incision into the gum" (Sample, 2004). The bud starts to grow into a normal tooth as it fuses to the jaw. "It releases chemicals that encourage nerves and blood vessels to link up with it" (Sample, 2004). The group claims the procedure should also work in humans, as the procedure would be the same.

A tooth is a lot easier to grow from scratch than a heart, but it is definitely progress towards that goal. One day an organ may be failing, and it would just be a simple trip to the doctors to get a new one grown up in the lab. There would be no organ transplant list to wait for while death could come at any moment. Additionally, there would be no organ rejection because

the organ would be grown from the same individual's cells. Future breakthroughs will shock and amaze, as the quality of life improves.

Conclusion

Stems cells do appear to be a miraculous cure in an age where focus on health has become important. Technically, embryonic stem cells do have the most medical potential as they are able to form any tissue or any cell type in the body. Yet, many have moral hang-ups in their use, as the destruction of the embryo used to obtain them could be considered infanticide or akin to abortion. Regardless, human trials will eventually happen, exactly when and where is debatable until it does happen. Animal studies with ES cells have shown stunning results, but this is still a far cry from actual human application. A solution has been to investigate the healing qualities of adult and umbilical stem cells. Despite a more limited cellular path, they do have an enormous utility in regenerative medicine. Several examples have been presented of the myriad of success stories in humans using umbilical and adult stem cells. Additionally, parthenote-derived ES cells will become a viable option, when the technology is perfected. This will offer the benefits of embryonic stems cells but with the generally accepted ethical standing of adult and umbilical stem cells. From spinal injuries to pre-birth heart defects, the future of stem cells in regenerative medicine is bright indeed.

CHAPTER-3: STEM CELL ETHICS

To understand the ethical debate surrounding stem cells, we will briefly review the types of stem cells as previously discussed in Chapter-1. Stem cells are normally classified into 3 main categories: embryonic, adult, and umbilical. The latter two categories are frequently lumped together since they do not destroy an embryo. Cells within each category have different potencies. The earlier in development a stem cell is harvested, the more potency it has. The newly fertilized egg is considered totipotent. Totipotent cells are able to generate an entire organism. The fertilized egg will grow into a morula (6-8 cells) whose cells are also totipotent (see fig 1). These cells can regenerate virtually any tissue in the body. If the cells are allowed to grow to the blastocyst stage (day 5-6) the embryonic stem (ES) cells of the inner cell mass are pluripotent (see fig 2). These cells can regenerate the majority of cells in the body (Conan-Davies, 2002). Hematopoietic stem cells (HSCs) are also present in the newborn's umbilical cord, but are only multipotent, able to develop into a limited type of cells (i.e. those related to blood). Adult stem cells can be pluripotent (i.e. bone marrow HSCs) or unipotent (i.e. neuronal stem cells).

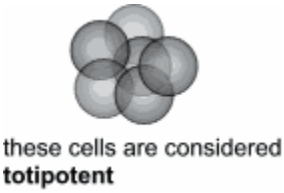


Figure 1. Morula
Early stage of growth approximately 8 cells
(Conan-Davies, 2002).

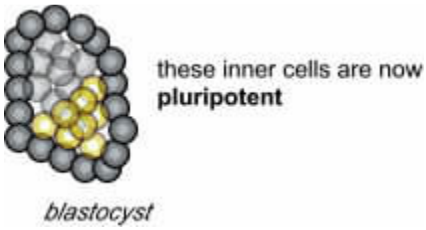


Figure 2. Blastocyst
Stage of growth several days after fertilization.
(Conan-Davies, 2002).

Which Stem Cells Cause the Most Heated Debate?

Although stem cells have great promise for treating a variety of diseases, their use is highly controversial. Adult and umbilical stem cells are the least controversial, but also have the least potentials. All four of the world's major religions support the use of umbilical and adult stem cells, so long as they are used to support the "common good". The problem comes with ES cells that are taken from the inner cell mass of the blastocyst, and usually destroy an embryo to obtain them. Is it right to use these cells, is it murder to do so?

Embryonic Stem Cell Ethical Issues

With umbilical or adult stem cells, the organism from which they are taken does not die when the cells are harvested. The cells are fairly easily taken from the umbilical cord, baby teeth, or bone marrow. Conversely, embryonic stem cells are usually taken from the blastocyst stage. When individuals are at high risk of having genetic defects and/or having trouble conceiving, fertilization is sometimes done *in vitro* (outside of the body). Sperm and egg are united in vitro, and the embryo is allowed to grow. Sometimes a pre-implanation genetic diagnosis (PGD) is performed to test the embryo prior to implantation in the uterus. "PGD is actually a number of procedures that when combined have the ability to determine the genetic makeup of an embryo while it is at the 8-cell to blastocyst stage"(Socalfertility, 2005). Using this method, it can be determined if the individual has a genetic predisposition to a certain disease (such as cystic fibrosis). If the embryo is healthy, its remaining cells are implanted. While this procedure is less controversial than regenerative medicine it still raises key ethical issues, such as who decides which embryos to re-implant, and who can use a couple's donated eggs after they are done with them.

One of the main issues is whether an embryo is considered a life. If it is, then its use to harvest ES cells which results in its ultimate destruction could be viewed as murder. Murder is universally considered ethically reprehensible. At what point does life begin? Is it the moment of fertilization, or if not, at what moment after? This normally comes down to religious morality. Catholicism considers life to start within the womb. The Christian Bible states in Isaiah 44:2, 21, 24 "the Lord who made you and formed you from the womb." Catholics traditionally consider life to begin at embryo implantation (day 6). Because implantation occurs near the time of blastocyst formation the Pope considers destroying a blastocyst immoral, although not all Catholics agree with this stance. Some Catholic philosophers argue that the blastocyst is not yet "individualized" so it has less moral status than a fetus (Shannon, 2001). This stance allows ES cell research so long as it supports the common good. Thus from a traditional Catholic perspective, embryonic stem cell harvesting could be considered murder. To stop embryo development is a sin. The previous catholic Pope John Paul II, stated, "It is immoral to produce human embryos destined to be exploited as disposable 'biological material'", in his *The Gospel of Life.* Christian/Judaism philosophy claims man is made in the image of God, of whom controls life. Strict interpretation of this research is considered by some as tampering with God's work.

Yet, not all Christian denominations and other religions view stem cell research in the same light. Some Christian churches view working with ES cells as helping the sick, and ultimately good. "Jesus set an example, by his ministry of healing and caring for the sick and disabled, challenging us to follow his example by supporting the healing and caring ministry in our own day" (Currie, 2005). In the same stance, the stem cell treatments could be used to help the infirmed. Especially if the ES cells or established ES cell lines already exist, it is wasteful to

discard them, as the “murder” has already occurred and lives could potentially be saved. Other Christians take a more strict view. “Most notable is the Christian concept that we may not do evil so that good will results. So, even though people may be cured through embryonic cell therapies, the destruction of human life (i.e., evil) prevents its use” (Deem, 2004). If life starts in the womb, at what point is it a human life? If it is at conception, then embryonic stem cell use would be ethically wrong. Not all Christian churches believe life starts at conception, and thus support for embryonic stem cell research varies.

