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STEM CELLS AND SOCIETY

An Interactive Qualifying Project Report

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By:

Divya Panickar

Nirali Parekh

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APPROVED:

Prof. David S. Adams, Ph.D.
WPI Project Advisor

ABSTRACT

Stem cell research has been a controversial topic for a long time with strong effects on society. Misinformation about the subject seriously complicates the issue. Stem cells are undifferentiated or 'blank' cells of a multi-cellular organism that are capable of developing into many different cell types that perform different functions, and thus they show medical potential for treating various diseases. In this project, various types of stem cells are discussed, along with how they have been used to benefit society. Also discussed were their ethical and legal issues.

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PROJECT OBJECTIVES

The intention of this IQP was to investigate the controversial topic of stem cells as an example of the effects of technology on society. Information was provided on the various kinds of stem cells and their applications to help dispel myths about their use and potentials. The effect of this new stem cell technology on society was investigated in four such chapters. The first chapter discussed the various types of stem cells, how they are classified, and their potencies. Chapter-2 describes various examples of how stem cells have been used medically, and their future prospects. Chapter-3 discussed the ethical issues of stem cells, and noted the views of the five major religions on this very controversial topic. Chapter-4 examined the laws that govern these cells in the U.S. and other countries. Finally the authors provided their own conclusions on the use of stem cells.

Chapter-1: Stem Cell Types and Sources

Nirali Parekh

Although stem cells were first discovered in animals decades ago, the contentious topic of stem cells is not very old. Since the journal *Science* declared advances in stem cell research to be the "breakthrough of the year" (Chamany, 2004), the field has continued to expand, catching the interest of businessmen, policy-makers, ethicists, and many more scientists. Stem cells are long lived cells with the ability to form new tissues, and are the basis of the new field of regenerative medicine. But when referring to "stem cells", most people mistake all stem cells to be embryonic stem cells. Actually there are many different types of cells with various levels of potency, so the purpose of this chapter is to introduce the reader to the various stem cell types.

All types of stem cells have three common properties, 1) the capability to renew and divide for an extensive time period, 2) unspecialization, and 3) the ability to give rise to more specialized cells (Stem Cell Basic, 2005). Stem cells are unspecialized, meaning that they do not participate in the functions performed by the cells they give rise to. For example, hematopoietic stem cells do not transport oxygen through the bloodstream, although they give rise to the blood cells that do. When unspecialized stem cells give rise to specialized cells, the process is termed "differentiation". Every cell in the body was initially a stem cell which then developed into a specific functional cell like the heart, kidney, or muscle cells. Unlike many specialized cells, stem cells can replicate themselves numerous times over an individual's entire life span. A symmetric division, where the daughter cells carry the exact chromosome copy of the mother cells, occurs about 10 times in the life of a specialized cell. But when stem cells divide, they retain the ability to generate another unspecialized cell. Thus, stem cells can be considered to be

"immortal". This type of stem cell division is termed asymmetric division, where one of the daughter cells becomes a new stem cell and the other cell becomes specialized (Stem Cells… 2001).

Stem Cell Classification by Potency

Stem cells are usually divided into four main categories that describe the extent to which they can differentiate (**Figure-1**). The first type is *totipotent cells*, which have the ability to give rise any kind of cell, including any cell in the body or extra-embryonic tissue like the placenta. Only newly fertilized zygotes and cells through the 8-cell stage are totipotent. After a few days of fertilization, the totipotent cells start to specialize. The first stage of differentiation occurs as two cell layers are formed in the blastocyst. The inner cell mass of the blastocyst are the *pluripotent cells* (embryonic stem cells), which have the ability to differentiate into almost all kinds of cells in the body that arise from the three primary germ layers, but they cannot form placenta. The pluripotent cells then give rise to *multipotent cells*, which have a more limited range of differentiation. This type of stem cells is limited to forming several types of related cells. An example of a multipotent cell would be a hematopoietic stem cell, which forms all the cellular components of blood. Then there are the *unipotent cells*, which can give rise only to one particular type of cell, and cannot regenerate indefinitely. Unipotent cells develop into their specified and final cell type. An example of this might be a skin stem cell which forms only skin epithelium.

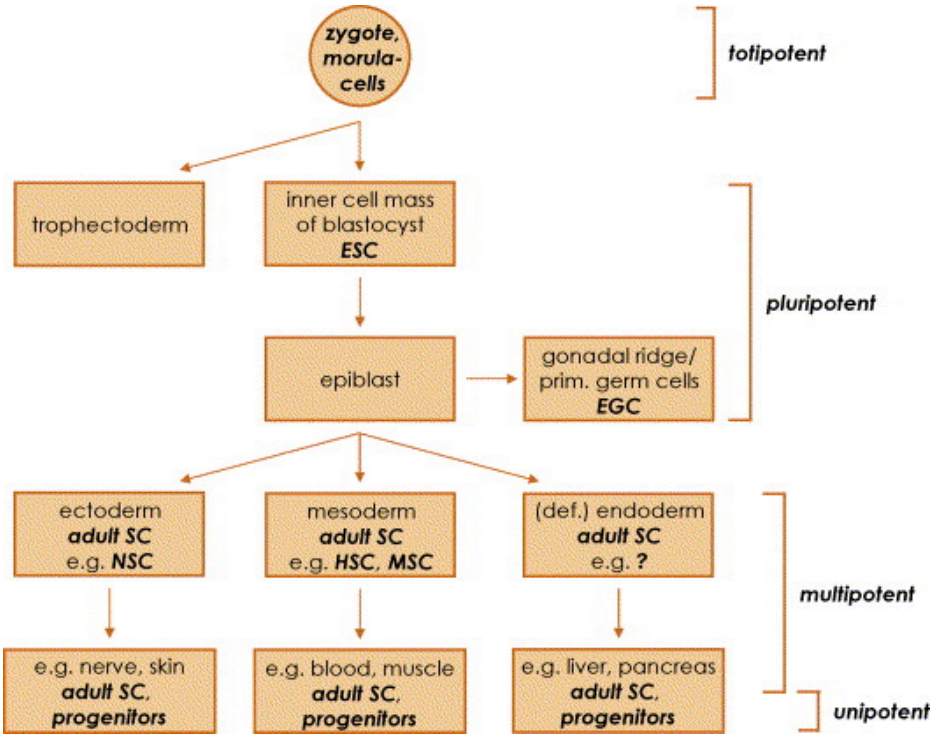

Figure-1: Diagram of Various Stem Cell Potencies. Shown are the various levels of stem cells from totipotent cells to unipotent. (Keller, 2005)

Stem Cell Classification by Source

Another way to classify stem cells is by source. As mentioned above, embryonic stem cells are isolated from the inner cell mass of a blastocyst embryo. These cells are pluripotent, and because they destroy the embryo to obtain them are ethically controversial. However, stem cells are found not only in developing embryos but also in the fetus umbilical cord blood, the placenta, and many adult tissues. By far, adult stem cells (ASCs) are the most widely researched, as some of them (hematopoietic stem cells) have been used for decades to treat various forms of blood cell cancers. Hematopoietic stem cells (HSCs) (Frequently…2004) are

the precursors of all mature red and white blood cells. Other adult stem cell types can be found in the brain, blood, cornea, retina, heart, intestines, and several other areas (Weiss, 2005).

Adult Stem Cells

Adult stem cells are isolated from adult tissues. These cells are rare in the body, so are hard to isolate. They are also more difficult to grow than ES cells. But because they are ethically less controversial, scientists hope to use them to treat diseases whenever possible. **Table-I** shows the various types of adult stem cells, some of which will be discussed below.

Table-I: List of Adult Stem Cells.

Stem Cell	Source	Types of Cells Produced
Hematopoietic	All types of blood cells	Red blood cells, B lymphocytes, T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, macrophages, and platelets
Bone Marrow Stromal (mesenchymal)	Connective tissues	Tendons, osteocytes (bone cells), adipocytes (fat cells), and chondrocytes (cartilage cells)
Neural	Parts of the nervous system	neurons, astrocytes, and oligodendrocytes
Epithelial	Lining of the digestive tract	Absorptive cells, goblet cells, Paneth cells, and Enteroendocrine cells
Epidermal	Basal layer of the epidermis	Keratinocytes (forms the protective layer of the skin)
Follicular	Base of hair follicles	Hair follicles and the epidermis
Hepatic	Liver	Hepatocytes

Source: Stem Cell Basics, 2005.

Research in the field of adult stem cells has given us much insight into what could be done with these cell lines, such as controlling and protecting vital organs from inflammatory and destructive autoimmune reactions (van Laar and Tyndall, 2006), treatment of cancer (Weiss, 2005), and their possible use in the treatment of several other debilitating disorders. The

problem with adult stem cells is they are limited in their usage. They are rare in the body, are hard to identify and isolate, are hard to grow, and are limited in their ability to differentiate.

Hematopoietic Stem Cells

Blood cell replacement through bone marrow transplantation is one of the best characterized applications of stem cells, and has been used to treat blood disorders and blood cancers. Hematopoietic stem cells (HSCs) are traditionally obtained from bone marrow, but are also present in umbilical cord blood, an especially rich source. Cord HSCs have the advantage of being more primitive than bone marrow-derived HSCs, and therefore are less likely to be rejected by the patient. Umbilical cord HSCs have been used for transplantation to reconstitute blood in patients exposed to radiation or chemotherapy. They have also been used to treat some types of genetic diseases, transplantation of umbilical cord blood cells can give patients a new blood forming system that can carry genetically corrected cells (Frequently, 2004). These therapies will be described in more detail in Chapter 2.

Mesenchymal Stem Cells

Another type of stem cell found in bone marrow is the mesenchymal stem cell (MSC). MSCs are multipotent, and can form bone, muscle, fat, and cartilage (Glossary, 2004). MSCs are also involved in repairing bone and cartilage. Once these cells divide, their progeny become committed to one particular function characteristic of a specific tissue (e.g. cartilage) (Caplan, 1991).

Neural Stem Cells

Another type of adult stem cell is the neural stem cell (NSC). These cells can be isolated from adult brain tissue and grown in culture media (Frequently, 2004). Earlier dogma stated that brain and spinal cord were incapable of regenerating, but this dogma has now been overturned. **Figure-2** shows a diagram of the pathway for forming neural stem cells. Multi-potent stem cells form neural progenitor cells that differentiate into committed neural progenitor cells. Then the committed cells differentiate into functional neurons (Gage, 2000). "The term 'neural stem cell' is used loosely to describe cells that (i) can generate neural tissue or are derived from the nervous system, (ii) have some capacity for self-renewal, and (iii) can give rise to cells other than themselves through asymmetric cell division" (Gage, 2000). Adult NSCs were first isolated in 1989 (Temple, 1989), and later research by Clas Johansson showed that new neurons are being continuously generated in specific areas of the adult nervous system, apparently from adult multi-potent stem cells (Johansson et al., 1999). Rats with spinal cord injuries were shown to have increased ependymal cell proliferation. Ependymal cells give rise to cells that proliferate rapidly and that generate neurons. This data lead the researchers to believe that these ependymal cells were in fact neural stem cells, and are involved in the process of repairing central nervous system injuries (Johansson et al., 1999).

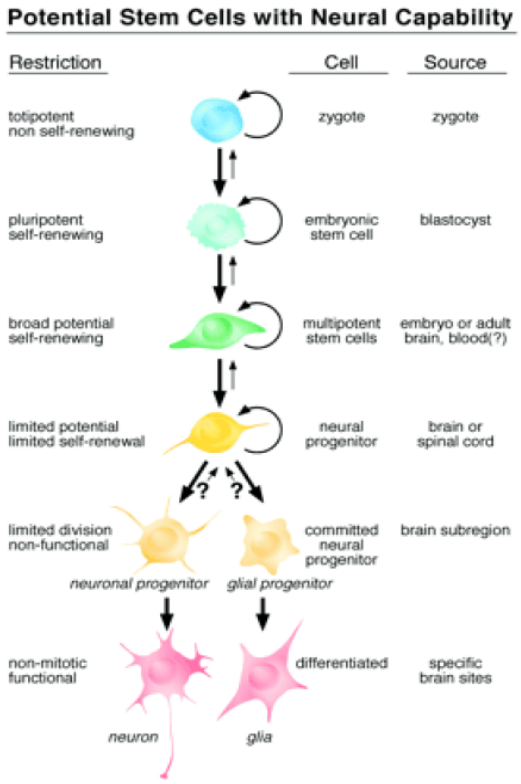

Figure-2: Diagram of Neural Stem Cell Formation and Differentiation. Neural progenitor cells form from multi-potent stem cells. The progenitor cells form committed progenitors that differentiate into neurons (Gage, 2000)

In the adult brain, neurogenesis (the generation of new neurons) occurs in just two regions: 1) the subventricular zone lining the lateral ventricles, and 2) the subgranular zone (Bjorklund and Lindvall, 2000). These findings show that the brain has a latent capacity for self-repair, although it appears to be severely limited (Bjorklund and Lindvall, 2000). NSCs located in the central nervous system are limited in their mobility and accessibility, however they have been found to initiate and perform repairs (Johansson et al, 1999). If scientists can determine how to maintain a cell line of these NSCs, many degenerative brain diseases could be stopped and perhaps reversed.

