HUMAN STEM CELLS

AN ETHICAL OVERVIEW

CONTENTS

PART I

WHAT ARE STEM CELLS AND WHAT DO THEY DO?

What are stem cells?

Stem cells are "blank" cells found in human beings that are capable of developing into the many different kinds of cells you find in the human body. The human body contains stem cells because all human beings start out as only one cell, a **zygote**, which is a fertilized egg. The zygote grows into a human **embryo** by dividing first from one cell into two, then from two cells into four, and so on. In the first few divisions in the human embryo each cell contains the ability to make all the cells in the human body.

As the cells of the human embryo continue to divide, the cells begin to specialize. The new cells are no longer completely "blank" because they begin to take on the functioning of a particular tissue or organ, such as the lungs or the nervous tissue. The process in which the cell function becomes specialized is called **differentiation**. After a cell has differentiated, it cannot develop or change into a different kind of cell.

Stem cells are cells that have not yet differentiated, and they have two unique properties: 1) stem cells can divide and multiply themselves in the undifferentiated state for long periods of time, perhaps indefinitely,[1] and 2) stem cells can differentiate into different types of specialized cells.[2]

How are stem cells able to multiply themselves indefinitely? Most cells in the human body cannot self-renew or divide themselves indefinitely. The cells have a certain number of divisions determined by a person's **DNA**. After a cell has divided its specified number of times it could not divide further without the cells containing error or breaking down. For example, the human skeleton grows until adult height is reached. At that point the skeletal cells no longer divide and the skeleton remains the same size for the rest of a person's life, and if a bone were to be removed from the skeleton it would not grow back. Stem cells are unique in that they do not have a programmed break down in their cellular DNA and can therefore continue to multiply themselves for a very long time, if not forever.

In the laboratory, scientists use the stem cells' ability to divide repeatedly without error to multiply them over and over again into **stem cell lines**. Stem cell lines consist of cells that have been copied from one original stem cell. One stem cell can produce hundreds of genetically identical stem cell lines.

Stem cells are also different from other cells in the human body because they can differentiate into two or more kinds of specialized cells. Inside the developing human embryo and the embryo's environment are triggers that prompt the stem cells to begin the differentiation process. Similarly, stem cells found in the adult human body can also be triggered to produce specialized cells. Scientists working with stem cells in the laboratory attempt to imitate the signals and triggers that cause stem cells to differentiate. They experiment by putting them into a **medium** containing different nutrients and chemicals.

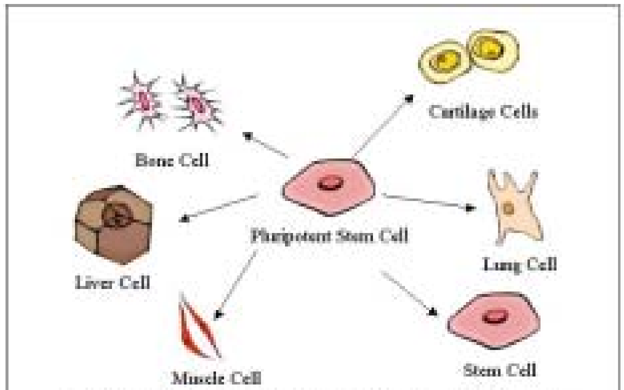
These are the properties that make stem cells unique – the fact that they can divide thousands of times without error and without breaking down, and that they can differentiate into a variety of different kinds of cells. Scientists anticipate using stem cells to expand the available knowledge on human biology and develop new and innovative medical therapies.

Different types of stem cells

Not all stem cells are the same. There are ranges in a stem cell's ability to differentiate into a variety of specialized cells. Some stem cells can differentiate into a greater variety of cells than others. There are four types of stem cells, and they are categorized by their range of flexibility. The categories are totipotent stem cells, pluripotent stem cells, multipotent stem cells, and progenitor stem cells.

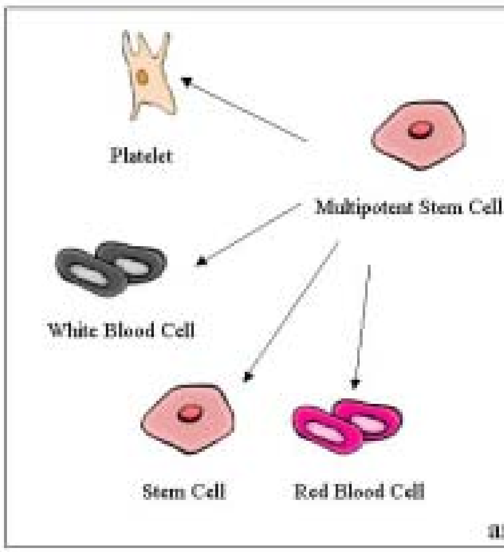
Totipotent stem cells can differentiate into the widest variety of cells. They are considered the "master" cells of the body because they contain all the genetic information needed to create all the cells in the human body in addition to the **placenta**, which nourishes the human embryo in the womb. Human cells are only totipotent during the first few divisions of a fertilized egg. After three to four divisions of the totipotent cells, the cells start to specialize.[3] At this point, the cells become pluripotent.

Pluripotent stem cells can give rise to all the different cell types in the human body but do not contain the genetic information to make a placenta. These stem cells are primarily found in the human embryo during its earliest stages. Pluripotent stem cells are typically what people are referring to when they generically refer to stem cell research.



Pluripotent stem cells can give rise to all of the different cells found in the human body

Multipotent stem cells are cells that can divide and grow into several differentiated cell types within a specific type of tissue or organ. For example, a multipotent skin stem cell could divide and grow into a hair follicle cell or a sweat gland cell; however, it would not be able to grow into a nerve cell or heart cell or any other kind of cell. A multipotent skin stem cell could only divide and grow into the different types of cells found in the skin tissue. These multipotent stem cells can be found in many places in the adult human body, including the skin and bone marrow.



