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STEM CELLS

An Interactive Qualifying Project Report

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ABSTRACT

Because stem cells have the potential to cure and treat a myriad of diseases, they have become one of the most exciting areas of current medical science. However, this new technology has ethical and legal implications. We have examined this complex area of medical science, examining stem cell sources, types, applications, ethical considerations, and legal issues.

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EXECUTIVE SUMMARY

Stem cells hold the potential to cure many diseases. It is because of this potential that stem cell research is among the most exciting areas of current medical science. This project examined the sources, types, applications, ethical considerations, and legal issues of stem cells. Stem cells are the fountainhead of all mature cells in the body. They retain the ability to self-renew and differentiate into a variety of different tissues. Recent studies show that stem cells are not restricted to one lineage, but can differentiate along different lineages when placed in the appropriate environment.

Strong proof of the existence of stem cells comes from animal studies, specifically those conducted on mice. Our best characterized stem cells are the hematopoietic stem cells (HSCs) present in bone marrow and umbilical cord blood. These cells have saved hundreds of thousands of lives in bone marrow transplants, where they are used to reconstitute the blood system following chemotherapy or radiation therapy. Known surface markers have been used to isolate hematopoietic stem cells to aid in gaining knowledge of a stem cell's appearance, and to isolate and freeze these cells for saving future lives.

Chapter-1 in this project explores the different kinds and locations of stem cells in the human body as discovered via the internet, periodical, and literature research. Embryonic stem (ES) cells are derived from blastocysts as their inner cell mass, and have the potential to make a variety of tissues for therapeutic purposes. Because an embryo is destroyed to obtain ES cells, these cells are the most ethically controversial. Adult stem cells are obtained from adult tissues, and have far fewer ethical considerations since their

use does not destroy an embryo. Such cells include hematopoietic stem cells found in the bone marrow, mesenchymal stem cells that can potentially differentiate into a number of connective tissue types, intestinal stem cells, stem cells found for the skin, liver and neuronal stem cells.

Chapter-2 in this IQP focused on stem cell applications. The stem cells found in the human body and the human fetus offer a vast number of potential medical applications. Because ES cells have the greatest medical potential (they can create the greatest variety of tissues), the pressure is to use these cells for research even with their controversial ethical considerations. Human ES cell studies may also deliver insight into how undifferentiated cells become differentiated. In addition to understanding human development, stem cells could serve a purpose in understanding and testing new drugs. Arguably the most valuable and promising potential use of human stem cells is the generation of new cells, tissues, and organs for use in cell-based therapies.

The most researched stem cell applications are for the HSCs. Bone marrow transplantation and stem cell therapy is used to treat leukemia and lymphoma patients. There is also the potential for treating diabetes and lupus. Hematopoietic stem cells have also been derived from umbilical cord blood and used in transplantation. ES cells have been used with success for the treatment of heart failure. ES research is progressing toward possible repair of degenerative diseases, and there is potential ocular treatment with ES cells on the horizon.

Chapter-3 in this IQP focused on stem cell ethics. The concerns of embryonic stem cell research combine the ethical concerns of abortion and cloning, while creating hope for the most incredible and potentially the most important advances to date in

medicine. In the purely scientific community, free of religious implications, the question of sentience concerns the limits of research on an embryo. This project undertook the question of ethics in regards to stem cell research. The topics examined were stem cell sources, religious perspectives, somatic cell nuclear transfer, pre-implantation genetic diagnosis, adult non-embryonic stem cells, parthenotes, embryonic stem cell lines, and stem cells and immortality. Our research strongly supports the use of adult stem cells as potential replacements for ES cells in those cases where adult stem cells have been identified. It also strongly supports the use of somatic cell nuclear transfer as a possible source of histo-compatible tissue when the donor nucleus is not diseased, and the derivatation of new ES cell lines as a renewable source of ES cells.

As stem cell ethics became more widely debated, the demand for legislation followed. In the fourth chapter of this project, the most restrictive and most liberal current policies on embryo research were described. Germany currently has the most restrictive policies. In Germany, it is criminal to use a human embryo for research. The current U.S. policy is only slightly more liberal. President George Bush restricted the U.S.'s policy on embryo research in 2001, stating that federally funded laboratories can only work with ES cell lines established prior to August 2001. However, most scientists agree that this policy places a severe restriction on the number of cells actually available for research. Sweden currently has a liberal policy where the research must, "improve infertility treatment, to improve contraceptive methods or…develop knowledge of embryonic development and the causes of embryo defects." The United Kingdom is most liberal in the world on embryo policy with only two main restrictions. Informed

consent of embryo donors is required, and the Human Fertilization and Embryo Authority must decide if the embryo use is “necessary or desirable”.

In conclusion, this project touched on stem cell sources, stem cell medical applications, stem cell ethics, and stem cell politics. We strongly support the use of adult stem cells when applicable, the use of somatic cell nuclear transfer to produce histo-compatible tissues, and believe the current U.S. legislation is too restrictive.

PROJECT OBJECTIVE

The purpose of this IQP was to describe new technologies involving stem cells, and investigate how this new field of medical biology affects society. This IQP goal was accomplished by describing what stem cells are, where they are found (chapter-1), what they are used for (chapter-2), and what are their main ethical concerns (chapter-3) and legal issues (chapter-4). The final chapter-5 discusses the authors conclusions based on the research performed for this project.

Chapter 1: Stem Cell Types and Sources

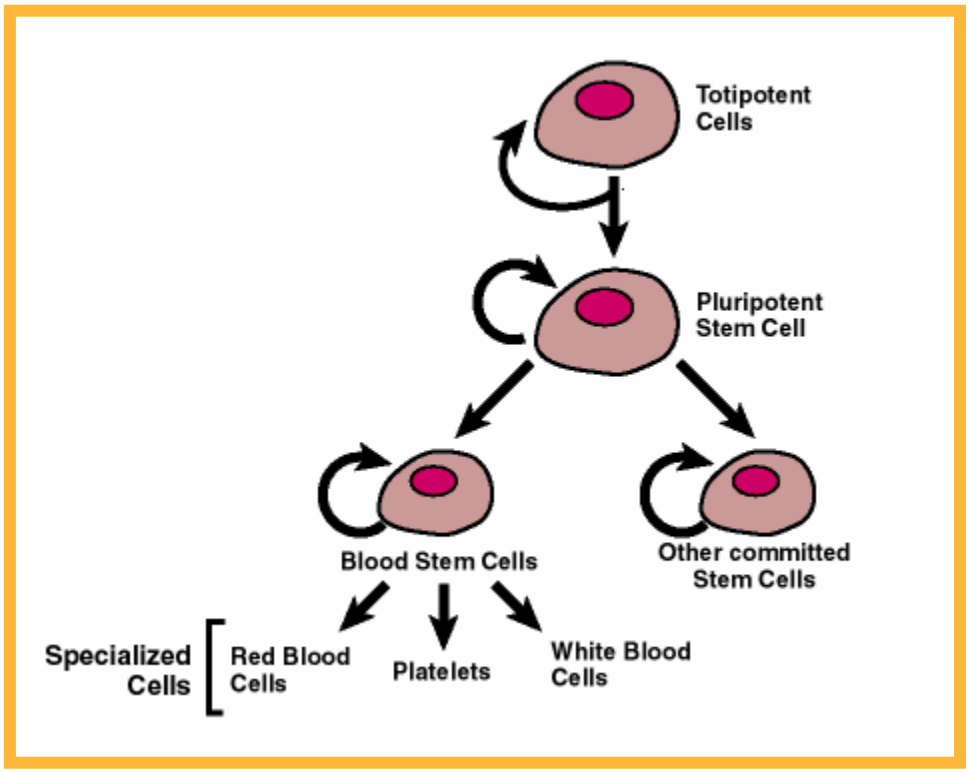
Stem cells are the fountainhead of all mature cells in the body. The body is a composition of dynamic tissues with trillions of cells that are involved in a constant cycle of death, creation, and replacement. Most of the body's cells are mature, differentiated cells. The small remainder of the body's cell population (approximately 1 out of every 10,000 in bone marrow, for example) is characterized by stem cells. It is this small population of stem cells that the rest of the body's mature, differentiated cells derive from (Stem Cells and the Future of Regenerative Medicine, 2001).

Stem cells are cells that retain the ability to self-renew, and (depending on the type of stem cell) they can differentiate into a variety different tissues. This makes stem cells potentially useful for regenerative medicine applications. However, strictly speaking, stem cells can not renew indefinitely. Although there is evidence that telomeres in immature hematopoietic cells do shorten with increased cell doublings *in vitro*, telomere shortening in stem cells is finite in rate and may be slower than in other somatic (non-germline) cells. Telomeres are noncoding repeating sequences that are found on the ends of chromosomes when linear DNA is replicated. In non-germline human cells, telomeres are shortened each replication, giving rise to a so called "mitotic clock" that aids in cell-cycle ceasing (Palsson and Bhatia, 2004).

Levels of Stem Cell Differentiation

In addition to self-renewal, stem cells possess the potential to differentiate along one or two lineages. Science has historically believed that stem cells produce large

numbers of progeny, dividing without limit over a lifetime. Thus, stem cells are named by the kind of progeny they can produce. Unipotent stem cells (lower right cell in Figure 1) can produce one cell type. Adult neural stem cells are of this type, only able to generate other neural cells. Pluripotent stem cells (middle and lower left cells in Figure 1) can produce many cell types. For example, embryonic stem (ES) cells can produce muscle, nerve, and kidney, among others; and hematopoietic stem cells can produce several types of red and white blood cells. Totipotent stem cells (upper cell in Figure 1) can produce all cell types. A newly fertilized egg is an example of a totipotent stem cell.



NIH, 2000

Figure 1. Levels of Stem Cell Potentials

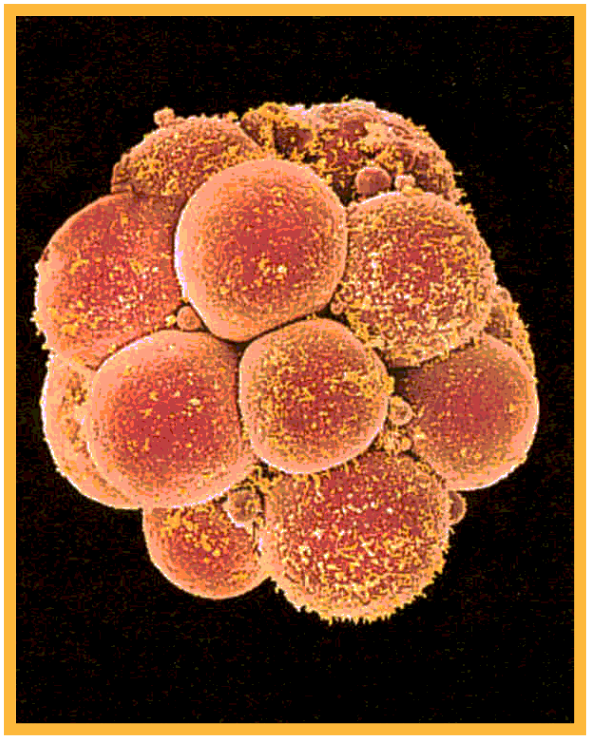
Although stem cells can have the ability to differentiate along one or two lineages and can produce large numbers of progeny, it was believed that once a stem cell is committed to a certain tissue, it is restricted to that same lineage. However, recent studies indicate that when some adult stem cells are placed in the appropriate microenvironment, they can differentiate along different lineages. This type of activity is known as plasticity. An example of such a phenomenon would be a hematopoietic (blood forming) stem cell differentiating into a hepatocyte, myocyte, or neuron (Stocum, 2002).

Proof of the Existence of Stem Cells

Strong proof of the existence of stem cells comes from animal studies, specifically those conducted on mice. Mice that would normally die from hematopoietic failure because of lethal irradiation can be rescued with as few as a half-dozen selected stem cells which can reconstitute multi-lineage hematopoiesis (Osawa et al, 1997). Additionally, experiments with diffusion chambers with implanted 1 micrometer pore size membranes (pores large enough to allow nutrient passage, but not cell passage) filled with bone marrow cells produce cartilage and bone after three weeks *in vivo*. The implanted marrow-derived stem cells created newly formed bone and cartilage. Investigations like these and others of this nature serve to establish a belief of immature hematopoietic cells having multilineage potential and their persistence over long time periods *in vivo*.