Most Jewish scholars see embryonic stem cell research as justifiable. “Judaism has no problem with "playing God,"…the concept of emulating God is implicit in the mandate to heal and provide effective medical relief wherever possible…only two "professions" ascribed to God Himself are those of teaching and healing. By teaching and/or healing, we fulfill the obligation to "play God." ”(Jakobovits, 2002). According to Jewish law, using such technology to heal is allowed. Only when done for cosmetic/improvement would it be forbidden as described in the laws of cross-breeding. But the Torah does assert that life is to be protected as a sacred thing, and that aborting a fetus only for the purpose of stem cell research would be forbidden. Even though before 40 days the fetus is considered “mere water”, it is interfering with what would become life. “While the destruction of pre-embryos in the course of fertility treatments or to prevent disease may be permitted, this does not mean that pre-embryos may be destroyed without compunction” (Eisenberg, 2001). Pre-embryos from fertility treatments were not made for use only to be used in treatment thus, could be used to help heal others, in accordance with Jewish laws.

Similarly, Islamic convention holds that “Each of you possesses his own formation within his mother’s womb, first as a drop of matter for forty days, then as a blood clot for forty

days, then as a blob for forty days, and then the angel is sent to breathe life into him." Thus, life only begins only after the fetus shows significant development (Weckerly, 2004). Islamics also generally believe the soul does not enter the body for 120 days after fertilization (well after blastocyst formation). Thus Islam allows ES cell research. Buddhism (despite many factions) takes a similar stance that the soul does not enter the body until the formation of the pineal gland or third eye (which occurs after blastocyst formation). The Hinduism perspective on embryonic stem cells is somewhat unclear as well. Hindus do believe life starts at conception, and a fetus is a person. "Yet Hindus do permit abortion, when it is performed to save the life of the mother" (Hinduism Today, 2004). But those views are not held universally. If the stem cells from an aborted fetus could save the mother's life, then it would be allowed. At what point using such cells is right is not well defined. Thus, opinions do differ in every religion; however, in general all four major religions support the use of adult or cord stem cells, and three also support the use of ES cells, so long as the treatment is used to help preserve life. Religion generally preaches a message to preserve life, but the point at which it begins remains debatable.

Religious Stance on Adult and Umbilical Stem Cell Usage

Though the morality of embryonic stem cells is highly contested, adult and umbilical cord stem cells are a completely different story. Here Catholic and Christian camps are in agreement. "Research with adult stem cells does not require the killing of a prenatal embryo to obtain the cells, therefore, this type of research is not necessarily immoral" (Conte Jr., 2004). There is no harm done to the adult or child when adult stem cells are taken, thus it would be not considered a violation of the commandment "thou shall not murder." Umbilical cord stems would normally be discarded when the placenta and other afterbirth are thrown away. They have

shown the ability to be become many types of blood cells and help individuals with various diseases. Some preliminary evidence even exists that HSCs can be transdifferentiated into neuronal cells (Snow, 2003). With more research on transdifferentiation, such cells could become very helpful and side-step many of the ethical objections in using cellular material from embryos.

Using umbilical and adult stem cells is also permissible in Jewish law. "There would… be no Jewish legal problem with using stem cells derived from adult tissue. Similarly, it would appear that using cells from umbilical cord tissue would be permissible." (Jakobovits, 2002). Again, there is no fetal sacrifice, and the Jewish religion encourages the healing of others. But these cells too, if used for cosmetic purposes would not be allowed. Treating a genetic disease would be acceptable, but changing one's height by any medical treatment would not be allowed. As tampering with God's image is not permissible, only restoring to its intended form would be approved.

Islam also allows adult and umbilical stem cell use. "If the origin were a live human being then this would be allowed with his consent. This is because the person has a legal (Shari) authority over his organs" (Latif, 2001). The umbilical cord, blood, and any part of the human body can be considered part of their organs. Thus, if the individual decided to allow their stem cells to be used in medical treatments, Islamic law permits it. The use of adult stem cells would also be compliant with Hindu law, which objects to embryonic stem cell research due to the abortion of fetuses, as "Killing a fetus is a sinful act" (Hinduism Today, 2004). Again, adult/umbilical stem cells would not conflict ethically as no fetus is killed.

Buddhism is a religion that is half philosophical in nature, so there are few authorities to make any official laws. Thus its view on adult stem cell research is a bit murky. There are only

guiding principles, which allow a lot of personal interpretation. Many even interpret embryonic stem cell research as allowable (others don't because they believe it does end life). Buddhism also places a great importance on knowledge and compassion in the "prospect of developing cures and treatments that alleviate human suffering should be welcomed… [and on the] principle of ahimsa, or non-harming, and therefore has grave reservations about any scientific procedure that destroys life — whether human or animal" (Keown, 2004). As adult/embryonic cell treatments do not destroy life and are compassionate in nature, they would definitely be allowed. Therefore, all the major religions don't have any major issues with either adult or umbilical stem cells as long as they are used for purposes of medical treatment.

The Ethics of Animal Research

Animal sacrifice in modern scientific research is fairly widespread. Mammals (especially mice) have long been used to model many human conditions and disorders. Although many regulations oversee animal research to minimize needless animal suffering, animal research sometimes necessitates subjecting animals to incredible suffering. These animals are indeed alive, and because they have a central nervous system (or equivalent) they can feel pain. Painkillers are used to minimize pain, and animals are sacrificed as soon as possible to avoid needless pain. Yet most of the public see the medical value of using mice in research, and approve of it with strong oversights. The mice are viewed as having less moral status than a human, which justifies their sacrifice so long as they are used for medical gains. Studies often produce results for human application to help treat ailments. But how does this relate to embryonic stem cells? The embryos used to obtain ES cells do not feel pain in any way, because they are taken well before any type of nervous system has developed. Yet animals tested in

medical research experience pain/death, but this research is allowed. Does it matter whether the animal has a 'soul'. Most religions do contend that all humans do have souls, and each religion has views as to when ensoulment occurs that generally agrees with their stances on when life begins. Animal souls are somewhat in question.

The consumption of animals is also justified as necessity for human survival. In many countries, animal suffering in the food industry is quite high. Is it right to overfeed pigs, put them in pens so small they can't move, and then electrically prod them into the slaughter house (even when they have broken legs). Yet most people do not know of the abysmal treatment of animals as food. Is scientific animal research on the same level or any more unfair? Is one more justifiable than the other? Some Buddhists even abstain from meat out of respect for the life of animals. Both animal and stem cell research is performed to advance our medical knowledge to advance the common good.

Animals such as pigs are quite intelligent and even see in color, and we serve them up without a second thought. An organism may truly have a soul when it's able to think, to have a sense of reality, to understand. 'I think therefore I am.' A stem cell has none of these properties. Some stem cell research might involve implantation of stem cells into humans. Does this transplant represent some sort of quasi-cannibalism? If the cells come from a developing human, one is drawing benefit from another human's cells. Organ transplant could be seen in the same light. It is taking part of one human and using it to extend the natural life of another. Organ transplant is seen as more morally justifiable since the donor is normally dead. Thus the act of transplanting stem cells into another human to save his life is not as controversial as destroying the embryo to obtain the stem cells in the first place.

