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STEM CELLS

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Abstract

Stem cell research is an emerging field of biology that has great medical potential and controversy. We will examine the science, hopes, morality, and policy issues regarding stem cells with intent of educating ourselves and the general public on the facts of stem cell research. Using this knowledge the authors were able to better understand why this area of research is so crucial to the medical community, and how its many benefits outweigh its disadvantages.

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1.0 Executive Summary

"In late 1998, a group of scientists led by University of Wisconsin-Madison developmental biologist James Thomson became the first in the world to successfully isolate and culture human embryonic stem cells." (ES Cells Research at UWM, 2003)

When most people first think of stem cells, they automatically think of one type, embryonic stem (ES) cells that normally come from human embryos. Because destroying human embryos is such a controversial subject, the public is often quick to dismiss the immense benefits stem cells bring, and instead work to outlaw all research, including the use of non-embryo stem cells. While embryonic stem (ES) cells clearly have the most medical potential because they can differentiate into almost any cell type for therapeutic purposes, they are not the only types of stem cells we have access to, and recently scientists have even devised ways of deriving ES cells without working with embryos.

Stem cell therapy makes use of new techniques and technologies to replace diseased or dysfunctional cells with healthy, normally functioning cells derived from stem cell colonies. The end purpose of this therapy is to treat diseases at the root of the problem instead of treating the symptoms as many conventional medicines do. For example, this new therapy has the potential to cure blinding diseases of the retina by replacing dead retinal cells with new ones.

Each type of stem cell holds for us a potential to develop treatments and preventative measures for many of the afflictions that we are currently unable to treat. Each variant of embryonic and adult stem cells have their own innate properties that distinguish them from other types of stem cells. The unique properties of these cells is

what scientists believe gives each of these stem cell types separate niches as sources for treatments and as knowledge bases (McKay, 2000).

Predictably, the President Bush's policy on stem cell research has been decidedly conservative. While Bush recognizes the broad medical potentials ES cells have to offer, he refuses to risk angering his conservative following by giving anything more than his very limited support; allowing federal dollars to support only research on previously established ES cell lines derived using only acceptable means as determined by him. On cloning, he has latched onto and fostered the social stigma around human cloning and rejects the practice outright. On the final issue of adult stem cell research where he faces little if any controversy, the President can and does fully back the research without any fear of alienating his conservative following.

These limitations on ES research have left most scientists in the stem cell field with a bad taste in their mouths. Many of these scientists argue that the 78 ES cell lines made available for legal use are not enough to build a competitive research program in the United States.

One of the dangers of overly restrictive regulation of stem cell research in the U.S. is the possibility that the U.S. may be shut out of the expanding field entirely. If laws in the U.S. restrict research too much, companies will relocate to countries with less restrictive laws governing the research. In that way the U.S. stands to lose not only the medical benefits of such a technology, but also to lose a potentially massive industry, and all the money and jobs that a large biotech industry has to offer. The U.S. also stands to lose economic advantages since foreign companies would be more likely to patent stem cell technologies before American companies.

2.0 Project Objective

Stem cells are cells capable of differentiating into a wide variety of adult tissues. This property gives them great potential to vastly improve the treatment for patients who in some cases would have no other treatment available to them. For example, hematopoietic stem cells (HSCs) have the ability to reconstitute all the cellular components of blood. This ability makes HSCs ideal for treating patients with immune systems suppressed by radiation or chemotherapy. The purpose of this IQP was to research this new technology, first describing what stem cells are, then asking, what are their types? Where do we get them? And, what are their medical uses? We will then describe their effects on society namely, the ethics of their use and legislation governing their use. Using current technology, stem cells are not easy to isolate, and many hurdles still exist in applying them. This IQP describes what stem cells are and will look into the moral, legal and scientific hurdles as well as the great medical potential that surround stem cell research.

3.0 Stem Cell Types and Sources

"In late 1998, a group of scientists led by University of Wisconsin-Madison developmental biologist James Thomson became the first in the world to successfully isolate and culture human embryonic stem cells." (ES Cells Research at UWM, 2003)

When most people first think of stem cells, they automatically think of one type, and that type comes from human embryos. Because this is such a controversial subject, they are quick to dismiss the immense benefits they bring, and instead work to outlaw all research, including the use of non-embryo stem cells. While embryonic stem (ES) cells clearly have the most medical potential, they are not the only types we have access to, and recently scientists have even devised ways of deriving ES cells without working with embryos.

3.1 Stem Cell Properties

A stem cell, regardless of its source, has three basic properties:

1 – They are capable of dividing and renewing themselves indefinitely.

2 – They are unspecialized.

3 – They differentiate into other specific cell types.

Unlike cells like blood cells or muscle cells that can not renew themselves indefinitely, stem cells are considered immortal. Stem cells can replicate themselves many times over. This allows lab workers to start with a small population of stem cells, and when grown over a few months, can end up with a population of millions of cells. As long as they stay unspecialized like the parent stem cells, they are capable of

maintaining this cell division long term. However, if they start to turn into specialized cells, like blood cells or bone cells, they lose their ability to keep this up, and eventually stop replication.

When we say stem cells are unspecialized, we mean that stem cells lack the structure of normal mature cells. For example, they can not work together to move an arm like muscle cells could. The benefit of this is undifferentiated state is that they can give rise to specific cells, thus they can be used for therapeutic purposes.

When an unspecialized cell creates a specialized one, this is called differentiation. We are just beginning to understand how this biological process happens, and what signals cause this. However, biologists have come to realize that stem cells have this ability to change into a variety of cell types, giving them the potential to treat a number of degenerative diseases requiring new tissue formation. In fact, totipotent stem cells obtained from 1-8 cell embryos can differentiate into any tissue in the body. ES cells derived from blastocysts are multipotent, but not totipotent.

3.2 Types of Stem Cells

There are three basic types of stem cells: Totipotent stem cells, Embryonic Stem cells (which contain both Pluripotent and Multipotent cells), and Adult Stem cells.

Totipotent stem cells: are derived from newly fertilized eggs at the 1-8 cell stage. These cells are obtained by in vitro fertilization, and have the potential to become any tissue in the body, so are termed totipotent. The first few cell divisions in embryonic development produce more totipotent cells, but after four days of embryonic cell division, the cells begin to specialize into Pleuripotent stem cells. Totipotent stem cells however

fail the one of the major desired therapeutic properties; they are unable to make more of themselves.

Embryonic Stem (ES) cells: are causing the current controversy, solely based on the way they are harvested. Embryonic cells, as the name suggests, are derived from human embryos. ES cells are the inner cell mass of a blastocyst which is formed after four or five days. These cells are called pluripotent (not totipotent) stem cells because while they can become nearly any human tissue, they cannot do so without the outer trophoblast layer.

Multipotent stem cells: The offspring of the pluripotent cells become the originators of such cell lines as blood cells, skin cells and nerve cells. At this stage, they are multipotent, in that they can become one of several types of cells within a specialized organ. For example, a hematopoietic stem cell (HSC) can develop into red blood cells, white blood cells or platelets.

Adult stem cells: As their name implies, adult stem cells are taken from adult tissue, not from embryos. They are undifferentiated but found among differentiated cells in tissues or organs. These cells are not totipotent, or even multipotent. They are only capable of renewing themselves, and can differentiate to create the major specialized cell types of the tissue or organ they came from. Their role is to repair and maintain whatever part of the body they are found in.

3.3 Stem Cell Sources

Embryonic stem (ES) cells are cells that have been developed from embryos resulting from fertilized eggs in an in-vitro fertilization clinic. These cells have been fertilized in a laboratory dish or an artificial environment. They are no longer taken from

abortions or fertilized in a human body, which is a very important distinction to make. Because far more embryos are created for donors than are reimplanted for pregancy purposes, most fertility clinics have excess embryos that can be used for research with donor consent. The embryos are usually 4 or 5 days old before the ES cells are extracted. At this stage, the embryo is a hollow microscopic ball of cells called the blastocyst. The blastocyst is formed by 3 layers. The outer layer, called the trophoblast, which is a layer surrounding the blastocyst. Inside is the blastocoel which is the hollow space in-between the trophoblast and the inner cell mass, which is where the stem cells come from. This cell mass is approximately 30 cells, and is extracted to be grown in a laboratory dish.