Renal Stem Cells

Another example of adult stem cells is the renal stem cell (stem cells from the kidney). These cells have the potential for treating a variety of kidney disorders; however, we are still not completely sure if they exist (Watorek and Klinger, 2006). A significant amount of data points to their existence, so they may have uses in treating kidney failure, renal diseases, and cancer of the kidney (Watorek and Klinger, 2006). To determine if renal stem cells could generate the cell types found in the kidney, researchers examined the "differentiation potential of metanephric mesenchymal cells isolated on the first day of kidney development" (Oliver et al., 2002). The cells were examined and found to be "kidney-specific mesenchymal cells" that could indeed differentiate into specific cell lines found in the kidney, suggesting that these stem cells were specific to the kidney organ (Oliver et al, 2002).

Embryonic Stem Cells

ES cells are pluripotent, so they have the ability to become any cell type in the adult body, making ES cells a primary target for medical research. ES cells are easier to isolate and grow to large quantities than adult stem cells. But they are ethically controversial because they are isolated from the inner cell mass of a 5 day old blastocyst, which destroys the embryo during the isolation process.

Human ES cells were first isolated in 1998 at the University of Wisconsin (Thomson et al., 1998). Scientists at the Wisconsin Regional Primate Centre in Madison in November of 1998 isolated human ES cells from excess embryos they had obtained from various *in vitro* fertilization clinics (Weiss, 2005). One year later, scientists at John Hopkins University isolated

their human ES cells from primordial germ cells of aborted foetuses (Shamblott et al., 1999). These scientific teams expected their discoveries would bring applause and admiration, but instead the discovery was overwhelmed with controversy and debate, as it re-ignited old debates about the use of embryos in research that had been raging since the first human IVF procedures were performed in the late 1960's and early 1970's. As will be discussed in Chapter-3, some religious groups argue the destruction of the embryo is murder, so oppose working with embryos. Some went to the extent of terming this new ES cell isolation process as "cannibalism" (Weiss, 2005). However, not all religions are against working with embryos, and as more diseases are being researched for treatment, more people are starting to rethink their earlier ideas about stem cells.

The pluripotent ability of ES cells to develop into almost any type of cell in the body is the primary reason these cells are of great interest to scientists. Scientists hope to be able to learn how to differentiate ES cells *in vitro* into all cell types, including nerve cells, heart muscle, organ tissue, and many other types (**Figure-3**) in the hope of curing a variety of diseases and increasing life expectancy. Some of the advances in this direction will be discussed in Chapter-2.

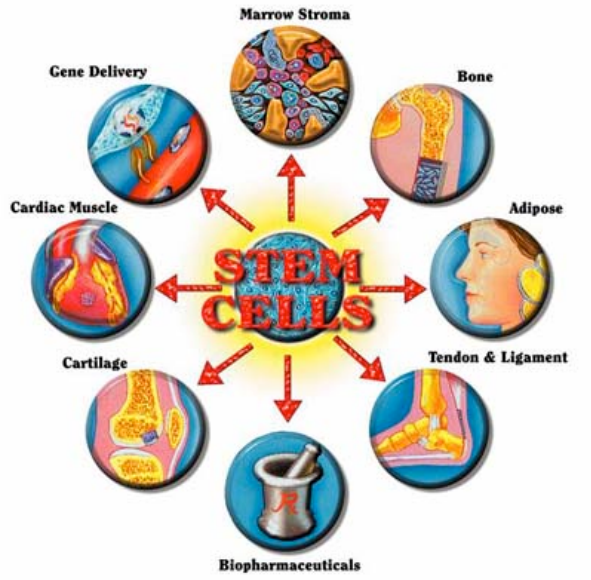

Figure-3: ES Cell Differentiation. Diagram shows the various types of tissues scientists hope to be able to differentiate ES cells into *in vitro*. (Mohit, 2010)

The problem with ES cells is they destroy an embryo to isolate them. In the US, embryos for this use are obtained from reproductive IVF clinics. It is currently not legal in the US to create embryos solely for research purposes, so they must be obtained from excess IVF embryos with donor consent (In Vitro Fertilization, 2006). After the IVF zygote is created, it progresses through several cell divisions until it becomes a blastocyst which takes about five days. The blastocyst consists of an inner cell mass (containing ES cells) and the outer cell mass. Extracting the inner cell mass from the embryo destroys it. Usually during reproductive IVF procedures excess embryos are created. If those embryos are not used by the parents, with their signed consent the embryos can be donated for research purposes (Weiss, 2005).

The isolated inner cell mass cells are plated on a feeder layer to provide a scaffold for growth. Initially, the feeder layer was irradiated mouse fibroblast cells, but to avoid possibly contaminating the ES cell lines with animal products from the animal feeder layer the protocols were adapted to use human cell feeder layers. Once an ES cell line has been established, research can commence.

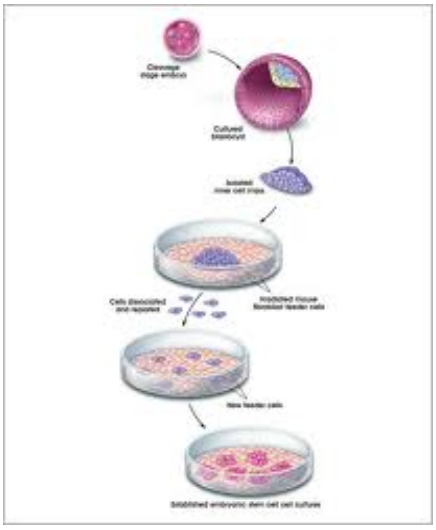

Figure-4: Isolation of ES Cells from Blastocyst Embryos. Diagram illustrates the process of isolating the inner cell mass (blue) from 5-day old blastocysts, and plating them on a feeder layer (yellow) to provide a scaffold for growth. (Winslow and Duckwall, 2001)

Although human ES cells have been differentiated *in vitro* into cells secreting dopamine (for treating Parkinson's disease), insulin (for treating type-I diabetes), or myosin (for creating muscle cells), scientists are still researching ways to differentiate them into all known tissue types.

iPS Cells

Because many people still view sacrificing an embryo to be murder, scientists are constantly seeking ways to create pluripotent stem cells without using embryos. One of the hottest topics in all of stem cell research in the past few years is the induction of pluripotent stem cells directly from skin cells using genetic reprogramming. These cells are termed induced pluripotent stem (iPS) cells. iPS cells were first derived from skin cells from mice (Takahashi and Yamanaka, 2006) and a year later were derived from skin cells in humans (Takahashi et al., 2007). Initially the reprogramming was performed by using a virus to deliver four genes encoding transcription factors for Oct3, Sox2, c-Myc, and Klf4 into the skin cells. The transcription factors bound DNA in the cells to induce a reprogramming to a pluripotent-like state. In some cases the implanted iPS cells causes tumor formation, so later protocols omitted the c-Myc oncogene component, and also eliminated the virus method of delivery. This process does not destroy embryos, so these cells are potential replacements for ES cells, so long as they are truly pluripotent. However, recent experiments indicate iPS cells may contain DNA mutations (Lister et al., 2011), so further research will be required to determine whether iPS cells can be used for therapies.

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CHAPTER-2: STEM CELLS APPLICATIONS

Divya Panickar

For years, doctors and researchers struggled to cure many diseases, but little did they realize that every human is born with, and retains, a special type of cell that might help treat many types of disorders. Because of their ability to divide and to differentiate into a variety of tissues, stem cells represent the medicine of the 21st century. As discussed in Chapter-1, these cells (depending on their type) have the ability to form heart tissue, neurons, skin cells, and various other tissues (**Figure-1**). Adult stem cells are found in our own organs and tissues such as fat, bone marrow, umbilical cord blood, placenta, brain, and olfactory tissue (Hughes, 2005). The purpose of this chapter is to go beyond a discussion of stem cell types to document the various *ways* that stem cells are being used. Such "benefits to society" are important to document prior to our discussion of stem cell ethics.

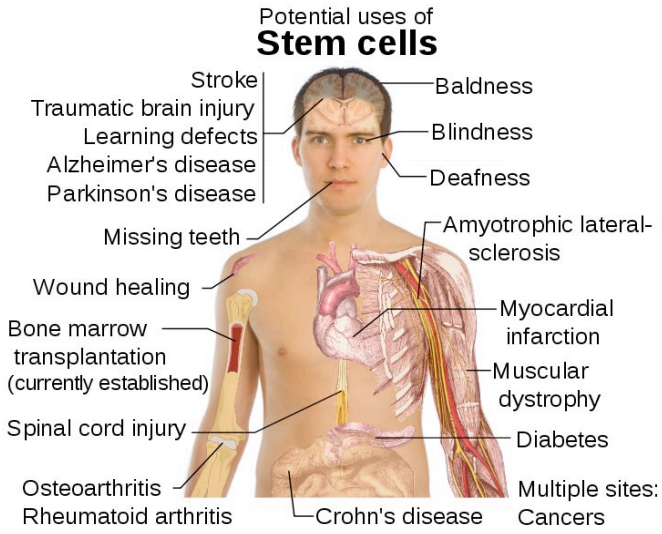


Figure-1: The Potential Uses of Stem Cells. The figure shows the various uses of stem cells for treating diseases affecting different parts of the body. (New Stem Cell Research, 2010)

The potential stem cell applications discussed in this chapter include blood cancers, spinal cord injuries, diabetes, heart attacks, and lung cancer. In each case, an attempt is made to update the reader up on the use of either embryonic stem (ES) cells stem cells or adult stem cells (ASCs) to treat either animal models of a disease or human patients. Adult stem cells are less controversial since they can be isolated from adult tissue samples or from umbilical cord blood, and do not require embryos, but these cells are hard to obtain and hard to grow. So it is important to note whether ACSs can effectively treat a particular disorder, or must ES cells be used. However, ES cell lines are harder to obtain funding for, and may produce tumors upon implant. Data will be provided for induced pluripotent stem (iPS) cells when available, since these cells do not destroy an embryo to obtain them, yet they appear to be pluripotent. In addition to academic labs, many drug companies are also showing strong interest in stem cell technologies. Roche, for example, made a deal with Harvard University and Massachusetts General Hospital to focus on stem cell-based drug screening. Other companies that have made similar deals include Pfizer, GE healthcare, Novocell, GlaxoSmithKline, AstraZeneca and Cellartis (Baker, 2010).

Hematopoietic Stem Cells (HSCs) Applications

Hematopoietic stem cells (HSCs) are multi-potent stem cells that can give rise to all types of blood cells using myeloid and lymphoid lineages (**Figure-2**). The main uses of HSCs are bone marrow transplants (BMT). In a bone marrow transplant, the patient's diseased bone marrow is destroyed by chemotherapy or irradiation, and healthy marrow is infused into the patient's blood stream. HSCs are used to treat leukemia, lymphoma, aplastic anemia,

thalassemia, sickle cell anemia, and autoimmune diseases. Bone marrow transplants have been performed for decades now, saving thousands of lives, making HSCs the best characterized of all types of stem cells (reviewed by Donnall, 2000).

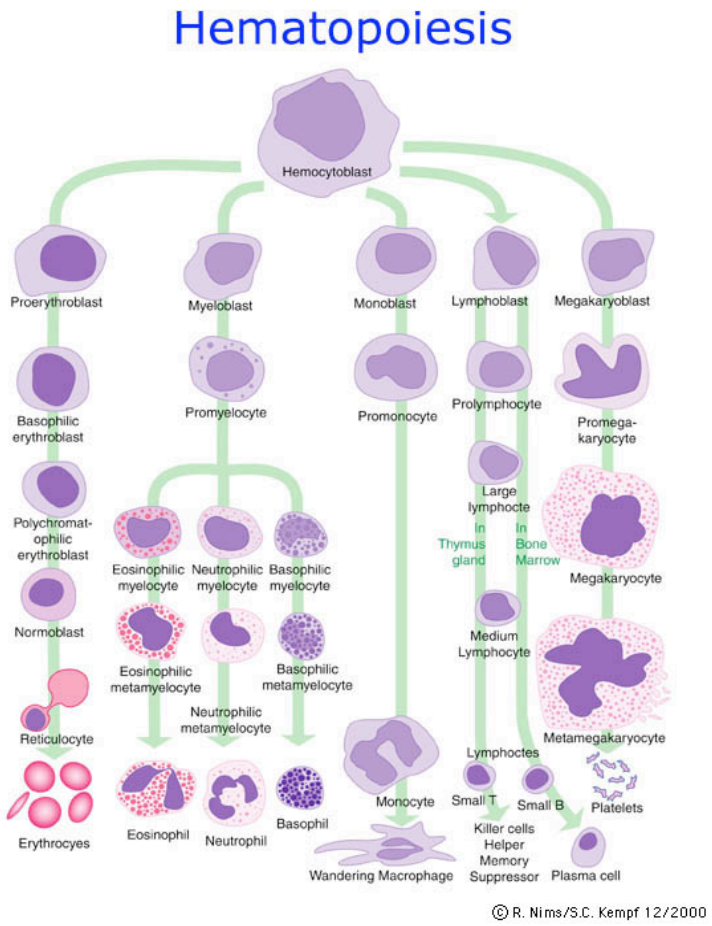


Figure-2: Diagram of Hematopoiesis. Diagram shows the formation of all blood cell types from a hematopoietic stem cell (upper center, cell labeled hemocytoblast). (Histology, 2000)

Leukemic cells are known to be highly sensitive to irradiation. Chemotherapy or irradiation kills the affected cells and also normal cells of the bone marrow. So transplantation of a new healthy marrow is required. Early attempts to treat leukemia in mice by BMT, in 1956 by Barnes, included the treatment of leukemic mice by supra-lethal irradiation, followed by the

infusion of normal mouse marrow. The allogeneic (histo-compatible, although not identical) marrow cells became successfully engrafted.