Parthenotes: Alternative Source of Stem Cell Lines

In the laboratory it has been observed that human eggs sometimes divide for seemingly no reason, without being fertilized. Since these eggs are unfertilized, there is no way in which they could become a human life. Thus, this could yield a "valuable source of stem cells that could bypass the moral, ethical, and some of the tissue rejection problems associated with fetal and embryonic stem cells, particularly for the woman donating the egg" (Bedford Stem Cell Research Foundation, 2004). Without the ability to become an embryo, these cells bypass religious objections to the destruction of potential human life. A developing embryo needs genetic material from both parents to develop into a human, yet parthenotes only contain that of the mother. So far, scientists have been able to successfully derive parthenote stems cells from monkey and human eggs, but have only been able to derive parthenote ES lines from monkeys (Bedford Stem Cell Research, 2004). The eggs are stimulated electrically or chemically to divide and produce parthenote stem cells (see figure 3 for more detail). Such cells have even been helpful in treating monkeys that have been induced to have Parkinson's disease (Bedford Stem Cell Research Foundation, 2004). Primate trials give hope that these cells could be beneficial in treating human aliments as well.

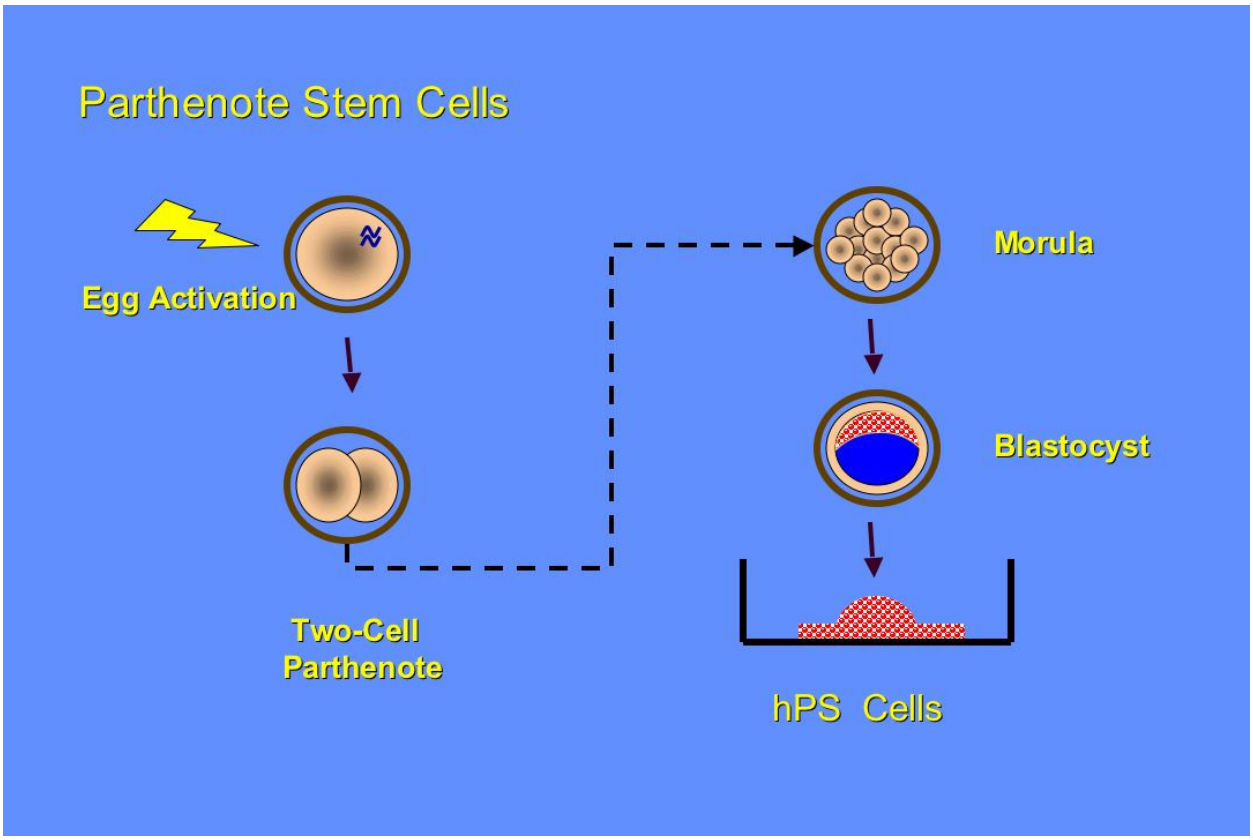


Figure 3. How Parthenote stem cells are made.
An unfertilized egg (top left) is induced by chemically or with electrical jolt to divide. The egg divides into increasing smaller (bottom left) and smaller (top right) cells. When it has divided into about 100 cells, outlying cells form a sealed layer that contains a fluid-filled cavity with several interior cells (Blastocyst). The inner cells (red dots) are then removed and put onto a petri dish (bottom right), these cells will continue to multiply as parthenote stem cells (Bedford Stem Cell Research, 2004).

Stem Cell Ethics In The Light Of Other Similar Issues

Embryonic stem cell research could even be considered a form of very early abortion. Normally, a fetus that would be aborted would be much further developed before being killed. Initially, abortion procedures were intended to be used only in extreme cases. It was first applicable when the child was deformed, had a genetic disease, or was a product of rape. Doctors also recommend aborting one or more of the fetuses when several are present if it increases the survival chances of the remaining fetuses. Having many babies at once greatly lowers the chance of survival of the others. Despite its initial intention, abortion has become more and more prevalent, even as a way to avoid an unwanted healthy pregnancy. "Approximately

1,370,000 abortions occur annually in the U.S. according to the Alan Guttmacher Institute" (Katz, 2005). It has been determined that 48 percent of abortions are performed after 9 weeks, when the fetus can feel pain (BBC News, 2000). Unlike the early stem cells, many aborted human fetuses are able to feel pain. And what is the medical benefit? In cases of terminating unwanted healthy pregnancies, the benefit is often not bringing an unwanted or unaffordable child into the home.

To most religions, late term abortion is debatably forbidden. "Judaism holds that the fetus is not yet a full human being, and thus killing a fetus is not murder. But abortion, when necessary, must take place before the first 40 days, when the fetus is referred to as 'mere water'" (Wikipedia, 2005). Catholic views generally do not permit any form of abortion. Other Christian religions vary in their stance, especially Protestant churches. If the fetus is a life, abortion is considered wrong. Anglican churches do allow abortions, while Evangelical generally do not allow it in any form. "Islam discourages abortion, but allows it as permissible under certain circumstances. Additionally, Hinduism teaches that abortion is a great crime and one of the worst sins. Moreover, abortion thwarts a soul in its progress towards God" (Wikipedia, 2005). Thus a late term abortion, if the fetus is considered a life, would be considered infanticide.

A developed fetus is not a lump of cells. Some abortions even occur when the fetus would be able to survive outside the mother (but usually with help). It would appear this is much closer to homicide than stem cell harvesting. A blastocyst is sensationless, nerveless, dividing ball of cells, which certainly can not develop into a human outside the body. It is stopped from growing into a healthy human. Many aborted fetuses are highly developed with brains, arms, legs, lungs, and beating hearts (heart also starts beating around 9 weeks). Many consider the point the heartbeat starts as the moment life begins. It marks a point where the fetus starts to

take control and becomes an independent organism. Unlike early embryonic stem cell research that can save many lives from the ES lines established from one embryo, abortion to terminate an unwanted pregnancy does not produce anything of value, other than economic or psychological benefit to the mother. Many fetuses are thrown away, the mother affected adversely by the procedure and nothing of value gained. Using embryonic stem cells to help cure paralysis is a much more beneficial procedure. Even so, one or both may be still considered murder by the traditional Catholic stance.