In order to grow these ES cells, you must first prepare a culture dish. This dish must contain two things (NIH, 2002). First, it must contain a nutrient broth called "Culture Medium", and on the bottom of the dish there needs to be a layer of embryonic fibroblast, (a connective tissue cells "which secretes an extra-cellular matrix rich in collagen and other macromolecules") (Genetic Home Reference, 2003) these are usually skin cells from mice (NIH, 2001). Scientists call this layer of skin cells the "Feeder layer". This feeder layer serves two purposes; it releases nutrients and growth factors into the Culture Medium so the stem cells don't waste away and also serves as a sticky surface for the ES cells to attach. Unfortunately, this co-culture process opens the door for the possibility to have some form of contamination from the mouse cells into human cells. Recently because many new growth factors required for stem cell growth have been identified and manufactured, the feeder layer is no longer necessary. (NIH, 2002)

Over several days, the ES cells begin to multiply. Once they begin to fill up the culture dish, the lab technicians gently remove them from the original dish and put them

into several fresh dishes. This expansion process is continued over and over again over a course of several months, and at that time the original thirty cells has created a cell line of millions. This process usually takes about 6 months, and as long as the cells do not differentiate, stay unspecialized, and have not been genetically altered, a new embryonic stem cell line is created.

The origin of adult stem cells in mature, developed tissue is currently unknown. There is clear evidence that hematopoietic stem cells (HSCs), that are capable of forming new blood and immune cells, exist in bone marrow and the umbilical cord (Cord Blood FAQs, 2003). Such cells are the basis of bone marrow transplants that have been in use for 30 years now, and have saved hundeds of thousands of lives. However, recent findings indicate that neuronal stem cells exist in rat brains (Ma, 1998), but still other scientists believe that such cells do not exist. As time and research continues, these findings are gaining more support. (Polli, 2003)

The recent developments in adult stem cell research have many scientists very excited. They have discovered adult stem cells in many more tissues than they had originally thought possible. This has led them to question if those cells could be used for transplants, instead of the highly controversial ES cells. Scientists have also recently discovered that adult stem cells may have the ability to transdifferentiate into other kinds of cells (NIH, 2001). For example, an adult brain stem cell might be able to make muscle tissue. This ability to transdifferentiate, should scientists find it to be valid, could post a great boon for researchers because they would not be restricted to working with cells derived from human embryos. Being able to use these types of cells for research instead of the Embryonic Stem Cells, while having less potential, provides a much greater pool

of sources to pull from. This in turn could help them quickly discover defects in cell lines or look at cells from people off different nations and with different diseases.

Adult stem cell locations identified to date include the brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin and liver. These cells are thought to reside dormant in a specific area of the parent tissue until activated by injury or disease. However, while they do appear to reside in many locations in the body, the pool of cells available to draw from is relatively small. This is why finding them is so difficult.

Scientists have not yet agreed on a specific set of criteria that should be used to identify and test adult stem cells. However, many scientists often use one or more of the following three methods:

1 – Labeling the cells in a living tissue with molecular markers and then determining the specialized cell types they generate. (NIH, 2002)

2 – Removing the cells from a living animal, labeling them in cell culture, and transplanting them back into another animal to determine whether the cells repopulate their tissue of origin. (NIH, 2002)

3 – Isolating the cells, growing them in cell culture, and manipulating them, often by adding growth factors or introducing new genes, to determine what differentiated cells types they can become. (NIH, 2002)

Also used, is the fact that a single adult stem cell should be able to generate a line of genetically identical (clone) cells which should be able to form all of the appropriate differentiated cell types of the tissue.

"Scientists tend to show either that a stem cell can give rise to a clone of cells in cell culture, or that a purified population of candidate stem cells can repopulate the tissue after transplant into an animal." (NIH, 2002)

Recently, Scientists have been able to demonstrate that individual adult stem cell clones do in fact have the ability to repopulate injured tissues in a living animal by infecting those adult stem cells with a virus that gives a unique ID tag to each individual cell.

With all that we know about adult stem cells, there are still a vast number of questions that remain unanswered. The following list from the National Institute of Health gives an example of the wide range of questions scientists are striving to answer.

- How many kinds of adult stem cells exist, and in which tissues do they exist?
- What are the sources of adult stem cells in the body? Are they "leftover" embryonic stem cells, or do they arise in some other way? Why do they remain in an undifferentiated state when all the cells around them have differentiated?
- Do adult stem cells normally exhibit plasticity, or do they only transdifferentiate when scientists manipulate them experimentally? What are the signals that regulate the proliferation and differentiation of stem cells that demonstrate plasticity?
- Is it possible to manipulate adult stem cells to enhance their proliferation so that sufficient tissue for transplants can be produced?
- Does a single type of stem cell exist — possibly in the bone marrow or circulating in the blood — that can generate the cells of any organ or tissue?
- What are the factors that stimulate stem cells to relocate to sites of injury or damage?

3.4 Embryonic Stem Cells vs. Adult Stem Cells

First and foremost, the most basic difference between these types of stem cells are in the number and types of cells they can become. ES cells can become all cell types of the body because they are pluripotent. Adult cells however are limited to differentiating into cells types of their origin tissue.

Embryonic stem cells can be easily grown in a culture lab into large numbers, but adult stem cells, being rare and having little known about them, have not had the conditions for growing them worked out. Because large numbers of stem cells are needed for cell therapy, this is an important difference. Should we discover a way to continually grow and maintain adult stem cells, they could become a viable source for stem cell replacement therapies. (NIH, 2002)

One advantage to using adult stem cells in replacement therapies is that the host's own cells would be used for therapy. They would be harvested, expanded in a culture lab, and then reintroduced into the patient. By using their own cells, there would be no rejection by the immune system, allowing the patient to recover without relying on immunosuppressive drugs to combat the body's rejection of the new cells (NIH, 2002). It is thought that embryonic cells that are introduced into a patient could cause a potential transplant rejection, but since human trials are only now underway, it is difficult to determine what, if any, the reaction would be.

The National Institute of Health says "the promise of stem cell therapies is an exciting one, but significant technical hurdles remain that will only be overcome through years of intensive research." We still have a long way to go before we have mastered

stem cell research, control, and applications, but right now the potential benefits far outweigh the moral outrage of the conservatives.

4.0 Stem Cell Potentials and Therapies

With the use of stem cell research and its derived therapies, scientists foresee the treatment of many illnesses and injuries that are currently untreatable using conventional medicine. By far the most publicized use of stem cells is to cultivate them in order to use them in cell transplants. While these therapies do play a large role, they are far from the only benefit that increased knowledge of stem cells has to offer us. Further research into the nature of each type of stem cell promises us a deeper understanding of the molecular, cellular, and genetic processes that drive our own growth and development. Unfortunately, there are significant scientific, ethical, financial, and governmental hurdles to overcome before many of these therapies and research can be successfully realized. This chapter will take a closer look into what scientists predict will be the potential uses of stem cell research and the therapies it may give rise to.

4.1 Potentials

Each type of stem cell holds for us a potential to develop treatments and preventative measures for many of the afflictions that we are currently unable to treat. Each variant of embryonic and adult stem cells have their own innate properties that differentiate them from the others. The unique properties of these cells is what scientists believe gives each of these stem cell types separate niches as sources for treatments and as knowledge bases (McKay, 2000).

4.1.1 Embryonic Stem Cells

Embryonic stem (ES) cells are infamous for the controversy they create as they are usually obtained by destroying a human embryo, and simultaneously famous for the medical hope they inspire from their innate ability to fully differentiate. In terms of science, ES cells are most popular for their potential to be used in all types of cell therapy – replacement of damaged tissue; this application will be discussed further later in the chapter – but these cells have several other potentials that have not been as well publicized.

An embryonic stem cell is defined by its origin, the blastocyst stage of an embryo. The blastocyst stage occurs approximately 3-4 days post fertilization when the embryo forms a small hollow ball. ES cells can be isolated from the inner cell mass (epiblast) of this hollow ball. Such cells are pleuripotent (not totipotent), meaning that they have the ability to maintain themselves in an undifferentiated state during replication and amplification, and to differentiate into a large variety of cell types given certain environmental conditions and stimuli. So, in addition to using ES cells for cell therapy, scientists believe that human ES cells could one day be used as a window to study the events that transpire during the early stages of human development. This research could provide us with insight to the causes and possible treatments for many of the still unexplained events that can cause congenital birth defects and placental abnormalities that lead to spontaneous abortion (NIH, 2001). These cells could also be used to explore the effects of chromosomal abnormalities in early childhood development and to better monitor the development of early childhood tumors of embryonic origin (NIH, 2001).