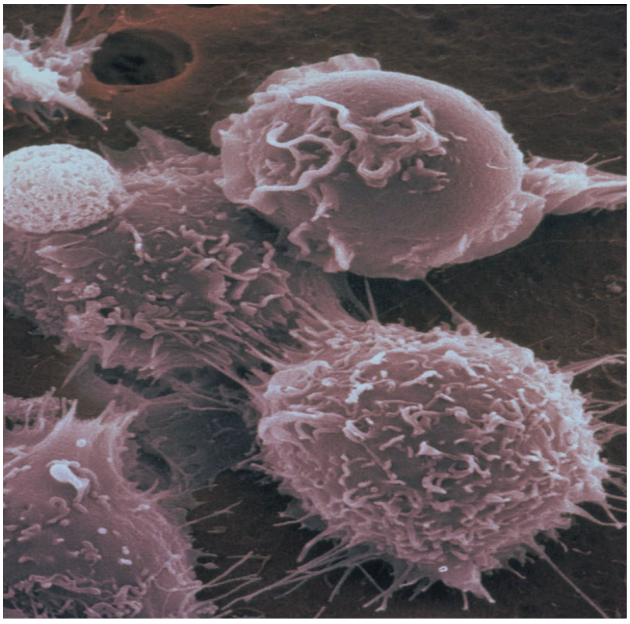
Stem Cell Morphology

Known surface markers have been used to isolate hematopoietic stem cells to aid in gaining knowledge of a stem cell's appearance. Stem cells are "small spherical cells that are about 6 to 8 μm in diameter and have no particular morphological features, though they do have a high nuclear-to-cytoplasmic ratio (Palsson and Bhatia, 2004)." Furthermore, it appears that stem cells express receptors for most of the known hematopoietic growth factors. They divide rarely and commit to growth and differentiation in a stochastic manner. The following figures 2 and 3 illustrate embryonic stem cells and hematopoietic stem cells in bone marrow, respectively.



Newsweek, July 9, 2001

Figure 2. Embryonic Stem Cells



(2001) Nature 414: 129

Figure 3. Hematopoietic Stem Cells in Bone Marrow

Stem cells have two highly scientifically relevant characteristics that distinguish them from other types of cells in the body. First, these unique cells begin as unspecialized cells that renew themselves over lengthy periods through cell division. Second, stem cells that experience certain physiological or experimentally induced conditions can be prompted to become cells with special functions such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas (Stem Cells: Scientific Progress and Future Research Directions, 2001).

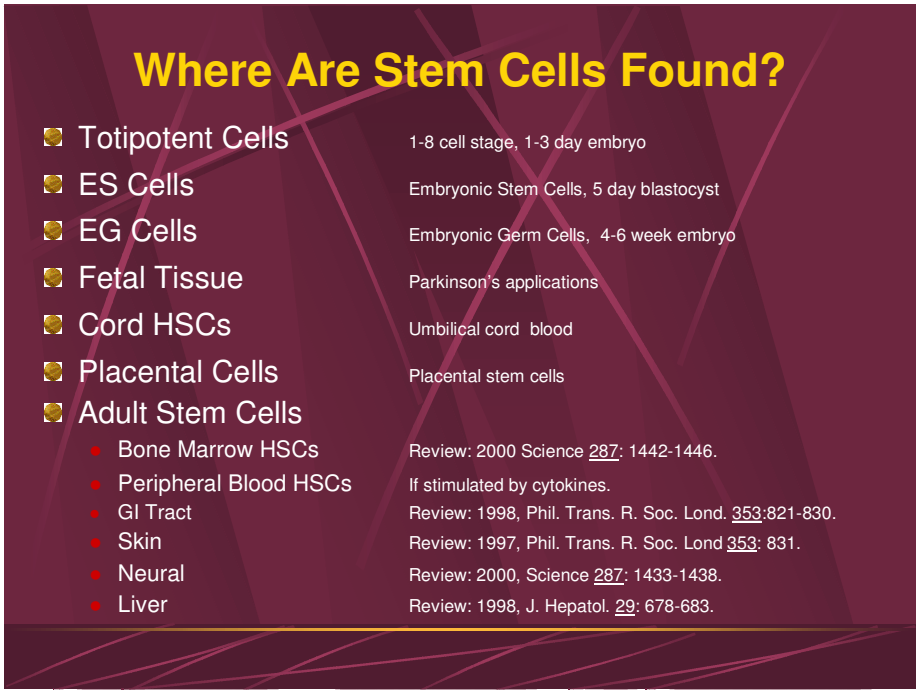
Stem Cell Kinds and Locations

Stem cells are found throughout the body (see Figure 4). Different tissues in the body that stem cells reside in have their different characteristic replacement times. "The more rapidly proliferating tissues, such as bone marrow, small intestinal epithelium, muscle, and skin, all appear to have stem cell systems. The same now seems to be true for organs with slow turnover times, such as the liver, brain, and even beta islets in the pancreas (Palsson and Bhatia, 2004)."

Hematopoietic Stem Cells

The bone marrow is the site where hematopoietic stem cells (HSC's) are found. Bone marrow is red and cell producing at birth but changes to adipose, non-cell producing tissue after time. However, this change in the marrow tissue is reversible in times of stress and disease. In the red marrow is the stroma, a sponge-like network of tissue with sinuses and sinusoidial capillaries within that provide the blood supply for the marrow cavity. The stroma is where blood cells are constantly being formed and sent

through the sinusoidial capillaries so as to reach the circulating bloodstream (Dee et al, 2002).

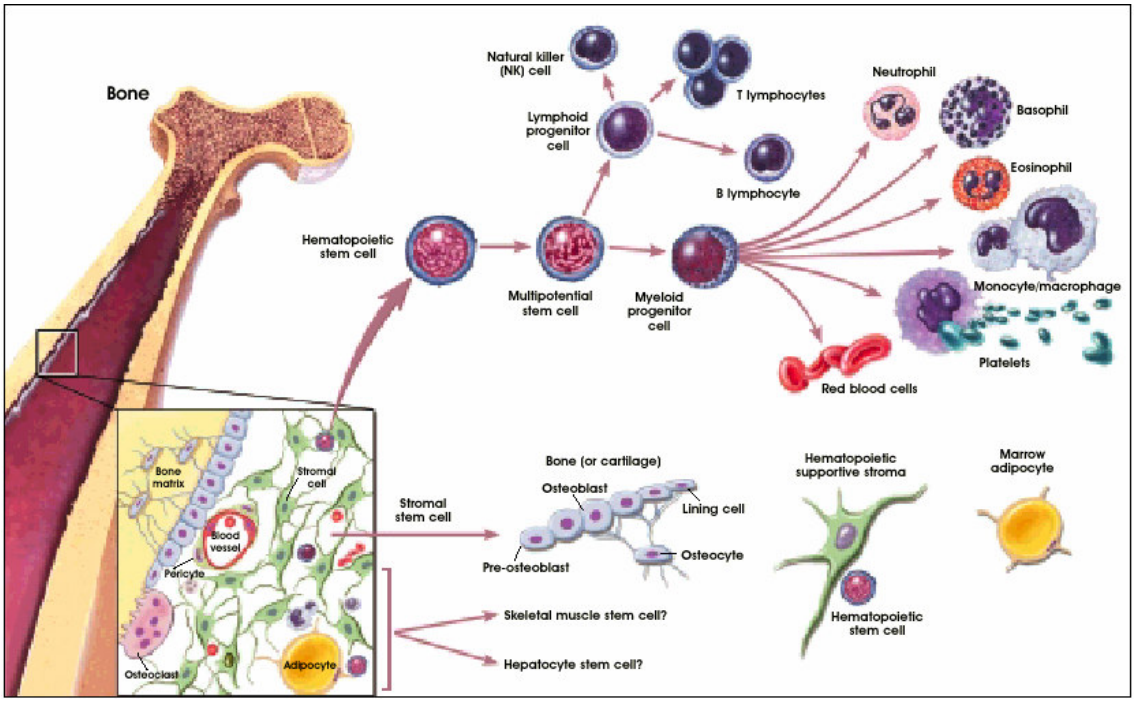


Adams, 2004

Figure 4. Description of Where Stem Cells Are Found

"The word *hematopoietic* is formed from *hema,* meaning 'blood,' and *poietic*, meaning 'forming (Dee et al, 2002).'" All blood cells originate in the bone marrow and develop through the blood cell formation process, hematopoiesis (see Figure 5). The hematopoietic stem cell (HSC) that is the origin for the cells that circulate in the bloodstream is pluripotent. The pluripotent hematopoietic stem cell (PHSC) can replicate and differentiate into two new stem cell types, the lymphoid stem cell and the myeloid stem cell. The lymphoid stem cells leave the bone marrow to the spleen, thymus, and lymph nodes of the lymph system. They eventually produce the white blood cells of the

lymphatic system, known as lymphocytes. Myeloid stem cells remain in the bone marrow and produce the red blood cells (oxygen-carriers), platelets (blood clotters), and leukocytes (defenders against foreign objects).



NIH Stem Cell Report, May 2000

Figure 5. Illustration of Blood Cell Regeneration (Hematopoiesis)

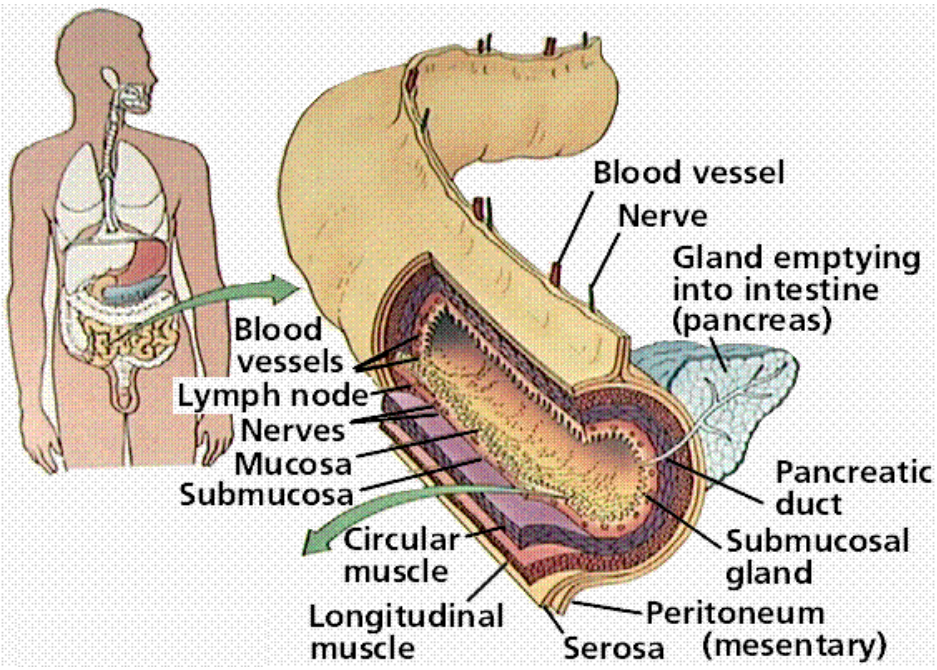
Mesenchymal Stem Cells

In addition to the presence of stem cells that produce the blood-borne cells of the body, there is a cell population in the human bone marrow that can potentially differentiate into a number of connective tissue cell types. Osteocytes, chondrocytes, myoblasts, fibroblasts, and possibly adipocytes are all mature cell types that can be derived from a purified population of supposed mesenchymal stem cells. Tests have been conducted to find the validity of the idea of a multipotent human mesenchymal stem cell.