Multipotent stem cells can give rise to the various cells found in a particular tissue or organ.

Pictured here is a multipotent stem cell found in the bone marrow which makes the different cells found in the blood and lymphatic system.

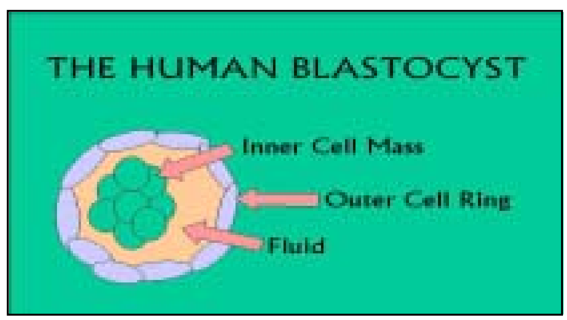
Progenitor cells are the least flexible stem cells. They are also called precursor or pre-specialized cells, and are more differentiated than multipotent stem cells. They are found in adult human beings and are best described as immature cells that have been pre-written to specialize into specific types of cells existing in human adult tissues and organs. While they have not yet differentiated and therefore share that property with other types of stem cells, their ability to differentiate is limited to only a few specific cell types.[4]

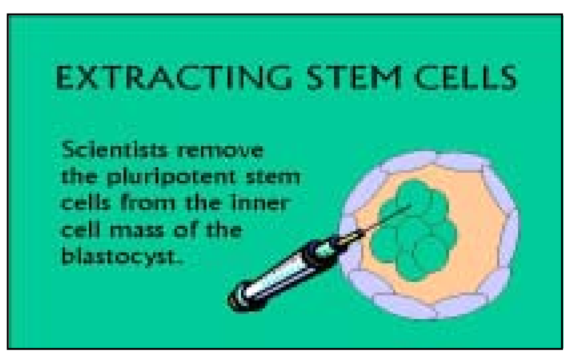
<u>Different sources of stem cells</u>

Different types of stem cells are derived or isolated from different places. Pluripotent stem cells are derived and isolated when researchers first identify the stem cells within the human embryo, and then extract them. Multipotent stem cells found in adults are isolated by using tools that identify cell surface markers and functional markers that allows discrimination between stem cells and the other cells in the tissue, or by placing a cluster of cells into a medium that specifically supports stem cells. These processes are then followed by placing the pluripotent or multipotent stem cells into different cultures that will either stimulate growth of the stem cell lines or cause the stem cells to differentiate. The different types of stem cells are embryonic stem (ES) cells found in human embryos, embryonic germ (EG) cells isolated from an aborted **fetus**, and adult stem cells found in different organs and tissues in the human body.

Embryonic stem (ES) cells are pluripotent stem cells derived from the inner cell mass of a **blastocyst-stage embryo**. A blastocyst-stage embryo is a human embryo that has not been implanted into a uterus about five days after being fertilized ***in vitro*** (*in vitro* means "in an artificial environment").[5]

A blastocyst has two parts. The first part is the **trophoblast**, or **outer cell ring**. The outer cell ring is shaped like a hollow ball and is made up of the specialized cells that would eventually form a placenta if the

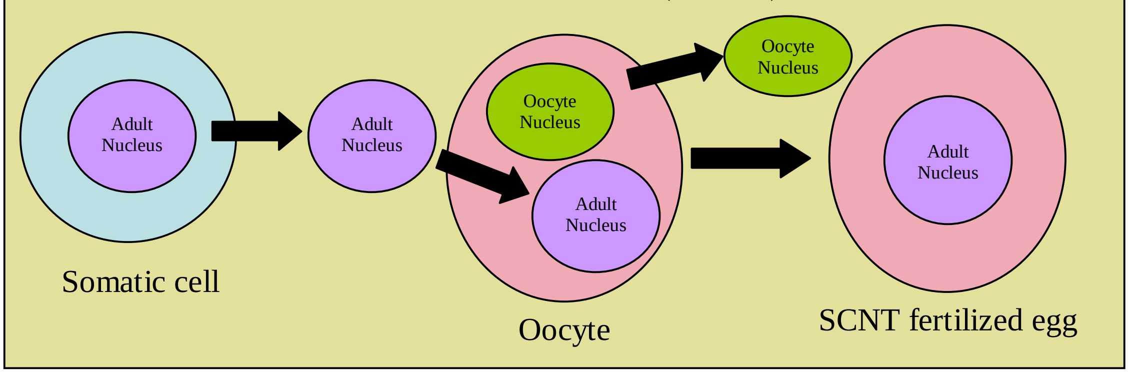




embryo were implanted. Inside the outer cell ring is a mass of about 30 cells referred to as the **inner cell mass**. The inner cell mass is made up of pluripotent stem cells and these stem cells can be extracted and isolated by researchers, which was first done in 1998 at the University of Wisconsin.[6] While many researchers believe the potential and flexibility of ES cells makes them especially valuable for research purposes, it is important to note that extracting the ES cells destroys the embryo.

ES cells can come from embryos created via ***in vitro* fertilization (IVF)** procedures, but they could also come from embryos created with the **somatic cell nuclear transfer (SCNT)** procedure, otherwise called **therapeutic cloning**. The SCNT procedure consists of first removing the nucleus, containing the genetic information, or DNA, of an adult, from a **somatic cell** (any cell found in the human body that is not an egg or sperm cell). Then the somatic cell's nucleus is inserted into an **enucleated oocyte**. Enucleated oocytes are the cells in the female body that develop into eggs from which the nucleus has been removed.[7, 8] This is the same procedure used in reproductive cloning.