Traditionally HSCs are obtained under local anesthesia from bone marrow using a syringe. However, more recently scientists obtain HSCs from peripheral blood from individuals treated with hematopoietic growth factors (GM-CSF or G-CSF) to stimulate the release of HSCs into the peripheral blood system. HSCs can also be obtained from cord blood.

BMTs have also been used to treat autoimmune diseases. Total body irradiation followed by an allogeneic stem cell engraftment is the most curative approach; however it includes complications from T-cells similar to those stated for the treatment of leukemia, immune rejection. Some scientists have tried storing a patient's own peripheral blood HSC s for future morrow rescue, then giving a higher dose of immunosuppressive agents to see whether there is an improvement over conventional chemo doses. Others who prefer a more conservative approach give myeloablative and lymphoablative chemotherapies together followed by purified (lymphocyte-free) HSCs. Third, and most likely to be curative, is myeloablative and lymphoablative therapy followed by HSCs from an HLA-identical matched family member with subsequent short methotrexate and cyclosporine treatment to control GVHD (Donnall, 2000).

Another successful application of HSCs is in the transplantation of umbilical-cord blood in babies with infantile Krabbe's disease, a disease with no cure. In some experiments, 100% survival was obtained in the transplantation of umbilical-cord blood from unrelated donors in *asymptomatic* newborns with infantile Krabbe's disease, while only 43% survived in transplantation in babies *after* symptoms had developed (Escolar et al., 2005; NIND, 2011).

Surprisingly, HSCs also find their application in muscle regeneration. This is an application outside the normal ability of HSCs to differentiate, and shows their possible plasticity.

Genetically marked bone marrow transplantation performed in immune-deficient mice has shown that the HSCs migrate to degenerated muscle and differentiate to regenerate the damaged muscle fibers. These marrow-differentiated myogenic progenitors could be used to target affected/degenerated muscles, thus offering an alternative successful treatment of muscular dystrophies (Ferrari et al., 1998).

Another remarkable possibility in the application of HSCs is their use in providing neurons. It was shown that in a strain of mice incapable of developing cells of myeloid and lymphoid lineages, transplanted adult bone marrow cells migrated to the brain and differentiated into cells that expressed neuron-specific antigens. Thus, an alternative source of neurons might be obtained from bone marrow cells differentiated into a neuronal lineage. This would help treat patients with neurodegenerative diseases or central nervous system injury (Mezey et al., 2000).

Spinal Cord Injuries

Spinal cord injuries can be caused by direct damage to the cord itself or by damage to surrounding blood vessels, bones, or tissues which destroy the spinal cord support system. These injuries cause destruction or damage of various cells including neurons. In acute CNS injuries, the axons carrying signals from the brain to the body, and vice versa, do not function properly, which can lead to total paralysis or in other cases a lack of sensation in some parts of the body.

Astrocytes are star shaped glial cells found in the brain and spinal cord that perform a variety of functions in the CNS including repair. Transplantation of rat astrocytes derived from embryonic glial-restricted precursors has shown healthy axon growth and restoration of locomotor function following acute transection injuries of the adult rat spinal cord. The ability of such astrocytes to fill the injury site, suppress gliosis, realign host tissues, and delay expression

of axon-growth-inhibitory proteoglycans, suggests that these cells are unusually effective in providing an environment that supports axon growth for acute CNS injuries (Davies, 2006). In adult rats with motoneuron injuries, embryonic stem (ES) cell-generated spinal motoneurons were transplanted into spinal cords. The cells extended long axons, formed neuromuscular junctions, and induced muscle contraction when co-cultured with myoblasts. It was found that about 3000 of these motor-neurons (25% input) survived for over a month in the spinal cord of each animal. The axonal growth was inhibited by myelin, however this inhibition was overcome by administration of dibutyryl cAMP (dbcAMP) *in vivo* and *in vitro*. These studies are important since they show the potential of creating neural circuits *in vivo* after deriving the cells *in vitro* (Harper et al., 2004).

After these initial rat studies, experiments with human ES cell-derived neurons were performed, although the human cells were transplanted into rats not humans. Human ES cells have been shown to be capable of forming several types of CNS tissue, including neurons, oligo-dendrites, and astrocytes (**Figure-3**). Since spinal cord trauma causes demyelination which contributes to loss of functioning of the axons, a potential therapeutic strategy involves re-myelination of the axons. This requires myelin-forming cells to repair the damaged neurons. Transplantation of human ES cell-derived oligo-dendrite progenitor cells (OPCs) into the spinal cord of adult rat suffering spinal cord injuries has been shown to enhance re-myelination and promote improvement of motor function. Rats that were injected with OPCs 7 days after injury showed enhanced re-myelination and substantially improved locomotor ability, while those injected with OPCs 10 months after injury exhibited no enhanced re-myelination or locomotor recovery. These studies show that in both cases the transplanted cells survived, redistributed over

short distances, and differentiated into oligodendrites, but the transplants are helpful in treating spinal cord injuries only when provided at early stages (Kierstead et al., 2005).

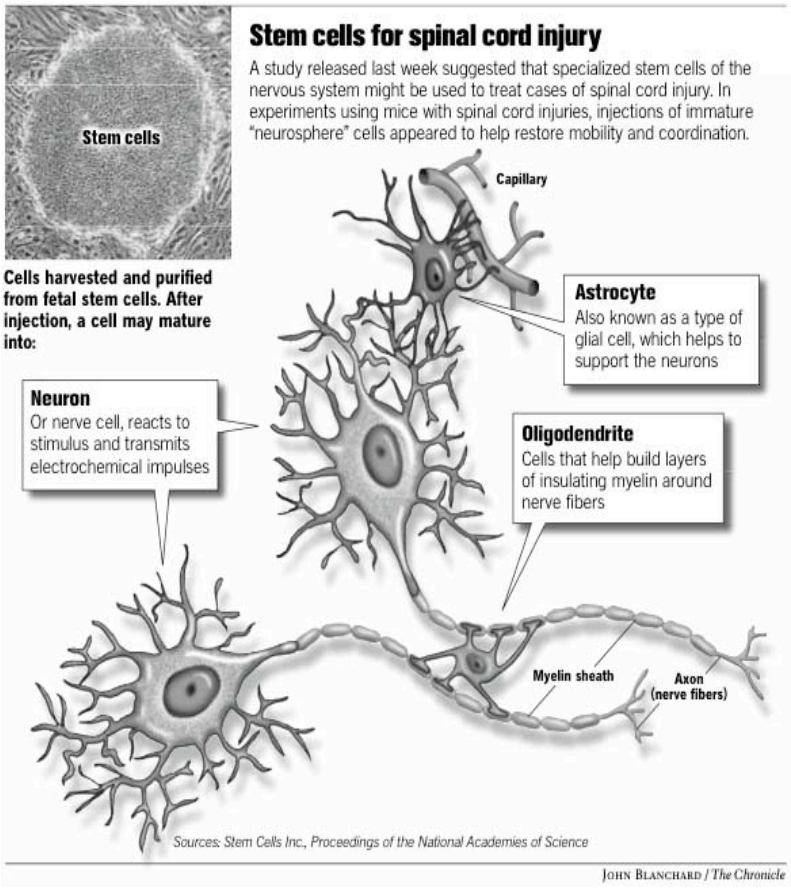


Figure-3: Cell Types Derived from ES Cells to Help Repair Spinal Cord Injuries. Human ES cells have been shown to be capable of forming neurons, oligo-dendrites, and astrocytes *in vitro*. (Hall, 2005)

The world's first human clinical trial of cells derived from human ES cells has been approved and has begun a little more than 10 years after the first human ES cells were isolated at the University of Wisconsin (Thompson et al., 1998). The Food and Drug Administration only recently approved the human stem cell clinical trial for treatment of spinal cord injuries to Geron Pharmaceuticals. The trial is in its first phase with no data yet available. Years of testing will be required before the treatment will be available to more patients. Some scientists have expressed

concern with the safety of these trials, arguing that the animal tests performed previously showed success only in moderately injured animals. Others fear that when ES cells are put into the body, chances are high that they will form unwanted tumors. Even if not malignant, any tumor in the spinal cord could further damage the nerves. Dr. Okarma of Geron however said that they had done numerous studies showing that these differentiated cells did not contain residual ES cells, and did not form tumors in animals even after one year. Geron submitted over 22,000 pages of data to the FDA, perhaps the largest application ever to begin a clinical trial, before gaining permission (New York Times, 2009).

Treatment of Diabetes

Diabetes mellitus, simply known as diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin or the body fails to respond to the insulin produced. Diabetes currently affects about 7% of the world's population, nearly 250 million people worldwide (Goldthwaite, 2006). All forms of diabetes have been treatable (but not curable) since insulin became available. Type-I diabetes is treated with insulin injections, while type 2 diabetes, the more common type, is controlled with diet, exercise, and other medications.

Researchers have been considering cell replacement therapy as a potential strategy to treat type-I diabetes, since patients with this form of the disease have lost all pancreatic β-cells. These cells normally provide insulin for controlling blood sugar levels (**Figure-4**). Cell replacement therapy might also help treat type 2 diabetes since replenishing β-cells would help prevent their insulin deficiency. However, a major challenge in cell replacement therapy is an

insufficient supply of β-cells from human organ donors. Thus, researchers have been exploring stem cells as a possible therapeutic option.

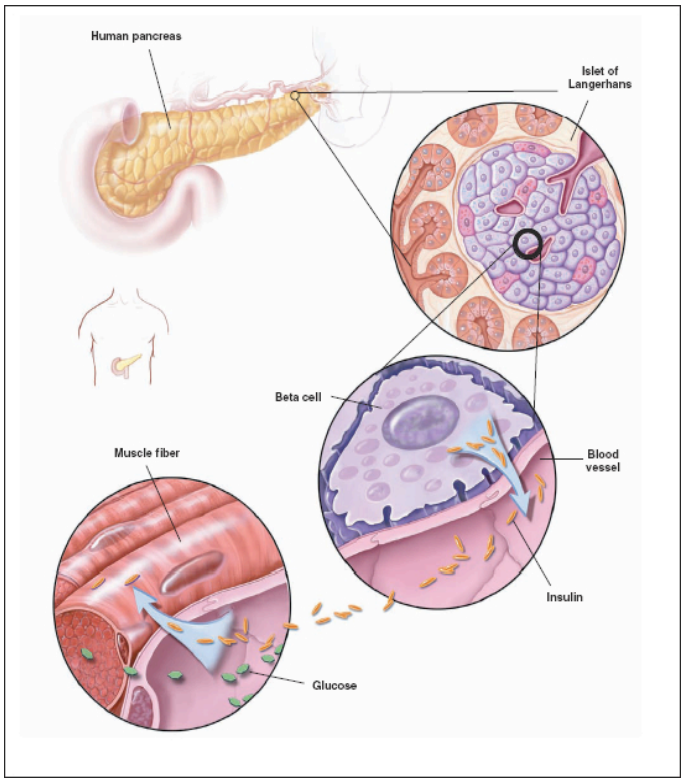


Figure 4: **Diagram of the Human Pancreas**. The pancreas consists of β-cells that produce and release insulin into adjacent blood vessels. Insulin facilitates the uptake of glucose into cells of tissues such as muscles, and is lacking in patients with Type-I diabetes. (Terese et al., 2001)

In cell therapy for type-I diabetes, stem cells capable of differentiating into β-cells in response to molecular signals could be introduced into the body, where they can migrate and differentiate into insulin producing β-cells. Alternatively, stem cells could also be allowed to differentiate into insulin producing β-cells *in vitro*, then could be transplanted into the patient. ES cells have already been shown to be capable of a differentiation process similar to *in vivo* pancreatic organogenesis. In this process, the human ES cells are directed through embryonic

stages resembling endoderm, gut-tube endoderm, pancreatic endoderm and endocrine precursor, which eventually form endocrine cells capable of synthesizing the pancreatic hormones insulin, glucagon, somatostatin, pancreatic polypeptide, and ghrelin. These ES cell-derived insulin-expressing cells release C-peptide (a peptide indicating the synthesis and maturation of true insulin) in response to multiple secretory stimuli. The cells also have an insulin content approaching that of adult islets (D'Amour, 2006).