Studies demonstrate that there is a subpopulation present in bone marrow that has the potential to bear several cell types in different organs. However, evaluation is still in the relatively preliminary stages that can only provide strong support, not proof, for the identity of human mesenchymal stem cells (Stem Cells: Scientific Progress and Future Research Diretions, 2001).

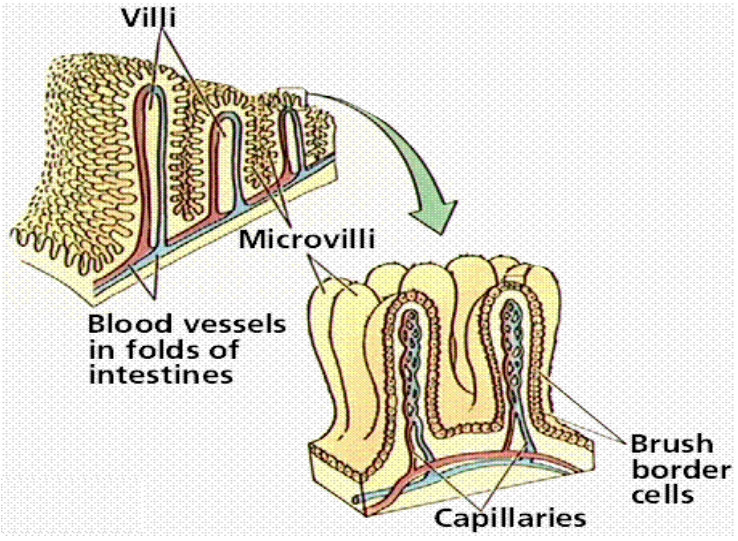
Intestinal Stem Cells

Like the bone marrow, the small intestinal epithelium is a more rapidly proliferating tissue with a stem cell system. Its cellular content turns over approximately every five days, making the small intestine the body's second most prolific tissue next to the bone marrow. The lining of the small intestine is comprised of minute projections called villi (Figures 6 and 7). The villi work as nutrient absorbers for the tissue. In between the villi are tube shaped epithelial infoldings. Each infolding is known as a cryptus. The bottom of the cryptus is where all the intestinal epithelial cell production takes place. A ring of about 20 slowly dividing tissue specific stem cells resides in each crytus. After division, the daughter cell becomes a rapidly cycling progenitor cell that has a cycling time of 12 hours. These cells, known as transit amplifying cells, move up the crypt and differentiate. Upon leaving the crypt, the cells are mature and enter the base of the villi. Then they take about five days to travel to the top of the villus, where they die and slough off.



Purves et al, 1998

Figure 6. Layers of the Intestine

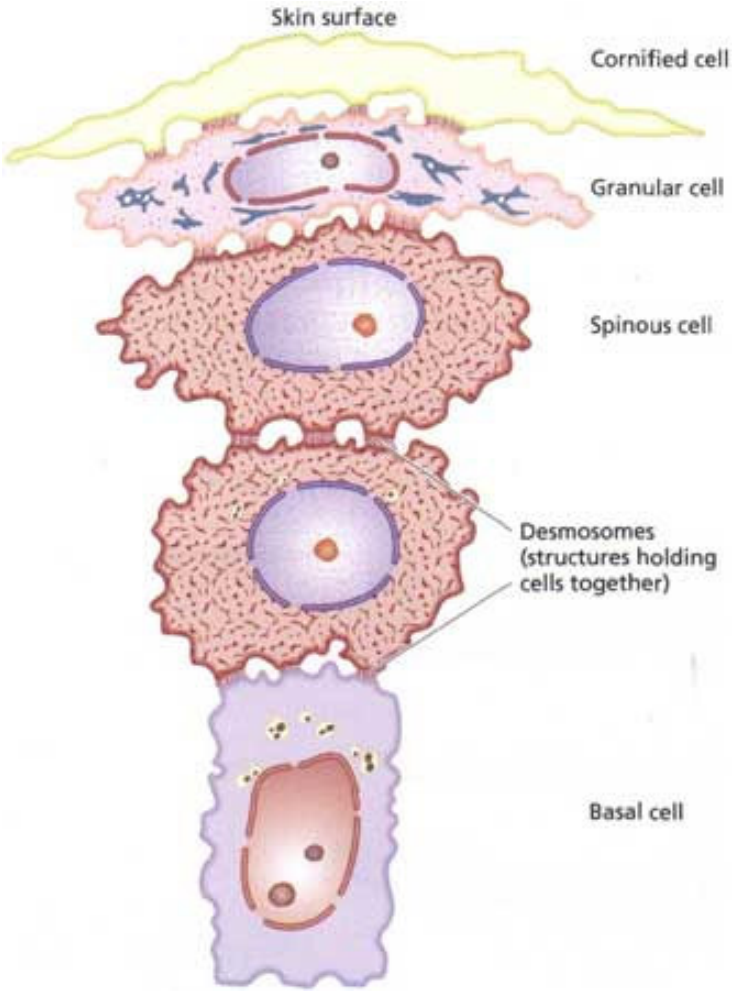


Purves et al, 1998

Figure 7. Villi of the Intestine

Skin Stem Cells

Behind the bone marrow and small intestinal epithelium, the skin is the body's third most prolific tissue. The turnover of skin is typically a few weeks. The skin's two principle cell layers, the dermis and the epidermis (Figure 8), are separated by a collagen-based basal lamina layer. The dermis is under the basal lamina and is comprised mainly of fibroblasts while the epidermis is above the basal lamina and is comprised of differentiating keratinocytes. The epidermis has a columnar organization with the cells located at the basal lamina replicating and the cells above differentiating. Thus, the cells at the bottom of the epidermis are the stem cells that undergo differentiation as the leave the basal lamina. Approximately one in 10 to 12 basal cells is an epidermal "progenitor" cell that is responsible for the cell production in the squamous column above it (Purves et al, 1998).



Procter & Gamble, 1997

Figure 8. Different Forms of the Cells of the Epidermis

Liver Stem Cells

Dissimilar from the bone marrow, small intestinal epithelium, and skin, the existence of a liver stem cell is a topic cloaked in controversy and debate. "For example, some investigators believe that hepatocytes at the beginning of the sinusoid are stem cells. There they proliferate, differentiate, and 'stream' down the sinusoid where they will ultimately die. Others propose that the liver is sustained by division of mature hepatocytes. However, when their division is inhibited, and the liver has sustained

dramatic injury, a quiescent cell population become activated. These oval cells are therefore only 'opportunistic' stem cells (Palsson and Bhatia, 2004)." In any case, recent work clearly illustrates the residence of cells in the bone marrow that can repopulate the liver under some circumstances. These cells essentially act as stem cells but do not serve as sufficient proof to end the disagreement over the identity and role of stem cells within the liver in normal liver homeostasis.

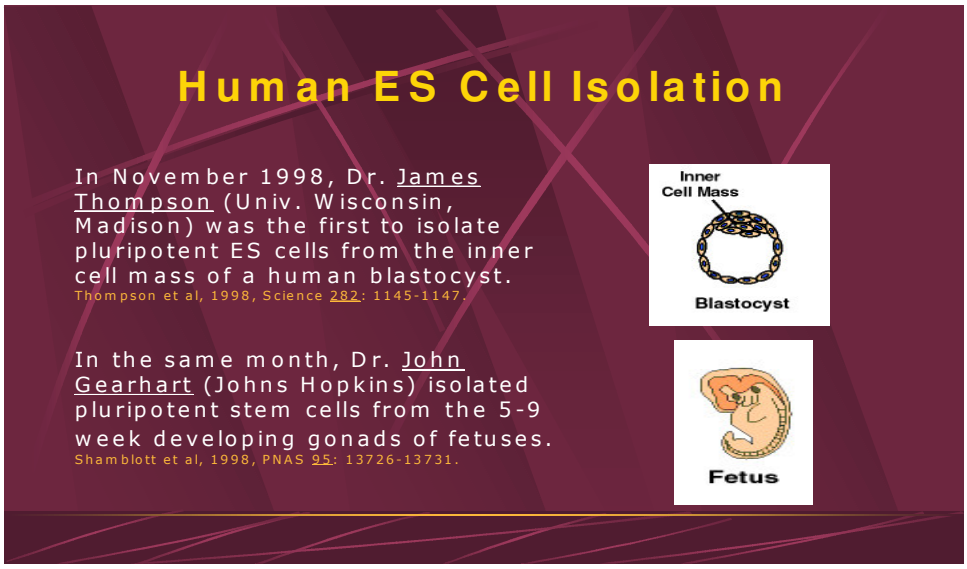
Neuronal Stem Cells

Lineage differentiation of neural stem cells can be diagrammed thanks to demonstrations and studies on human fetal brain cells. Cells isolated from the ventricular zone in the human fetal brain have been cultured clonally and induced into differentiation of major cell types in the neural tissue. When these cells were experimentally transplanted into brains of newborn mice, the cells migrated and differentiated into neuronal lineages (Zigova and Sanberg, 1998).

Embryonic Stem Cells

The aforementioned mentioned stem cells described above are each capable of producing the cells for each respective tissue. However, it is their specific designated tissue that these specialized stem cells are limited to. For example, the stem cells in the small intestinal epithelium give rise to the cells only in the small intestinal epithelium. In contrast, embryonic stem cells, or ES cells, have been found to have potential for vast capabilities. Stem cells, present in the earliest stages of embryo development, are capable of generating all of the cell types in the fetus and, subsequently, the adult. Thus ES cells hold the most promise for regenerative medicine (Stem Cells: Scientific Progress and Future Research Directions, 2001).

ES cells were first harvested from the inner cell mass of murine blastocysts in the early 1980's. In 1998, embryonic stem cells were successfully grown in the laboratory for the first time (Thomson and Hskovitz-Elde, 1998) (see Figure 9). Presently, ES cells from several mammals, including humans and primates, have been made. "Among the types of cells derived from cultured mouse ESCs are fat cells, various brain and nervous system cells, insulin-producing cells of the pancreas, bone cells, hematopoietic cells, yolk sac, endothelial cells, primitive endodermal cells, and smooth and striated muscle cells, including cardiomyocytes—heart muscle cells (Stem Cells: Scientific Progress and Future Research Directions, 2001)." In addition, human ES cells have been shown to form tissues that resemble gut, bone, nerve, cartilage, and kidney.



Adams, 2004

Figure 9. Representation of Human ES Cell Isolation

The extraordinary versatility that scientists are realizing from embryonic stem cell research gives great hope for transplantation therapy in the future. Controlling the

organization of these cells is something not yet understood, so efficient production of various cell types and control of tissue structure will be key for the future use of ES cells for creation of replacement tissues.

Chapter 2: Stem Cell Medical Applications

"The development and application of human stem cells offers a vast number of potential applications, including the prevention, diagnosis and treatment of human diseases (Strode, 2003)." This statement speaks of the expansive potential for medical stem cell applications. Each year over 30,000 children and adults are diagnosed with life-threatening diseases like Leukemia, which could potentially be cured by stem cell treatments (NMDP, 2004). However, for the full potential to be reached, many technical hurdles need to be overcome through extensive research and clinical trials.

One of the greatest visions of stem cell applications are human embryonic stem cell studies, which may deliver deep insight into how undifferentiated cells become differentiated. It is known that turning genes on and off is integral to differentiation. However, there is not yet a full understanding of the signals that turn genes on and off. Cancer and birth defects, for example, originate from abnormal cell division and differentiation. A better understanding of genetic and molecular controls of cell division and differentiation could give rise to new strategies for therapy for such diseases (Stem Cells, 2002). Additionally, investigation of many pathogenic viruses which only grow in human or chimpanzee cells (such as human immunodeficiency virus and hepatitis C) is largely held back by a lack of *in vitro* models. Current animal models for diseases such as Alzheimer's disease only shed a very partial light on the disease's underlying processes. "ES cells might provide cell and tissue types that will greatly accelerate investigation into these and other viral diseases (Stem Cell Research and Applications, 1999)." Furthermore use of ES cells has the potential to greatly enhance our

understanding of the rudimentary processes which govern human development on all levels. “The potential benefits to human health are huge, and range from generating new neurons for treating patients with Parkinson’s disease, to learning about the molecular processes that drive the development of tumors (Stem Cells – Hype and Hope, 2000).”