Somatic Cell Nuclear Transfer (SCNT) Procedure



Theoretically, after the SNCT procedure, the fertilized egg could then be grown *in vitro* to the blastocyst stage and the stem cells from the inner cell mass could be extracted, just as is done for embryonic stem (ES) cell research with embryos from *in vitro* fertilization procedures. This has not yet been accomplished with human cells and no human embryo has as yet been produced using this procedure.

In the SCNT procedure, the derived stem cells would be genetically identical to the cells of the adult who donated the somatic cell.[9] This fact would make these stem cells particularly valuable for medical therapies, because the organs and tissues can be cultivated from stem cells that are genetically identical to a person who requires an organ or tissue transplant. The problems of transplant rejection could be greatly reduced, or even eliminated, thus increasing chances for recovery.

Embryonic germ (EG) cells come from an aborted human embryo/fetus. These cells would have developed into the reproductive cells (egg and sperm) of the human body. The EG cells are typically extracted from a five- to nine-week old aborted embryo or fetus and placed in a medium to produce EG stem cell lines just as is done in ES cell procedures. The first derivation of stem cells isolated from aborted human embryos/fetuses occurred in 1998 at Johns Hopkins University.[10] Researchers are finding these cells have more potential to differentiate into a wide variety of cells than they originally believed.

Adult stem cells are pluripotent, multipotent, and progenitor stem cells found among the differentiated cells of a particular tissue or organ in the human body.[11] Adult stem cells found in the body are used to replace and repair the tissue or organ in which they are found. For example, the stem cells of the **hematopoietic** (blood and lymph) system are multipotent stem cells found in the bone marrow that make red blood cells, blood clotting cells, and white blood cells.

Scientists have been conducting research with adult stem cells for over 40 years.[12] However, until very recently, researchers believed that adult stem cells were only multipotent. Research by Catherine Verfaillie and colleagues at the University of Minnesota's Stem Cell Institute recently found that some adult stem cells, from the bone marrow and other tissues, have pluripotent stem cell properties and can be manipulated into making cells for other tissues and organs in the body, not merely the cells from the tissues or organs where the stem cell originated.[13]

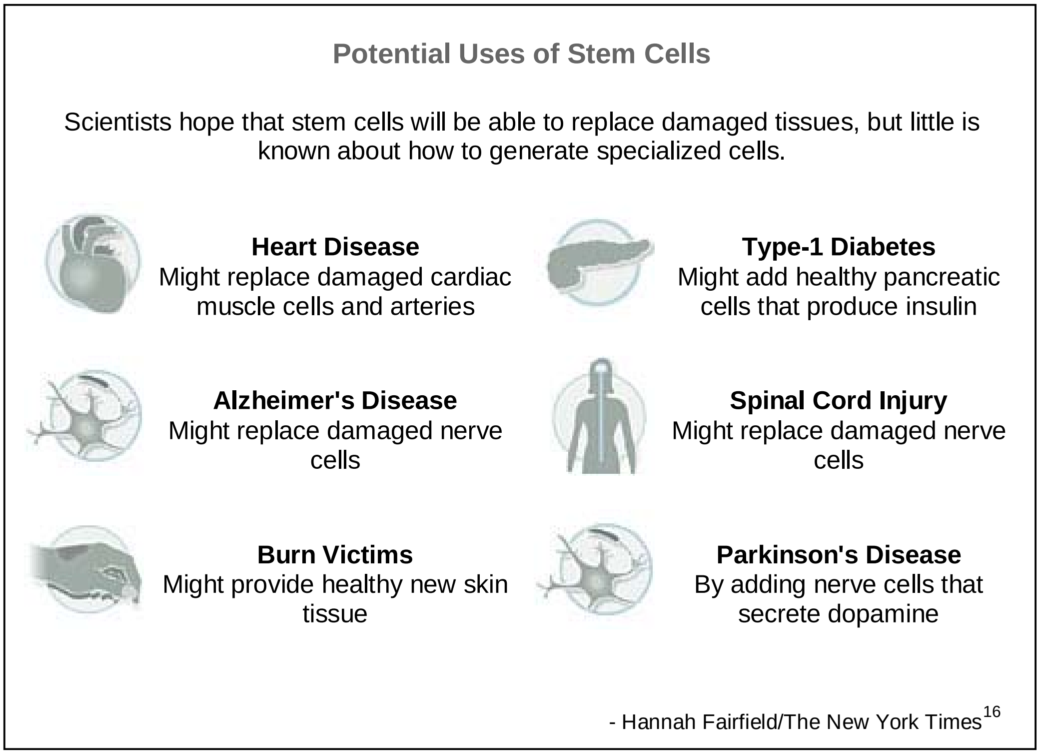
Preliminary findings and research possibilities

Why is everyone so excited about stem cells? The enthusiasm comes from the possible therapeutic uses of stem cells. The basic properties of stem cells (they can divide many, many times and differentiate into different types of cells) leads researchers to hope stem cells can eventually be manipulated and used in the laboratory and clinical medicine. Scientists believe pluripotent stem cells could primarily be used either to develop and test pharmaceuticals or for a variety of medical therapies.[14, 15] Scientists working with multipotent stem cells are interested in potential medical therapies as well as therapies where stem cells are actually used for what they are – stem cells – in the adult human body.

Pluripotent and multipotent stem cells could find use in medical therapies by a process of **grafting** healthy cells into a human body. Grafting is achieved by growing stem cell lines in order to produce healthy cells that can replace damaged ones, particularly if cells lose their function or die. Grafting could also take cells grown from stem cells and insert them into a tissue or organ where they could co-exist or repair an injury without removing the damaged cells. People with diabetes, spinal cord injuries, or heart disease, to name a few, might one day benefit from therapies of this nature.