Worldwide Permissiveness

Despite all humans having a common bond, worldwide there is much dissention on what is moral, what is the right religion, and what should be law. Perhaps this springs from the great diversity in cultures and languages our world possesses. Varying perspectives and influences do change ethical/moral decisions of countries with regard to what scientific research is allowed. Figure 4 below details quantifies individual countries' permissiveness towards stem cell research. It's notable how the United States has many stem cell research facilities, but one of the strictest rules regarding research. With countries that aren't as ethically inclined as the United States the potential exists for abuse and/or great discovery.

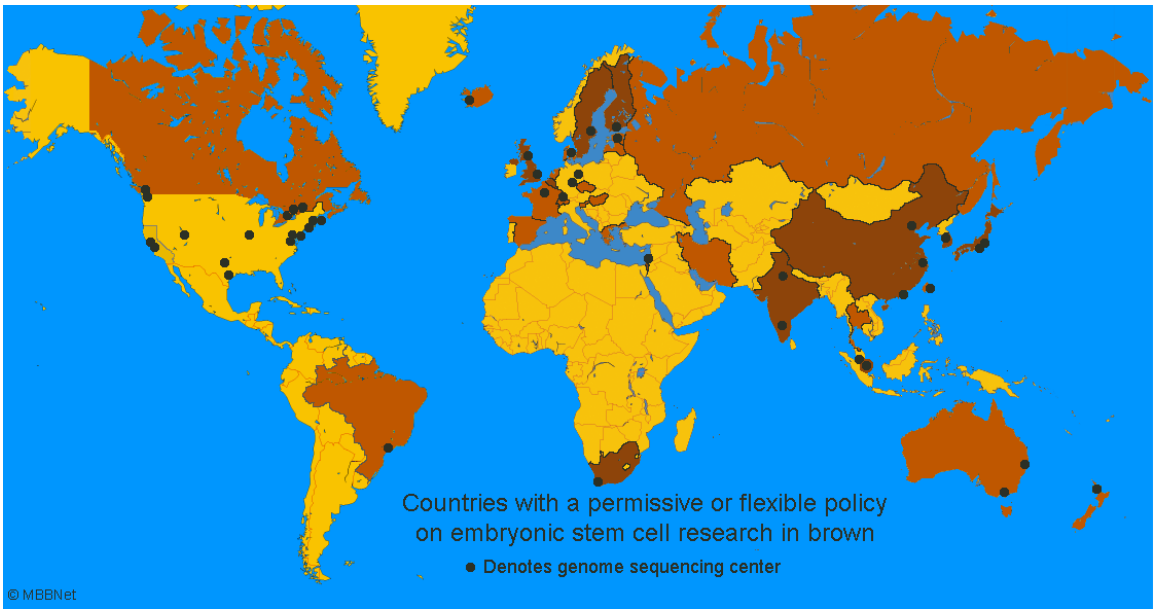


Figure 4. World Wide Stem Cell Laws.
Permissive stem cell laws: labeled in dark brown, allow several uses and therapeutic cloning. Includes United Kingdom, Belgium, Sweden, Israel, India, Singapore, China, Japan, South Korea, South Africa and others– 2.7 billion people. Flexible stem cell laws: labeled in light brown, only fertility clinic derivatives can be used, and no therapeutic cloning. Includes Australia, Brazil, Canada, France, Spain, The Netherlands, Taiwan and others – 800 million people. Restrictive stem cell laws: yellow. Includes the U.S., most of Africa, half of South America, Italy, the Balkans, Saudi Arabia, Malasia, and Tibet (Hoffman, 2005).

Stem Cell Payment Issues

Another problem aside from moral objections is the potential cost of stem cell treatments. Pharmaceutical companies claim to have the health of the consumer in mind, but often charge very high prices for medications. These companies invest hundreds of millions of dollars hoping to produce a drug/vaccine that can be useful in medical treatment. Yet, stuck with an overwhelming research bill, the medicines are priced quite high to pay for it. Is it right to charge such high prices when the treatments were first intended to help all people, including those who can't afford them? It is also significant to note that almost all medicines, vaccines, and medical procedures begin expensive, then significantly cheapen as production grows more efficient. Though these prices do come down over time, people die in the meantime. The moral thing to do would be to provide stem cell treatments to those whom were on the verge of death or whose

quality of life was greatly diminished. The cut off point of who is worthy seems blurred at best, but some would greatly benefit from it. However it does seem clear that any cosmetic use of stem cells should be paid for by the individual themselves, not by HMO's that would transfer the costs to all patients with escalated premiums. But offering cosmetic stem cell therapy could open a Pandora's box of stem cell abuse, much like that of plastic surgery. Non-essential misuse of medical technology takes the focus from individuals in dire need of help. For those in true need, the money still has to come from somewhere, perhaps from taxes. Many countries do offer free health care supported by higher taxes. However, it is morally suspect the amount of money some nations spend on intrinsically immoral actions. The United States has spent a purportedly $170 billion dollars on the recent Iraqi war. This same money could have gone into stem cell research, or to pay for many treatments of those in need. War seems counter-intuitive to the message of protecting life the United State supposedly has. Money is out there to pay for stem cell treatments, but it seems only good HMOs are there to foot the bills.

Conclusion

At the end of the day, stem cells do hold an immense medical potential. However, the question remains whether it is ethically responsible to use material from a cellular mass with the potential to become as real a person as yourself. If one was paralyzed in an accident, and a stem cell implant is your only hope for walking, would you favor their use? If a new technique was available to prolong the human life span, who would be able to refuse? The author of this report agrees with the stance of all four major religions that the use of adult and cord stem cells is justified so long as they are used for medical benefits, not cosmetic purposes. The author also agrees with their stance that parthenote derived ES cell lines are an acceptable alternative to ES

lines derived from fertilized eggs (once we have figured out how to obtain the lines in humans instead of primates). The author is against using any kind of stem cells (adult, cord, or ES) for cosmetic purposes, especially if paid by taxpayer money. The author also agrees that frozen IVF embryos slated for discard by the parents should be the preferred method of obtaining embryos if parthenotes are not available.