In addition to understanding human development, stem cells could serve a purpose in understanding and testing new drugs. Much like cancer cell lines that are currently used to screen potential anti-tumor drugs, new medications could be tested on differentiating human pluripotent cell lines. But, to screen drugs effectively, exact cell culture conditions must be replicated between different experiments. Unfortunately, there is not nearly enough known about the signals controlling cell differentiation to allow consistent and identical culture conditions (Stem Cells and the Future of Regenerative Medicine, 2001).

Arguably the most valuable and promising potential use of human stem cells is the generation of cells, tissues, and organs for use in cell-based therapies. While more than 70 diseases such as Hodgkin’s Disease, Sickle Cell Disease, and numerous Leukemia’s are currently treatable by a blood stem cell transplant, the conditions which may potentially be treated in the future by various cell-based therapies are extensive (NMDP, 2004). These treatments offer immeasurable hope to those patients who suffer from these diseases. The generation of cells, tissues, and organs is often referred to as tissue engineering. “The promised miracle is the generation of ‘personalized’ replacement tissues to combat the ravages of ageing and disease (Can They Rebuild Us?, 2001)”. Current tissues which we are already capable of engineering include skeletal tissues, and a wide range of epithelial surfaces such as skin, cornea and mucosal

membranes (Stem Cells in Tissue Engineering, 2001). Present medicine uses donated tissues and organs to replace ailing or destroyed tissues and organs. However, the need for transplants overwhelmingly surpasses the available supply. An additional complication is the rejection of foreign tissues and organs by the recipient's immune system. Conversely, by using one's own stem cells to grow replacement tissues, such rejection would be avoided. It is hoped that soon it will be possible to culture healthy cardiac muscles in the laboratory and transplant them into a patient stricken with chronic heart disease. In addition to heart disease, stem cell based therapies have the potential to treat Parkinson's disease, Alzheimer's disease, spinal cord injury, stroke, burns, diabetes, osteoarthritis, and rheumatoid arthritis, to name a just few (Stem Cells and the Future of Regenerative Medicine, 2001).

Traditional Cell Therapies

The future of cell-based therapies is bright because some cell therapies are currently successful. Cell-based therapies are not new. Blood transfusions of red blood cells into anemic patients have been a successful practice for decades (Palsson and Bhatia, 2004). Similarly, blood platelets have been transfused successfully into patients who have blood-clotting defects.

A cell-based therapy that has direct stem cell relevance is the bone marrow transplantation (BMT). The hematopoietic stem cells (HSCs) found in bone marrow are transplanted into cancer patients whose hematopoietic system has been destroyed by the radiation or chemotherapy used to fight cancer. BMT has been used to benefit hundreds of thousands of patients for nearly three decades.

Before bone marrow transplantation, cancer treatment options consisted of radio- and chemotherapies that attacked rapidly dividing cells. This left bone marrow susceptible to damage, limiting the dosage of such therapies. BMT was developed to overcome this challenge (Thecancer.info, 2004). While BMT's have been used to treat a vast range of conditions, nearly 75% of all BMT's are preformed on patients with forms of leukemia (NMDP, 2004).

Bone marrow transplantation can be performed in an autologous (marrow harvested from the patient himself) or allogeneic (marrow harvested from a donor) format. In an autologous setting, the patient's bone marrow (presumably cancer free) is harvested from the body prior to radio- and chemotherapies. While the patient undergoes treatment, the bone marrow is kept in cryopreservation. Following a few treatments with chemotherapeutic drugs, the bone marrow is rapidly thawed and returned to the patient. After put into circulation intravenously, the hematopoietic stem cells "target" the marrow cavity and restore bone marrow function. This treatment is frequently applied to lymphoma (cancer of the lymphatic system) patients to rebuild the hematopoietic tissue via the bone marrow stem cells contained in the transplant.

In an allogeneic setting, the donor's hematopoietic stem cells target the recipient's marrow cavity and repopulate it, just as in an autologous setting. In this case, the patient's bone marrow can not be used for transplant since it may be tumorigenic, so a histologically compatible donor's bone marrow is used. The paramount challenge in allogeneic transplantation is overcoming the immune rejection that can lead to Graft-versus-Host Disease (GVHD) (mortality of 10 to 15%) (Horowitz and Rowlings, 1997).

Treatment of Autoimmune Disorders

As mentioned before, the potential importance of stem cell research and application in the biomedical field is very high. One of the conceivable areas that could be affected by stem cell medical applications is the treatment of autoimmune disease (Stem Cells and the Future of Regenerative Medicine, 2001). An autoimmune disease is characterized by the body's inability to distinguish between the cellular components of "nonself" (infectious, invading organisms) and "self" (its own body). Consequently, the immune system fails to recognize self cells and attacks them as if they were foreign organisms. Common autoimmune diseases include rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis, Sjogren's syndrome, inflammatory bowel disease, and type 1 diabetes.

Diabetes Treatment

Type 1 diabetes is an autoimmune disease because the body's immune system sees its own insulin producing pancreatic islet cells as "nonself". As a result, the body attacks and destroys the body's insulin producers, leaving the body without insulin. This is different from type 2 diabetes. Type 2 diabetes develops when the body still produces insulin, but is unable to use it effectively. In either case, without insulin, the body has an excess of glucose in the blood that can lead to complications such as blindness, heart and kidney damage, or amputation (Diabetes.org, 2004).

Doctors, researchers, and diabetes patients turn their hopes to embryonic stem cells as one source to possibly cure diabetes in the future. "In theory, embryonic stem cells could be cultivated and coaxed into developing into the insulin-producing islet cells of the pancreas. With a ready supply of cultured stem cells at hand, the theory is that a

line of embryonic stem cells could be grown up as needed for anyone requiring a transplant (Stem Cells: Scientific Progress and Future Research Directions, 2001)." The cells could be engineered to avoid immune rejection, although there is some evidence that differentiated cells derived from embryonic stem cells might be less likely to cause immune rejection.

Lupus Treatment

Lupus is one such autoimmune disease. It generally affects women of child-bearing age and is three times more common, and often times more severe in African Americans and Hispanics/Latinos (NIAMS, 2004). Some current treatments for autoimmune diseases incorporate the use of anti-inflammatory drugs and immunosuppressive and immunomodulatory agents. The drawbacks of these therapies are the inability to induce a significant remission in certain patients and the dampening of the immune system (i.e. leaving patients susceptible to life-threatening infections). Researchers have recently begun contemplating the use of hematopoietic stem cell therapy as an alternative treatment for autoimmune disease (Stem Cells: Scientific Progress and Future Research Directions, 2001). "Many patients with severe forms of lupus have limited treatment options that may offer only temporary relief of symptoms and no disease regression. For these patients, stem cell transplantation therapy may offer hope for a normal functioning immune system," said Stephen Stephen I. Katz, M.D., Ph.D., director of NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) (National Institutes of Health News, 2004). Autoimmune diseases can incite immune-mediated injury in an organ-specific or non-organ specific manner. In the case of lupus, there is no specific target site on/in the body that the disease inflicts upon.

Poorly responsive, life-threatening cases of lupus can affect muscles, skin, joints, kidneys, and even nerves and the brain. The objective of hematopoietic stem cell therapy for lupus patients is to destroy the faulty immune cells then generate a new, properly functioning immune system via HSCs.

In most clinical human trials of hematopoietic stem cell therapy, the patient's own stem cells are used (autologous setting). To initiate the treatment, the patient receives injections of a growth factor that persuades the bone marrow to release large numbers of hematopoietic stem cells into the blood stream. The cells are then harvested from the blood, purified away from mature immune cells, and stored. When an appropriate amount of hematopoietic stem cells are taken from the patient, he/she undergoes a cytotoxic drug and/or radiation regimen that kills the mature immune cells in the body. The hematopoietic stem cells are then returned into circulation in the patient's bloodstream via a blood transfusion. The cells migrate to the bone marrow and differentiate to become mature immune cells and restore the immune system. Of course, up until that point of immune restoration, the patient's defense is compromised and is at a high risk of infection (Stem Cells: Scientific Progress and Future Research Directions, 2001).

Richard Burt and colleagues conducted a one to three year follow up of seven lupus patients that were subjected to this treatment to record the efficiency of the procedure. They found that each patient remained free from active lupus and improved consistently after the transplantation, without dependence upon immunosuppressive medication. In addition, Burt and his colleagues found that the levels of T cell diversity

were not representative of lupus patients, but were restored to levels of healthy individuals (Traynor et al, 2000).

Problems with Hematopoietic Stem Cell Transplants

Although isolating hematopoietic stem cells from a patient's blood has seen success, the procedure is far from perfect. There are drawbacks that leave room for future improvement or a different procedure altogether. The harvesting of cells from the patient's own peripheral blood puts the patient in a position where it is possible for the autoimmune disease to become antagonized. Additionally, success is compromised for some patients because of the contamination of the purified hematopoietic stem cells with the patient's mature autoreactive T and B cells. These problems could be attended to with the ability to generate unlimited numbers of hematopoietic stem cells outside of the body, and by using differentiation markers on the surface of mature T and B cells to identify and remove them from the perfused cells.

Hematopoietic Stem Cells Derived from Cord Blood

Medical research currently sees umbilical cord blood with its embryonic origins as rich sources of hematopoietic stem cells outside of the body. We have learned that umbilical cords are packed full of hematopoietic stem cells. Normally discarded at the time of birth, cord blood units (CBU's) which have undergone cryopreservation, offer a positive alternative for bone marrow HSCs in stem cell transplantation. Umbilical cord blood could provide a reliable alternative to autologous cells for transplants in the future (Autologous Peripheral Stem-Cell Transplantation, 1995). However, whether transplantation with ES cells is superior to HSCs remains unproven: "Whether

embryonic stem cells will provide advantages over stem cells derived from cord blood or adult bone marrow hematopoietic stem cells remains to be determined (Stem Cells: Scientific Progress and Future Research Directions, 2001)." Embryonic stem cell research is as ongoing as the debate whether or not to use it. However, cord blood sourcing is a tangible solution that has seen success. "Cord blood has been used to effectively heal many cancers since the early 1980's. To date, 2,000 cord blood transplants have been safely performed at universities and medical clinics all over the world with spectacular restorative effects, ranging from significant improvements to complete remissions (Stem Cell Treatments Started in Georgia, 2003)." CBU's also offer many competitive advantages over BM cells. CBU's are a better source of Hematopoietic stem cells because they are less likely to be rejected by the patient therefore we see less graft rejection. In fact, "on a per cell basis, CBU's engraft 10 to 50 fold better in xenogenic hosts than BM progenitors (Hematopoietic Stem Cells for Transplantation, 2002)." Also a CBU is less likely to contain bacteria or viruses which may be present in marrow or PBSC's (Peripheral Blood Stem Cells) harvested from adults (NMDP, 2004). Additionally umbilical cord blood is a richer source of stem cells, that is to say the blood has a higher percentage of stem cells than those in bone marrow. The same immunological immaturity of the T-cells contained in a CBU which accounts for lower occurrences of GVHD subsequently provides a better option for patients unable to locate a fully matched or a one-antigen-mismatched donor (Hematopoietic Stem-Cell Transplants Using Umbilical-Cord Blood, 2001). Finally, for patients with diseases that progress rapidly, speed of transplantation may be a factor. CBU's can normally be obtained in about one month, and sometimes as quick as two weeks, whereas the

necessary time to acquire a marrow or PBSC transplant averages around four months (NMDP, 2004).