Another treatment might include bone marrow derived stem cells to regenerate a damaged pancreas. Experiments were performed by transplanting adult bone marrow-derived stem cells (expressing the cell surface marker c-kit) into mice with pancreatic damage. The majority of transplanted cells localized to islet and ductal structures, and their presence caused proliferation of recipient pancreatic cells resulting in the production of insulin. This experiment showed that the transplantation of adult bone marrow-derived cells expressing c-kit reduced hyperglycemia in mice with streptozotocin-induced pancreatic damage (Hess et al., 2003). With respect to the treatment of diabetes with induced pluripotent stem (iPS) cells, a specific combination of three transcription factors [Ngn3 (also known as Nuerog3), Pdx1 and Mafa] was found to reprogram differentiated mouse pancreatic exocrine cells into cells closely resembling β-cells (Zhou et al., 2008). This was a controlled process of adult reprogramming, and the induced β-cells were indistinguishable from endogenous islet cells in size, shape, and ultrastructure. They could secrete insulin and ameliorate hyperglycemia. This type of controlled conversion is essential to avoid cancer formation (Zhou et al., 2008).

In another experiment, a new model of β-cell regeneration was tested combining pancreatic duct ligation (PDL) (to stimulate *in vivo* cell formation) with the elimination of pre-existing β-cells with alloxan (Chung et al., 2010). A large number of β-cells were generated in

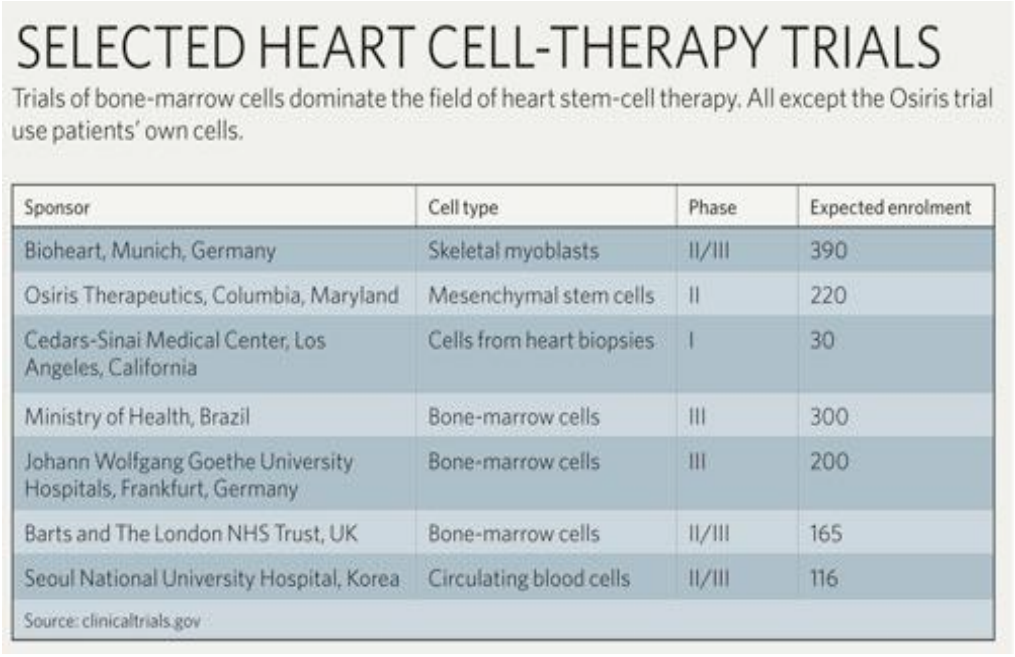
only 2 weeks. The neogenic β-cells appeared to arise primarily from alpha-cells by direct conversion, with or without intervening cell division. Within a week following the approach, an intermediate cell type between β-cells and alpha-cells was observed, and by the end of 2 weeks most of the intermediate cells were observed as mature β-cells, which lacked glucagon (an alpha cell marker) and expressed Mafa (a β-cell marker). Since the conversion is an efficient and rapid process, its application in treating diabetes holds great potential (Chung et al., 2010).

Treatment of Damaged Heart Muscles

When heart muscles are damaged due to a heart attack, bone marrow stem cells travel to the site of damage to help repair and restore the cells. However, for some reason, the molecular signals that recruit these stem cells to the heart are present only for a very short period of time, leaving most of the repair work undone. The partially repaired tissue makes the heart work harder and less efficiently, which can eventually lead to a second heart attack (Stem Cell Therapy, 2009). A cell therapy trial conducted by researchers in Germany and Switzerland involved infusing heart attack survivors with a solution including progenitor cells from their own bone marrow and other patients with a placebo solution. The study results showed that after two years, no patients that received the progenitor cells had suffered a second heart attack, while seven patients that received the placebo solution did. The progenitor cell-treated patients were also less likely to die, need new revascularizations, or be re-hospitalized for heat failure (Science Daily, 2009).

Ischemic cardiomyopathy is a term used to describe patients who have reduced heart pumping capacity due to coronary heart disease. This causes a reduced supply of blood and oxygen to the heart muscles. As the current therapies to treat ischemic cardiomyopathy have

their limitations, researchers have aimed at regenerating and repairing ischemically damaged myocardium though stem-cell therapy, to restore the thickness of the affected myocardium and reduce infarction so that the heart could pump more efficiently. Various clinical trials using skeletal myoblasts and autologous bone-marrow stem cells shows results such as 60% wall thickening across the ischemic myocardium, improved systolic function, improved exercise capacity, improved cardiac function, significant reduction in infarct size, and an increase in stroke volume (Rosenstrauch et al., 2005). The cell therapy approach has initially proven so successful that a variety of clinical trials are ongoing (**Figure-5**).



SELECTED HEART CELL-THERAPY TRIALS

Trials of bone-marrow cells dominate the field of heart stem-cell therapy. All except the Osiris trial use patients' own cells.

Sponsor	Cell type	Phase	Expected enrolment
Bioheart, Munich, Germany	Skeletal myoblasts	II/III	390
Osiris Therapeutics, Columbia, Maryland	Mesenchymal stem cells	II	220
Cedars-Sinai Medical Center, Los Angeles, California	Cells from heart biopsies	I	30
Ministry of Health, Brazil	Bone-marrow cells	III	300
Johann Wolfgang Goethe University Hospitals, Frankfurt, Germany	Bone-marrow cells	III	200
Barts and The London NHS Trust, UK	Bone-marrow cells	II/III	165
Seoul National University Hospital, Korea	Circulating blood cells	II/III	116

Source: clinicaltrials.gov

Figure 5: Cell Therapy Clinical Trials for Heart Disease.
Shown are the trials undertaken by various sponsors, the stem cell types used, and the current phase of the clinical trial (Baker, 2009).

A striking new experiment undertaken by researchers at the John Hopkins Institute for Cell Engineering demonstrated a highly efficient system for the differentiation of human ES cells and human iPS cells to a cardiac lineage to produce functional cardio-myocytes. The system

employed the forced aggregation of contracting human embryoid bodies (hEB) (to provide ES cells). The produced cells contained a high percentage of cardiac troponin I(+) cells that looked morphologically like cardiomyocytes, and uniform electrophysical profiles responsive to cardio-active drugs. The system appears to be cost-effective, and produces unlimited functional myocytes that can be used for cardiac disease modeling (Burridge et al., 2011).

Human umbilical cord stem cells have also been used to treat animal models of heart attacks (**Figure-6**). In an experiment conducted in mice following myocardial infarction, human umbilical cord blood (hUCB) cells were injected intravenously. They migrated to the damaged tissue, not normal myocardium, and engrafted, participated in neo-angiogenesis, and influenced tissue remodeling (Ma et al., 2005).

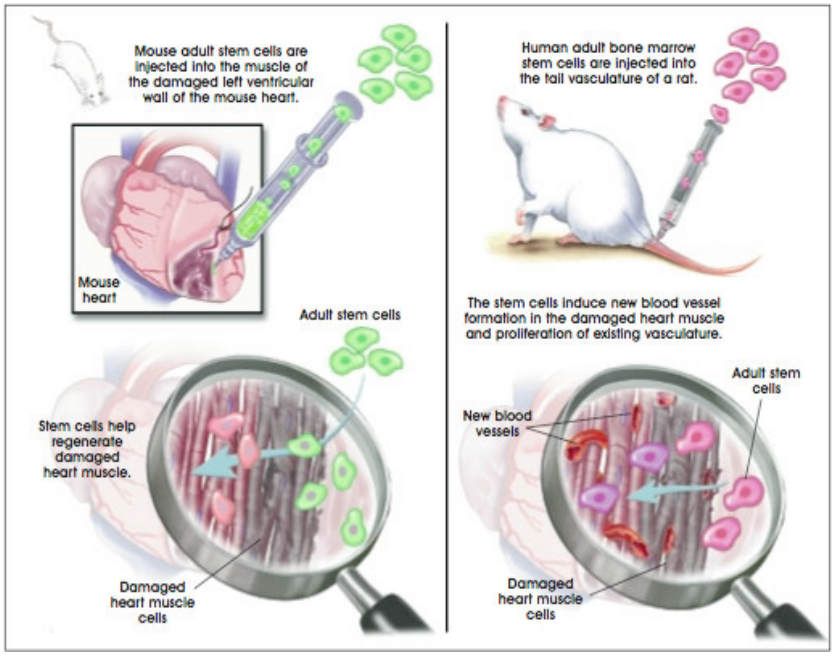


Figure-6: Use of Adult Stem Cells to Treat Heart Attack Damage. When the adult stem cells of a mouse were injected into damaged myocardium, the stem cells regenerate and repair the damaged heart muscle. When human adult bone marrow stem cells were injected into a rat tail, the stem cells induced new blood vessel formation. (Terese et al., 2001)

Lung Cancer

An uncontrolled cell division in the lungs is lung cancer. The two types of lung cancer are small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). SCLC is the more common type, caused mainly by smoking. The current therapies used for SCLC are surgery, radiotherapy, or chemotherapy etc. The main issue with chemotherapy/radiation therapy is much normal tissue is destroyed along with the tumor, which causes patients to experience fatigue and other side effects. So researchers have explored the use of stem cells to treat lung cancer (**Figure-7**).

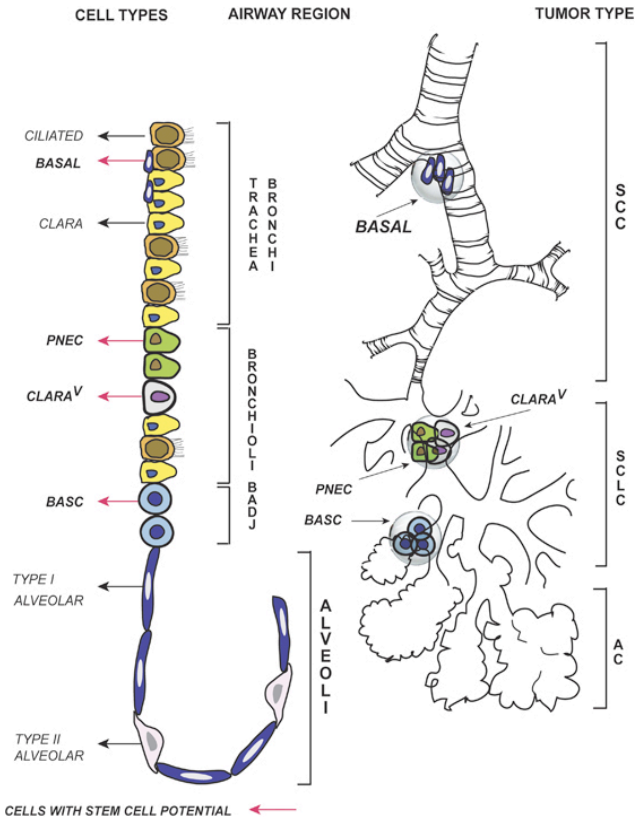


Figure-7: Tumor Formation in the Lung. Schematic representation of the airways and the cell types present in each region of the lung. The red arrows indicate cells types having stem cell potential, also possibly linked to tumor formation. The circles on the right side diagram of the bronchi indicate the locations of different lung cancer forms. Abbreviations are: **AC**-Adenocarcinoma; **SCLC**-Small Cell Lung Cancer; **SCC**-Squamous Cell Carcinoma. (Eramo et al., 2010)

Generally, patients receiving intensive radiotherapy followed by radiotherapy seldom survive. However, the use of stem cell-enriched whole blood during intensive chemotherapy has now been shown to enhance chest radiotherapy in SCLC (Calderoni et al., 2002). In a short 10 weeks treatment, 18 patients were treated with intensive chemotherapy with the support of unprocessed stem cell-enriched whole blood and chest radiotherapy. The results were compared with a previous treatment including six cycles of standard chemotherapy followed by chest radiation. It was clear that the short and intensive radiotherapy regimen in the presence of cell therapy was well tolerated and showed promising survival results (Calderoni et al., 2002).