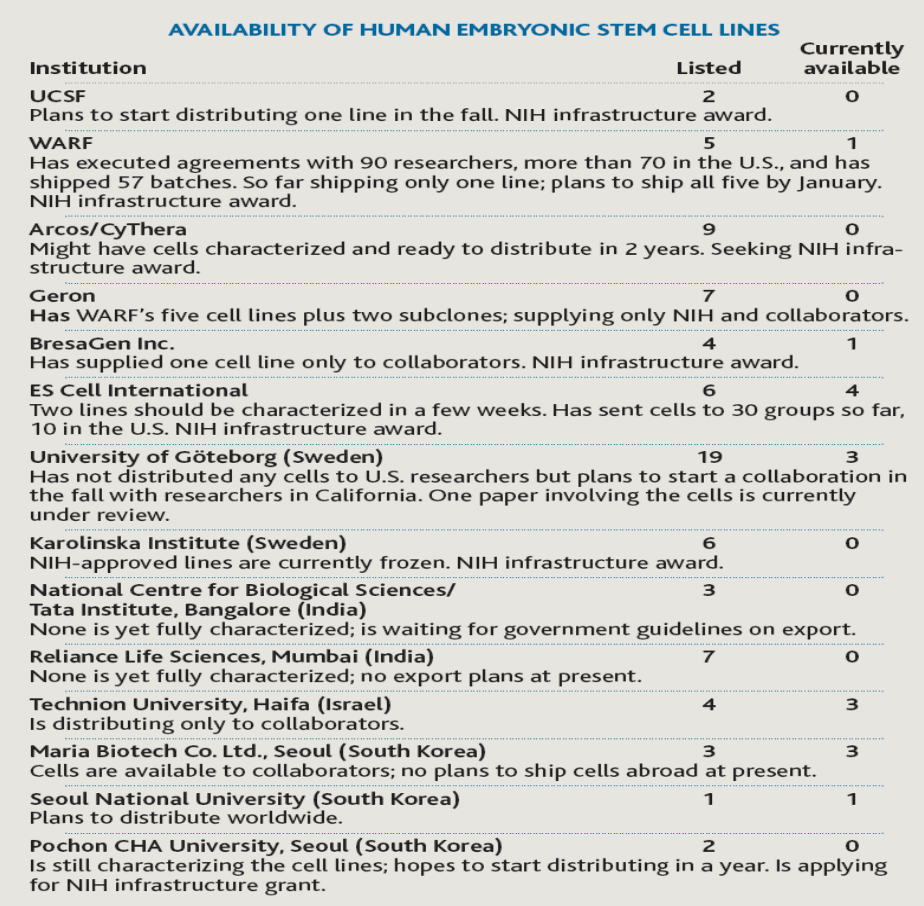
CHAPTER 4: STEM CELL LEGALITIES

In this chapter, we will address the various laws governing stem cell use in several countries. Due to the ethical controversies surrounding ES (embryonic stem) cells, there are laws in place to regulate their use, which vary greatly. Some laws increase restrictions, while others are passed to lessen them.

United States of America-

Arguing that destroying human embryos for research purposes is akin to murder, President Bush banned the use of federal money for human ES (hES) cell research on any cells derived from blastocysts after 9:00pm, on 9 August 2001 (Holden and Vogel, 2002). Prior to that date, if an embryo had already been destroyed to create a cell line, if it could potentially save patients lives, it could be used for research. The purpose of this legislation was to prevent any future embryonic "murders". As a result of President Bush's legislation, there are very few available embryonic stem cell lines available for use and even fewer available for distribution (See Figure 1 below for details).

However, in May of this year, a bill was circulated in Congress to lessen the restrictions on federal funding and research with hES cell lines- a bill which Bush stated he would veto if the bill made it to his desk since he maintains it still constitutes murder.



AVAILABILITY OF HUMAN EMBRYONIC STEM CELL LINES

Institution	Listed	Currently available
UCSF Plans to start distributing one line in the fall. NIH infrastructure award.	2	0
WARF Has executed agreements with 90 researchers, more than 70 in the U.S., and has shipped 57 batches. So far shipping only one line; plans to ship all five by January. NIH infrastructure award.	5	1
Arcos/CyThera Might have cells characterized and ready to distribute in 2 years. Seeking NIH infrastructure award.	9	0
Geron Has WARF's five cell lines plus two subclones; supplying only NIH and collaborators.	7	0
BresaGen Inc. Has supplied one cell line only to collaborators. NIH infrastructure award.	4	1
ES Cell International Two lines should be characterized in a few weeks. Has sent cells to 30 groups so far, 10 in the U.S. NIH infrastructure award.	6	4
University of Göteborg (Sweden) Has not distributed any cells to U.S. researchers but plans to start a collaboration in the fall with researchers in California. One paper involving the cells is currently under review.	19	3
Karolinska Institute (Sweden) NIH-approved lines are currently frozen. NIH infrastructure award.	6	0
National Centre for Biological Sciences/ Tata Institute, Bangalore (India) None is yet fully characterized; is waiting for government guidelines on export.	3	0
Reliance Life Sciences, Mumbai (India) None is yet fully characterized; no export plans at present.	7	0
Technion University, Haifa (Israel) Is distributing only to collaborators.	4	3
Maria Biotech Co. Ltd., Seoul (South Korea) Cells are available to collaborators; no plans to ship cells abroad at present.	3	3
Seoul National University (South Korea) Plans to distribute worldwide.	1	1
Pochon CHA University, Seoul (South Korea) Is still characterizing the cell lines; hopes to start distributing in a year. Is applying for NIH infrastructure grant.	2	0

Figure 1- Chart showing the availability of the approximately 70 human embryonic stem cell lines as of Aug. 9, 2002. The chart shows where they are held, how many each company has, and how many are actually available for use. Information obtained from Science magazine.

When Republican Mike Castle (Delaware) proposed this bill, along with Diana DeGette D- Colorado, he stated that the use of unwanted IVF embryos should be morally acceptable even to those opposed to abortion since lives could potentially be saved. Bush responded by locating a few families with children from donated embryos, known as "Snowflake babies," and arguing that even unwanted embryos have the potential for life and therefore cannot be destroyed. As he stated in an interview on May 13th, "I've made it very clear to the Congress that the use of federal money, taxpayers' money, to promote science which destroys life in order to save life- I'm against that. And therefore if the bill does that, I will veto it" (CBS News, 2005).

Much to President Bush's chagrin, the House of Representatives passed the bill on May 24th by a vote of 238-194. Although this is nowhere near the two-thirds majority needed to override a presidential veto, it did send a message to President Bush that despite his threats, the Congress still felt differently than he on this issue. Another bill was circulated along with this one that provided $79 million in federal funding for stem cells derived from adults and umbilical cords and establishes a national database for anyone in need of a match, as opposed to using the ES cells. This one passed 430-1 (CBS and ABC News, 2005).

Some supporters of the embryonic stem cell bill have stated that it is the obligation of Congress to fund research that could lead to cures for diseases like Parkinson's and Alzheimer's. Rep. James R. Langevin, D-RI, who was paralyzed at 16 as the result of a gun accident stated that "Being pro-life also means fighting for policies that will eliminate pain and suffering" (CBS News, 2005).

Despite all the controversy and bickering occurring in the U.S. government, in several other countries there are relatively few restrictions on stem cell research which is allowing them the opportunity for the first time, to surpass the United States in scientific research. There have been numerous American scientists that have left the U.S. due to all the restrictions on research here. Many have fled to England, while others go to Sweden, Singapore, Japan, or China in order to conduct the kind of research they want to with regard to hES cells.

Perhaps the realization of this fact has led to Congress wanting this new bill to be passed. However, it is also because of this that President Bush is so wary of supporting the bill. In South Korea, researchers were able to develop a highly efficient procedure for obtaining ES cells using nuclei from adult patient skin cells and transferring them to enucleated human eggs. These embryos were then cultured to the blastocyst stage to generate ES cells for treating the same

patient the nucleus was taken from, so the stem cell will not be rejected by the patient (Hwang et al, 2005).

Stem Cell Legislation in Individual States

Now, in response to Bush's legislation, a few states have granted state funding for research: California, Connecticut, New Jersey, and Pennsylvania. California was the first state to set aside funds for ES research. Most recently was Connecticut which supplied Connecticut companies with $100 million for ES research. In Massachusetts a bill was circulated to lessen restrictions on stem cell research in the Bay State and although Gov. Mitt Romney was opposed to and even vetoed the bill, it was overridden and passed. Due to the passage of this bill into law in Massachusetts, the governor of Connecticut has stated that if this issue comes up while she's still in office, she will support any stem cell bills that make it to her desk.