In 1999, a 16 year old leukemia patient by the name of Nathan Salley experienced the benefit of a cord blood transplant. Salley underwent intensive radiation and chemotherapy over an 18 month period only to find that the disease still resided within his system. Doctors suggested a bone marrow transplant to give Salley a new, leukemia-free blood system. However, when they were unable to find an adequate match for a bone marrow donor, doctors turned to an umbilical cord blood transplant for the answer. A match was found in Spain where a mother had donated her child's umbilical cord after birth. Since cord blood only has a limited number of cells available, not enough for a teenage patient, Salley's doctors decided to utilize an experimental procedure where some of the cells were treated in a laboratory with vitamins and growth factors to increase quantity. Salley received three days of intensive radiation and chemotherapy to eliminate his own leukemia producing bone marrow. He received 60% of the original cord cells in a transfusion while the remaining cells were treated in the laboratory. Ten days later he received the lab-expanded cells to complete his treatment. The procedure worked to successfully eliminate his leukemia. "He now has an infant's immune system that will build up over his life (Townsend, 2001)."

ViaCell,, Inc., a cellular therapy company located in Boston, MA, is a company which has been dedicated to enabling the widespread application of human cells as medicine. ViaCell offers expecting families the option of preserving their baby's cord blood stem cells. At the time of birth the umbilical cord blood is collected. It then undergoes a patented purification processes which essentially removes differentiated B

and T cells on antibody columns, and grows additional stem cells. Since the amount of Hematopoietic stem cells found in the cord blood is only enough to save a child, growing additional cells enables an alternative cellular therapy capable of saving an adult patient. For about $1,500 initially, and about $100 a year for storage, ViaCell will cryogenically preserve your child's umbilical cord stem cells. Should your child develop a life threatening illness later in life, these cells can be thawed out, transplanted, and potentially save the patients life. Again one of the advantage's in using ones own cord blood cells is that rejection no longer becomes an issue. Furthermore in the event that the patient develops some condition later in life, for example the deterioration of cardiac cells, there is the future potential of generating new heart tissue from ones own stem cells which were preserved at birth.

Adult Stem Cells

As recently as the mid-1990's, it was believed that neurons in the adult human brain and spinal cord couldn't regenerate. Once dead, the neurons of the central nervous system were believed to be gone for good. Neurological research and therapy was focused entirely on limiting any further neurological damage and compensating for the tissue that was now missing. However, things changed in the middle of the 90's when neuroscientists found that some parts of the human brain do regenerate new neurons. Moreover, it was found that the new neurons arise from "neural stem cells" in the brain. These discoveries lead researchers to believe that it may one day be possible to repair damage from degenerative diseases such as Parkinson's disease, Alzheimer's disease, and

amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's Disease) by culturing neural stem cells isolated from the patient's own brain.

To combat degenerative neural disease, researchers are employing two basic strategies. One strategy is to grow differentiated cells in a laboratory that are adequate for implantation by starting with undifferentiated neural cells. The objective behind this strategy is to either persuade the cells to differentiate toward the appropriate neuronal cell type *in vitro* before implantation, or to allow the signals inside the body to direct the maturation and differentiation of the cells after implantation. A variety of different stem cells could be used to accomplish this task. Neural precursor cells (cells that are committed to differentiation into neurons but have yet to do so) or pluripotent embryonic stem cells (cells that can become any cell type in the body and can be maintained in culture for a long time without differentiating) could be used in the procedure.

An alternative strategy hinges on finding growth factors, hormones, and other signaling molecules that help cells survive and grow that can stimulate a patient's own stem cells into action for coping with damage from disease or injury (Stem Cells: Scientific Progress and Future Research Directions, 2001).

Embryonic Stem Cell Therapies

In 2001, researchers at Johns Hopkins University made a significant advancement, reporting preliminary evidence that cells derived from embryonic stem cells can restore movement in an animal model of ALS. Amyotrophic lateral sclerosis is a disease that destroys motor neurons in the spinal cord. Those inflicted with the disease

experience gradual muscle weakening that begins in the limbs and results in paralysis and death (Alsa.org, 2004).

ES Treatment of ALS

In the study, researchers used rats as the animal model. The rats were exposed to the Sindbis virus, which destroys the motor neurons in the spinal cord, much like ALS. The inflicted rats developed paralyzed muscles and weakened limbs in their hindquarters. The researchers then mimicked the 1998 protocol of Gearhart and colleagues, isolating embryonic germ cells from human fetal tissue, and allowing the cells to make unchanged reproductions that clumped together to form embryoid bodies. Research has shown that when subjected to certain laboratory conditions, the embryoid bodies begin to look and function like normal neurons. So the scientists at Johns Hopkins prepared the embryoid bodies and injected them into the fluid surrounding the spinal cords of the rats. What they found was promising. Three months after the injections, many of the treated rats were able to move their hind limbs and walk, although somewhat clumsily. Meanwhile, the untreated rats were still paralyzed. The autopsy showed that the cells derived from human embryonic germ cells had migrated throughout the spinal fluid with continual development (Kerr et al, 2001).

ES Treatment of Parkinson's Disease

Like ALS, Parkinson's disease is a disorder of the nervous system that has the potential to be overcome through stem cell application in the future. Parkinson's Disease is a progressive movement affliction that results in highly compromised motor ability. The neurons that die in Parkinson's Disease are emitters of a dopamine, a neurotransmitter that works to regulate the nerves that control body movement (Pdf.org,

2004). The objective in cell or tissue transplantation therapy for Parkinson's disease is simple: replace the lost dopamine-releasing neurons with implanted cells into the brain. Accomplishing this task, however, is very difficult because the cells not only need to survive transplantation, they also need to make appropriate connections in the brain to function accordingly.

In the early 1970's, Lars Olsen and colleagues documented that fetal tissue transplanted directly from embryonic mice into adult rats continues to mature into fully developed dopaminergic neurons (Dunnett et al, 2001). By the early 1980's, Anders Bjorkland and others found that fetal tissue transplanted into damaged areas of the brains of rats and monkeys could reverse Parkinson's-like symptoms (Dunnett et al, 2001). In 1999, scientists extracted stem cells from the brains of rats and turned them into neurons in a Petri dish. The new neurons were then implanted into the brain of a 57 year old man with Parkinson's disease in an experimental procedure. To test for the effectiveness of the new neurons, the man received transplantation in only one side of his brain. Four years after the procedure, the treated side of the brain is doing well and the man "wants to get the cells implanted on the other side (Westphal, 2003)."

Evan Snyder of Harvard Medical School has also seen success in preliminary experimentation with cell transplantation that holds potential for future Parkinson's treatment. Snyder originally isolated neural stem cells from newborn mice and found the cells divided in tissue culture. This in essence meant that he had a limitless supply of therapeutic cells. After grafting the stem cells back into mice, Snyder found that the stem cells differentiated into all the different cell types found in the nervous system. These cells include nerve cells, supporting glial cells, and cells of peripheral nerves.

In a later experiment, Snyder used stem cells isolated from the brain of human fetuses. He injected the cells into the brain ventricles of monkey fetuses to find that the cells migrated out of the ventricles and developed into a variety of cell types throughout the brain. With encouragement of results like these, Snyder is researching the possible use of these cells to treat children that have disorders of the nervous system. His reasoning is such that the transplanted cells may provide enough of the necessary enzymes that are missing in the patient so that there is prevention of mental retardation or death (Freed and Simon, 2002).

Parkinson's researchers ultimately desire a renewable source of cells that can differentiate into functional dopamine neurons after transplantation. Growing cells derived from stem cells appears as the best potential alternative source for transplantable material. "One way to get these is to find the right combination of growth factors and cell-culture conditions to grow undifferentiated cells in a culture dish to a point where they are committed to becoming dopaminergic neurons, then implant them to finish growth and differentiation in the host brain. Another possibility is to put less committed cells into a damaged brain and rely on "environmental" signals in the brain to guide them into becoming the right kind of replacement cell (Stem Cells: Scientific Progress and Future Research Directions, 2001)."

In addition to cell transplantation approaches, Parkinson's research is also focused on finding a way to trigger the repair mechanisms found naturally in the human brain. The goal is to stimulate these repair mechanisms to mend damage that is otherwise beyond their capacity. Although the strategy has not seen as much progression as cell

and tissue implantation, repair mechanism inspiration still holds promise for the future (Bjorklund and Lindvall, 2000).

James Fallon and colleagues studied the effects of transforming growth factor alpha (TGFα) on normal and Parkinson's rat brains. TGFα is a protein found naturally in the body from the early stages of embryonic development onward. The protein is important in activating normal repair processes in the body. Fallon found that when TGFα was injected into a healthy rat brain, stem cells in the subventricular zone proliferated for several days. When TGFα was injected into a rat brain with damaged nigro-striatal neurons, the stem cells migrated to the damaged areas and differentiated into dopamine neurons. Moreover, the brain-damaged rats that were treated with TGFα were found to no longer display the abnormal behavior tendencies that were seen prior to treatment (Fallon et al, 2000).

Tumor Cell Purging

In 1999, Meck and colleagues presented their research for purging neuroblastoma cells from autologous stem cells at the proceedings of the American Association for Cancer Research. Neuroblastoma is one of the most common solid tumors found in babies and young children, with origins in the sympathetic nervous tissue (Cancerindex.org, 2004). Neuroblastoma is commonly treated with surgery, chemotherapy, and stem cell rescue. However, studies demonstrated that reinfusing stem cells with an autologous origin possibly contributes to relapse due to contamination of tumor cells that are undetectable morphologically. Meck et al reported that they chose an adenovirus-based method for purging the stem cells of neuroblastoma cells because

adenovirus is more toxic to neuroblastoma cells than to hematopoietic cells. They found through their research that their method allows 70% survival of progenitor cells while eliminating clonogenicity of tumor cells (Method Purges Neuroblastoma Cells from Autologous Stem Cells, 2000).

HSC Treatments for Sickle Cell Disease

Sickle cell disease is a chronic and often incapacitating disorder among a group of inherited red blood cell disorders. The sickle cell mutation is due to a single change in the amino acid chain of the oxygen transporting protein, hemoglobin. Instead of a glutamic acid at position 6 of the beta-globin chain we find instead an amino acid called valine. When the sickle hemoglobin releases oxygen in the tissues, the globin molecules tend to stick together and form long chains or polymers. These rigid polymers distort the cell and cause it to bend out of shape. The deformed cells block the flow of cells and interrupt the delivery of oxygen to the tissues which results in damage to the tissues and organs. Scientists believe hematopoetic stem cells may provide reliable treatment for sickle cell anemia through bone marrow transplantation. Researchers from 27 North American and European transplant centers conducted a study which resulted in very promising results. From 1991 to 2000, fifty-nine patients ranging from 3 to 16 years of age received sibling marrow allografts. Fifty-five patients survived and most impressive, 50 survive free from sickle cell disease. Of these 50 patients, 13 developed stable mixed donor-host hematopoietic chimerism (Stable Mixed Hematopoietic Chimerism after Bone Marrow Transplantation for Sickle Cell Anemia, 2001). While these results are promising, further studies and clinical trials will be necessary before HCT treatments

may be deemed reliable. Phase I-II clinical studies are underway for 30 children with sickle cell disease and is currently recruiting patients. This current study will combine "a non-myeloablative pre-transplant hematopoietic cell transplantation (HCT) therapy with modulated post-grafting immunosuppression to control host-versus-graft and graft-versus-host reactions (ClinicalTrials.gov, 2004)".

ES and HSC Treatments for Heart Failure

In the United States, 4.8 million people are afflicted with congestive heart failure, the ineffective pumping of the heart caused by the loss or dysfunction of heart muscle cells (Healthlink.mcw.edu, 2004). Heart muscle cells are destroyed by hypertension, coronary artery disease, or a heart attack. Researchers are working to use stem cells to replace damaged heart cells and restore cardiac function for future congestive heart failure sufferers.

Three cell types that are important to a properly functioning heart are cardiomyocytes, vascular endothelial cells, and smooth muscle cells. Cardiomyocytes are heart muscle cells that contract to eject blood from the ventricle (the heart's main pumping chamber). Vascular endothelial cells form the lining of new blood vessels and smooth muscle cells from the wall of new blood vessels. Vascular endothelial cells and smooth muscle cells are specialized cells that are critical for developing a new network of arteries to bring nutrients and oxygen to the cardiomyocytes after a heart has been damaged. The stance of researchers is to explore the possibility of stem cells developing into these three cell types so that they can be used to restore function to the damaged heart.