Another treatment possibility is to use stem cells in **gene therapy**. Stem cells could find use as **vectors** (a tool used to deliver genetic information between cells) where they serve as the agents used to transfer genetic material from one cell to another. For example, hematopoietic stem cells could theoretically be genetically altered to make them resistant to HIV and AIDS and then inserted into a person who has HIV or AIDS. The genetically altered cells may take on the function of healthy cells thereby helping the person with HIV or AIDS fight off infection and illness.

Multipotent stem cells from adults can be used as what they are in medical therapies. For example, persons who have diseases of the bone marrow could be injected with healthy hematopoietic stem cells that produce healthy blood cells, replacing the function of their own non-functioning bone marrow. These stem cells could come from healthy adult donors or the umbilical cord blood of a related sibling, for example. Currently, hematopoietic stem cells (or at least preparations of cells containing hematopoietic stem cells), skin stem cells, and corneal stem cells are used clinically for medical therapies of this nature.



Focusing on human embryonic stem (ES) cells

Current discussion usually focuses on the ethical issues surrounding embryonic stem (ES) cell research as opposed to ethical research issues with the other sources of stem cells – embryonic germ (EG) cells and adult stem cells. ES cell research is usually at the center of the stem cell research debate for several reasons.

First, research with ES cells was recently excluded from federal funding unless the ES cells were isolated from an approved blastocyst prior to August 9, 2001. This has placed limits on research by curtailing available federal funding and specifying which stem cell lines are eligible for use in federally funded research. Therefore the public policy issues surrounding federal funding for ES cell research are very timely.

As opposed to the ethical issues associated with ES cell research, the policy debate surrounding the ethical issues for embryonic germ (EG) cell research is not being addressed at the moment. EG cells can already legally be used in federally funded research projects and therefore this topic is frequently left off the agenda. According to the National Institutes of Health Revitalization Act of 1993, "The Secretary [of Health and Human Services] may conduct or support research on the transplantation of human fetal tissue for therapeutic purposes."[17] There are a number of restrictions on research involving an aborted fetus or embryo, but EG cell research is, in fact, included under this act.

Research with adult stem cells is considered less ethically problematic than research with ES and EG stem cells. The ethical issues surrounding adult stem cell research is considered similar to conducting research with other bodily tissues found in the adult human body. However, there are ethical issues, such as informed consent, that arise from time to time. Even considering ethical issues of informed consent, adult stem cell research is typically considered ethically sound research and finds itself on the policy agenda most frequently as an ethical alternative to conducting research with ES cells.

ES cells from embryos created via SCNT procedures raise ethical issues that are unique to the fact that these cells are cloned, such as whether the procedure may "open the door" to the use of cloning for reproductive purposes. It also raises issues about creating embryos for research purposes only, but this ethical issue is also included in the debate around ES cell research with embryos left over from IVF procedures. If one looks beyond the method of production, the basic ethical issues surrounding the derivation of stem cells from an SCNT embryo are similar to the ethical issues of deriving stem cells from IVF embryos, assuming SCNT procedures can actually give rise to human embryos, a point which is still unresolved.

PART II

ETHICAL ISSUES IN HUMAN EMBRYONIC STEM CELL RESEARCH

The status of the human embryo

One of the most heated ethical issues surrounding embryonic stem (ES) cell research is independent of the research goals or outcome possibilities. This ethical issue involves the status of the human embryo. The discussion about the status of the embryo has been in the forefront for many years in the United States. The debate becomes more impassioned during legal proceedings regarding abortion and political campaigns. Since the ethical issue regarding the status of the embryo has never been resolved, it continues to be contentious and rises to the surface whenever people discuss stem cell research.

In general, people adopt one of four stances towards using human embryos for research, and ES cell research in particular.[18] The stances vary along a range from *embryos are human individuals* to *embryos are a mere cluster of cells.* The majority of people do not subscribe to either end of the spectrum of beliefs, but tend to gravitate to a position between the two. It is helpful to examine the different stances people take towards human embryos as America considers the ethics of stem cell research, since these views shape how they approach stem cell research policy.

POSITION #1: Embryos are human individuals and should not be used or destroyed for research purposes.

One position contends that *embryos are human individuals* and therefore deserve the same respect and protection as all human beings. From this perspective, a human embryo ought to enjoy all the rights and protections as any other human being. This position considers the destruction of a human embryo to be immoral and often equates it with other types of murder. People who adhere to this belief oppose ES cell research, because the process of extracting stem cells destroys the human embryo. One argument offered by supporters of this position is that researchers should exhaust less ethically controversial sources of stem cells – like stem cells found in human adults or animals – before considering the use of human embryos for scientific and medical advances.

A subset of individuals subscribing to this belief do not believe destroying an embryo is equal to murder, but still consider its destruction reprehensible and immoral. Many state that while they understand the value that stem cell research could one day yield, the ends (potential benefits) do not justify the means (destroying a human embryo), particularly considering that the ends in this instance are hypothetical benefits that could one day yield helpful medical therapies.

One possible way to continue to conduct stem cell research without destroying embryos is to use stem cell lines for research derived from embryos that have already been destroyed. Defenders argue that it is acceptable to use ES cells that have already been derived, as long as no new human embryos are destroyed. The argument presented in favor of this position is that while the actual act of destroying a human embryo is wrong, it cannot be reversed, and therefore the stem cells from embryos that have already been destroyed are permissible for use in research. This is current federal policy for federal funding, announced by President Bush on August 9, 2001.

Some criticize this position saying that using the by-products of a destroyed embryo means the user is "complicit" in the destruction of that embryo, or at least taking advantage of someone else's immoral act. Therefore, using ES cells already derived from embryos is in direct conflict with the belief that destroying embryos in order to extract their stem cells is wrong. The United States' policy on federal funding for research seems to many to be inconsistent in its argument because of this implied complicity.