Human ES cells also have the potential to be used to greatly improve the quality and efficiency of new drug screening processes. Currently, before candidate drugs are tested in human volunteers, they are subjected to a vast barrage of overly expensive and time consuming preclinical tests. These tests typically include drug screening in animal models, either in vivo using a living animal, or in vitro using cells derived from animals. While these animal tests have been a mainstay of pharmaceutical research, these trials cannot always accurately predict the effects that the candidate drug will have on human cells (NIH, 2001). Therefore, cultures of human cells are often used in these trials to better foresee the effects of drugs on humans. However, these cultured cell lines have usually been maintained in an in vitro environment for extended periods of time. While being maintained in vitro, these cells tend to develop different characteristics than those typically seen in vivo. These characteristic differences naturally hamper the accuracy of any conclusions drawn from in vitro trials. Scientists hope ES cells will one day fill this niche. If human ES cells can be made to differentiate into specific cell types that are important to these drug screenings, such cells may be more likely to mimic the in vivo response of the cells or tissues of the human body (NIH, 2001). Using embryonic stem cells in this capacity offers increased accuracy and therefore safer drugs, as well as potentially cheaper models for drug screening.

Along the same vein, ES cells could be used to screen potential toxins. The reasons for their use in this capacity are similar to the reasons described above for their use in drug screening. Toxins often have different effects of different animal species; using ES cells could provide us with the most accurate results short of using living human test subjects.

4.1.2 Hematopoietic Adult Stem Cells

Most of the public is unaware that stem cells have been used for over 30 years now in bone marrow transplants for treating myeloablated cancer patients. The "active" component of the bone marrow that provides the reconstitution of the patient's immune system and blood are hematopoietic stem cells (HSCs). Such cells are termed adult stem cells because they are found in adults. Adult stem cells are not pleuripotent like ES cells, so they can only differentiate into the tissue they were derived from. But such applications may provide an alternative source to using ethically controversial ES cells. Although, coupled with this benefit comes the scientific challenge of locating and identifying these cells which seems to be an even larger hurdle in the case of adult stem cells which appear to be quite rare in adult tissue.

Among the first clinical uses of HSCs is the treatment of leukemia and lymphoma. These two cancers of the blood result in uncontrolled proliferation of white blood cells. In this treatment, the patient's own hematopoietic cells are destroyed using radiation or chemotherapy and then replaced using a transplant of bone marrow containing HSCs collected from a donor, typically a brother or sister of the patient so as to reduce the risk of tissue rejection. This transplant of HSCs has come to be more widely known as a bone marrow transplant. Bone marrow transplants have also been used to treat hereditary blood disorders, such as different types of inherited anemia (a failure to produce blood cells) and several other genetic disorders characterized by defects in the enzymes needed to produce essential body components or degrade chemical by-products (NIH, 2001). The blood disorders include aplastic anemia, beta-thalassemia, Blackfan-Diamond syndrome, global cell leukodystrophy, sickle cell anemia, severe combined

immunodeficiency and Wiskott-Aldrich syndrome. The other genetic disorders, referred to as inborn errors of metabolism that are treated with bone marrow transplants include: Hunter's syndrome, Hurler's syndrome, Lesch Nyhan syndrome and osteopetrosis. Unfortunately, bone marrow transplantation carries a significant risk of death. Therefore, it is a treatment reserved only as the last resort for otherwise fatal diseases.

Further research is now being conducted on hematopoietic stem cells to find further applications for other diseases. Among the hopeful applications are the treatment of such autoimmune diseases as diabetes, rheumatoid arthritis and system lupus erythematosis. In the case of autoimmune diseases, the body's immune system attacks its own body tissues. The treatments being explored are similar to the approach applied to cancers; scientists hope that they will eventually be able to use hematopoietic stem cells to reconstitute or reprogram the body's immune system (NIH, 2001).

4.1.3 Non-Hematopoietic Adult Stem Cells

HSCs are certainly not the only useful type of adult stem cell out there. Central nervous system stem cells are also a remarkable class of adult stem cell. Central nervous stem cells are easily grown in a lab environment, and given the right conditions and cues they can be persuaded to differentiate efficiently into neurons, oligodendrocytes (cells that insulate the electrical signals passing down axons in the nervous system and astrocytes, another type of non-neuronal cell in the nervous system) (McKay, 2000). Scientists hope that they will eventually be able to use central nervous stem cells to treat brain disease. In one form of stem cell therapy currently being developed, scientists are trying to cultivate central nervous stem cells that can be grafted and incorporated into

host tissues in order to correct brain diseases characterized by a loss of neurons. This type of treatment would be ideally suited for Parkinson's disease (McKay, 2000).

4.2 What is Stem Cell Therapy?

Stem cell therapy makes use of new techniques and technologies to replace diseased or dysfunctional cells with healthy, normally functioning cells derived from stem cell colonies. The end purpose of this therapy is to treat diseases at the root of the problem instead of treating the symptoms as many conventional medicines do. For example, this new therapy has the potential to cure blinding diseases of the retina by replacing dead retinal cells with new ones.

For stem cell therapy to work, the stem cells must first be obtained through one of the methods described in the previous chapter. Once taken, the stem cells must be stored and grown in culture. The culture is a special solution in a test tube or petri dish that provides all the factors needed for the stem cells to survive and grow. Through isolation and manipulation of the cells within the culture, scientists are able to grow cell colonies that can be transplanted to replace diseased or damaged cells in organs rather than transplanting the entire organ.

When growing a cell colony from stem cells, there are two primary factors that determine the resulting type of cell colony. These two factors are the stem cell line – its type and source – and the environment that it is grown in. By careful selection of the stem cells and precise control of their environmental conditions, scientists are able to control the type of cell colonies that divide from the original stem cells. The ability to control the type of progeny stem cells produce is intrinsically imperative to the success of stem cell therapy to treat a wide variety of diseases.

Another recent success is one recorded by the French scientific journal, *The Lancet* (Mending, 2003). In this case adult stem cells from a 72 year old patient's thigh were transplanted onto his heart in an effort to strengthen the heart after the patient had suffered a heart attack. *The Lancet* reported that the stem cells had evolved into well developed, fully functional cardiac tissue and had improved both blood flow and overall heart function of the patient.

4.3 Scientific Challenges

One of the first great challenges that scientists are now faced with is the problem of identifying stem cells in the cluttered mass of cells found in a tissue culture, which contain numerous different types of cells. Scientists are still discovering new cell types today. The process of finding and identifying specific stem cell types will still require a good deal more research in the field.

With the location and isolation of the desired stem cell comes the next hurdle that scientists face. That is, the determination and development of the correct biochemical solution that would cause the stem cells to differentiate into the desired cell type. This too will take a great deal of time and effort devoted towards experimentation.

For these cultivated stem cells to be useful to us as a means to replace diseased and dysfunctional cells we must be able to cope with issues inherent in implanting these cells into a person. In order for a treatment to be successful, these cells must be seamlessly integrated into the patient's tissues and organs. This means that the implanted cells have to adapt so that they may function in concert with the body's natural cells. One excellent example of the need for adaptation is a cardiac cell beating in a culture. When implanted, the cardiac cell must learn to beat in time with the other native cardiac cells.

The implantation of cultivated stem cells still challenges scientists with yet another significant problem; a problem that stem cells themselves offer a limited solution for. This is the phenomenon of tissue rejection. Just as seen in organ transplants, the body's immune system recognizes implanted cells as foreign bodies setting off an immune response that may cause serious complications and endanger the patient. Cell recipients would also have to take drugs that temporarily suppress their immune systems, which in itself could be dangerous to the patient. The use of adult stem cells taken from the patient circumvents this issue. Since the transplanted cells come from the patient's own body there is no chance of the patient rejecting them. However, this is a rather restrictive solution since according current scientific research, while adult stem cells are still able to differentiate into different cell types they lack much of the plasticity that ES cells have. This lack of plasticity in adult stem cells means that they are only able to differentiate into a relatively limited range of cell types. The end result of this restriction is that adult stem cells cannot be used to remedy as wide a variety of afflictions. Thus, the use of the patient's own adult stem cells to circumvent rejection issues involved in cell transplantation serves only as a solution to patients suffering from afflictions treatable by therapies using adult stem cells.

In order to widen the range of treatable afflictions using stem cell therapy it is imperative that scientists are able to control the differentiation of stem cells. Finding the appropriate environmental factors for each type of stem cell to produce the desired type of cell colony is currently one of largest hurdles that scientists must overcome before stem cell therapy treatments can be applied to a wider range of afflictions. This is one

hurdle that can only be cleared with painstaking experimentation and a better, more thorough knowledge of how stem cells work.