California:

Last year, the state of California approved Proposition 71 to recruit scientific research companies (GEN, 2005). It allowed for $3 billion dollars to be used for stem cell research over the next 10 years (CBS News, 2005). They were the first state to do such a thing after Pres. Bush's ban on federal funding of embryonic stem cell research. In a recent poll conducted by Genetic Engineering News, of the people polled, 72% of them believe that other states should be worried about loosing their scientific research companies and falling behind in the research field. As demonstrated by the fact that the setting aside of funds for research has led several companies, including some from Massachusetts and other states to relocate to California to make it easier to conduct their research since there was money available to do so. Also, when the state of California put aside this money for research they initiated talk in other states for similar

purposes, especially states that had started to lose businesses as a result of their relocations to California.

Massachusetts:

Senate Bill, No. 2039 was recently circulated through the Massachusetts state Senate which called for a lessening in restrictions from the state of Massachusetts for stem cell research (Mass.gov, 2005). The bill allows for therapeutic cloning of human embryos for research and also sets up an advisory board to resolve any lingering issues with the bill. Governor Mitt Romney, R, was not in favor of this bill for moral reasons and as a result, vetoed it.

Gov. Romney has said that he approves of the research when it is done on adult stem cells or cells extracted from leftover frozen embryos from fertility clinics, but does not support cloning for medical research. He has stated that it is akin to creating human life in order to destroy it. He suggested that the legislature make amendments to the bill such as "including language defining the beginning of life as the moment of conception, banning the production of embryos for other research purposes and limiting compensation to women who donate their eggs." The Legislature however, rejected all of his proposed amendments.

Prior to this bill's passage, Massachusetts state law required that any scientists who wanted to conduct embryonic stem cell research would first need to get the approval of the local district attorney. Now, with its passage, that requirement is gone and the state Health Department has been granted some regulatory controls. However, with Romney's veto, it has put him at odds with some of the top research facilities (including university owned ones) in Massachusetts, including the Harvard Stem Cell Institute, which are trying to keep up with institutions in California (boston.com). Unfortunately for Gov. Romney, the bill passed with

enough votes to override his veto, and when the bill went back to the Senate after his veto, the bill was easily passed and made into law.

New York:

As a result of California's $3 billion for stem cell research, New York feared losing some of their best research institutions and scientists to California and tried to pass a bill of their own allowing for $1 billion to be used for stem cell research. The bill would allow for $100 million be reserved for research each year.

Sen. Nicholas Spano, R- Yonkers, the man proposing the bill, stated that it is "an investment we have to make," and that "we can't afford to fall behind other states." However, Senate Majority Leader, Joseph Bruno, R-Rensselaer County and Gov. George Pataki were somewhat apprehensive about the bill, specifically about where the money for this measure would be found. Joseph Bruno stated that "we support, generally, stem-cell research. We don't support destroying embryos to get cells" indicating that he might be opposed to this measure. Gov. Pataki however was a little less open about his feelings regarding the bill because when asked whether or not he supports embryonic stem-cell research, he replied with "I haven't seen their proposal" (The Journal News, 2005).

A few other states have managed to set aside state funds to attract research companies and scientists, such as New Jersey- $380 million, and Connecticut -$100 million over 10 years (CBS News, 2005). However, Massachusetts and California are the only two that have been successful in passing laws setting aside money for stem cell research and/or regulating the research. States such as Maryland and South Carolina have tried to pass their own legislation to allow for funding of stem cell research, but as of yet, all attempts to do so have failed. Also, even with states now setting aside their own funds for stem cell research, for many, it is still not

enough, and these companies relocate to another country where the debate over stem cells is minimal, if at all.

Stem Cell Laws Outside the U.S.

Now that we have seen what the laws are like in the U.S. and in particular a few individual states, we will visit other countries to find out their laws governing stem cell use. Figure-2 below shows a world map indicating whether each country has permissive (dark brown), moderate (orange), or restrictive (yellow) stem cell laws.

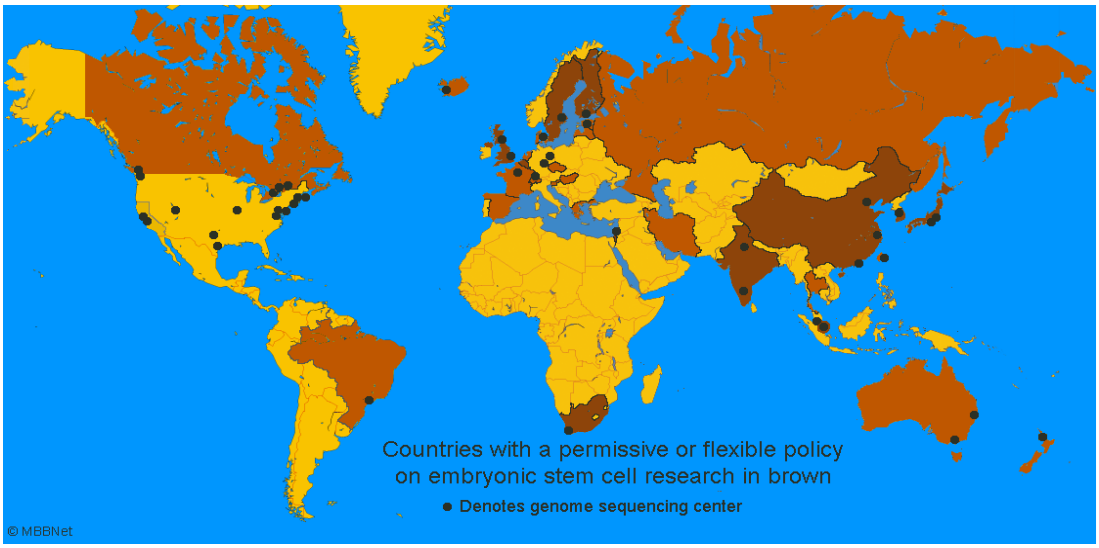


Figure 2- Worldwide Stem Cell Laws. **Permissive** stem cell laws: labeled in dark brown, allow several uses and therapeutic cloning. Includes United Kingdom, Belgium, Sweden, Israel, India, Singapore, China, Japan, South Korea, South Africa and others– 2.7 billion people. **Moderate** stem cell laws: labeled in orange, only fertility clinic derivatives can be used, and no therapeutic cloning. Includes Australia, Brazil, Canada, France, Spain, The Netherlands, Taiwan and others – 800 million people. **Restrictive** stem cell laws: yellow. Includes the U.S., most of Africa, half of South America, Italy, the Balkans, Saudi Arabia, Malasia, and Tibet (Hoffman, 2005).

Sweden:

Sweden is one country in which there is little controversy surrounding stem cell research, and because of this, they are considered to be at the forefront of science and technology in stem cell research. Not only are they experimenting on and with adult stem cells, but they are also

experimenting on and with hES cells, complete with governmental support. This is due in large part to the country having strong public support, strong government funding, a favorable bioethical climate, and a tradition of science and research. There are currently 30 research groups and nearly 300 people at nine Swedish institutions involved in stem cell research ("Sweden's Stem Cell Success.", 2005).

In Sweden, there are large numbers of people working in the stem cell research field which has led them to surpass Singapore, Great Britain, and the US in advances in stem cell research. Due to their progress, people who support advancing the science, such as Michael J. Fox, owner of the Michael J. Fox Foundation for Parkinson's Research, awarded $4.4 million (U.S.) dollars to Swedish companies.