POSITION #2: Embryos do not have the same status as a fetus or a baby and can be used for research.

A second position regarding human embryo status holds that *embryos are not nothing, but they don't have the same status as a fetus or a baby* and can therefore be used to derive stem cells for research. From this position, embryos do not deserve the same protections as a fetus or a baby, and therefore the rights and potential benefits for people that are currently alive outweigh the rights of the embryo.

Supporters of this position believe that embryos are unique and have special properties because of their potential to become human beings, but they are not as valuable as the lives of living human beings suffering from disease or illness who might benefit from ES cell research outcomes. Many persons who support using embryos for stem cell research contend that stem cell research is so valuable that medical advances will be held back without their use, even if research with alternatives, such as adult stem cells, continues.

POSITION #3: Embryos should not be created for research, but can be used if they are left over from *in vitro* fertilization (IVF) procedures.

A subset of people who believe that embryos can be used and destroyed for stem cell research also believe that *embryos should not be created or cloned for use in research but can be used and destroyed for research if they are left over from* in vitro *fertilization procedures and are going to be unused anyway*. This position is referred to as the "nothing is lost" principle.[19] The "nothing is lost" principle means if an embryo is not going to be used for its original purpose of reproduction and would be discarded in the future, then science should be allowed to make use of the embryo prior to its destruction for research that might benefit people who are alive and suffering from a disability or illness. Many believe using embryos destined to be destroyed in the future for research is justified because it is simply varying the method and timing of the embryo's destruction and not the fact of whether it will be destroyed or not.

There are currently more than 200,000 "excess embryos" frozen in fertility centers around the United States.[20] Excess embryos are created because harvested eggs cannot be frozen for later use, while embryos can. Therefore, unless the eggs are fertilized and made into embryos, a woman would need fresh eggs harvested at each fertility treatment attempt. When the people seeking infertility treatment complete the IVF process and do not plan to pursue reproductive treatments further, they decide what to do with their remaining embryos. One possible option is to donate their embryos to research.

POSITION #4: Embryos are clusters of cells no different from other cells and can be created specifically for use in research.

The final viewpoint regarding the status of the human embryo is that *embryos are a mere cluster of cells* no different from any other cluster of cells in the body and they can be derived, created, and used in any way people see fit to use them. Supporters argue that even if the embryo deserved special deference because it has the information inside of it to create a human life, that it is this very property which makes the embryo so valuable for research.

Embryos created for research are either produced by *in vitro* fertilization (IVF) or somatic cell nuclear transfer (SCNT) procedures. Supporters of this viewpoint frequently present the argument that if it is ethical to use human embryos in research, then it should be considered ethical to create embryos for that purpose, the intent of the original creation of the embryo is effectively irrelevant.

Many advocates of ES cell research (and even some who traditionally adopt a pro-life position) support the creation of human embryos by somatic cell nuclear transfer.[21] One potential of ES cell research with SCNT created embryos is related to the possible medical therapies capable of generating tissues that could be incorporated into a failing organ or tissue. Many hope this therapy would be superior to current transplant therapies, because using stem cells from embryos with specific properties, particularly cloned embryos, might reduce or even eliminate transplant rejection and adverse immune responses. Advocates also contend that current research will be limited unless embryos possessing specific genetic properties can be created and studied in conjunction with the creation of tissues and cells from other sources of ES cells.

A variety of organizations and individuals object to creating human embryos for research purposes for several reasons. One primary argument is that the potential for exploitation and abuse is too great to open the door to creating embryos for research, particularly if there is potential for monetary benefit for the person donating the egg, sperm, or embryo. Another ethical concern regarding the creation of embryos for ES cell research is donation of surplus embryos for research should be, and is in fact, different from creating embryos explicitly for research. Persons opposed to creating embryos for research argue that creating a human embryo simply to destroy it is an immoral and disrespectful action. Others who object to creating embryos for research have said it is simply “unnatural” to create anything for the sole purpose of destroying it.

Research conducted with cloned embryos created via SCNT procedures raises unique issues from research with embryos created via IVF procedures. The concerns stem from a fundamental moral concern about opening the door to cloning humans for reproductive purposes. President Bush, in his August 2001 remarks to the nation regarding stem cell research stated, “I strongly oppose human cloning, as do most Americans. We recoil at the idea of growing human beings for spare body parts, or creating life for our convenience.”[22] According to popular opinion polls, Americans make distinctions between cloning for reproductive purposes and research, or therapeutic, cloning. In a 2002 Gallup Poll of over 1,000 adult Americans, 90% were opposed to reproductive cloning. However, 61% objected to cloning human embryos for use in medical research, while the same poll shows 51% favoring the cloning of human cells taken from adults for use in medical (including SCNT) research.[23]

Donating embryos

While the use of surplus embryos remaining from infertility treatments is less controversial than the creation of embryos for research, there are other ethical issues to consider. One group of ethical issues involves the donation of human embryos for embryonic stem (ES) cell research. These issues are often similar to those involved in organ donation. U.S. federal law makes payment for organ and tissue donation illegal under the National Organ Transplantation Act (NOTA) of 1984.[24] People are encouraged to give their organs and tissues, or those from a deceased loved one, out of a feeling of obligation and sympathy for people suffering from disease. Concerns center around the possible exploitation of potential donors and inequitable, or uneven, distribution of organs to those with greater ability to pay. Financial incentives for renewable tissues do exist. For example, women can currently be compensated for donating their eggs for fertility treatments to women who cannot use their own eggs to have children. In addition, people are compensated for donating blood or plasma, with no real ethical objections being raised in regard to this practice.

Even though eggs (and/or oocytes) are considered renewable tissues and can be donated for compensation, many people have qualms about financial incentives for egg donation. People fear ES cell research will force the burden of donation to fall disproportionately on poor women, while the benefits of research outcomes would be enjoyed by all. This is due to the fact that eggs are necessary for both SCNT and IVF procedures.