Lastly, there is a concern in the possible risk of cancer. Cancer is the result of uncontrolled cell division. Researches must strive to find the precipitous balance between encouraging the growth of new cells to heal damaged tissues and making certain that the cells don't lose negative controls for their growth, thereby becoming cancerous.

4.4 Conclusions

Stem cell research holds for us a wide variety of potential benefits of which some have already been reaped and others that still lie over the horizon. Scientists have already put stem cells to use in a small variety of treatments and clinical uses. These applications however are only the tip of the iceberg. With continued research scientists will only broaden their knowledge of the workings of stem cells and thereby take steps towards realizing the benefits they now tout.

5.0 Ethics of Stem Cell Research

This chapter will focus on what is certainly the most controversial aspect of stem cell research and that is the ethics that are involved in this medical zeitgeist. The writer feels that stem cell research is ethical if the means to obtain the stem cells themselves was also ethical. The possible benefits, in this writer's opinion, are far too great to ignore. The purpose of this chapter will be to observe arguments from both sides of the imaginary line: those that feel that stem cell research is ethical for the advancement of modern medicine, as well as those that feel that stem cell research is unethical when looking at it from a pro-life standpoint. From the facts presented, the author has decided that stem cell research is ethical as long as partial birth abortions are not used as the means to acquire the fetuses that are used in the process.

Bio-ethicist Bonnie Steinbock feels that whether the embryo is perceived as a human being or a human subject would determine what kinds of research, if any, it may be used for (Green, 2001). What she means by this is that if the embryo were to be considered a complete human subject, then the amount of research that could be done on said embryo would be decreased. In January of 1999, Harriet Rabb stated Federal funding may not be used for research in which a human embryo or embryos are destroyed. However, insofar as hES cells themselves are not embryos, federal funding for research on them is not prohibited (Holland, 2002). The major ethical debate arises from the issue of how the stem cells were obtained. Partial birth abortions are, in this authors opinion, a very inhumane process. In this procedure one gets pregnant for the sole purpose of aborting the fetus for use with tissue research. According to the National

Right to Life Committee, "this procedure is used to abort women who are 20 to 32 weeks pregnant -- or even later into pregnancy.* Guided by ultrasound, the abortionist reaches into the uterus, grabs the unborn baby's leg with forceps, and pulls the baby into the birth canal, except for the head, which is deliberately kept just inside the womb. (At this point in a partial-birth abortion, the baby is alive.) Then the abortionist jams scissors into the back of the baby's skull and spreads the tips of the scissors apart to enlarge the wound. After removing the scissors, a suction catheter is inserted into the skull and the baby's brains are sucked out. The collapsed head is then removed from the uterus. (Butler, 2003). The author feels that this procedure is essentially murder since babies that are born after 23 weeks or more have a good chance to survive outside of the womb. However, partial birth abortions are an ethical storm of their own and should not influence one's opinion on stem cell research since the procedure is no longer used to obtain ES cells.

Having discussed one negative aspect of stem cell research, a positive aspect of stem cell research will now be discussed. Stem cells themselves are able to be grown in cell culture, and are suitable for use in gene therapy due to their being amenable to DNA manipulation. It is much easier to make gene insertions in stem cells than it is in other kinds of cells, this and their differentiation potential makes stem cells a very powerful tool. It would be quite simple for a scientist to genetically alter the stem cells in order to combine them with a disabled blastocyst to create an embryo that was created solely from the stem cells (Holland, 2002). The result of this could be an almost limitless supply of new stem cells, as more could be derived from the newly created alternate embryo only to repeat the process over again.

Another positive aspect of stem cell research that is always quick to come up in debates is that it could cure many diseases that have been affecting humans for a long time. The cure for cancer has always eluded scientists as it is a very complex disease and no one cure has ever been able to target all the different forms of cancer. Our scientists are at the threshold of learning how to coax stem cells into growing into the many kinds of organs and tissues needed by our gravely ill citizens, without the potential problems of rejection seen in most transplants. Thus, our researchers may soon be able to generate pancreatic cells to save children with diabetes and those with liver cancer (Stalcup, 2000). It most certainly is a noble stand to want to heal those who have life threatening illnesses, as well as prevent others who might follow in similar footsteps from ever contracting these deadly diseases. Attention must be paid to the reality of the medical abilities. In the case of HSCs, their applications for treating certain forms of cancer are very well proven.

One of the biggest problems that arises with stem cell research is the origin of the stem cells that the scientists use in their experiments. The NBAC claimed in its draft report on stem cell research that "Whereas researchers using fetal tissue are not responsible for the death of the fetus, researchers using stem cells derived from embryos will typically be implicated in the destruction of the embryo. This is true whether or not researchers participate in the derivation of embryonic stem cells. As long as embryos are destroyed as part of the research enterprise, researchers using embryonic stem cells (and those who fund them) will be complicit in the death of embryos." That is a very true statement, however, one must understand what is going to happen to these donated fetuses if they are not used in scientific research.

If a fetus comes from an abortion it is certainly not going to given the environment to develop into a child. Allowing the doomed fetus to possibly heal the many people in the world that are coming down with deadly illnesses would be a much greater use than to just dispose of the fetus. It seems that a lot of the people who are against the destruction of the human embryos should be using their energy to debate against the legality of abortion. At least with stem cell research the scientists are allowed to turn a tragedy into a possible miracle. Sometimes the greater good needs to come into view, even if it does involve the destruction of a human embryo, even though knowing that the human embryo would probably be disposed of if not used in the research.

Current President Bush legislation only allows the use of ES cells derived from embryos prior to summer 2001, and the embryos must have been obtained during in vitro fertilization experiments, not abortions. The Clinton Administration debated a modified version of this legislation. This goes back to the previous point, that if these embryos are not used to help with stem cell research they will most likely not be used for anything and left to die, thus never becoming the human being that the bioethics followers believe makes destroying human embryos unethical. If however no life is going to evolve from said embryos, how is there any harm in using them to bring a great good to many ailing individuals? Some of these patients are children with untreatable diseases. An embryo, if you will, is signifigant in the development of a human. What sense would it make to willing allow both of these to die when the one embryo that certainly has no future could bring a future to the child?

There was a new twist added to the stem cell research debate in 2001 when the company Advanced Cell Technology, located in Worcester, Massachusetts, had

confirmed that they were working to use human cloning to create human embryos. The embryos were going to be used to provide stem cells rather than to create clones of human beings. This type of research does not fall under the government funding plan described above, but private funding to do this work would be permissible by law. This compromise that President Bush came up with was that research will go forward on cell lines already derived from embryos discarded by fertility clinics, it would not approve of the destruction of more embryos for experimental purposes. It is no doubt unethical to breed embryos just to be destroyed, that would be comparable to having children just to make them slaves in a concentration camp where the would inevitably die.

Another point that needs to be addressed is that of whether science and ethics are being divided by President Bush's decision, and if it's necessary to do so. Paul Greenberg feels that "The president's well-organized points and counterpoints come across as contrived and artificial, a way of avoiding the basic moral questions involved. And maybe only for a little while. For we all know that, having crossed the line, it will be that much easier to cross the next. Already there is a clamor in the U.S. Senate to finance experiments not just with existing stem cell lines but using embryos still living." (Stalcup, 2000). Greenberg makes the point that the President's decision was artificial and contrived, when at the same he makes a very ludicrous statement himself. He completely dodges the issue that Bush focused on namely not destroying any new embryos, thus making the debate worthless. Bush did not agree with the destruction of fetuses at all, and what line did he cross?

He goes on to make another obvious, yet completely unrelated, point later on when he brings up the Japanese experiments on dead prisoners of war in the 1940s. After

the war all the medical records from these experiments remained untouched. "Those records were set aside unread, unopened, untouched, unused. What a waste. And yet no one at the time thought so. No scientist or priest, politician or ethicist. Because all shared a single value system, deeply rooted from the time immemorial that told them: This work is contaminated. Not in any scientific sense but in a much older, almost instinctive way. It was contaminated by evil, another concept that has grown hazier since that time." (Stalcup, 2000). Of course these records would not want to be touched at the time, but this is because of who conducted the experiments. The Japanese were seen as the enemy at the time. Would these same people feel the same way if United States scientists conducted experiments on dead Japanese prisoners of war?