In 2000, Itskovitz-Eldor et al reported advancement in embryonic stem cell work in relation to the heart. The researchers demonstrated that human embryonic stem cells can reproducibly differentiate in culture into embryoid bodies. Cells were noted to have the physical appearance of cardiomyocytes, show cellular markers consistent with heart cells, and demonstrate contractile activity similar to cardiomyocytes when observed under the microscope (Itskovitz-Eldor et al, 2000).

Orlic and colleagues reported in 2001 on an experimental application of hematopoietic stem cells for the regeneration of heart tissue. In their study, they induced heart attacks in anesthetized mice by tying off the left main coronary artery. They then isolated bone marrow cells with a high capacity to develop into cells of multiple types. When these cells were injected into the damaged wall of the ventricle, there was formation of new cardiomyocytes, vascular endothelium, and smooth muscle cells. The newly formed myocardium occupied 68 percent of the damaged ventricle nine days after transplantation. The researchers reported the mice that received the treatment survived in greater numbers compared to the mice that suffered heart attacks without treatment (Stem Cells: Scientific Progress and Future Research Directions, 2001).

Stem cell application for heart repair has not only seen success in rodent models, but also in human clinical trials. In Germany, Gustav Steinhoff at the University of Rostock purified stem cells from bone marrow removed from the hips of six heart attack patients. The following day the stem cells were injected, during a bypass operation, into the boundary between the living and dead heart tissue of each patient. "For all six patients, the heart's strength and blood supply improved, suggesting the stem cells had differentiated into heart muscle and blood vessel cells (Randerson, 2003)." In Japan, a

group reported similar results with stem cells injected via a catheter without bypass surgery. Although the greater improvement was seen from the patients with the stem cell/bypass treatment combination over patients with just bypass treatment, Steinhoff urges that this was strictly a preliminary feasibility study.

At the Texas Heart Institute, fourteen dying heart failure patients underwent stem cell treatment. Each of the patients had stem cells harvested from their own bone marrow. These stem cells were injected back into the patients, each receiving fifteen injections of roughly 2 million cells per injection. Another group of heart failure patients of less critical condition did not receive the stem cell injections. After two months, the treated group was able to pump more blood and experienced less chest pain than the untreated group. The improvement in blood pumping power withstood the length of the study (four months) and there were no instances of heart attacks or irregular heart rhythms (Fischman, 2003).

In 2003, sixteen year-old Michigan resident Dimitri Bonneville was accidentally shot in the heart with a nail gun. He suffered a heart attack from the gun wound. His prognosis appearing bleak, doctors decided to use an experimental stem cell treatment to salvage the boy's damaged heart. Stem cells were harvested from Bonneville's blood and transfused with a catheter into the damaged portion of his heart. As of four months after the procedure, Bonneville "continues to do well and improve (Westphal, 2003)."

Stem Cell Treatment of Pulmonary Fibrosis

On August 2nd, 2004 researchers at the University of California at Los Angeles had a remarkable finding relating to the treatment of pulmonary fibrosis. Researchers

found a particular type of adult stem cell which they determined plays an important role in pulmonary fibrosis. Then went on to inhibit its ability to migrate to the lungs where it produces collagen which ultimately leads to the excess scar tissue formation present in pulmonary fibrosis (Phillips et al, 2004). Dr. Robert M. Strieter and his colleges showed this adult stem cell could be blocked which can reduce the amount of build up in the lung thus reducing pulmonary fibrosis. The findings are available in the Journal of Clinical Investigation (Phillips et al, 2004).

Stem Cell Treatment of the Eye

For years it was assumed that the eye did not contain stem cells. However, Derek van der Kooy of the University of Toronto reported "several years ago (Dead Could Help the Living See, 2003)" to have found retinal stem cells in the eyes of mice. Following that discovery, van der Kooy and his team of researchers isolated stem cells from the black ring around the iris of the human eye. Using eyes from the Eye Bank of Canada, the team proclaims each eye to provide about 10,000 cells and each of these cells can provide 15,000 progenitor cells. When injecting the stem cells into the eyes of baby mice, van der Kooy and colleagues reported that there is generation of all retinal cell types, including the light detecting rods and cones. In the future, the team of researchers plans to inject stem cells into adult mice in an attempt to make blind mice see.

In 2002, Martin Friedlander and colleagues reported that "non-hematopoietic stem cell lineages specifically interact with astrocytes both during normal angiogenesis and during pathological vascular degeneration in the retina (Senior, 2002)". The team studied the behavior of bone marrow cells in a neonatal mouse model of retinal angiogenesis.

Bone marrow cells were isolated from adult mice, marked, and injected into the eyes of two day-old infant mice. They found that the injected cells were adhering to the retina and had the appearance of elongated endothelial cells. Additionally, the cells colocalized with astrocytes and became incorporated into the developing vasculature. Friedlander expressed that "the results suggest that there is a population of endothelial precursor cells that can promote angiogenesis by targeting reactive astrocytes and incorporate into an established template without disrupting retinal structure (Senior, 2002)".

CHAPTER-3: STEM CELL ETHICS

The concerns of embryonic stem cell research combine the ethical concerns of abortion and cloning, while creating hope for the most incredible and potentially the most important advances to date in medicine. This combination of pros and cons cannot be immutably debated because it asks each of us to make a decision based on the worth of one individual against the worth of the many. No writer or questionnaire, no matter how widely distributed, could compile every ethical implication that this topic creates. As embryonic stem cell research continues to grow and be perfected by the insatiable expanse of humans' control of the world, more controversial, world-changing decisions will be made that the greatest philosophers cannot foresee. The success of embryonic stem cell research will drastically change a world that hundreds of countries and many religions are desperately trying keep in balance. While world has every right to fear this technology, religions are offended by the pride of humans as we approach a reality where we really are gods, creating life, ending life, and living forever. Although frightened, the world must realize the amazing medical benefits this technology creates, and steps should be taken now to ensure this new technology is used appropriately.

In the purely scientific community, free of religious implications, the question of sentience concerns the limits of research on an embryo. Even scientists free of religious morals oppose the tests on a human embryo aware of its own existence, not in a philosophical sense but through the capability of sensing pain. Ethical decisions are required even when determining the point at which an embryo senses pain. Pain receptors begin to grow in the embryo at approximately seven weeks, and the

spinothalmic portion of the brain begins to develop at thirteen weeks, but the spinothalmic portion of the brain does not connect to the cerebral cortex until twenty-six weeks. Research has found that the embryo seems to react to stimuli at seven weeks. This is not a conscious reaction however because the nerve cells are not connected to the brain at this time. Even after the spinothalmic portion of the brain has developed, the reaction to pain would be no different than the reaction at seven weeks because the stimuli cannot pass from the spinothalmic portion of the brain to the cerebral cortex due to an underdeveloped connection within the brain. At twenty-six weeks the cerebral cortex is connected to the spinotalmic portion of the brain and the response to pain stimuli is a conscious effort of avoidance created by an individual. In countries such as England, the United States, and Sweden, their legislation avoids the question of sentience entirely by prohibiting research on embryos beyond 14 days, at which time the embryo becomes a blastocyst and the earliest signs of the nervous system have not begun development. However, the opposite side of this argument states that "killing developing human beings earlier as opposed to later is no improvement" (Kilner, 2004).

Stem Cell Sources and Ethics

Sources of stem cells are another concern of people with or without knowledge of stem cell research. The primary source of embryos used for research come from in vitro fertilization clinics. Consent from couples using in vitro fertilization is required for the excess embryos to be used for research. In fertilization clinics, consent is provided each time a couple agrees to donate embryos for stem cell research. Those who oppose stem cell research doubt that the decisions of ordinary couples on such a delicate topic are well

measured based on the limited information available on the outcome caused by such research. It seems the opponents to embryonic stem cell research believe the full extent of ethical implications would not be taken properly into account. The opponents of stem cell research are also usually unaware of some of the alternatives to ES cell research, including the use of adult stem cells, and the use of parthenotes.

Ending life is more obviously objectionable than creating life or living forever because it is the only one of these three that is prohibited without challenge everywhere government exists. Embryonic stem cell research usually requires the termination of an embryo at the blastocyst stage (in which the ES cells constitute the inner cell mass) to avoid that termination becoming murder from the government's perspective.

Religious Perspectives

A world based on stem cell medicine would be entirely different in the way we respect human life; "We need to be careful lest misguided compassion move us to pursue a quick fix that will foster a way of thinking that will harm a much larger number in the long run." (Kilner, 2004) This is an excellent comment, summing the fears of all who oppose stem cell research. However this comment is only true if one believes this new way of thinking would harm people. Regardless, a compromise must be reached to decide when life officially begins, whether it is to prohibit embryonic stem cell research or allow it. The Catholic Church asserts that life begins at conception, when the sperm first unites with the egg. The Jewish Church however believes "an unborn child may not be aborted, but to do so is not killing. It is wrong." (Ayon, 2002). Jews believe that any embryo or fetus outside the mothers womb is not a human being. Furthermore, "Judaism

does not see the artificial growth of human cells on a laboratory dish as a human life." The Jewish religion shares the feelings of many scientists, believing "the greatest accomplishment and advancement in human endeavour have been in the eradication of suffering, disease and needless mortality." Muslims also have beliefs that may be a benefit to future embryonic stem cell research. The Muslim sacred text, the Koran, suggests, "moral personhood is a process and is not granted at the embryonic stage." (Pizzi, 2002) Muslim beliefs hold "abortion as wrong but …life does not begin until the fertilized egg attaches to the womb wall" (Derbyshire, 2001).

What is surprising to most in the U.S. is that of all the religions, Christianity displays the most extreme opposition to stem cell research. Christians have found ways to oppose every form of embryonic stem cell creation, even when the potential for life was not harmed, leading me to believe that Christians are as much concerned with the changes in culture and society brought about by stem cells as with the morality of destroying an embryo, and may invent reasons condemn stem cell research.

Somatic Cell Nuclear Transfer

The cloning debate merges with the stem cell debate through Somatic Cell Nuclear Transfer (SCNT). This avenue of embryonic stem cell research is the most controversial but potentially the most useful if perfected. An embryo that could become a human being is created, however it is a clone of an existing human being. If a universal egg was developed, capable of accepting any person's nuclear contents, and this new embryo divided properly to the blastocyst stage to provide ES cells, a person requiring embryonic stem cell therapy would have access to stem cells perfectly matching their

own cells. Again, opposition to this technique does not trust that the technique would be used purely for the acquisition of stem cells. The opposition fears that clones of the embryo may be developed into a cloned human being, while still opposing the use of an embryo for anything except its full development into a human being. There are also the uneducated population, unwaveringly opposed to cloning of any sort, though they do not understand the difference between cloning "Polly the sheep" and a single cell that would at most develop into an organ. A possible immoral use of SCNT may be to grow a clone to be killed when its organs are required by the origin of the clone, or if a brain transplant is perfected in the future the clones body may be used as a full body replacement. Even more extreme ideas are that clone armies would be created, making the blond, blue-eyed German racial dominance of the early 20th century too insignificant for mention in future history books. This is unrealistic because the clones would have to develop for approximately 18 years and undergo a life full of training before being useful as a soldier. The hardships in the life of this soldier would be more ethically objectionable than the cloning procedure from which he or she was created. The extraction of stem cells from the SCNT technique has foreseeable benefits to humans now and the constant opposition is a healthy form of checks and balances ensuring that SCNT or any drastic scientific advance will not be taken for granted and morality will be properly taken into account.