As is true with all research situations, researchers working with ES cells have a variety of incentives. Possibilities for financial gain and prestige motivate researchers. If these incentives are overwhelming, researchers might be encouraged to practice less-than-ideal (i.e. flawed or unethical) research. Incentives for research come from the belief in the potential therapeutic uses of stem cells. If researchers believe they are only a few steps away from curing Parkinson's disease or leukemia, there is a fear that they would overlook some of the ethical safeguards in order to more quickly attain their goals. Curing one of these diseases would bring prestige within the field and monetary rewards and these incentives can be difficult to put aside or overlook in the quest for knowledge and ethically sound research.

The incentives of prestige and financial gain might become even more controversial if there are allowances for patents of ES cells and their products. Many people object to giving patents for stem cell lines and the products of stem cells because it might be equated with patenting the function of a pancreas or a lung. For this reason, several countries have banned the issuance of patents for stem cells and products of stem cell derivatives and the European Union has recommended that patents be issued only for stem cell lines that have been "modified by inventive processes for industrial use."[25]

Federal funding for human embryonic stem (ES) research

On August 9, 2001, President George W. Bush announced that federal funding for embryonic stem (ES) cell research in the United States would be limited to research with approved stem cell lines derived on or before that date. Research with existing stem cell lines derived from human embryos can be federally funded if the stem cells are included on an official list of authorized lines.[26] Authorized stem cell lines have to meet the following criteria, in addition to being derived prior to August 9, 2001, as stated by the National Institute of Health:

> The stem cells must have been derived from an embryo that was created for reproductive purposes, the embryo was no longer needed for these purposes, informed consent must have been obtained for the donation of the embryo, and no financial inducements were provided for donation of the embryo.[27]

The announcement of this federal policy had two direct impacts on stem cell policy and research. First, it prompted public discussion and proposed legislation around human stem cell research. Each chamber of the United States Congress was quick to introduce legislation to address the following issues: use of embryonic stem (ES) cells in research, the donation of ES cells for research, the creation of embryos for ES cell research, cloning of embryos for ES cell research, and federal funding of ES cell research. None of these legislative efforts have been successful so far, although this continues to be an active policy issue.

Second, the impact of President Bush's policy is being felt by researchers. Testimony from researchers demonstrates difficulty in obtaining stem cell lines from approved sources. There are only 78 available and eligible stem cell lines which are approved for use in federally funded research. Only 27 of these are in the United States, making physical procurement of the ES cell lines cumbersome,[28] while a mere 9 of these 27 stem cell lines are available to researchers.[29] In addition, all of the eligible stem cell lines were derived using private money and these private holders are under no obligation to share or sell their stem cell lines. As a result, the cost of both the administrative support needed to work with organizations to buy stem cells lines and the cost of the stem cells themselves rose sharply, according to testimony before the United States Senate. Other difficulties with the Bush policy include doubts researchers have about the quality of the eligible stem cells and their genetic diversity.[30, 31]

Federal funding for ES cell research receives a great deal of attention because a large proportion of biomedical research funding conducted in the United States comes from the federal government. About 45% of medical and health research is conducted with federal dollars. The remaining 55% comes from private business, foundations, and charitable giving.[32] Within the global community, the United States government spends more than any other country on biomedical research. Since the federal government is the largest single source of funding for biomedical research in the world, many see the issue of U.S. federal funding for ES cell research as critical and crucial to the hopes of medical therapies from these research efforts.

The United States funded some research with human embryos resulting from IVF procedures until 1975, shortly after the Roe v. Wade abortion case re-sparked the debate on the status of the human embryo. At that time, a **moratorium** was placed on federal funding for IVF and embryo research. Since that time, there have been several boards and commissions appointed at the national level to make recommendations regarding policies for the use of human embryos in research. The results have been published, discussed, and partially implemented periodically since the mid-1970s. It is an ongoing, politically-charged process resulting in fragmented state laws and federal regulations about what is and is not acceptable practice.

In September of 1999, the National Bioethics Advisory Commission (NBAC) published recommendations concerning the use of human embryos for use in stem cell research. The NBAC's first recommendation was the continuation of federal funding for embryonic germ (EG) cell research, which uses tissues from aborted embryos/fetuses. This recommendation was consistent with the Fetal Tissue Transplantation Act of 1993 which allows federal funding for research on discarded fetal tissue.

The second recommendation from the NBAC was to federally fund embryonic stem (ES) cell research with embryos left over from *in vitro* fertilization treatments, but to not federally fund research with embryos created specifically for research. Funding for ES cell research using embryos remaining after *in vitro* fertilization treatment hinged on whether the donors of the embryo were made fully aware that: a) research will destroy the embryo, b) the embryo will not be implanted in another woman, c) the funding source for the research, d) the intention and context of the research, and e) that decisions to donate will not impact the donor's current or future medical care.[33]

Shortly after the release of the NBAC report, in December of 1999, the National Institutes of Health (NIH) drafted guidelines for federally funding research on ES cell lines derived in the private sector. President Clinton backed the guidelines and they were finalized in August of 2000. At the time the guidelines were finalized, then-candidate for President, George W. Bush, denounced the guidelines and made statements opposing the destruction of human embryos for research purposes.[34]

After his inauguration and a review of the NIH guidelines, President George W. Bush announced the current federal policy. He also formed a new bioethics advisory group to address bioethical issues including cloning and stem cell research, called the President's Council on Bioethics. The Council's mission is to advise the President regarding policies involving ethical issues, including human stem cell research. As of December 2002 there had been no formal recommendations concerning embryonic stem cell research, but the Council did publish their recommendations (based on a 10 – 8 majority) on stem cell research using cloned or SCNT embryos: "We propose a congressionally enacted…four-year national moratorium (a temporary ban) on human cloning-for-biomedical-research." This ban would apply to all organizations and individuals in the United States whether or not they are receiving funding from the federal government.[35]

Regarding privately funded ES cell research, opinions are varied. Many suggest that if federal funding of ES cell research doesn't apply to private research, there will be no rules to ensure an ethical standard. They believe policies would be more effective if they applied to all forms of research and not limited to only federally funded projects. On the other side of the debate are those who state that the "freedom to conduct research" is a right, and private research should be encouraged to be conducted both ethically and publicly. Traditionally, federal regulations on research involving human subjects have strongly influenced the ethical conduct of research in the private sector and the same result could occur for policies regarding ES cell research with human embryos.