Greenberg then goes on to declare that Bush is not a great president because he does not feel the same way as he does. The whole article seems very one sided and doesn't address any of the real issues involved in the moral debate of stem cell research. Such a practice does not seem like it would be uncommon however, as the goal of the debate is to persuade others into believing ones opinion, generally by whatever means necessary. With all of this looking at how there are holes in the anti stem cell research debate it would not be fair to ignore holes in the pro stem cell research debate. The next portion of this chapter will indeed focus on that topic. Before starting though, it should be pointed out that the holes involved on the pro stem cell research side don't dodge the topic at hand nearly as much as the anti stem cell research side.

In one article the author tries to win the audience over by making them feel bad for young children. "Ask my friend Doug, who has a 7-year-old son with diabetes. Every night he and his wife are awake in the wee hours, monitoring their son's blood, worrying

that they have missed the balance and that their beloved child will slip into a coma." (Stalcup, 2000). While this is a very sad story, the main issue is where the stem cells are obtained from, so there is really no need to beat a dead horse with sob stories.

Another issue that comes up is that while the Government won't fund the destruction of human embryos, there is nothing to stop companies from getting private funding to do this. This comes down to sounding like "we are going to do what we want whether you like it or not." That is not the kind of thought one wants to put in peoples minds when they are trying to convince them of their point. Who is to say that these companies that push for the greater good with human embryo research aren't going to use very unethical means to obtain the embryos. Going back to very early in this chapter in the partial birth abortions section it is clear that such a procedure is disgusting and inhumane. Sucking the brain out of a fetus until it dies is widely seen as a very evil procedure, right up there with experimental work of Dr. Joseph Mengele during Nazi Germany. However, the author feels that such barbaric procedures would not be undertaken by the majority of the privately funded companies.

It is also important to recognize that research that involves human embryos outside the womb-- such as those produced in the laboratory by in vitro fertilization or cloning-- has never received federal funding. (Stalcup, 2000). In 1993 the Human Embryo Research Panel recommended to the National Institutes of Health that certain kinds of harmful non-therapeutic experiments using human embryos receive federal funding. However, these recommendations were rejected in part by President Bill Clinton, and then rejected in their entirety by Congress (Stalcup, 2000). Basically what these quotes are saying is that there has never been federal funding for research done on

human embryos that were created for the sole purpose of being experimented on. Such a practice has always been seen as immoral.

To try and persuade others to support stem cell research, in the past scientists would come up with new medical terms such as pre-embryo with the intent of showing that the work that was being done on these embryos was being done on a "pre-embryo" that was not yet a full embryo and therefore not yet a human being. This brings up the point of when life truly begins. The anti-abortion and anti-stem cell research activists would argue tooth and nail that life begins the moment the egg and the sperm are united. Others argue that it begins the moment that the embryo can live on its own outside of the womb. Neither view can be marked as either correct or incorrect since the are both just opinion, however the embryo is indeed living when it's still inside the womb, whether it could live without the womb is really a moot point. This topic, however, could easily turn into an abortion debate and not the real issue at hand and that is often what happens in a lot of stem cell research debates.

Despite an existing congressional ban on federally funded human embryo research, the department of Health an Human Services determined on January 15, 1999, that the government may fund human embryonic stem cell research. The stated rationales behind this decision are that stem cells are not embryos and that research using cells obtained by destroying human embryos can be divorced from the destruction itself. (Stalcup, 2000). This is where the anti stem cell research side begins to get a little weak in their delivery. The statement that the destruction of the embryos is not connected to the research itself seems to be based on flawed logic. President Bush himself stated that he will not fund research using cells that are obtained by such measures. The authors

strongly support this decision. We argue that the origin of the embroys is extremely important, and support research from IVF embryos not obtained via abortions.

The same article quoted above later goes on to say "The HHS's decision and the recommendations of the NBAC to federally fund research involving the destruction of human embryos would be profoundly disturbing even if this research could result in great scientific and medical gain. The prospect of government-sponsored experiments to manipulate and destroy human embryos should make us all lie awake at night." (Stalcup, 2000). The last line is especially laughable, considering that the embryos are going to be destroyed anyways if they were obtained from abortion. It might be a stretch, but if these cells are still living would they not also be living when they are curing a patient with a serious ailment? They would be able to live and flourish in life that they themselves saved.

The same people that claim to be pro-life seem to contradict themselves heavily. What exactly does "pro-life" really means? Would a child growing up in a broken household and goes on to become a murderer or rapist because it was an unwanted child and did not receive any love be considered "pro-life"? What about when animals are experimented on? They are living organisms themselves. What about the grass that is cut every day and weeds that are destroyed in a garden, are they not living? That is one of the largest problems with the truly self-righteous. To their own ideals and goals they are perfect, even if some of their ideals must be altered to show this. Once again this appears to be turning into an abortion debate, but that is where the whole pro-life stance originates from.

All debates seem to have each side completely oblivious to the points that the other side is making only trying to hammer home their own points. This makes debates a very poor source for someone wanting to discover information on a topic. It is too easy to become influenced by one side's opinion before even realizing that they do not address anything that the other side is saying. This could be called spotty evidence, as it is generally true in its own right but hardly providing the answer that one is searching for. The best way for one to decide for themselves how they feel about stem cell research is to read the history on it, read what it had and can accomplish, and read what the dangers in the past have been. It is certainly a very interesting science that brings a glimmer of hope to many people, while at the same time sets off a fire alarm in the heads of those who just love to argue.

To conclude this chapter it seems necessary to go back to the decision that was made by President Bush back in 2001. He perfectly sums up the entire argument when he states that he will not fund research from the destruction of human embryos, only those embryos that are "left over". Whether certain research boards will stick to this should not influence ones opinion on stem cell research. Address such issue when they happen, don't let the thought of it slow down something that could cure many of the diseases that have been threatening humans for a long time. On a personal note, cancer runs very rampant in this author's family so he feels that anything that might help cure it is a very good thing. Don't confuse science with ethics, match individuals with ethics. Everyone has the ability to make their own decisions and if these decisions are seen unethical they should be prosecuted on a case-by-case basis.

6.0 Stem Cell Legalities

6.1 Administration Policy

On the evening of August 9th 2001 from his Crawford ranch, President Bush addressed the nation to "discuss a complex and difficult issue, an issue that is one of the most profound of our time." He was referring to the controversial issue of embryonic stem (ES) cell research. That evening President Bush took time to tackle that hot topic, and to lay out the stance of his administration on the issue.

This statement was pivotal to the future of ES cell research as it carries behind the full weight of the Presidential office. With that weight follows the federal funds that drive much of the research in the US, as well as laws that govern the research and its sharing. For ES cell research to be successful in the US, it is imperative that it gains support from both current and future administrations.

In his speech, the President struggled to strike the balance at "a difficult moral intersection" by "juxtaposing the need to protect life in all its phases with the prospect of saving and improving life in all its stages." He considers the medical strides and public benefit that stem cells could offer, and weighs them against his own moral views pertaining to what must be done to acquire these stem cells. In particular, Bush asked himself two fundamental questions. First, "are these frozen embryos human life?" And second, "If they are going to be destroyed anyway, shouldn't they be used for a greater good?" While Bush offers us no insight into what he sees as the proper answer to these

questions, he does reach what he feels to be a moral compromise in his August 9th speech.

> "As a result of private research, more than 60 genetically diverse stem cell lines already exist. They were created from embryos that have already been destroyed, and they have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research. I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made." (Remarks by President, 2001)

In the end, this statement boiled down to 3 criteria that must be met before any federal funds can be issued for research using human embryonic stem cells.

- The derivation process (which begins with the destruction of the embryo) was initiated prior to 9:00 p.m. EDT on August 9, 2001.
- The stem cells must have been derived from an embryo that was created for reproductive purposes and was no longer needed.
- Informed consent must have been obtained for the donation of the embryo and that donation must not have involved financial inducements.

The National Institute of Health reports that with respect to these guidelines, there are currently 78 embryonic stem cell derivations eligible for federal funding (NIH, 2003).

At the low-key bill signing that enacted this policy into law, the President warned that "any piece of legislation that undermines what I think is right will be vetoed." His policy left many of those at the center or left with a bad taste in their mouths, prompting Senator John Edwards, D-North Carolina to comment: "He's sort of made a pre-emptive strike and set down very rigid guidelines in an area where we have many questions that remain to be answered." While he also faced criticism from religious leaders and

conservative lawmakers such as Rep. Chris Smith, R-New Jersey who feels that Bush's decision "legitimizes the killing of those embryos."