The main reason for all the support of ES cell research is because all of the ES cells being tested in Sweden have come from IVF (in vitro fertilization) clinic embryos which are no longer viable for use in an IVF situation. Therefore, the government sees no reason why not to support the science and this avoids the debate of paying women to donate their eggs specifically for ES cell purposes.

Germany:

In January 2002, 340 of Germany's 618 parliamentarians voted in support of allowing embryonic stem cells to be imported for research, but only under close government supervision. The National Ethics Council which was created by Chancellor Gerhard Schröder recommended limited importation of stem cells in November of 2001. However, a special parliamentary commission was in favor of a strict ban.

The existing German laws ban research on human embryos and only allow embryos to be created in labs for in vitro fertilization purposes. The embryonic protection law, which was

passed over a decade ago, however, did not take into account stem cells, as they had not yet been discovered and therefore did not explicitly ban their importation.

Deputy chair of the National Ethics Council and specialist on health technology assessment at the University of Hamburg, Regine Kolleck, stated that "the import was not prohibited before, it was completely free. Now we'll have a very restrictive law on the way the import is regulated, and that is more than we had before." She also said that she would have favored a freeze on ES cell imports and still has hopes for the research on adult stem cells since they do not require embryonic destruction (Kim, 2002).

Dr. Alexander Kekulé, director of the Institute for Medical Microbiology in Halle, believes that this act of parliament puts German researchers at a serious disadvantage. The German Parliament decided that researchers are only allowed to use stem cells which have already been created and prevents German researchers from creating more cells. Dr. Kekulé has called this act "a lame compromise" and believes that Germany has a handicap and will "have to do research with cells that will soon be obsolete" (Kim, 2002).

Drs. Jochen Taupitz and Kolleck, though colleagues, have quite different opinions on what the effect of this resolution may have on other countries. Dr. Taupitz, a member of the German National Ethics Council and a law professor in Mannheim believes that "Germany has some of the strictest laws in the world and so even with this resolution we are pretty isolated in Europe." While Dr. Kolleck believes that what happens in Germany may have a ripple effect on smaller countries which also have restrictive laws such as Austria, Portugal, and Ireland.

Switzerland:

In November of 2004, Swiss voters approved a new law on embryonic stem cell research. This law came into effect on March 1, 2004 and allows researchers to take stem cells from

"supernumerary" human embryos. These embryos are created for in vitro fertilization but not actually needed for implantation. (Tognina, 2005)

The law was passed in December of 2003 by the Swiss parliament but some anti-abortion groups organized a referendum opposing the legislation, delaying the actual enactment of the law. There were even some left-wing environmentalists who opposed the law. The environmentalists are skeptical about developments in genetic research. Some opponents of the law even went so far as to liken researchers to the Nazi "angel of death," Dr. Josef Mengele in an attempt to discourage voters from supporting the government's passage of the bill into law (ABC News, 2004).

This law provided that any existing stem cell projects be declared to the Federal Health Office within three months from March 1st and that new projects be subjected to authorization by the office based on the recommendations of a specially appointed ethics committee.

On top of those requirements, the law sets strict limits on the type of research that can be done. For example, it forbids the production of embryos for research purposes, creating clones, chimeras (part-human, part-animal organisms), or hybrids. Stem cells can only be obtained from embryos in the first seven days of their development and the use of any embryos for commercial purposes is not permitted. Also, the use of the supernumerary embryos is permitted only if the donor couples concerned have given written consent, and have been fully informed about the research project. Anita Holler of the Federal Health Office's Biomedicine Division believes that couples will willingly donate embryos for research. Also, anyone who is found to have violated the provisions of the law are liable to a fine of up to $427,460 (US) or five years in jail (Tognina, 2005).

Spain:

On July 25, 2003, the predominantly Catholic, and rather conservative Spain, passed legislation that allows for the use of embryonic stem cells for research. They are the first Catholic country to authorize hES cell research. There were conditions placed on how the embryos were to be obtained such that they can only come from IVF clinics and must be excess embryos bearing the "parent's" consent (Bosch, 2003).

This law is an update of a former law which was enacted in 1988, which allows for spare embryos frozen for 5 years or more in IVF clinics to be used for research purposes. The 1988 law allowed for embryos to be frozen for up to 5 years, but did not allow for research to be conducted with these embryos. Since the law did not state what the IVF clinics were to do with embryos that had been frozen for over 5 years, advocates of ES cell research lobbied to amend the law to permit these embryos to be used for research (Bosch, 2003).

The lobbyists won in 2003, as embryos up to 14 days old, regardless of how long they have been frozen, can be used for research, so long as the parents' have given their informed consent. For couples who have donated embryos for the use of other couples, the embryos will remain up for adoption for 5 years, after which point, they will be moved to the national center for research purposes. Also, any embryos whose parents (or mother) are unknown and/or informed consent has not been provided within a year, will remain available for donation to other couples for up to 4 years, and then transferred for research if still unused (Bosch, 2003).

United Kingdom:

In December of 2000, Britain approved a governmental measure to extend their current legislation to allow research to be conducted with human embryos as a source of stem cells. To get this issue resolved, both sides engaged in extensive lobbying. In the end, members of

parliament were allowed a free vote on this issue and ended up voting more than 2-1 for the cloning/stem cell research plan, and passed but a margin of 366-174 ("UK Parliament Approves…," 2000).

Some opponents of the measure criticized how quickly the decision was reached and argued that there was insufficient time allowed for debate on the subject. Since the passage of the Human Fertilization and Embryology Act (HFEA) of 1990, Britain has allowed licensed research to be conducted on human embryos up to 14 days old but it was strictly limited to problems of infertility. The new regulations amended this law so that unborn children in the early stages of development could also be used for the purpose of research on non-congenital diseases before being killed ("UK Parliament Approves…," 2000).

British Prime Minister, Tony Blair, even backed this proposition when he stated that this type of research is vital to maintaining Britain's position as Europe's leader in biotechnology. These proposed amendments to the 1990 HFEA also asked that cloning be allowed for research purposes which sparked an even bigger debate about how if cloning for these purposes was allowed, how much longer it would be before cloning for reproductive purposes was asked of the Parliament. As a result of Tony Blair's position, some protestors dressed in white lab coats and wore identical Tony Blair masks and urged the members of parliament to "Vote no to Cloning" ("UK Parliament Approves…," 2000).

With the allowance of the amendments to the 1990 HFEA, in May of 2004 the UK opened the world's first ES cell bank, located in Hertfordshire, England. Its purpose is to supply and store stem cell lines aimed at research and treatment for chronic diseases. This stem cell bank was funded by the Medical Research Council and the Biotechnology and Biological Sciences Research Council, both based in the UK. This new stem cell bank will also act as a

library for cell lines derived from multiple sources and will make these cells available for researchers ("World's first …", 2004).

Even Ireland wants to be included in the stem cell research and other biotechnology fields as a major contender. As a result, they recently opened a new stem cell research center at the National University of Ireland (NUI) Galway. This research facility is the Regenerative Medicine Institute (Remedi). At the opening of the Remedi center, the Minister for Enterprise Trade and Employment, Micheál Martin TD said "The Remedi center brings together a top team in gene therapy and stem cell research, continuing the Government's investment in the clinical and academic infrastructure in the west and putting Ireland on the world map in this ground-breaking area of scientific research and development." (Skelly, 2005)

The Science Foundation of Ireland (SFI) is the group responsible for funding Remedi, and is giving the research center €15m ($17,917,500 US) over five years. This is the second time in as many years that SFI has donated a substantial amount of money to NUI Galway. The Remedi center is focusing their research on adult stem cells rather than the more controversial ES cells. This new research center is partners with healthcare industry leaders Medtronic and Biolabs which have been developed due to SFI's Centers for Science, Engineering and Technology (CSET) policy as well as to "…ensure that the research undertaken is practical and relevant to Ireland's economic development and that Remedi remains internationally competitive, results oriented, and focused on delivery." -Micheál Martin (Skelly, 2005).