Better than treating lung cancer would be to prevent it. Scientists have identified lung stem cells in the lung airways that are believed to initiate cancer formation (Pine et al., 2008). These stem cells have pro-tumorigenic characteristics, including a high proliferative capacity, multi-potent differentiation, drug resistance, and long lifespan. If scientists can re-program these stem cells to not form tumors, perhaps lung cancer could be prevented. Stem cell signaling and differentiation pathways are maintained for distinct cancer types, and a destabilization of this machinery might help control tumor formation. However, this application is just a theory (Pine et al., 2008).

Researchers have also used ES cells to treat lung cancer in mice (Science Daily, 2006). Vaccination of mice with ES cells prevented lung cancer when cancer cells were transplanted into them following the stem cell vaccination. However, these studies are in the early stages, and human clinical trials are not underway yet (Science Daily, 2006).

Stem Cells and Food Applications

Stem cells might also be used to create animal tissues that when cultured with the right amounts of proteins can mimic the taste and texture of meat. This could be a revolutionary achievement since artificial meat could offer a green alternative to raising livestock, help alleviate world hunger, and help prevent animal slaughter (Cheng, 2010). According to the analysis by scientists at Oxford University and Amsterdam University, lab-grown meat would reduce greenhouse gases by up to 96% in comparison to raising animals, reduce energy requirements by 7%-45%, and use only 1% of land and 4% of the water associated with conventional meat raising (Harvey, 2011).

Several groups in the U.S., Scandinavia, and Japan have been researching ways to create meat in the laboratory, but the Dutch project may be the most advanced as they have been working on this since 2006, but they have not yet achieved the right texture or taste. So far, they have succeeded in creating 1cm long strips of pork (**Figure-8**).

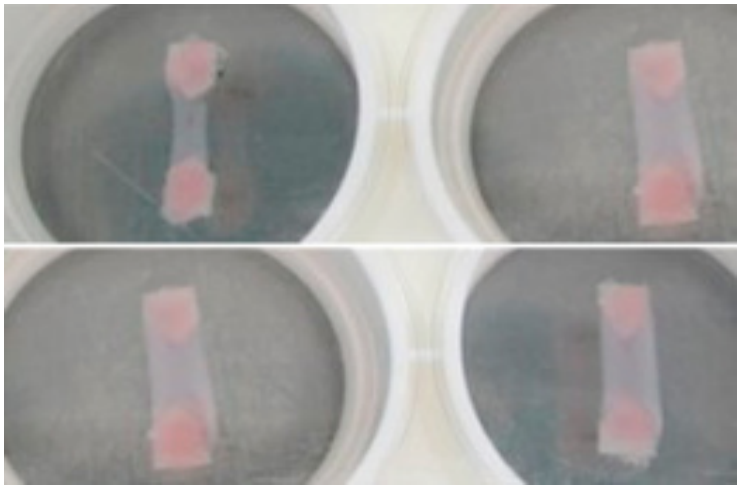


Figure-8: Photograph of Artificial Meat. Shown are strips of pork 1cm long created from pig stem cells. (Cheng, 2010)

To create these strips, a pig's muscle-derived stem cells were isolated and placed in a nutrient culture that helped the cells replicate. It took about 30 days to grow a centimeter long pork strip. The texture of the strips however was soft like scallop, and moist due to lesser protein compared to conventional meat.

On a similar note, fish stem cells could be used to produce healthy omega-3 fatty acids, which could be mixed with the lab-produced pork to create a healthier product, perhaps for use in sausages or hamburgers. The main problem is reproducing the protein content in regular meat: In livestock meat, protein makes up about 99% of the product; the lab meat is only about 80% protein (Cheng, 2010). Creating edible artificial meat is a win-win situation for all, so hopefully this will be successful in the near future.

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CHAPTER-3: STEM CELL ETHICS

Nirali Parekh

Although stem cells carry with them a great power to heal, some types also carry a great deal of ethical roadblocks. Considering the sources of embryonic stem cells, many people feel that certain types of work should be deemed unethical, immoral, or even murder. Not since the *Roe v Wade* Supreme Court decision of 1972 legalizing some types of abortion has there been so hotly debated a topic (*Roe v Wade*, 1972). The purpose of this chapter is to frame the stem cell debate, and to discuss the various religious stances on the topic, as an example of the effects of technology on society.

Framing the Stem Cell Debate

From Chapter-1, we know there are several types of stem cells. Adult stem cells (ASCs) are isolated from an adult tissue and do not destroy embryos to obtain them. Examples include hematopoietic stem cells, neuronal stem cells, stromal stem cells, and epithelial stem cells, etc.). Embryonic stem (ES) cells are usually isolated from a blastocyst, an embryo about 5 days old, the size of the period at the end of this sentence. The blastocyst has the potential to become an adult if implanted into the uterus, so some call its destruction murder.

In September 2005, a Gallup poll of 1,002 adults nationwide (**Table-I**) asked their opinions about the origins of human life, how much this opinion affected their life, and whether their religious and scientific beliefs conflicted (CNN, 2005). It shows that 84% of people believe that God had at least some role in the evolution of humans, and 76% of people have thought about the origins of man at least a moderate amount (CNN, 2005). Though this only illustrates

the idealism of a monotheistic, or the belief in a singular entity in religions like Christianity or Judaism, this poll shows that the United States could be even more divided on whether humans should interfere with the "natural process of life," especially when 66% of the people polled believe that their theological beliefs about creation mean a great deal or moderate amount to them (CNN, 2005). Some religions believe that stem cell usage is murder, and that scientists are playing God (Ayon, 2002). What makes this question even more complicated is that stem cells are not all alike, and the religious views differ on each type. As the poll shows, 35% of people find that their religious and scientific beliefs conflict with each other (CNN, 2005).

"Which of the following statements comes closest to your views on the origin and development of human beings? Human beings have evolved over millions of years from other forms of life and God guides this process. Human beings have evolved over millions of years from other forms of life, but God had no part in this process. OR. God created human beings in their present form exactly the way Bible describes it." Options rotated

	Evolved, God Guided %	Evolved, God Had No Part %	Exactly As Bible Describes %	Other (vol.) %	Unsure %
9/8-11/05	31	12	53	1	3

"How much have you, personally, thought about these different explanations for how human beings came to exist on earth: a great deal, a moderate amount, not much, not at all?"

	A Great Deal %	A Moderate Amount %	Not Much %	Not At All %	Unsure %
9/8-11/05	41	35	17	6	1

"How much does it matter to you which of those theories is correct: a great deal, a moderate amount, not much, not at all?"

	A Great Deal %	A Moderate Amount %	Not Much %	Not At All %	Unsure %
9/8-11/05	40	26	19	14	1

"Which comes closer to your view about the relationship between science and religion? They generally agree with each other. They generally conflict with each other. OR. They are not related to each other in any meaningful way."

	Generally Agree%	Generally Conflict %	Not Related %	Unsure %
9/8-11/05	24	35	36	5

Table-I: CNN/USA Today/Gallup Poll. Sept. 8-11, 2005.
N=1,005 adults nationwide. MoE ± 3 (CNN, 2005)

Almost all religions accept adult stem cells, but some believe that the use of embryonic stem cells is sacrilegious, depending on whether they view life as beginning at conception (thus working with a 5-day embryo is murder) or life begins at day-40 or birth (thus working with a 5-day embryo is not murder). As it can be imagined, religious controversy about stem cells is a major obstacle for the continuation of its research. For this reason stem cell ethics is a worthwhile discussion.

Number of Embryos Destroyed versus Lives Saved

Some individuals may not be aware of the power that is at our disposal with stem cells. One human embryo can produce about forty primary ES cells (Weiss, 2005), and these primary cells can sometimes be grown in ES cell lines to create millions of cells. In addition, *in vitro* fertilization (IVF) clinics usually create excess embryos not used by the parents for reproduction, so there is a debate about what to do with the approximate 400,000 frozen embryos in storage inside IVF clinics (Freking, 2005). Should the excess embryos (with donor consent) be used to try to save lives? Those forty ES cells could be cultured in a medium and under the right conditions can produce millions of healthy cells, and can replicate infinitely. The number of people that can be saved from these cells would be endless (Scientists Match ….2005). So, every embryo has the potential to save many lives through ES cell lines. Why should we throw away many existing lives for the sake of one *potential* life the size of a dot.

Religious Stances on Stem Cells

Hinduism and Buddhism Ethics

Hinduism is a dominant Asian religion that varies significantly in traditions and beliefs. Closely related to Hinduism is Buddhism. A fundamental tenet of Hinduism and Buddhism is the importance of practicing compassion toward others. Medical research, with its aim to help others is, therefore, viewed favourably in these religions, so adult stem cell research is widely accepted (Knowles, 2011). The traditional Hindu belief is that life begins at conception, which is the point when a person is reborn from their previous life, or reincarnated. Some believe that 'ensoulment' or the beginning of personhood takes place between the 3 and 5 month of gestation. However, Swami Tyagananda, a Hindu chaplain at the MIT Religious Activities Center, argues that ES cell research and therapy may be justifiable as it is considered an "extraordinary, unavoidable circumstance," and an act done "for the greater good" (Reichhardt, 2004). While abortion and any other kind of killing of the fetus at any stage are considered murder, abortion is still practiced in some rural parts of India in the Hindu culture because of the cultural preference for boys. So as is typical of many religions, the theoretical may differ from the actual practice.

An additional central tenet of the Hindu religion is the mandate to avoid harming other living things. Life in all its forms is viewed as sacred, and this mandate to avoid harm mediates against ES cell research since the embryo is seen as a living being. While views on the moral status of the human embryo differ, in traditional Hindu belief, conception is the beginning of a soul's rebirth from a previous life. Some Hindu traditions place the beginning of personhood between three and five months of gestation, while few believe that the soul's rebirth can occur as late as the seventh month. Most Buddhists have adopted the classical Hindu teaching that personhood begins at conception (Knowles, 2011).

Buddhism does not believe in a "divine creator, whose plan might be distorted by human tinkering with nature" (Frazzetto, 2004). They follow the teachings of the Buddha Sakyamuni. In Buddhism, ethics is more a matter of personal choice; principles like the one of 'non-harming' should be followed as guidelines" (Schlieter, 2004). Therefore, there are many interpretations of when life begins and what the consequences are to your karma. Karma is believed to be a sum of all of your actions in your current, past, and future lives. Therefore, how you act in one life will affect your reincarnation, or rebirth.

Damien Keown, a well-known expert on Buddhist biomedical issues, explains that "Buddhism teaches that life may come into being in a variety of ways, of which sexual reproduction is but one, so sexual reproduction has no divinely sanctioned priority over other modes of procreation" (Frazzetto, 2004). Buddhist teachings about embryology assume "that the transmigration of consciousness is sudden rather than gradual" (Hughes and Keown, 1995). However, an article by James Hughes, from the MacLean Center for Clinical Medical Ethics and by Damien Keown, of the University of London, explains that there are a variety of views of when Buddhists believe ensoulment occurs:

> "Based on the findings of modern neuro-embryology, Buddhists today might maintain that the fetus does not fully embody all five skandhas and the illusion of personhood until after birth; this is the argument developed by most Western ethicists to defend abortion. If the fetus is not yet a fully embodied person, then the karmic consequences of abortion would be even less than the killing of animals, which Buddhism teaches do have moral status. This neurological interpretation of the skandhas may be more consistent with Western Buddhism, which often sees the doctrine of rebirth as peripheral or interprets rebirth metaphorically rather than literally" (Hughes and Keown, 1995).

Consequently, the actual definition of when life begins is not an exact time. Therefore there are two main interpretations about this in Buddhist teachings. A small segment of Buddhists believes that incarnation or conception "does not occur until as late as the seventh month." Though there

is another larger segment that believes the "transmigration of consciousness occurs at conception, and therefore that all abortion incurs the karmic burden of killing" (Hughes and Keown, 1995). Though abortion occurs later in the development of the fetus (well after a day5 blastocyst), it could be inferred that this segment of the Buddhist would believe that stem cell research would have the name moral effects as abortion because the status of the fetus is the same at any point of its development. Though this might seem a reasonable rationale, it is still not so clear what Buddhism's view on stem cells is. Buddhism "encourages placing a strong value on respecting every living being, which includes fertilized embryos used for research activities" (Frazzetto, 2004).