On the issue of using cloning as a source of ES cells President Bush was a staunch advocate of a bill introduced in 2001 banning all forms of cloning including the use of cloning to derive stem cells, despite its potential benefits. This bill later passed in the house but stagnated and died in the senate in the wake of September 11th.

Bush cites three reasons for his support of a ban of cloning in any form. First, he believes that "anything other than a total ban on human cloning would be unethical. Research cloning would contradict the most fundamental principle of medical ethics, that no human life should be exploited or extinguished for the benefit of another." In the case of research cloning this seems to be a contradictory statement since he implies that embryos are human life. Were this accepted as true, then we have stood by as mass murders are committed daily when the excess human embryos that result from in vitro fertilization are discarded. As we discussed in Chapter 3, it is not well established in the bioethical community that destroying embryos is the same as committing a murder, since embryos only have the potential to make an independent human being. They are not yet independent beings.

Secondly, Bush addressed the issues that would arise if the government would attempt to enforce a ban on reproductive cloning but not research cloning. He stated that "anything other than a total ban on human cloning would be virtually impossible to enforce. Cloned human embryos created for research would be widely available in laboratories and embryo farms. Once cloned embryos were available, implantation would

take place. Even the tightest regulations and strict policing would not prevent or detect the birth of cloned babies."

And lastly, the President remarked on the state of the current research on ES cells, noting that "the benefits of research cloning are highly speculative." While advocates for research cloning are hopeful that this technique could one day be used to circumvent the problem of tissue rejection, the President cited animal studies in which the transplanted tissue was indeed rejected.

The bill enjoyed strong bipartisan support in the House in 2001 when it passed easily. But the bill soon died in the senate facing opposition from democrats and a loss of public interest after the events of September 11th. The bill has since been picked up again but is facing deeper criticism than its first run through.

On the topic of adult stem cell research where there is very little moral controversy, the President has given his support. Bush has supported the funding of adult stem cell research projects and has asked congress to increase the National Institute of Health's budget so that it can better foster research in the field.

Predictably, the President's policy on stem cell research has been decidedly conservative. While Bush recognizes the broad potential benefits ES cells have to offer, he refuses to risk angering his conservative following by giving anything more than very limited support. On cloning, he has latched onto and fostered the social stigma around human cloning and rejects the practice outright. On the final issue of adult stem cell research where he faces little if any controversy, the President can and does fully back the research without any fear of alienating his conservative following.

These limitations have left most scientists in the stem cell field with a bad taste in their mouths. Many of these scientists argue that the 78 ES cell lines made available for legal use are not enough to build a competitive research program in the United States. The main arguments to this point were considered in a series of special congressional Subcommittee of the Committee on Appropriations hearings. In these hearings scientists went before the committee to argue their points regarding the allocation of federal funds for stem cell lines. The primary arguments scientists made for the availability of federal funds for use in research of a wider range of stem cell lines were as follows (Senate, 2002):

- The stem cells that the President has made available have all been subject to mutations, it may be preferable to use fresh cells that have not accumulated as many mutations.
- All existing E.S. lines have been cocultured with animal cells or animal products, which presents potential hazards.
- Existing E.S. lines are all genetically very similar with similar properties, providing little variety in their suitable potential applications.
- As new technologies for generating E.S. cells are continued to be developed scientists may be forced to use only the stem cell lines that are now in existence and preclude using new stem cells that may better suit an application. Much like being forced to use a vinyl record instead of a CD when they it is developed, except that this issue far outweighs sound quality

6.2 Administration Statements

In August of 2001, there were several administrative statements released regarding stem cells. Released over a course of two and a half weeks, the string of statements was kicked off with the President's Address to the nation on August 9, 2001. In his 11 minute speech, he explained to the nation the background of stem cell research, its benefits, but also its potential ethical and moral problems. As the President continues his address, he talks about the potential cures to illnesses and the different types of stem cells available, but continuously returns to the dilemma he faced in deciding what to do. He says "As I thought through this issue, I kept returning to two fundamental questions: First, are these frozen embryos human life, and therefore, something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they be used for a greater good, for research that has the potential to save and improve other lives?" (Radio Address, 2001). In order to come to his decision to put $250 million towards research, he explains how he came to his decision. Only by discussing the two questions with "other scientists, scholars, bioethicists, religious leaders, doctors, researchers, members of Congress, my Cabinet, and my friends. " was he able to come to the decision to proceed with stem cell research, but with "great care", and only on existing ES cell lines (Radio Address, 2001). Closing his address to the nation he states that he will be appointing a council to monitor the research, to recommend possible regulations, and to consider all the possible outcomes of continuing with this research, both good and bad.

Also released on that day were two other Administrative Statements and one statement by NIH. First there was the one page document entitled *White House Fact Sheet on Embryonic Stem Cell Research*, which gave a quick rundown on the President's address to the nation, how the federal funding would be used, who would be heading up the newly formed council, and explain further the role stem cells face in medial research. The third statement released that day was a statement by Secretary Thompson regarding the President's decision on stem cell research. Secretary Thompson's response was short and to the point, stating "This is not a decision based on rigid lines of ideology, nor is it based on unrealistic expectations that science might or might not be able to fulfill. It keeps the door open and allows us to move forward in a careful and measured manner." (Regarding, 2001) and continued with his support for the President's decision, and his thoughts on the potential created by the research funding.

NIH released a statement in response to the President's August 9th address as well. Drafted by the NIH Acting Director, Ruth Kirschstein, M.D., the statement expresses their approval of the President's decision and then comments on the benefits of the funding.

On August 27, 2001, NIH released yet another statement (NIH) naming the ten laboratories throughout the world which house the 64 stem cell lines that met the President's criteria for federal funding. The main idea was that by restricting federally funded workers to performing research only on existing ES cell lines, the embryos needed to make those immortalized cell lines had already been "destroyed" so no new embryos would need to be destroyed to continue the stem cell research. He continued by

explaining how they were going to implement the President's decision and what is going to happen next.

This statement was responded to by Secretary Thompson who reiterated the ten laboratories, explained the workload ahead of them, and explained what NIH was up to at the time. "The NIH wants to expedite this work and is aggressively pursuing several initiatives to facilitate research on all forms of stem cells. The NIH is creating a registry of the embryonic stem cell lines that meet the eligibility criteria so researchers can contact the owners and gain access to them. The registry will contain basic information about the cells, a unique identifier, the name of the company or laboratory that derived the cells, and contact information about that company or lab. The registry will list these 10 laboratories as well as any other owners of stem cell lines meeting the eligibility criteria who come forward in the future. Also, the NIH is welcoming grant applications for federal funds, including use of existing funds, for stem cell research." Secretary Thompson, August 2001.

Personally, I feel that the current legislation is slightly too restrictive for proper research. While I am not sure exactly how I feel about the current state, I do feel it is headed in the wrong direction. With more restrictions into this potentially huge field, I fear that we may stifle any future discoveries that would have been found with broad analysis. With the current restrictions, scientists are only going to be able to do research into pre-approved areas.

While many people in the world today feel that ES research destroys a life, I disagree. There is not enough research out in order for me to make an informed decision I am comfortable with. However, I believe what the current research tells me, that a

human life begins at a certain stage, and these stem cells used are created before that stage. The potential for finding treatments for life threatening diseases and injuries is just too great to shut the door on.

6.3 International Policies

One of the dangers of overly restrictive regulation of stem cell research in the U.S. is the possibility that the U.S. may be shut out of the field entirely. If laws in the U.S. restrict research too much, companies will relocate to countries with less restrictive laws governing the research. In that way the U.S. stands to lose a potentially massive industry, and all the money and jobs that a large biotech industry has to offer. The U.S. also stands to lose economic advantages since foreign companies would be more likely to patent stem cell technologies before American companies. We will now take a look at what types of policies foreign nations have enacted with regards to stem cell research.

Not too long ago the E.U. finally published its proposed guidelines for funding human ES cell research (Scott, E.U. Guidelines, 2003). This occurred after a prolonged debate on whether to lift the ban on E.U. funding of ES cell research outright. Reactions in the research community to the proposed guidelines have been mixed. While they are pleased that the ban has been lifted and that a step in the right direction has been made, many believe that the guidelines do not go far enough to promote funding. The following are the proposed guidelines that the E.U. has published:

- The stem cells can only be derived from excess "supernumerary" embryos donated for research after informed consent by parents.