Pre-Implantation Genetic Diagnosis

Pre-Implantation Genetic Diagnosis (PGD) is one area of embryonic stem cell research that has not attracted enough debate. While SCNT may be extraordinarily useful when a patient requires stem cells due an accident of some sort, if a person were diseased

a clone of their stem cells could fill their body with more diseased cells. PGD has already been used to solve this problem in two different ways. First PGD can select an embryo not carrying the disease in question, so the mother will not carry a diseased child to term. Secondly, and more controversially, parents have used PGD to select an embryo not carrying the same disease as their existing child that, once born, would be a compatible adult stem cell donor for the existing child. The opposition to PGD is concerned that the second child may not be loved or given the proper respect because he or she is a metaphorical tool. Thus far, the children developed using PGD have been loved as any child should, but the concern remains. If the procedure to save that child's older sibling is a failure, the parents may blame the PGD child. Of course this is immoral but it would be naïve to trust every set of parents to act appropriately, especially in such an extreme situation as the potential loss of a child. This avenue of stem cell research should receive more opposition because it is occurring presently, and opposition to this practice should demand legislation be developed immediately to properly protect these children, grown for the purpose of another human being.

PGD has obvious connections to adult stem cells as mentioned above, but it is also inseparable from the embryonic stem cell debate. Preventing an unfortunate diseased life is an excellent use of embryonic research, relatively free of moral implications. Objections arise when considering the excess embryos from the procedure that must be terminated or stored at great cost by cryogenic freezing. These embryos have an important role in embryonic stem cell research. Scientists have the opportunity to observe the pathology of various diseases in the first weeks of life due to PGD, and potentially find cures or remedies for persons currently living with the disease. This

research has not been met with the same objections as SCNT, or even the objections to the use of excess embryos from in-vitro fertilization clinics not using PGD. Although there are more immediate uses for the research of the pathology of diseased embryos, by not opposing the research and termination of these embryos, the opposition evidently gives more respect to the life of a healthy embryo than a diseased embryo. These embryos also have the potential to become human beings. If legislation must be created to decide which embryos could be used for research and which must be allowed to die naturally, the worth of the embryo would be defined by the how diseased it is. Lastly, the excess embryos from in-vitro fertilization clinics supply most of the embryos used for research. Opponents to the use of these embryos believe the use of these embryos for research is morally objectionable. However, these embryos are extras, and if they were not used for research they would be left to die naturally. Assuming this embryo is an individual, it seems objectionable to allow these embryos to die without allowing the embryos to contribute to mankind.

Adult Stem Cells

Adult stem cells are currently in use, and have far fewer ethical concerns than ES cells. Opponents to ES research argue that adult stem cells should receive more financial attention. Until recently however, the use of adult stem cell has been limited to hematopoietic stem cells present in bone marrow transplants, therefore ES cells with their pleuripotency seemed vastly superior medically. As more kinds of adult stem cells are discovered, this kind of therapy may increase further. From a societal standpoint,

research on adult stem cells may provide medical usefulness, at least in the near future, without wasting financial potential while fighting in courts or fighting an ethical battle.

Unfortunately, even adult stem cells are sometimes opposed simply through ignorance. Much of the population do not understand the difference between embryonic stem cells and adult stem cell. ES cells are pluripotent, capable of becoming a vast number of different bodily tissues, while adult stem cells are unipotent or at best multipotent capable of becoming few different types of bodily tissue. The greatest ethical difference is that adult stem cells are acquired from bone marrow, umbilical chord fluid and various other sources completely unrelated to the destruction of embryos. The potential to create a new human being from an adult stem cell is no greater than from a common skin cell.

Parthenotes

The public is usually not aware that embryos are not the only source of pluripotent stem cells. Parthenotes are eggs stimulated by chemicals that trick the egg into acting as though it were joined with a sperm cell. The egg begins to divide as though it were an embryo, but this pseudo embryo does not have the potential to become a person, they usually divide only to the blastocyst stage. But at least parthenote blastocysts can be used to derive ES cells. Male genes are required for complete development in mammals. Parthenotes have been grown to the fetus stage from mice, and ES cells have been extracted and made into ES cell lines from monkey parthenotes. Those monkey parthenote ES cells "turned into intestine, skeletal muscle, retina, hair follicles, cartilage, bone…, heart cells beating in unison…., nerve cells that secreted the

brain chemical dopamine, the kind of cell that is gradually lost by Parkinson's patients." (Weiss, 2001) Given enough research, we may be able to grow replacement cells and tissues from a patient's own eggs so they would not be rejected by her immune system.

Although parthenotes do not carry the potential for human life they still have their opponents. Douglas Johnson of the National Right to Life Committee is unconvinced that parthenotes deserve no protection. Mark S. Latkovic says, "the current scientific data does *not* allow us to deny that the 'parthenote'/embryo is a human being. Regardless of whether we could produce "human babies" this way, there are enough credible voices saying that even though the present day technology is unable to get the 'parthenote'/embryo past the blastocyst stage, this does not mean that the developing embryo should not *already* be viewed as a human life, albeit a seriously damaged or defective human life…. it seems to me, we are faced with the problem of creating what is a kind of 'deformed embryo,' but an embryo nevertheless….I think that this research ought to be absolutely discontinued in humans. (Latkovic, 2002) Latkovic, a Christian scholar, is making this condemnation based on Pope John Paul II beliefs that human life must not be considered simple biological material to be thrown away. The debate over parthenotes will likely be resolved with a compromise over the status of the normal embryo.

ES Cell Lines

Current technologies allow ES cells to be immortilized into ES cell lines. Such cell lines can be grown indefinitely, and provide a rich source of ES cells for subsequent therapies, without destroying more embryos. Typically, critics of stem cell research

mention the murder of an individual to obtain stem cells. Often it is not mentioned that with the destruction of one embryo, stem cells can be obtained that will divide perpetually creating immortal cell lines. This means the destruction of one embryo could theoretically produce stem cells that could help an infinite number of people. Obviously, opposition to embryonic stem cell research claims there are moral objections to the destruction of even one embryo. Every life saved by that embryo would not be righteous because that life is based on morally objectionable actions. People who believe it is unethical to use those immortal stem cell lines that have already been created are a presently a minority. However, the creation of new cell lines, each requiring the destruction of one embryo is widely opposed. Determining if new cell lines should be created or not requires that the in the early stages of development the embryo is not considered a human being. Hence, in the debate of sentience versus conception, sentience is the victor. Otherwise for the creation of new cell lines to be permitted, a choice would be made favoring the the benefit of many lives over the destruction of one embryo. Aside from the fact that I believe sentience is required for the destruction of an embryo to be considered immoral, the fact that there is no proof that destroying an embryo is the same as killing a human being, and that the destruction of one embryo can save so many lives, I am completely in favor of creating new stem cell lines.

Stem Cells and Immortality

Another reason for stem cell critics to request a halt to stem cell research is that immortality could become reality. Although this debate seems ridiculous based on the distance from our present skills in the science of stem cells, it has attracted very

formidable opposition. Leon Kass, of Presidents Bush's Council on Bioethics is arguably the man most responsible for future of stem cell research in the United States. In a meeting with stem cell researchers at the University of Pennsylvania, Kass made weak comments intending to defend the present way of life in which we wait patiently for death, and we try to make the most of the time we are given. "The self-perception of oneself in an aging body is somehow part of our experience." He made jokes during this meeting, attempting sarcasm on the topic of 75-year-old men playing ice hockey. To me that sounds more like aspiration than humor. All the researchers who attended this meeting seemed to be in favor of stem cell research. As Kass introduced the idea that prolonged life may be a negative result of stem cell research, Dr. Sweeney said, "I think you'd probably be outvoted by the population in general." (Sweeny, 2002) Just as there are differences in opinions between the scientific community and the religious community, there seems to be differences in opinions between generations. Wrinkled old men who probably will not enjoy the benefits of ES science should not make these decisions. They have apparently chosen to accept their slow "natural" decline towards a healthy death, and may be making peace with their god. Kass believes the pleasures of life would not increase proportionately to years. He asks, "Would professional tennis players really enjoy playing 25% more games of tennis?" He is not providing reasons to stray from the goal of immortality. In contrast to Kass's comment about tennis players, immortality would create unforeseen enjoyment of life; "There will never be a shortage of new activities, new understanding, and new experiences…. There will always be innovative art -music, graphic art, writing, dance, and forms as yet unconceived. There are no limits to the personal relationships we can create and develop." (More, 1991)

With people on the earth living longer, more relationships would be made between countries creating a more diplomatic, peaceful world based on more wisdom than could be attained from reading a history book.

There are real concerns with immortality as well. For instance, if stem cell therapy becomes as widely used as the microwave, would a person who wants to die not be allowed to die naturally? This person may receive a voice mail one day stating their doctors concern over a missed stem cell treatment, then police come to your front door accusing you of committing suicide. Also if nearly everyone lives forever, who would be granted permission to reproduce? Would children cease to exist? These topics are genuinely frightening, but only because it requires us to imagine a vastly different world.

In conclusion, the concept of immortality and its benefits can relate to the universal theme of the stem cell debate. I will not say that the positive aspects brought about through immortality outweigh the extinction of children or the prohibition of natural death, but we should find a way for our society to coexist with a world where immortality coexists with children and choice, because the benefits are dictated by what we create and are worth our effort.

CHAPTER-4: STEM CELL LEGALITIES

As stem cell ethics became more widely debated, the demand for legislation followed. The wide variety of current legislation between countries demands increasing attention as trade between countries is greatly affected by domestic policies. As with the ethics of stem cell research, a major concern of the courts in every country allowing any sort of stem cell research is the determination of a time limit for allowing research on an embryo and the status of the embryo in general. The most restrictive and most liberal current policies on embryo research will be described in this chapter.

Germany's Stem Cell Policies

Germany's history of experimentation in eugenics rebounded into one of the most restrictive human embryo policies in the world. Simply stated, "existing German law bans research on human embryos and only allows the laboratory creation of an embryo for the purposes of in vitro fertilization." (Kim, 2002) It is a criminal offence in Germany to dispose of a human embryo whether it is taken from the mother or created in vitro, punishable with a fine or imprisonment. Embryos may not be acquired for anything other than their maintenance with the goal being the full development of the embryo. In January 2002, Germany finally relaxed its restrictions on embryonic stem cell research after being purely restrictive with the Embryo Protection Act of 1990; with the Stem Cell Act of January 2002, research involving imported stem cell lines has been allowed, with conditions:

> "the stem cells were derived from embryos prior to 1 January 2002; the embryos from which the cells were derived were created for use in assisted conception; the informed consent of the donating couple is obtained without the offer of compensation of other benefit; there is no equally effective alternative, and finally the research proposal is worthy and is approved by the 'Central Ethics Commission on Stem Cell Research'" (Davies, 2003).

A large number of contingents argue that Germany is still extremely restrictive after the Stem Cell Act, but if any restrictions are lifted in the near future it will likely be in very small portions.

U.S. Stem Cell Policies

The U.S. is another restrictive country, though research on embryos is not as severely punishable as in Germany. President Bush, in August 2001, decided to restrict the U.S.'s policy, created by the National Institute of Health, to be more morally conscious, while still allowing some research. The NIH in 2000 said it would accept applications for stem cell projects in which stem cells were taken from frozen, excess embryos. Bush's 2001 restrictions completely restrict this potentially liberal policy, only allowing the use of stem cell lines created before January, 2001 to receive federal funding. Bush's policy is still liberal towards private funding of stem cell research, and private stem cell institutes have been formed at Standford and Harvard. However there are few companies prepared to take the risk of spending the large amounts of money

required for the research and development of such technologies. Furthermore, most stem cell lines in the U.S. are currently held by extremely wealthy firms and individuals, unwilling to release them. Many of the available existing stem cell lines in the U.S. are corrupted by the use of animal growth factors in their development creating the possibility of unknown animal viruses or other factors in the stem cells that would compromise the research.

Bush's 2001 decision was largely swayed by by Leon Kass, the appointed chief of the President's Council on Bioethics, an avid opponent not only of stem research but the outcomes of successful stem cell research. Kass believes that embryonic stem cell research needs to be more tightly regulated. However, a restrictive policy on stem cell research is different than a regulated policy. To regulate, Bush must create policies under which stem cell research could exist and be controlled, learning how to best control it by learning from mistakes and experience. The conflict of stem cell research seems as though it would be restricted due the embryos potential for human life, however in 1996, "Congress attached a rider to the Health and Human Services appropriations bill that precludes federal funding of research in which human embryos are destroyed. The rider, attached again to the 2002 bill (which has yet to be signed into law) defines embryos to include parthenotes" (Weiss, 2001) incapable of becoming human beings. If signed into law now the restrictions under Bush's presidency would probably be too restrictive for the U.S. to complete with the rest of world in the race to embryonic stem cell success.