In September 2002, California passed a law allowing state funding of stem cell research projects and the derivation of ES cells from human embryos, including embryos created through SCNT procedures. The legislation includes a stipulation for the establishment of ethical review committees to review research projects in order to ensure ethically responsible research. The unique aspect of this legislation is that the law also applies to research conducted by private organizations, which will be subject to ethical review as well.[36]

Opinions

The opinions expressed below do not necessarily represent the opinions of all individuals or organizations within a specific group, but rather the majority or most popular opinion.

President George W. Bush President Bush has allowed federal funding to go towards research on stem cell lines derived prior to August 9, 2001. His policy states, "This allows us to explore the promise and potential of stem cell research without crossing a fundamental moral line, by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life."[37]
European Union The European Union's European Group on Ethics (EGE) released an opinion on stem cell research in November of 2000. Their findings concluded that: 1) the use of adult stem cells should require the same ethical consideration as tissue donation, 2) retrieving stem cells from umbilical cord blood after delivery should require the consent of the fully informed donor, 3) using foetal tissues to derive stem cells requires both informed consent and the rule that no abortion be induced for the purpose of obtaining tissues for stem cell research, and 4) the use of embryos for stem cell research should be up to each country within the European Union to decide.[38]
University of Minnesota The University of Minnesota is actively pursuing stem cell research through its Stem Cell Institue. Many research innovations have come out of the University including the first bone marrow stem cell transplant in the 1960s. The University follows all state and federal laws and policies relating to stem cell research, and hosts the Stem Cell Ethics Advisory Board to address ethical issues around stem cell research.

President's Council on Bioethics As of October 2002, the President's Council on Bioethics is currently still hearing from experts in the field and debating the ethical points for and against using embryonic stem cells for research, but they did recommend a 4-year moratorium on research with cloned (SCNT) human embryos.
Catholic Church Richard Doerflinger, in his 1999 opinion for the Catholic Church states, "Stem cell research that requires the destruction of human embryos is incompatible with Catholic moral principles, and with any ethic that gives serious weight to the moral status of the human embryo."[39]
Judaism In testimony to the National Bioethics Advisory Commission in 1999, Rabbi Elliot Dorff explained that one condition of Judaism is the body be preserved and health pursued. Rabbi Dorff interprets this to mean that God would encourage research of any kind that would help preserve one's body. Of course, many Jewish persons may not agree with his statement but he does recommend the advancement of stem cell research because of its great potential to do good.[40]
Protestant There are many different views held within by Protestants. The more conservative Protestant denominations would consider it unethical to destroy human embryos for use in research. Some of the more liberal denominations might be more permissive in their opinions regarding the use of an embryo, but would most likely still place limits on research.
Islam The Islamic tradition in general considers research with human pluripotent stem cells (from embryonic germ cells) obtained from an aborted fetus acceptable, with several conditions placed on using embryonic or fetal cells from different stages of development as stated in the Koran.[41]
General public In a public opinion poll taken by the Pew Research Center (n = 2,002 adults over 18) in April of 2002, 50% of people think the federal government should fund stem cell research, while 35% think that stem cell research should not be funded by the federal government. When asked what they thought was more important, research towards medical cures or not destroying human embryos, 47% thought research was more important versus 39% who favored not destroying embryos.[42]

Other ethical issues

The ethical issues around embryonic stem cell research, embryonic germ cell research, cloned (SCNT) embryo research, and adult stem cell research are varied and complex. The debate becomes more intense when people consider special situations ranging from current medical therapies developed with stem cells to issues that may occur in the future. Below are a few of the current and future ethical issues that require attention.

- *Future genetic manipulation of stem cells.* When working with SCNT embryos, there is currently no genetic manipulation, but that might not always be the case. Some worry that stem cell research is laying the foundation that will give scientists the knowledge they require to genetically alter human cells and thus change, fundamentally, the building blocks of humanity so significantly that the new cells created are no longer human.
- *Xenotransplanted stem cells.* **Xenotransplanted** stem cells are stem cells from animals that are used to create tissues and cells. These cells would then be used in medical therapies for humans. Ethical issues involving the abuse and exploitation of animals and animal rights concern many people. Medical concerns about using xenotransplanted stem cells involve the possibility of animal-human pathogens and illnesses that might not be anticipated by researchers.
- *Creating a life to save another.* In 2000, the University of Minnesota used **pre-implantation diagnosis** to create a child in order to harvest stem cells from the umbilical cord at birth for use in treatment for the child's sibling. Pre-implantation diagnosis occurs when embryos are fertilized *in vitro* and then screened for a particular characteristic. In this case, the sibling had a rare genetic disorder and needed a healthy donor from which to collect genetically-matched umbilical cord stem cells. Ethical concerns involved in cases like this one might include: debate over the pre-implantation selection, the intentions and motivations of the parents, and the creation of a child as a means to gather the stem cells from the umbilical cord.