Christianity Ethics

Christianity is the world's largest religion, and the beliefs vary for different denominations. Some Christians approve of ES cell research under certain conditions, while others believe that it is unethical under any circumstances. The majority of Christians believe that life begins at conception and is sacred from that moment on.

Catholic officials are strictly opposed to the destruction of embryos under any conditions. ES cell research is "immoral, illegal, and unnecessary," as said by the U.S. Roman Catholic Bishops (Religious Views…2001). Catholicism is the only major religion opposed to in vitro fertilization (IVF) methods which are the main sources for ES cells. The IVF clinics often destroy excess embryos not used for reproduction, and these embryos could be used as a source of ES cells. However, the Catholic Church believes that this popular method for allowing infertile couples to have children "breaks the God-given connection between sex and procreation" (Reichhardt, 2004). When speaking about embryonic stem cell research,

Archbishop Francis E. George stated that "history has shown that it is always the dispossessed, those whose lives are easily overlooked, who are subjected to the worst abuses of scientific research," and that the "so-called 'spare' human embryos are particularly vulnerable to this kind of moral blindness because so many people seem to have difficulty identifying with their humanity" (US Bishops, 2006).

Even those Christians that do not believe the embryo is fully human argue that they are still “deserving of respect”. They believe that life begins at fertilization, biologically speaking this is believed to be the beginning of a new human life (Shannon, 2006). Professor Thomas Shannon goes on to explain that “together with this affirmation is the correlative presumption that this is the time of the infusion of the soul. Although there is no official Catholic doctrine on this position, the attitude of the Church is that moral priority should be given to this position” (Shannon, 2006). The Catholic church believes that no matter how insignificant in size it may be, it is still life says Bishop Donald Wuerl, "while (a stem cell) is a tiny speck, it nonetheless contains the elements out of which comes the fully developed human person" (US Bishops, 2006). Pope John Paul’s II address to the diplomatic corps on January 10, 2005 seems to exemplify the Catholic position:

> “Conflicting views have been put forward regarding abortion, assisted procreation, the use of human embryonic stem cells for scientific research, and cloning. The Church's position, supported by reason and science, is clear: the human embryo is a subject identical to the human being which will be born at the term of its development. Consequently whatever violates the integrity and the dignity of the embryo is ethically inadmissible. Similarly, any form of scientific research which treats the embryo merely as a laboratory specimen is unworthy of man.” (Pope, 2005)

The Pope goes on to explain that “scientific research in the field of genetics needs to be encouraged and promoted, but, like every other human activity, it can never be exempt from

moral imperatives; research using *adult* stem cells, moreover, offers the promise of considerable success" (Pope, 2005).

There are a few within the Christian church that support ES cell research, arguing that the embryo represents the *potential* for life but does not yet have the moral status of a born child. This stance argues embryos should not be bought or sold (Farley, 2000), but can be used to save lives. Doctor Ronald Cole-Turner of the Pittsburgh Theological Seminary and a member of the Protestant denomination, the United Church of Christ, explains that the majority of the members believe "that embryos have an important but less status" (Cole-Turner, 2000). The General Synod, the church-wide counselling body which is the voice of the church on particular issues, released a statement that the "human pre-embryo" should be treated with the utmost respect, but that it has only the "*potential* to develop into full human personhood" and thus he supports "human pre-embryo research, including research that produces and studies cloned human pre-embryos through the 14th day of fetal development." Human blastocysts from which ES cells are obtained are usually day-5. The only recommended limitations were that the embryos be treated respectfully, not be implanted, and that there is public discussion of the current and future research (Cole-Turner, 2000). Thus, the Christian faith seems to be divided on their views about embryonic stem cell research, but the majority believes it to be immoral. They only all support the usage of adult stem cells as a community.

Judaism Ethics

A more liberal ethical stand on stem cell research is that of Judaism. A main theological certainty of this faith is that they accept "both natural and artificial means for overcoming illness" and that doctors are both "the agents and partners of God in the ongoing act of healing"

(Dorff, 2000). It is Jewish belief that they "have a duty to God to develop and use any therapies that can aid us in taking care of our bodies, which ultimately belong to God" (Dorff, 2000). The Union of Orthodox Jewish Congregations stated that, "an isolated fertilized egg does not enjoy the full status of personhood" (Religious Views…2001). In fact, some Jews believe that 'ensoulment' is not achieved until the moment of birth. So, while it is wrong to unnecessarily abort a fetus, it cannot be considered murder. However, an abortion is permitted if carrying the child is a threat to the mother's health, or if the fetus is "severely defective" or has a terminal illness (Dorff, 2002). In fact, due to Judaism's emphasis on protecting and healing the body, "an abortion must be performed to save the life or the physical or mental health of the woman, for she is without question a full-fledged human being with all the protections of Jewish law, while the fetus is still only part of the woman's body" (Dorff, 2002).

With respect to the Jewish stance on when life begins, Rabbi Yehiel Ben Ayon confirmed that "Judaism teaches that life begins at birth; hence the possibility to kill life can only begin at the same time as that life begins" (Ayon, 2002). In Judaism, an unborn child is not life but *potential* life. Certainly an unborn child may not be aborted without a valid reason, but to do so is not killing. "It is forbidden, but it is not killing" (Ayon, 2002). Dr. Rabbi Elliot N. Dorff, of the University of Judaism, explains that "Genetic materials outside the uterus have no legal status in Jewish law, for they are not even a part of a human being until implanted in a woman's womb, and even then, during the first 40 days of gestation, their status is 'as if they were simply water'" (Dorff, 2000).

Therefore, Jewish law and religious beliefs allow for embryonic stem cell research. They also believe that the use of adult stems "is always accepted and even welcomed" (Ayon, 2002). Rabbi Yehiel Ben Ayon continues that "Judaism does not see the artificial growth of human cells

on a laboratory dish as a human life" and that "it is routine in medicine today to grow human skin for use in skin grafts. Growing stem cells should then be seen in the same light" (Ayon, 2002). These quotes show that followers of Judaism believe that embryonic and adult stem cell research is moral and should be encouraged, as long as it is done for the common good. And the embryo from which the stem cells are isolated must be aborted legitimately under Jewish law if abortion is the source. They also support the use of excess embryos from IVF procedures, as embryos formed outside of a woman's body have an even lower status than those in the first 40 days of gestation (Dorff, 2002). The subject of creating embryos specifically for research purposes is more difficult. Some feel that this should never be permissible, while others believe that it can be permitted under the condition that the woman only does this once or twice in her life due to the increased risk of developing ovarian cancer from drugs causing hyper-ovulation (Dorff, 2002).

Islamic Ethics

Islamic beliefs are based on textual information, mainly the Qur'an, without a major religious institution to guide the opinions of the followers. There are two schools of thought, the Sunni and the Shi`ite. The Sunni make up the majority of Islamic followers, and interpret the text in a more traditional way than the Shi`ite (Sachedina, 2000). Both sects believe that they have an obligation serve society by using the knowledge that was given by God to help the common good (Frazzetto, 2004).

There are many ideas about when the embryo reaches moral status. A majority of Muslims believe that after the blastocyst stage, the fetus becomes a person; ensoulment occurs 120 days after conception (Frazzetto, 2004). The Shari'ah text goes further to make "a

distinction between *actual* and *potential* life, determining that the former should be afforded more protection than the latter. Under most interpretations, the embryo is therefore not considered to be a person, and using it to create stem cell lines would not violate Islamic law" (Frazzetto, 2004). Hassan Hathout, of the Islamic Organization for Medical Sciences in Kuwait, is quoted by Bill Broadway saying that "Islam opposes creating embryos with the intention of using them for research" (Broadway, 2001). However, Dr. Abdulaziz Sachedina of the University of Virginia explains that "it is correct to suggest that a majority of the Sunni and Shi`ite jurists will have little problem in endorsing ethically-regulated research on stem cells that promise potential therapeutic value, provided that the expected therapeutic benefits are not simply speculative" (Sachedina, 2000). It would be easy to presume that both Islamic sects would support the use of adult stem cells, since no life is destroyed in the process of cultivating them.

There is also Muslim disagreement over who could use the stem cells, as there is a great emphasis "on inter-human and familial relationships" (Frazzetto, 2004). Giovanni Frazzetto explains that "the preservation of the parent−child lineage is of utmost importance to Muslims, as are the spousal relationships that encourage parental love and concern for their children. Dr. Abdulaziz Sachedina explains further that "The Muslim focus of the debate on genetic replication and embryonic manipulation is concerned with moral issues related to the possibility, through these technologies, of creating incidental relationships between a man and a woman without a spiritual and moral connection between them" (Frazzetto, 2004).
Consequently, Islamic law prohibits surrogate parenting and adoption, but would allow "the adoption of human embryos," when excess embryos exist, for research purposes as long as they are used only by the couple who created them (Frazzetto, 2004).

The Islamic method of forming an opinion about controversial matters is *ijtihad,* where a panel of "qualified Islamic scholars" reviews current research, and through careful consideration decides on a position that conforms to Muslim belief (The Islamic Institute, 2001). This panel decided that stem cell research should proceed.

iPS (Induced Pluripotent Stem Cell) Ethics

iPS cells are adult somatic cells (usually skin fibroblast cells) genetically modified by the integration of up to four transcription factors genes (or their proteins) into the adult cell genome (N.B., 2008). Human iPS cells were first induced in 2007 in Yamanaka's lab in Japan (Takahashi et al., 2007). These cells do not involve risk of egg donors, nor does it destroy a human embryo or egg. The exact level of potency of iPS cells is still being investigated, but some scientists argue they may be as potent as embryo-derived ES cells. iPS cells even promise to correct numerous life threatening and disabling conditions. If iPS cell potency is pluripotent (or lower) most religious experts would accept the use of these cells as being similar to working with adult stem cells, as no embryos are destroyed.

But if iPS cells are ever shown to be totipotent, the ethics changes considerably, and many ethicists realize that the issues posed by these cells would be as "thorny" as ever (Lehrman, 2010). According to Francoise Baylis, an expert ethicist on ESC research and iPS cells, "there are some concerns which do not completely solve the ethical issues regarding iPS cells" (Brind'Amour, 2009). In an online article entitled "ES Cells and iPS Cells: A Distinction with a Difference" for the Hastings Center in March of 2008, Baylis said that if iPS cells eventually demonstrate *totipotency*, which is required for the generation of a new human life, they would essentially be human embryos, and this generation would negate any advantage iPS

cells may have over ESCs in terms of the destruction of early human life (Baylis, 2008). As of now, these cells haven't even been able to be manipulated to grow the outer layer of an embryonic cell required for the development of the cell into a human being (Brind'Amour, 2009). Michael Rudnicki, scientific director of the Stem Cell Network, agrees and says the promise of stem cell advances using iPS cells is staggering. He also notes "If iPS cells can be made safe for clinical therapies, it will ultimately make the delivery faster and more economical. But as a scientist I am cautious. So, much is based on future prospects and there is much work that needs to be done in the labs before it becomes a therapeutic reality" (University of Alberta, 2009).

If proven to be totipotent, in fertility clinics, iPS cells could enable prospective parents to choose embryos for desired traits more easily than they can with conventional assisted-reproduction technologies. The possibilities would raise radical questions about the moral status of human cells, said Jan Helge Solbakk, the head of research at the Center for Medical Ethics at the University of Oslo in Norway, and Chair of the society's Ethics and Public Policy Committee.

One major concern regarding iPS cells is privacy; it is impossible to maintain donor privacy if the donor only provides a skin cell to the process. This is because to study the cells or to treat diseases such as Parkinson's, juvenile diabetes or Alzheimer's, it is necessary to know the donor's health history and personal information (Sally Lehrman, 2010). Another similar problem is that the ethical norms of consent and withdrawal may not be feasible. What if someone doesn't want his/her tissues to be used for studies that involve the combination of both human and animal cells? The cells will be growing worldwide, so it won't be possible nor will it be fair for the donor to ask for the cells to be destroyed (Lehrman, 2010). However, other

scientists disagree, reminding us that iPS cell lines would be used to treat the patient that provided the skin cell nucleus, not other patients, as the latter would reject the transplanted cells.

Timothy Caulfield, research director of the Health Law Institute at the University of Alberta in Edmonton has noted "We have to recognize all the complicated issues that iPS research is engaging, and get a sense of how existing laws and policies play out" (Lehrman, 2010).

Chapter-3 Conclusion

The proponents of stem cell research argue that the time for "modern medicine" has arrived. Medical science to date has not cured many types of diseases, but stem cell therapies offer new hope. It is time to look towards regenerative medicine to hopefully get the job done. The opposition would say that medical science is here to save lives not take them.