Sweden's Stem Cell Policies

Sweden is among the most liberal Countries in the world where science is concerned, and that openess is reflected in their attitudes towards research on embryonic stem cells. Swedish research on embryos is still governed by the 1991 Act of Measures for Purposes of Research and Treatment Involving Fertilized Human Ova. After consent is obtained from the donors for research on their excess embryos, any sort of research is allowed as long as the embryo is terminated before day 14. The research must, "improve infertility treatment, to improve contraceptive methods or…develop knowledge of embryonic development and the causes of embryo defects." (Davies, 2003) This Act controls the use of embryos, but does not specifically mention embryonic stem cells. The Swedish Research Council has decided that the study of embryonic stem cells is included in the last of the three criteria for research of embryos stated above. Research on embryonic stem cells develops knowledge of embryonic development. As of 2003, the Parliamentary Committee on Genetic Integrity has proposed an amendment to allow the creation of embryos solely for the purpose of research and also allow somatic cell nuclear transfer as a method of creating embryos, a form of cloning. The cloned embryos still must be terminated at 14 days of development.

The United Kingdom's Stem Cell Policies

The United Kingdom is the most liberal country in the world with regard to embryonic stem cell research, not only in their research permissibility, but also their straightforward, public manner about such research in the global community. There are only two main restrictions of embryonic stem cell research in the United Kingdom.

Research is prohibited without a license granted by the Human Fertilization and Embryology Authority (HFEA), and the informed consent of embryo donors is required. The HFEA must decide that the use of embryos is "necessary or desirable" (quoted by Davies, 2003 from the Human Fertilization and Embryology Act 1990) for one of the following purposes:

> "promoting advances in the treatment of infertility; increasing knowledge about the causes of congenital disease; increasing knowledge about the causes of miscarriages; developing more effective techniques of contraception; developing methods for detecting the presence of gene of chromosome abnormalities in embryos before implantation or "for such other purposes that may be specified in regulations." (Davies, 2003 from HFEA 1990)

Much like Sweden there was substantial legal challenge to the 1990 Act arguing that SCNT was not included in the Act and therefore out of the scope of HFEA permits. It succeeded initially, but the House of Lords and the Court of Appeal defeated the appeal, allowing therapeutic cloning in the United Kingdom. However, reproductive cloning is still prohibited. Placing a cloned embryo inside a woman's uterus is a criminal offence in the UK due to the Human Reproductive Cloning Act of 2001.

The UK has made other great strides in creating a controlled environment where embryonic stem cell research may proceed. It has created a stem cell bank, where adult, fetal and embryonic stem cell lines may be grown and monitored by the Medical Research Council and the Biotechnology and Biological Sciences Research Council. A commercial contributor would pay towards the production of a stem cell line, and if the

creation is successful, these councils would control the distribution of these cells for research purposes. Ensuring all advancements in the field are valid, safe, and ethically constrained by their standards, the NFEA will not authorize the discoveries of research firms unless the firm first donates a sample of their stem cell lines to the bank for inspection. The bank will only take high quality lines that will be of benefit to other scientists. Other countries will also be allowed to use the Stem Cell Bank, but they will be required to follow the ethical and procedural regulations created for these lines in the UK. Creating the bank and having such a liberal policy on stem cell research, the UK is not ignoring the ethical and practical application of this new science, rather they have created an government controlled framework for the creation of safe practice methods and regulations to ensure unethical practices will not occur without punishment. The UK has been the most thorough in legislating this vulnerable field. In May, 2004, the first human embryonic stem cell line was donated to the Stem Cell Bank from King's College in London.

Other European Stem Cell Policies

Many European countries, such as Belgium, Ireland, Italy, Luxembourg, and Portugal still have no legislation related to stem cell research. France has no legislation, but is currently devising a policy. The European Union is an institutional framework for a united Europe, created after World War II for economic purposes, so another war among them would be unthinkable. The European Union takes the stance of the majority of their counterparts, which is a restrictive one. The EU is currently trying to create a directive that requires member states to ban the use of tissues or cells from cloned human

embryos, germ cells, or totipotent cells from humans or animals. This would be the most restrictive policy possible while still allowing in-vitro fertilization clinics to aid conception. If the stem cell debate is strong enough to force countries away from the EU, this Directive would have an effect on the economy far greater than the stem cells profit to the markets, throwing off-balance trade within Europe for goods or services not at all related to the field of biotechnology.

The authors of this IQP feel that Sweden and the UK have the correct ideas on the future of stem cell research. Sweden's advice is, "Be prepared for the long haul." ("Sweden's Stem Cell Success", 2001) Control over stem cell research cannot occur if a government is watching the advances from across its borders, or if it is occurring behind the government's back. If advances in embryonic stem cell research occur, the more restrictive countries throughout the world will likely change their policies quickly. Simple research alone will not impress anyone until its applications are proven.

CONCLUSIONS

The potentially extraordinary number of lives which could be saved as a result of human embryo experimentation affirms the need for ES research to progress and to become federally funded. Without federal funding for this area, the United States will pass up the opportunity to pioneer some of the greatest known advancements in the history of medicine. Those who suffer from illnesses which could be potentially cured or treated through the utilization of stem cells are at the mercy of those legislators who have due to their policies greatly prevented work on this vitally important area of science. It is also crucial that Stem Cell research progress with careful consideration to our deepest moral principles. The recent formation of the Human Embryonic Research Board composed of consumers, ethicists, lawyers, and scientists with vast knowledge of all aspects of human and animal stem cell research, will help maintain a balance between our moral beliefs and needed scientific progress.

The issue concerning the use of Parthenotes as a source of ES cells is highly debatable. The author's of this IQP were not in agreement on the issue of the use of parthenotes as a source of ES cells. One of us believes that parthenotes may *someday* have the ability to become a human, even though current technology does not permit this. This potential to become a human grants parthenotes a higher moral status, and one author is against their use as a source of ES cells. However, the remaining two IQP authors feel that because parthenotes do not currently have the ability to become a human, their moral status is lessened, and are in agreement with using them as a convenient source of ES cells. Even if current technology allowed parthenotes to develop

into adults, current legislation prohibits research of parthenotes beyond fourteen days, and we agree with this legislation. We also are in agreement with the current world-wide legislation banning human reproductive cloning.

We agree that adult stem cells should be investigated as potential alternative sources of material whenever possible. Because such cells have no potential for creating an individual person, such cells lack most of the ethical concerns of ES cells. However, adult stem cells are unipotent, or at most multipotent, they are not pleuripotent like ES cells. The limited potentials of adult stem cells still requires the complementation by further ES cell research.

ES cell research provides valuable insight into the development of human beings, and provides hope of better understanding a variety of diseases and human development. The destruction of human embryos at the earliest stages of development for justifiable scientific reasons does not necessarily undermine their moral status. Human cadavers used for medical research for example demonstrate how objects destroyed during scientific experimentation can be treated with respect. Researchers may dissect human cadavers respectfully, in an effort to expand scientific knowledge of the human body. Determining moral status has been compellingly elaborated by philosophy Professor Mary Anne Warren who contends that no one criterion determines an entity's moral status, but that seven different principles need to be considered. In accordance with these principles two philosophy Professors at the Santa Clara University in California, Michael Meyer and Lawrence Nelson, conclude that while an embryo has some moral status and disserves respect, this status is 'weak or modest'. While the truth of the moral status of embryos will continue to be contested and debated, the following passage exemplifies

these principles and speaks of the moral status of an embryo (Human Embryo Experimentation, 2002).

> *"The only intrinsic property that provides a reason to grant [the human embryo] moral status is its being alive. The embryo is neither an agent, a human being capable of sentience but not agency, a nonhuman sentient creature, nor an entity of ecological significance. Nor is an embryo a person, or an early stage of a person, in the typical understandings, both metaphysical and moral, of the muddled term 'person.' One often noted reason it isn't is that an embryo prior to the formation of the 'primitive streak' (which usually appears around fourteen days of development) is not clearly even an individual, as it can still be divided into twins. Personhood is usually taken to imply individuality. Another reason is that, if an embryo is maintained outside a woman's body and those who provide the gametes for it have not decided to permit its development in a womb, it is not effectively a stage in the early development of a person. Put differently, an extracorporeal embryo—whether used in research, discarded, or kept frozen—is simply not a precursor to any ongoing personal narrative. An embryo properly starts on that trajectory only when the gamete sources intentionally have it placed in a womb."*

Therefore we believe ES cell research should be allowed with restrictions in accordance with the principles of sentience. Furthermore, additional Embryonic Stem cell lines should be developed in order to obtain ES cell benefits, even if it involves destroying more human embryos. For the betterment of human kind, destroying a potential human life can be morally justifiable, and is well worth such a grave price, by potentially saving hundreds of thousands of lives at the cost of one single potential life.

Adult stem cell research should be encouraged due to its promise to become an alternative to destroying human embryos. However it is clear that the use of adult stem cells, at least currently, has some major disadvantages to ES cells. These disadvantages have already been discussed, and although adult stem cells have already saved hundreds of thousands of lives in bone marrow transplants, they still show limited capacities for differentiating into the number of tissues that ES cells can. Thus we agree that when a

particular disease in question can be cured using adult stem cells, that method should be used. But those cells may never have the potentials that ES cells do. These disadvantages must first be overcome in order to *fully* utilize their potential. It is possible that adult stem cells may someday become a viable alternative to ES cells, at which point such heavy ethical considerations about using ES cells will become moot. However, until Adult Stem cells do become a reliable alternative to ES cell therapies, cloning for therapeutic purposes should be allowed to continue.

While in the very earliest stages of development, Somatic Cell Nuclear Transfer could provide a reliable resource of engineered animal oocytes for medical research. Although NT technology may solve the problem of histocompatibility, an enormous hurtle faced while transplanting tissues during the treatment of diseases, it is necessary to strictly regulate these procedures to avoid potentially devastating ethical implications. These technologies are not intended to be used for the cloning of a human being; in fact most biotechnology companies and all current legislation claim to be clearly opposed to any efforts to clone a human. "ES and NT technologies…if properly applied, could lead to significant medical advances with life saving potential (Human Embryo Experimentation, 2002)."

President George W. Bush announced in August of 2001 that he would allow federally funded research on ES cell lines only if they had been developed before 9:00 p.m. on August 9, 2001. This legislation was a devastating set back to the scientific community largely because it made it difficult to obtain one of these existing ES cell lines. Bush announced that more than 60 cell lines were available to researchers at that point in 2001. Yet one year later, only sixteen lines were claimed to be available by their

suppliers, and of these even fewer were actually in the hands of those researches independent from the labs which had derived the cells ('Show Us The Cells, 2002). This availability issue, combined with the lack of federal funding, has prevented work on some of our most critical medical problems. George W. Bush and his advisors believe that the destruction of a human embryo even in the earliest stages of development should be considered murder. How can someone be so adamantly opposed to stem cell research and essentially hinder advancement in this fantastic area of medical science? How is it that someone who is in favor of capital punishment, that is the termination of a person's life, also believes that destroying cells in a petri dish in the earliest stages of human development for the advancement of scientific progress, is on the same level as murder? Scientists and concerned citizens alike should become more active in urging Congress to revise this 2001 legislation at once. We have the potential to make one of the greatest impacts on the quality of human life, and yet we are faltering in the heat of political squandering, while our loved ones with Leukemia's and life threatening illnesses needlessly suffer. Let us all do our part in securing a better future for our families and children. It is essential for us to stand together as a nation and support stem cell research now. Let our future provide the means to heal the sick and the suffering. While the decisions we make are not always easy, let us remember that we are making the right decision for the greater good, for those who are sick, for those who we care for, for our children, for generations to come, for a better tomorrow.

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