- *Parthenogenesis.* A new and innovative process of developing blastocysts in order to extract their stem cells for research is **parthenogenesis**. In this process, oocytes are activated through the use of chemical stimulation without requiring sperm or an SCNT procedure. Researchers recently derived stem cell lines from monkeys using this procedure, but have not been able to stimulate human oocytes into progressing this far. Scientists are doubtful that parthenogenesis could ever develop an oocyte into an advanced embryo or a fetus, and therefore, this potential source of stem cell lines could be used without creating a human embryo that could develop into a human being, which could serve to eliminate a great deal of ethical objections arising from the use of human embryos for research.

The future of stem cell research is in question. While federal funding is limited to a few available stem cell lines, private research continues at a rapid pace and federally-funded research with adult stem cells and embryonic germ cells also progresses. The future of stem cell research will offer new and additional scientific and medical advances, along with many ethical challenges. Society's challenge is how to balance them all.

PART III

SUGGESTED MATERIALS

Suggested Materials: Websites

American Society for Bioethics and Humanities
www.asbh.org

CNN: Ethics Matters with Jeffrey Kahn, PhD, MPH
www.cnn.com/HEALTH/bioethics

Do No Harm: The Coalition of Americans for Research Ethics
www.stemcellresearch.org

National Institute of Health Embryonic Stem Cell Research
http://escr.nih.gov

President's Council on Bioethics
www.bioethics.gov

University of Minnesota Stem Cell Institute
www1.umn.edu/stemcell/sci/page/pg/patch2gar2v2-8_6.htm

Suggested Materials: Books

Becoming Immortal: Combining Cloning and Cell Therapy. By Stanley Shostak. State University of New York, 2002.

Cloning and the Future of Human Embryo Research. Edited by P. Lauritzen, Oxford University Press, 2001.

Crafting a Cloning Policy: From Dolly to Stem Cells. By Andrea Bonnicksen. Georgetown University Press, 2002.

Hematopoietic Cell Transplantation. Edited by Donnall Thomas, Karl Blume, and Stephen Forman. Blackwell Science, Inc., 1999.

The Human Embryonic Stem Cell Debate: Science, Ethics, and Public Policy. Edited by Suzanne Holland, Karen Lebacqz, and Laurie Zoloth. MIT Press, 2001.

My Detour on Life's Highway: The Story of a Stem Cell Transplant Survivor. By Rosemary Champagne. Glacier Publishing, 2001.

Stem Cell Biology and Gene Therapy. Edited by Peter Quesenberry, Gary Stein, and Bernard Forget. John Wiley & Sons, 1998.

The Stem Cell Controversy: Debating the Issues. Edited by Michael Ruse and Christopher Pynes. Prometheus Books, 2002.

Suggested Materials: Articles

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PART IV

GLOSSARY

AND

REFERENCES

Glossary[43]

Adult stem cells – Stem cells found in various tissues and organs of the adult human body

Blastocyst-stage embryo – A blastocyst-stage embryo is a human embryo that has not been implanted into a uterus about five days after being fertilized *in vitro*

Differentiation – The specialization of a stem cell into one cell type

DNA – The genetic material of the human body found in every human cell

Embryo – The beginnings of a human organism from conception through the eighth week of development

Embryonic stem (ES) cell – Cells from the inner cell mass of a blastocyst-stage human embryo

Embryonic germ (EG) cell – Cells isolated from the gonadal ridge of an aborted embryo/fetus

Enucleated – A cell from which the nucleus has been removed

Fetus – An unborn child from the end of the eighth week after conception until birth

Gene therapy – Treatment of certain disorders accomplished by introducing specific engineered genes into a patient's cells

Grafting – Transplanting or implanting tissue surgically into a bodily part to replace a damaged part or compensate for a defect

Hematopoetic – The bodily system of organs and tissues, primarily the bone marrow, spleen, tonsils, and lymph nodes, involved in the production of blood

In vitro – An artificial environment

In Vitro Fertilization (IVF) – Fertilization of a egg outside of the human body in an artificial environment

Inner cell mass – Approximately 30 cells inside the blastocyst-stage embryo

Medium – A liquid or gelatinous substance containing nutrients in which tissues are cultivated

Moratorium – The suspension of an ongoing activity

Multipotent stem cell – A cell that can differentiate into the different types of cells found in a particular tissue or organ

Parthanogenesis – The process in which oocytes are electrochemically stimulated into forming a human blastocyst without SCNT procedures or being fertilized by a sperm.

Placenta – An organ that develops in women during pregnancy, lining the uterine wall and surrounding the developing fetus; also nourishes the fetus via the umbilical cord

Pluripotent stem cell – A cell that can differentiate into all the different cells of the adult human body

Pre-implantation diagnosis – A procedure that screens embryos fertilized *in vitro* for certain traits such as a genetic disorder

Progenitor stem cell – An immature cell that has been pre-specialized; also called a precursor cell

Oocyte – A cell from which an egg or ovum develops by meiosis

Outer cell ring – The cells forming the hollow outer shell of the blastocyst-stage embryo which would eventually develop into the placenta

Somatic cell – Any cell in the human body that is not a germ cell

Somatic Cell Nuclear Transfer (SCNT) – The procedure used to clone an embryo by taking the nucleus from an adult cell and inserting it into an oocyte from which the nucleus has been removed

Stem cell line – The replicates of an original stem cell

Therapeutic cloning – Cloning for research purposes; distinguished from reproductive cloning used to create offspring

Totipotent stem cells – Cells that can make all of the cells in the human body and the placenta

Trophoblast – The cells forming the outer cell ring of a human blastocyst.

Vectors – An agent that transfers genetic material from one cell to another

Xenotransplanted stem cells – Stem cells are first derived an animal species, then grown and cultivated into tissues, and finally the tissues are then transplanted into a human being

Zygote – A fertilized egg before it has divided or cleaved

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