All five major world religions support the use of adult stem cells, so long as they are used to save lives. Unfortunately these cells are harder to identify, harder to grow, and do not have the pluripotency of ES cells, but the authors of this IQP strongly support the use of adult stem cells whenever possible.

ES cells have been chosen by scientists to treat the bulk of diseases for two main reasons. The first reason is their ability to differentiate into almost any of the approximate 220 types of cells. Adult stem cells can differentiate into only about six types of cells at best. Those six types of cells are limited to neuronal activity and the blood (Weiss, 2005), although more are being discovered all the time. The second reason is that ES cells are much easier to culture and isolate than adult stem cells. Adult stem cells are scarcer in the body and, therefore, harder to identify and isolate.

The scrutiny that scientists have had to endure over this subject is enough to drive anyone insane. It is hard for the author of this report to envision how anyone could stand in front of someone and tell them that you don't think it is ethical to destroy embryos that have been fertilized on a lab bench while forgetting about the millions of existing lives that can be saved? How can someone call scientists murderers for destroying a cell mass barely visible, that has no brain or feeling, while condemning adult patients to death? By shutting down ES cell research, isn't it possible that some administrations are the bigger murderers. Too many times, people have a tendency to think about the present when it should be time to think about the future.

It is comforting to see that people are starting to warm up to the idea of hES cell research. In a recent poll taken in Boston, MA from June 6 to June 12, 2005, sixty-seven percent of the residents polled said they were in favor of using taxpayer money to fund stem cell research. Forty percent said they were strongly in favor (Wallace, 2005). The poll had reached only 405 residents of the Hub, but this is at least an indication that the people of this country are slowly being educated on this subject. It wouldn't be too surprising to find out that those who protest this subject know very little about the details involved with stem cell research, especially adult stem cell research.

It is not just Boston who has started to learn about stem cells. Wisconsin senator Scott Fitzgerald tried to push for a ban in Wisconsin and at the University of Wisconsin-Madison on stem cell research, but was denied on both accounts (Still, 2005). There is even a recent push in the House of Representatives for federal funding of stem cell research; one vote in May 2005, was 238 to 194 in favor of federal funding for stem cell research. When such bills reached former President Bush's desk, they were vetoed, but not with President Obama.

The author of this chapter believes it is acceptable to work with either ES cells or adult stem cells, although adult stem cells should be favoured for a particular disease if shown to be equally effective. With respect to embryo sources, the author believes excess IVF embryos created for reproductive purposes should be used first, and if those become exhausted paid donors may be used. We must do everything in our power now to prepare for the future. Who knows how many of us may soon develop a fatal disease.

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CHAPTER-4: STEM CELL LEGALITIES

Divya Panickar

However beneficial stem cell research may be, people cannot make use of this technology without setting rules and regulations to prevent misuse. Stem cell laws are tied in to embryo laws, and vary greatly from country to country. In making these laws, legislators must take into account where the stem cells are collected from, who funds the research, and what the definition of a human being is (Stem Cell Laws, 2005). So a particular country's laws on stem cells often reflect political and religious issues within that country. In this chapter, we discuss stem cell laws in specific countries and in the different states of the US.

Stem Cell Laws and Funding in Different Countries

Different countries have different policies mandating the level of stem cell and embryo research work that can be performed (**Figure-1**). Some countries permit almost all kinds of stem cell research, including human embryonic stem (ES) cell research, others are flexible about the extent of research work permitted (depending on the sources of funding and embryos), others completely restrict human embryonic stem cell research, and other countries completely lack any stem cell policies.

Countries that permit ES cell research or therapeutic cloning (dark brown in the figure) include Australia, Belgium, China, India, Israel, Japan, Singapore, South Korea, Sweden, and the United Kingdom. These countries represent more than 2.7 billion people. Countries that do not permit therapeutic cloning but allow research on excess embryos no longer needed for reproduction (light brown in the figure) include Brazil, Canada, France, Iran, South Africa,

Spain, The Netherlands, Taiwan, the USA, and others. Countries that outright prohibit human embryo research and permit limited research on only imported stem cell lines (yellow in the diagram) include Austria, Germany, Ireland, Italy, Norway and Poland (Hoffman, 2005).

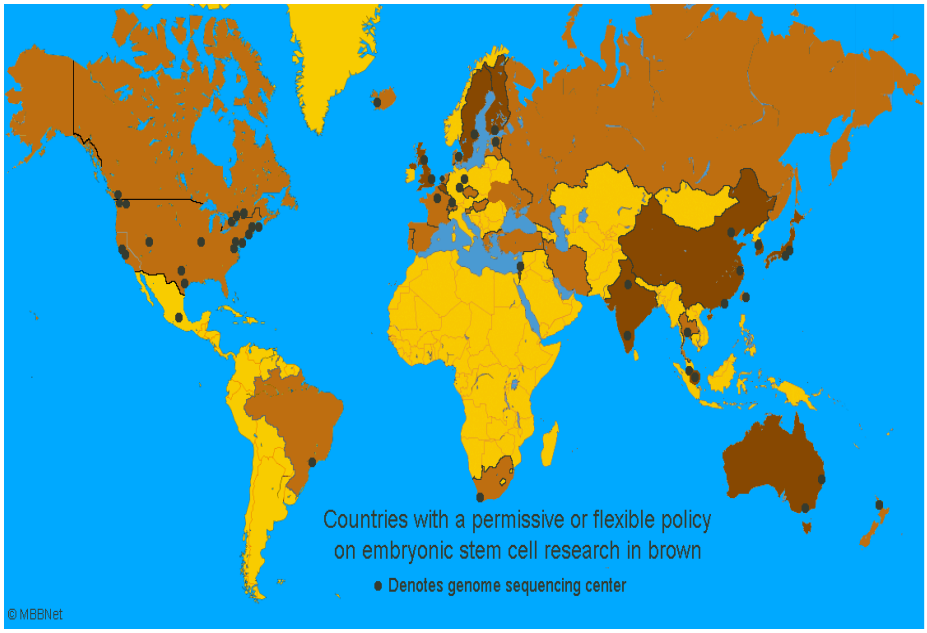

Figure-1: World Stem Cell Map. Map denotes the various countries relative to their stem cell policies. Color code: ■-Permissive ■-Flexible ■-Restrictive. Countries allowing human embryonic stem cell research represent 3.8 billion people. (Hoffman, 2005)

Some of the legislations are influenced by religious or ethical values in the respective countries. Many opponents, including some religious leaders, believe that stem cell research raises the same moral issues as abortion, declaring that life begins at conception, so destroying a 5-day embryo is murder. Some laws have been amended to allow experiments on special types of induced pluripotent (iPS) cells since researchers in Wisconsin and Tokyo announced that they had transformed ordinary human skin cells into those that appeared to have the same properties as embryonic stem cells (Vestal, 2008).

In Canada, stem cell research was restricted to adult stem cells until recently when new legislation permitting a small amount of human ES cell research was passed (Ebbin, 2007). Various Canadian institutes, including the government and health charities, fund the research but the largest source of funding is the Canadian Institute of Health Research (Ebbin, 2007).

Great Britain is the leader in ES cell research and has been for years because of their effective regulation, which appears to instill trust between scientists and the public. In the 1980s, Parliament organized a committee to address ethical concerns and research limitations. From that committee came the formation of the Human Fertilization and Embryology Authority in 1990. This organization controlled what scientists and doctors did with research and therapeutic applications, and instilled public confidence that the embryos and research are put to use for the better of mankind and not being misused in the wrong hands (Berroth, 2009). In Britain, the promise of societal good has always won out over ethical discomfort when it comes to embryo research. A few countries like Spain and Japan are developing their own stem cell banks, but Britain has taken the lead and its bank is likely to become a prototype, if not a resource, for the world. To support stem cell technologies, the British government spent $ 4.7 million to create the stem cell bank that would store all the embryonic stem cell lines in Britain and would be monitored by a British ethics panel (Rosenthal, 2004).

Israel was able to become a leader in ES research because they had the ability to tackle ethical, political, and regulatory issues early on. Israeli stem cell research is strictly regulated with requirements for publishing and peer-reviewing. Scientist and researchers must go before a committee to state an intent in research to gain permission for further study. They are also not permitted to pay for a woman's eggs or use research to clone a human being. Israel allocates public and private funds for stem cell research regulated by Israeli law (Berroth, 2009).

The Swiss Parliament is considering the possibility of allowing research on stem cells derived from stored excess embryos remaining at the end of assisted reproduction procedures if they were frozen at seven or fewer days of development. This legislation is notable because the Swiss Constitution strictly prohibits research using human embryos and even sets controls over the number of eggs that may be fertilized and developed outside a woman's body during fertility treatments. If the Swiss legislation passes, the thousands of frozen embryos of the nation would become available to researchers (Garfinkle, 2004).

China is the 'land of opportunity for stem cell research'. This is mainly due to its relaxed government laws regulating stem cell research. Since the Chinese culture has few religious or moral objections to the use of embryonic stem cells, the government has no qualms with funding this research for academic, educational, or therapeutic purposes. Although China may offer low barriers to stem cell research, it may come at the cost of risks of protecting intellectual property (IP). Enforcement of IP protection laws is still weak in China compared to Western countries. These laws are also unclear since Chinese biotech companies are partially supported by government-owned universities and research centers. Incidents of plagiarism and falsified results in Chinese researchers' work have been known to occur recently. Until China seriously addresses such issues, it will continue to sacrifice its competitive edge in the field of stem cell research (Barnes, 2006).

Japan pioneered the creation of induced pluripotent stem (iPS) cell technology. This was done at Kyoto University in Japan (Takahashi et al., 2006; 2007). Japan is now ramping up patent efforts to keep this iPS lead since the United States might be the first to commercialize this technology. On the same day that Kyoto University's Shinya Yamanka reported his human iPS cells, James Thomson's team at the University of Wisconsin-Madison separately published

similar results. In Japan and Europe, the patent is awarded to the researchers who file first, while in the US the patent goes to the group that can show it invented the technology first. Even though many researchers around the world give Yamanaka' 2006 work on iPS cells in mice the credit for being the starting point of the whole field, the race for the patent still continues (Cyranoski, 2008). Japan's guidelines, set in 2001 for stem cell research have done great damage to related research fields in Japan. The guidelines allowed Japanese scientists to derive new human ES cell lines, and research both homegrown and imported cell lines, but only after the specific research was approved. The big issue was the approval. Proposed projects had to be approved twice: first by a local institutional review board and then by a science-ministry committee. This resulted in only a quarter of the projects getting approval. Many Japanese researchers believe that although Yamanaka created iPS cell technology, the US stole the lead in iPS cell research since they did not have guidelines like in Japan that hindered further research. However, the Japanese government has been slowly trying to change the restrictions. New regulations were recommended by the Council for Science and Technology Policy, chaired by the prime minister. The latest guidelines remove the secondary approval step for working with ES cells. Now, only a local review committee must approve the work. But it might be too late to make a difference since most of the Japanese researchers have been pushed into iPS research through targeted funding programs and are unlikely to return to ES cell basics (Cyranoski, 2009).

Germany along with Austria, Poland, Slovakia, Lithuania, Luxembourg, and Malta are against the notion that the European Union (EU) should provide money for projects in some countries when the same research is prohibited in other member states. However, European Research Commissioner Janez Potocnik said that research funding should not rely on the ethical standards of either the most restrictive or the most liberal countries since it would be against the

principles of the EU. Laws on stem cell research vary largely across Europe with Germany enforcing a near total ban while the UK encourages it. A 2006 survey also showed that 59% of Europeans approved of the research, provided there was government oversight on the projects (Deutsche, 2006). International and European stem cell networks such as EuroStemCell and ESTOOLS had tried to convince the German parliament of the high potential of stem cell research and the impact of legislations in facilitating such research. By adopting four submitted proposals to amend the 'Act ensuring the protection of embryos in connection with the importation and utilization of human embryonic stem cells' with 346 out of 580 votes, the Bundestag (lower house of parliament) changed the future of German stem cell research. The general ban on creating and working on human embryonic stem cell lines was upheld, however Germany will still be able to import cell lines harvested prior to a cut-off date. The cutoff date was moved to 1st May 2007 from 1st January 2002. The Bundestag have also amended the scope of the Stem Cell act, which refers to the utilization of human embryonic stem cells in Germany and the work of German scientists abroad as not constituting a criminal offence (Herman et al., 2008).

USA- The Leading Publisher of Articles on Stem Cell Research

The US is currently by far the leader in stem cell research. The US publishes about 3.5 times as many stem cell articles as its nearest competitor Japan (**Figure-2**). But many US scientists fear that it is slowly slipping behind countries like the UK, Korea, Singapore, Sweden, Israel, Australia and China, due to the political changes in its policies under the past several administrations.