- The cells must have been created before June 27, 2002, the date of the adoption of the 6th Research Framework Programme.
- Project partners must seek ethical advice at national or local levels in member states where the research will take place.
- Research must meet "particularly important" research objectives.
- Research will be funded only if no adequate alternative is available.
- Embryo donor(s) will not be permitted to make any financial gain.
- Data and privacy protection of donors must be guaranteed, and traceability of stem cells will be required.
- Research consortia will be required to make their human embryonic stem cells available to other researchers.

Critics like Angelo Vescovi of the Stem Cell Research Institute in Milan argue that "This is the worst compromise they could have come up with, it's a political compromise that has very little to do with science, and it's going to make everybody unhappy on both sides [of the debate]." (Scott, E.U. Guidelines, 2003) The more upbeat members of the science community like George Radda, CEO of the Medical Research Council in the U.K. remark that the outcome is "a positive step for the future of health and medicine."

The national policies of individual member nations of the E.U. vary. In Germany, law bans the extraction of stem cells from human embryos. The British are a little more lax, law still forbids the extraction of stem cells from embryos or fetuses but it is legal for researches to import embryonic stem cells from abroad. In France, bioethics laws do not

allow research on human embryos, but a report recently adopted by the assembly general of the Conseil d'Etat recommends that embryonic stem cell research be allowed (McKay, 2000) Sweden is currently striving to be at the forefront of stem cell research. The Swedish government is in the process of passing legislation that would legalize the use of surplus fertilized eggs from in vitro fertilization. With its lax laws and well established medical industry, Sweden hopes to attract foreign investment from companies who wish to perform stem cell research (Sweden, 2002). Similarly liberal countries include Japan, Israel and Singapore. They all permit the creation of embryos for research purposes (if a sufficient number of embryos cannot be obtained by any other means) as well as stem cell research and therapeutic cloning while still banning practices such as reproductive cloning and payment for embryo donations (Wertz et al, 2003).

6.4 Pending Legislation

Since the discovery of stem cells, bills after bills have been introduced into Congress and the Senate over how to govern their research. Starting with the 107th congress, we find many bills being introduced for all aspects of stem cells.

6.4.1 107th Congress

H.R. 2059, *Stem Cell Research Act of 2001* was introduced on 6/5/2001 (LoC, 2001). The bill was sponsored by Rep Jim McDermott of WA, and was intended to "amend the Public Health Service Act to provide for human embryonic stem cell generation and research" (NIH, 2003). This bill made "it unlawful for any person receiving Federal funds to knowingly acquire, receive, or otherwise transfer any human

embryos for valuable consideration if such action affects interstate commerce." This bill, and the following bill were referred to the House Subcommittee on Health on 6/18/2001.

H.R. 2096, Responsible *Stem Cell Research Act of 2001*, was introduced on 6/7/2001 (LoC, 2001), by Rep Christopher Smith of NJ. This bill was introduced "to require the Secretary of HHS to maintain a stem cell donor bank containing stem cells derived from adult tissue, placentas, and umbilical cord blood" (NIH, 2003) and authorized the Secretary, through NIH, to conduct and support human stem cell research.

H. Con. Res. 17, *Expressing the sense of the Congress supporting Federal funding of pluripotent stem cell research*, was introduced on 1/30/2001 by Rep Carolyn Maloney of NY (LoC, 2001). Intended to express support for federal funding of pluripotent stem cell research (NIH), it was also referred to the Subcommittee on Health on 2/17/2001.

H. R. 2838, the *New Century Health Advantage Act* was introduced to require NIH to conduct human embryonic stem cell research and repeal the Human Embryo Research Ban contained within the Labor, HHS, and Education Appropriations Act. Sponsored by Rep Juanita Millender-McDonald, it was referred to the Subcommittee on Health on 9/17/2001 (LoC, 2001).

H.R. 2863, *Cell Development Research Act of 2001* , also sponsored by Rep Jim McDermott, was introduced to require the "establishment of an additional Food and Drug Administration (FDA) Advisory Committee to make recommendations on the field of cell development, including human embryonic stem cell research and therapeutic cloning." (NIH, 2003). Also referred to the Subcommittee on Health on 9/17/2001. (LoC, 2001)

H.R. 4011, *the Science of Stem Cell Research Act*, again sponsored by Rep Carolyn Maloney of NY on 3/20/02 moved to establish a Stem Cell Research Board within the legislative branch to conduct research on the effects of the President's August 9, 2001 stem cell policy. Once again, this bill was referred to the Subcommittee on Health.

6.4.2 108th Congress – House Bills

H.R. 534, *Human Cloning Prohibition Act of 2003*, introduced 2/5/2003 by Rep Dave Weldon, "Amends the Federal criminal code to prohibit any person or entity, in or affecting interstate commerce, from knowingly: (1) performing or attempting to perform human cloning; (2) participating in such an attempt; (3) shipping or receiving an embryo produced by human cloning or any product derived from such embryo; or (4) importing such an embryo or derived product." (LoC, 2001) included a criminal penalty of up to 10 years for violation of the provisions of the bill. On 2/27/2003 the bill passed in the House, 3/3/2003 Senate preparation for floor (LoC, 2001).

H.R. 801, *Cloning Prohibition Act of 2003*, On February 13, 2003, Representative Jim Greenwood introduced this bill to "prohibit any person (including governmental entities) from (1) using or attempting to use human somatic cell nuclear transfer technology to initiate a pregnancy; or (2) shipping, mailing, transporting, or receiving such product knowing that it is intended for such use. This bill precludes from such prohibition the use of somatic cell transfer technology to clone molecules, DNA, cells, tissues, or animals." (LoC, 2001). Referred to the Subcommittee on Health. On 2/26/03.

H.R. 916 *Human Cloning Research Prohibition Act*, Introduced on February 25, 2003 by Representative Cliff Stearns of Florida. The intent of the bill was to prohibit the

expenditure of Federal funds to conduct or support research on human cloning. The bill required the Director of the National Science Foundation to contract with the National Research Council for a review of the implementation of the Act. The bill also required Congress to express to other countries they should establish similar provisions. (LoC, 2001)

H.R. 938 *Human Cloning Prevention Act of 2003*, Introduced on 2/26/2003 by Rep Ron Paul. This bill prohibited any Federal agency from "making, or entering into any obligation to make, any grant, contract, or other payment to any individual, business, institution, or organization that: (1) has engaged in human cloning in the past year; or (2) controls, is controlled by, or is under common control with any such individual or entity." (LoC, 2001). Also referred to the Subcommittee on Health on 3/10/2003.

108th Congress – Senate Bills

S.303, *Human Cloning Ban and Stem Cell Research Protection Act of 2003*, introduced by Sen. Orrin Hatch of UT on 2/5/2003, moved to amend the Federal criminal code to prohibit: "(1) conducting or attempting to conduct human cloning; (2) shipping the product of nuclear transplantation for the purpose of human cloning in the United States or elsewhere; or (3) exporting to a foreign country an unfertilized blastocyst if such country does not prohibit human cloning" (LoC, 2001). On 2/5/2003 this bill was referred to the Senate committee.

6.5 Congressional Statements and Testimony

On May 22, 2003, The Senate Appropriations Subcommittee on Labor, HHS, and Education held a hearing on the status of research on embryonic stem cells. Two of the people who spoke were Dr. Elias Zerhouni, Director of National Institute of Health and

Dr. Ronald McKay, Senior Investigator, National Institute of Neurological Disorders and Stroke. When Dr. Elias Zerhouni's took the stand to discuss the recent developments of the NIH he was full of facts about the progress NIH has made:

"In FY2002, NIH spent approximately $11 million for human embryonic stem cell research to increase the availability of stem cell lines for federal research, train scientists how to use these technically-challenging cells, and conduct basic, pre-clinical research that represents the first steps toward understanding how stem cells might be used to treat injuries and diseases." (Senate, 2003). As he continues in his testimony he explains that more than 60 investigators at 48 institutions have received awards from the National Institute of Health, 14 of which are investigator-initiated grants and 44 administrative supplements (Senate, 2003) which are allowing the rapid incorporation of research on human embryonic stem cells into other works. "As you know, there are 78 lines fully eligible for Federal funding, in various stages of development. NIH support has helped increase to 11 the number of human embryonic stem cell lines that are widely available for all researchers. More lines will become available in the future, as we help the scientific community capitalize on this opportunity. I can report to you today that NIH's implementation of the policy set by the President on August 9, 2001 has enabled the field of stem cell research to advance. We continue to acquire new knowledge about human embryonic stem cells (hESCs). Some of the significant discoveries include the following research findings." (Elias A. Zerhouni, M.D, Director, National Institutes of Health, Senate, 2003). He concluded his testimony with the benefits of hESC research and the possible gains in medical science, and how the President's Policy has provided

them with the opportunity to be at the forefront of these discoveries, and expects the NIH to keep its place in front of the field for many years.