South Korea:

Lately, South Korea has been mentioned a lot in talks involving stem cell research, especially when talking about the possibility of lessening the restrictions on stem cell research and funding in the U.S. The reasoning behind their recent media coverage is due to their success

in making stem cells tailored to match an individual. The South Korean scientists were able to create 11 new stem cell lines using the genetic material from the skin cell of a patient and implanting it into a donor egg. The eggs that were the product of this process were grown to the blastocyst stage then their ES cells were isolated and used to derive ES cell lines. The cell lines were perfect matches for the patient, and as a result, could lead to treatments for certain diseases, such as diabetes, without the consequences that result from the rejection of the treatments.

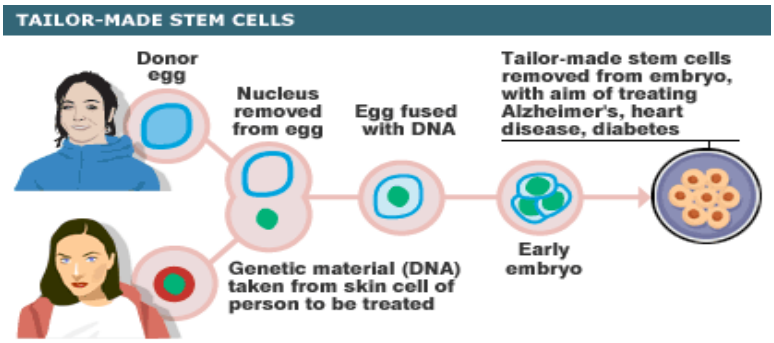


Figure 3- Diagram showing the method used for cloning and obtaining embryonic stem cells used in South Korea. ("Stem Cells Tailored to Patients," 2005)

However, since this process is a form of cloning, in many countries which are opposed to this practice, it stirs up unsettling feelings. Pres. Bush has stated in interviews that he is against cloning and even fears a world in which cloning may one day be an acceptable practice. Yet, this Korean advancement is a significant milestone in stem cell research. Since this is such a new area of research, some experts are skeptical as to how well these cloned cells will work and have warned that these cells could become cancerous. The Korean team that created these cells agrees that there is still much work to be done before these techniques can be perfected. Dr. Gerald Schatten from the University of Pittsburgh, US, who worked with the Seoul National University Team on this project, said that "In some cases, the cells might need to be manipulated before being used as a treatment." Professor Woo Suk Hwang "stated that researchers will also

need to develop ways to efficiently direct the growth of stem cells into stable cell types." Prof. Hwang and his colleagues successfully cloned human embryos last year (BBC News, 2005).

This advance has led to splits in the scientific community along with heated discussions about the ethics of such research. As we have seen, it has even triggered debates within countries whose laws governing stem cell research are fairly restrictive to want to lessen the restrictions. It also leads others to stand firm to their view that science is going too far, and needs to be monitored and if necessary, certain areas prohibited from being probed. In some countries the science and technology, the ethics, and government are entwined and therefore it is extremely difficult to make a ruling in favor or against the advancement of this science. Yet in others, the government has found a way to reach a happy medium, allowing the researchers to experiment and test new theories with minimal interference, while others wish to maintain a little more control over the science. Hopefully, soon all countries governments and researchers will be able to reach a compromise so that research can move forward with less controversy and stumbling blocks.

It seems to me that with the laws that are currently in place, the best countries to go to in order to practice stem cell research would be the UK, Switzerland, Sweden, or South Korea, as these countries have the least amount of restrictions on the type of research that can be done. Though they are not completely controversy-free because of their impact around the world, the scientists and governments in these countries seem to have been able to reach a compromise so that everyone can do their job and produce results without constantly hitting a road-block. Not to mention the fact that in the UK and Switzerland especially, money for research is being donated left and right from anyone who cares enough and has the means to support this type of research.

CONCLUSION

In this IQP we investigated what stem cells are, the different types of stem cells, and the legal and ethical ramifications of stem cell research, especially with regard to human embryonic stem cells (hESCs). Adult and umbilical stem cells are the least controversial, but also have the least potentials. All four of the world's major religions support the use of umbilical and adult stem cells, so long as they are used to support the "common good". The problem comes with ES cells that are taken from the inner cell mass of the blastocyst, and usually destroy an embryo to obtain them.

It is because of this destruction of an embryo that sparks all the debate and controversy, and has led to legislations being passed with some countries banning the practice, some banning government funding from being used for the research, and others simply restricting what can be done with the harvested cells. The U.S. government has taken the stance of banning the use of federal money for human ES (hES) cell research on any cells derived from blastocysts after 9:00pm, on 9 August 2001. Leaving funding of the research up to the individual states (or the companies themselves) to decide how much money they can devote to ESC research.

One of the trickiest parts about the debate is the destruction of the embryo. Most who are opposed to ESC research believe that it is essentially murder to destroy an embryo which has the potential to develop into a human being. As a result, it raises many questions of its own, such as when does life truly begin? Since this question can not be answered to anyone's complete satisfaction, some groups (primarily religious, for example, Catholics) have decided that life begins at conception, although some Catholic philosophers argue that the blastocyst is not yet "individualized" so it has less moral status than a fetus.

Unfortunately, for U.S. researchers, the government has sided with the Catholics that believe life begins at conception and that "there is no such thing as a spare embryo" as stated in an interview by Pres. Bush. As a result, some individual states have started passing their own legislations to support ESC research, such as California, Massachusetts, and New York. All of which have either set aside money for the companies to conduct their research, or have lessened the restrictions on what type of research can be conducted on these cells. However, for some scientists, this is still not good enough and they relocate to places where there is less opposition, governmental or otherwise, towards this type of research.

As for whether or not ESC research should be allowed to be conducted and supported by governments, we believe it should be. ESCs have tremendous potential for benefits to the medical community and should be allowed to be researched if there is a chance that they may provide cures for debilitating diseases such as Alzheimers' and Parkinson's. Especially in the United States where there is supposed to be a Separation of Church and State, there should not be so many debates based on religious standpoints as to whether this type of research should be allowed to be conducted or not.

We also support research that would lead to human parthenotes being acceptable replacements for ESCs once we have found a way to successfully create them. We believe that ESCs hold great potential for medicinal, especially the therapeutic, treatments of diseases as well as reparative, restorative, and regenerative aspects related to things such as spinal cord injuries. Yet, while we support this research, we do believe that it should also be monitored so as to make sure the research is being performed for medical rather than cosmetic benefit. Our preferred approach for obtaining embryos for research purposes is from IVF clinics in which these left-over embryos are just sitting in a freezer and are slated for destruction. Though we understand

the stance of people who say that there is “no such thing as a spare embryo”, since some families have donated their unused embryos to other families who were unable to parent children themselves, we do not see why these embryos who have not been placed up for adoption and are not going to be used cannot with the owners full consent be used to improve the quality of life for those suffering from debilitating diseases, or have encountered a horrible accident which has rendered them invalids.

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