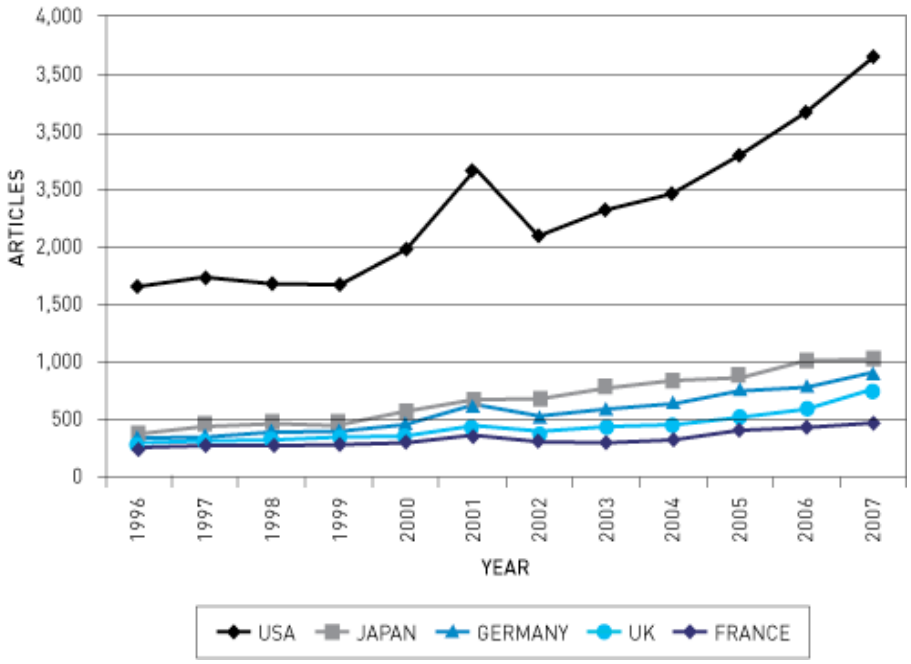

Figure-2: Top Five Ranking Countries in Stem Cell Research Based on the Number of Research Articles Published. The graph shows the number of research articles published by five countries over a period of 12 years. According to the graph, France is ranked 5th, UK 4th, Germany 3rd, Japan 2nd and the USA 1st based on the number of research articles published (Couffignal-Szymzcak, 2009).

US Historical Embryo Policies

Historically in the US, the stem cell policies have reflected which administration is in power (**Figure-3**). In 1973, the US government refused to fund ES cell research after abortion was legalized (Roe v Wade, 1972); this step was taken to discourage women from having abortions for research purposes. In 1993, when Bill Clinton became President, he formed the NIH Embryo Research Panel who recommended allowing some types of research on embryos created by IVF, but in 1995 the US Congress enacted the *Dickey-Wicker Amendment* that banned all embryo research (Robertson, 2010). In spite of a 2000 NIH Guideline recommendation to allow some forms of embryo research, in 2001 President George Bush continued the Dickey-

Wicker Amendment and banned all embryo research, although he allowed federal funding on ES cell lines established before 2001.

In 2005, Congress passed the *Stem Cell Research Enhancement Act*, allowing the federal funding of new ES cell lines, but it was vetoed by Bush. In that same year, the National Academy of Sciences also published their *Guidelines for Human Embryonic Stem Cell Research* (amended in 2007, 2008, and 2010), which was ignored by Bush. In 2007, Congress passed the *Stem Cell Research Enhancement Act*, but it was again vetoed by Bush (Robertson, 2010).

Figure-3: Stem Cell Research Timeline in the US. The figure shows a timeline of the progress of embryonic stem cell research in the US. Shown are when Bush announced the ban in 2001 and when Obama lifted it in 2009 (Genetics, 2009)

The ban on federal funding for ES cell research under Bush and the Dickey-Wicker Amendment drove most US embryonic stem cell research and IVF research into the private sector (Wertz, 2002). In a Washington Post-ABC News poll conducted in January, 59% adults were in support of relaxing the restrictions on federal funding for ES cell research, and even 40% of Republicans supported reversing the ban. In 2007, private funding in the US exceeded funding from the federal government (Ebbin, 2007).

Current US Embryo Policies

On March 9, 2009, President Obama lifted the eight-year-old ban, allowing federal funding for some types of embryonic stem cells, so long as scientists work with the approximately 61 ES cell lines already existing in the US. This means private fertility clinics and research centers are now eligible to receive billions of dollars of federal funding (Wilson, 2009). President Obama issued a presidential memorandum aimed at insulating the scientific decisions across the federal government from political influence. He also made it clear that human cloning would still not be permitted. Obama argued that the US has been falling behind in stem cell research because of the ban, and now that the ban has been partially lifted, he hopes that the US will play a leading role in exploring stem cell research frontier (Scadden, 2009). To some in Congress, it remains unclear whether Obama actually overturned the earlier Dickey-Wicker amendment that banned embryo research, so this issue has occasionally come into view.

Obama's policy was based on guidelines set by the National Institutes of Health (NIH) on embryonic stem cell research. The new guidelines explain which cell lines can be used in federally funded experiments. Some researchers were unhappy that the NIH did not recommend

allowing embryos for research purposes outside IVF clinics, allow somatic cell nuclear transfer (cloning), and allow parthenogenesis (from an unfertilized egg) (Holden, 2009).

Legislations in the Different US States

Especially important in the decade in which federal funding was banned for deriving new ES cell lines, individual states approved bonds to fund their own stem cell institutes. Seven big states are leading the world in political and financial support for ES cell research (**Figure-4**). They aim to get the best scientists from all over the world and become the hub for a multi-billion-dollar bioscience project.

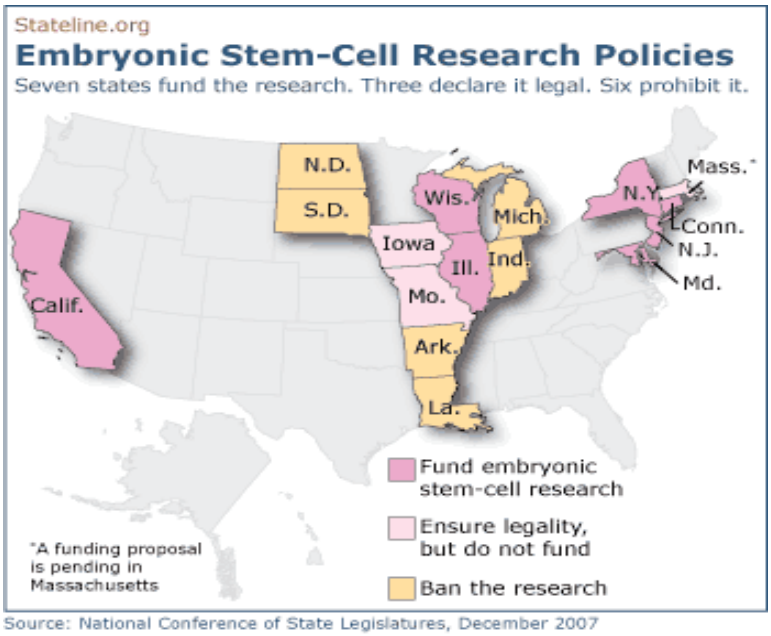

Figure-4: 2009 Policies in Various US States on ES Cell Funding. The figure explains which states in the US fund stem cell research, which ensure legality but don't fund research, and which ban research (Vestal, 2009).

In the past two years alone, California, Connecticut, Illinois, Maryland, New Jersey, New York and Wisconsin have awarded $230 million in grants. California is the bellwether with a $3 billion fund of taxpayer dollars being spent so far for research purposes (**Figure-5**). When all seven states' investments are totaled, a sum of nearly $5 billion over the next 10 years is obtained. Massachusetts has voted to add another $1 billion. Two other states, Iowa and Missouri, do not fund the research but have affirmed the legality of the research hoping to encourage scientists to work within their borders. Some states like Arkansas, Indiana, Louisiana, Michigan, North Dakota, and South Dakota have voted to ban embryonic stem cell research, and Arizona bars state funding for embryonic studies (Vestal, 2008).

State Support of Embryonic Stem Cell Research

State	Amount
California	$3 billion
Connecticut	$100 million
Illinois	$15 million
Maryland	$15 million
Massachusetts	To be Determined
New Jersey	$10 million
New York	$600 million
Texas	$41 million +
Virginia	To be Determined
Wisconsin	$375 million

Figure-5: 2008 ES Cell Research Funding by Different US States. The figure shows the amount of money funding ES cell research in 2008 different states. Such funding shows how the laws in specific states can over-ride the lack of federal funding in that state (Katz and Walker, 2008).

In 2004, New Jersey became the first state in the US to support stem cell research, allocating $10 million to be distributed over 10 years to university, non-profit and commercial labs in the states. Lawmakers have since allowed another $15 million for grants, and $9.5 million to cover administrative costs of the program. California voters quickly followed the path of New Jersey in 2004 by approving a 10-year $3 billion funding program. This program became embroiled in legal proceedings over patent issues, but after the funding stalled, former Gov. Schwarzenegger gave the program a state loan of $150 million in 2006. However, the state almost ran out of money in 2009 because the state's fiscal crisis and problems in the financial markets prevented it from issuing bonds. Connecticut Gov. Rell signed a measure in 2005 to provide $100 million in state funding over 10 years for embryonic stem cell research. Illinois Gov. Blagojevich directed their public health department in 2005 to grant $10 million from existing public health funds to stem cell projects over 10 years, and added $5 million more to the fund after 2006 after Bush vetoed a bill seeking to open up federal funding for the science. In 2007, Maryland Gov. Ehrlich also signed a measure in 2006 appropriating $15 million in general funds. The following year, first–term Gov. Malley appropriated another $23 million to be distributed in 2008. New York Gov. Spitzer signed a budget measure in 2007 that set aside $600 million for stem cell research over 11 years. Wisconsin Gov. Doyle created a $750 million investment fund, including public and private money to build a research facility where embryonic stem cell studies would be conducted.

With respect to Massachusetts, in 2005, the state legislature passed an act enhancing regenerative medicine in the commonwealth (An Act, 2005), but it was vetoed by then governor Mitt Romney. On May 15, 2007, Governor Deval Patrick announced his one billion dollar plan

to fund life sciences including stem cell research in the state (Estes, 2007), which was signed in 2008 (Life Science Bill Signing, 2008).

Some states do not fund ES cell research but do not specifically ban it. Michigan voters in 2008 approved a constitutional amendment making all forms of embryonic studies approved by the federal government legal in the state. Iowa Gov. Culver signed a bill in 2007 repealing a 2002 ban on the studies, and ensured the legality of all forms of stem cell research approved by the federal government (Vestal, 2009).

With respect to other forms of research, federal funding of research involving *cloning* for the purpose of reproduction or research is strictly prohibited. The Food and Drug Administration has claimed authority over the regulation of human cloning technology as an investigational new drug (IND) and stated that at this time, they would not approve any projects involving human cloning for safety reasons (Johnson, 2005), and in 2009 Obama banned human cloning.

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PROJECT CONCLUSIONS

Based on the research performed in this project, the authors now make their own conclusions on the topic of stem cells. The author of Chapters 1 and 3 believes that it is acceptable to work with ES cell lines, since stem cell therapies offer new hope to treat previously incurable diseases. The author of Chapters 2 and 4 also believes that ES cell lines should be used, since it is high time people accepted this new promising technology. Both authors also strongly support the use of adult stem cells whenever possible, as there are lesser controversies surrounding their use. However adult stem cells are harder to identify, isolate, and grow. The author of Chapters 1 and 3 also has a hard time questioning the destruction of a 5-day old embryo fertilized on a lab bench when millions of existing lives could be saved. The author of Chapters 2 and 4 believes that the embryo that is being destroyed for research purposes does not go through any pain and suffering since it doesn't have a developed brain or nervous system. However, the destruction of embryos should be used only until a better source of producing pluripotent cells has been developed, such as iPS cells. Both authors think iPS and ASCs should be used in countries where religious and ethical views have caused a ban in using ES cell lines for research. Both the authors, however, slightly differ in their opinion regarding having paid donors as the source of embryos. The author of Chapters 1 and 3 believes that excess IVF embryos created for reproductive purposes should be used first and if those become exhausted, paid donors may be used. The author of Chapters 2 and 4, on the other hand, believes that donors should not be paid, embryo donation should be allowed but purely on a voluntary basis, mainly to discourage frequent egg donations which may harm the woman. Many people might misuse donor money in third world countries to force women to donate eggs or to get an abortion to

make money. Both authors are in favor of using excess IVF embryos originally created for reproductive purposes for research with donor consent. Countries like the UK, USA, China, India, Israel, Sweden and Japan are countries that have strong government regulated stem cell policies to prevent embryo misuse, while allowing scientists some freedom to perform research. Finally, both the authors conclude that all types of stem cell experiments should be permitted, other than cloning.