The other speaker, Ronald McKay, Ph.D, Senior Investigator, National Institute of Neurological Disorders and Stroke had much of the same sentiment about the research potential of stem cell research. However, his testimony focused on what we do not yet know, and how to discover with continuing research.

> "As this area is new and rapidly developing, the major technical barriers that may slow our progress are not understood. However, some of the potential difficulties can be anticipated. The human ES cells may be difficult to grow and differentiate. Their genome may be unstable. The different cells may show very different properties resulting from their genetic origin. There may be unexpected difficulties in taking the cells to a point where they are clinically relevant. And once we have obtained the differentiated cells, it may be difficult to integrate these cells with the other cells of the body" (Ronald McKay, Ph.D, Senate, 2003)

By looking at testimonials like these over the past few years available by the OLPA, you can see how all of them focus on the need for continuing research, and the inevitable benefits we will receive. All of them express the importance of continuing support of their research, and the need to look at the subject with more than just an eye clouded by morality.

7.0 Conclusion

Stem cell research is something truly unique in today's world of science. It is the potential solution to many deadly ailments and diseases, yet at the same time continues to raise eyebrows around the world from human rights activists. As mentioned in the first chapter the whole movement on human stem cells began in 1998 at the University of Wisconsin-Madison by developmental biologist James Thompson. Thompson was likely aware that the zeitgeist had landed when he made this discovery. His discovery could have been one that was heralded from then on as being the work of a savior. Unfortunately this was not to be, as many ethical and legal questions were raised upon discovery of his work.

The stem cell itself is an amazing part of human development. It has the ability to turn into any cell in the human body if harvested early enough, or to replicate specific tissue and organ cells when taken from adults. The 3 types of stem cells all serve different purposes. The ideal kind: the totipotent, are the most valuable since they can differentiate to form any type of tissue, but they are also the most ethically controversial since they could be abused to clone human beings. The pluripotent stem cells are the most commonly debated type since they are taken from human embryos, so are termed embryonic stem cells or ES cells. They do not have the same differentiation power that the totipotent cells have, but they are sometimes obtained through the destruction of human embryos. Multipotent stem cells are taken from adults, and are limited as to what they can become from where they are taken. There is some evidence that shows the ability of such adult stem cells to transdifferentiate into other cell types, but this remains

controversial.

All the ES cells that are used in stem cell research today were taken from embryos donated from in vitro fertilization clinics, and cultured in a petri dish to the blastocyct stage where the ES cells are isolated. Recent developments in stem cell research brings a lot of excitement to scientists all over the world since they are allowing advances in the new field of regenerative medicine never seen as possible in the past. Scientists have also recently discovered that adult stem cells may have the ability to transdifferentiate into other kinds of cells which could eliminate the need for all hES cell research and quiet down the people who are strongly against stem cell research at this point.

The potentials of stem cell research are immense; the ability to treat the current diseases that are coined untreatable is a very amazing thought. Also the stem cells can unlock a lot of the mysteries surrounding human life today. Many questions that have always gone unanswered just because the key was not there could potentially be unlocked with the key that is stem cell research. Human embryonic stem cells have the potential to be used to greatly improve the quality and efficiency of the new drug screening process. It would reduce both the cost and time needed for such tests. Stem cells could also be used to screen potential toxins, learning how the body would react to the toxins, and find a way to cure a disease that might result from them.

As for adult stem cells it seems that the most promising type of the adult stem cells is the hematopoietic stem cell, or HSC, which can be found in peripheral blood, bone marrow and umbilical cord blood. It is very promising for the obvious potential for curing blood related diseases, and the way that moral issues are circumvented from the way these cells are obtained without the destruction of a human embryo. In fact, HSC's

play a large role in the success of bone marrow transplants over the last 40 years, saving lives in cases involving leukemia and lymphoma. More research is being conducted on hematopoietic stem cells to possibly cure other serious diseases such as diabetes, rheumatoid arthritis, and system lupus erythematosis.

While all of this sounds great for both science and humankind, there are too many moral and legal questions. The means by which the cells are obtained is a huge debate that is ongoing. Partial birth abortions where individuals were impregnanted for the sole purpose of aborting was one of the largest targets due to its inhumane procedure. Thankfully ES cells are no longer obtained in that way. But the questions are still raised that involve when life actually begins and whether it is moral to destroy a human embryo for the greater good of another human being. Because stem cell research is such a sensitive topic, bills had to be addressed to the President and Congress to determine if it should even be legal to perform stem cell research.

The pro stem cell research side emphasizes the potential benefits of the science to humankind. The goal of stem cell research is without a doubt one of great moral character. Stories of young children with cancer or diabetes frequent the articles that are pushing for stem cell research. These articles would make anyone who read them feel pity for the victims being discussed; it would only be natural to want to help these people. To give a young child a life that they might never see is reason enough for many to push forward with stem cell research, even though they may be pushing aside many legal and moral issues that arise. It's a double edged sword, one that will likely be debated for decades to come, unless alternatives are found for obtaining ES cells from embryos.

The anti stem cell research side seems to be the same people who are anti abortion and pro-life. This all makes sense due to the main argument being that the destruction of human life is immoral and illegal. It is also noted that while these embryonic stem cells have the potential to heal humans, a potential human life (the embryo is not yet living on its own) is destroyed in the process. It wouldn't be ridiculous to compare the research that goes on with embryonic stem cells to that done on twins by Nazi doctor Josef Mengele as well as the Japanese doctors experiments on prisoners of war in the 1940s. Human life is compromised in every case, while at the same time the possibility of using the research to cure diseases for a great many people is not an impossibility. The latter two subjects are seen as evil and are untouched by scientists today, but to their own people they weren't seen as evil and if it weren't for the circumstances surrounding World War II they could possibly be heralded as scientific heroes. The ethical debates surrounding stem cell research will likely continue indefinitely since it is such a sensitive topic.

In 2001 President Bush gave an 11 minute address discussing stem cell research. It was stated that research on stem cells obtained from the destruction of human embryos would not be funded by the government, and that federally funded labs could only work with ES cell lines already derived prior to summer 2001. The reason for this was that if it was morally wrong to destroy an embryo to obtain ES cells, with the embryos used to obtain said stem cells already being destroyed, perhaps these cell lines could be used to try to save lives, without having to destroy any more embryos. However, this would not prevent private funding for companies like Advanced Cell Technology (ACT)

(Worcester, Massachusetts). Current President Bush's legislation proposed three guidelines involving the funding of stem cell research:

- The ES cell derivation process (which begins with the destruction of the embryo) must be initiated prior to 9:00 p.m. EDT on August 9, 2001.
- The stem cells must have been derived from an embryo that was created for reproductive purposes and was no longer needed.
- Informed consent must have been obtained for the donation of the embryo and that donation must not have involved financial inducements.

Bush also noted that "the benefits of research cloning are highly speculative." Bush cited cases in animal studies when tissues were rejected, showing that it was not a fool proof science by any means. His bill that came from the address was popular in Congress until it received heavy rejection from the Democrats (as of the time of this writing the bill has passed in both houses and is law). So for now, federally funded U.S. ES stem cell researchers are to perform research with cell-lines that already exist. The problem is there is not a large amount of these cell lines available to the U.S. stem cell research program, so eventually the U.S. may fall behind competitor countries in this area.

The US faces severe scientific stagnation due to its strict policies regarding stem cell research. Any scientists that were seriously interested in the development of the field would be drawn to a country such as Sweden where there are very lax laws that effect stem cell research. In fact, Sweden hopes to be at the forefront of stem cell research in allowing studies to go on with little interference. Other countries such as Germany

totally ban the extraction of stem cells from human embryos. The differences in policies of different countries basically read like an ethics debate. Most likely the country that allows the research to continue uninterrupted will be the first to succeed in finding the cures for the diseases that stem cell research hopes to prevent.

There have been many bills that have been passed in both Congress and the House of Representatives which can be read about in chapter 4. In the future stem cell research has a future that is equal parts bright and grim. The moral issues will be furiously debated for a long time to come. At the same time there are many advances that are possible which could bring much hope to people all around the world. If stem cell research is allowed to continue it will without doubt have one of the largest impacts on the scientific community since the discovery of the double helix by Watson and Crick. The world is on the brink of discoveries that will push the envelope of science for the remainder of time.

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