CRG WHAT YOUR MOTHER NEVER TOLD YOU ABOUT STEM CELLS

Wouldn't it be nice to have a nickel every time the words "embryonic stem cells" were used on TV or in the newspaper? As with many other contemporary debates in biology and biotechnology, the stem cell controversy is hard to escape, yet is too often characterized by hype and confusion. This pamphlet will give you the facts you need to form your own views about this new technology.

WHAT ARE STEM CELLS?

Next time you look at yourself in the mirror, be amazed. You are made up of trillions of cells! These trillions of individual cells make up the different tissues of your body. Each type of mature cell is specialized to perform a specific function, such as photoreceptor cells in your eye that allow you to see the words on this page.

Photoreceptor cells, and all the other 200 known types of cells in our body, are derived from so-called *"stem cells."* Put simply, these are the cells from which mature, specialized cells stem.

Although some scientists dispute the exact qualities that define a stem cell, the following are generally accepted characteristics: Stem cells, like most other cells, have the ability to divide and produce more cells like themselves, a process often called *self-renewal.* They can also divide and form mature cells specialized for specific roles in the body.

Some stem cells can produce more than one specialized type of cell. As far as we know, populations of stem cells reproduce throughout our lives.

Stem cells existing in many tissues supply our bodies with new mature cells. For instance, there are stem cells underneath our skin that replace the cells that we lose through normal wear and tear.

Although stem cells lie in tissues that perform specialized functions, they do not exhibit the specialized appearance and function of the cells to which they give rise.

Some stem cells produce *precursor* or *progenitor* cells, and these add an additional step in the maturation pathway. Precursor cells are similar to stem cells in that they have the ability to produce at least one functionally specialized type of cell, but unlike stem cells, they are unable to self-renew.

If a stem cell has the potential to produce more stem cells and only one kind of specialized cell it is known as *unipotent.* Stem cells are said to be *pluripotent* if they can produce many different types of specialized cells.

The cells of the embryo in the very early stages are considered *totipotent*, and can produce any type of cell necessary for the survival of the embryo. However, they are not considered to be stem cells because the number of cell divisions before further specialization is limited.

(No known cells are *omnipotent* . . . and so the meaning of life remains a mystery.)

WHERE ARE STEM CELLS FOUND?

Adult stem cells (ASCs): from many tissues such as bone marrow, brain, and muscle.

Umbilical cord blood of newborns: these are also considered ASCs.

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Placental tissue: another source of ASCs.

Fetal tissue: "Embryonic" germ cells (EGCs) are stem cells derived from fetal gonads, and have been misleadingly dubbed embryonic stem cells in recent reports. They are derived from aborted fetal tissue, and cannot be produced in a petri dish or test tube like embryonic stem cells can.

Embryos: source of Embryonic stem cells (ESCs) derived from a 5 day old embryo. These are the cells that can give rise to all known cell types in our bodies.

HUMAN EMBRYONIC STEM CELLS

Embryonic stem cells have been the recent focus of the popular media. As far as we know, these stem cells develop into the greatest number of different types of cells and they proliferate rapidly. Due to their special properties, some scientists feel that research on ESCs should be federally funded, despite ethical concerns that have restricted funding for embryo research.

On August 9th 2001, President Bush announced his decision to allow federal funding for research on embryonic stem cell lines that has been derived from embryos left over from in vitro fertilization prior to his announcement. He prohibited federal funding for research on embryos produced solely for research purposes, and on cloned embryos. President Bush's decision does not affect privately funded ESC research.

Researchers collect embryonic stem cells from the inner cell mass of a *blastocyst.* No, the blastocyst is not a new punk band, it is the structure formed at the stage of development just before the embryo would normally implant in the lining of a woman's uterus. At this stage, the cells of the embryo begin to separate into two domains, the *trophoblast* and the *inner cell mass (ICM).* The trophoblast forms a hollow ball that will later give rise to the placental tissue. The ICM is a cluster of cells attached to the inside of the hollow sphere, and it gives rise to the tissues of the body of the developing fetus.

Embryonic stem cells are derived from the inner cell mass (ICM) cells, removed from the embryo at 5 days post-fertilization. The procedure destroys the embryo. Cells from the ICM are placed into a culture medium.

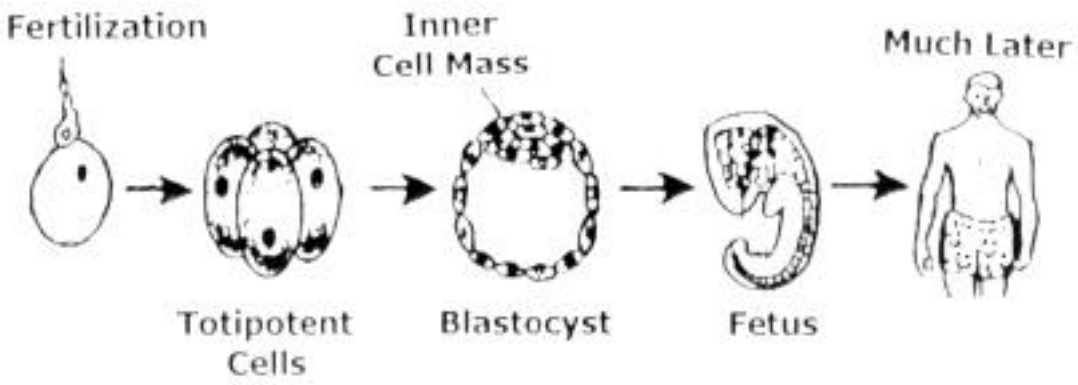
Most of the cells divide a few times and then die, but a few continue to proliferate. These are the embryonic stem cells.

Embryonic stem cells can divide and produce further identical stem cells, thereby generating ESC "lines."

ESCs can be produced in three ways. To date, most of the research has been conducted with embryos that were produced during in vitro fertilization but were not implanted in a woman's uterus.

However, in July 2001, scientists at the Jones Institute for Reproductive Medicine produced human embryos solely for research purposes. They did so by paying women for their eggs and men for their sperm and producing an embryo in vitro.

A third way to collect more embryonic stem



cells is to produce cloned embryos. If a bill recently passed in the House of Representatives becomes law, this procedure would be outlawed in the United States. In Great Britain, however, embryo cloning is legal.

POTENTIAL USES OF STEM CELLS

Many stem cells have the ability to proliferate readily and divide to form different types of cells. Researchers are attempting to become efficient at directing the development of a specific types of cells by culturing them in the presence of different growth factors and hormones.

It has been proposed that stem cell technology will lead to treatments for various diseases. However, none are currently used for the treatment of human diseases except for one type of adult stem cell. Research on most types of stem cells is still in the animal testing stage.

STEM CELL HYPE HAS CREATED MYTHS

The positive potential of embryonic stem cells has often been grossly exaggerated in the media. In addition, the debate has been reduced to "pro-lifers" vs. "scientists searching for cures to end human suffering". Media hype is a disservice to the public and creates myths that must be dispelled.

Myth: This is a pro-life vs. pro-choice debate.

A person can be pro-choice in terms of a woman choosing whether to continue with her pregnancy and be opposed to the production of embryos for research. There is a difference between a woman deciding to bring a child into her life and scientists controlling the fate of an embryo in a laboratory.

Myth: By questioning embryonic stem cell research we are allowing people to suffer and die every day.

People suffering from diseases have been very vocal throughout the debate, pleading to save

A COMPARISON OF HUMAN STEM CELL TYPES

	Adult Stem Cells (ASCs)	*Embryonic Stem Cells (ESCs)*	*Embryonic Germ Cells (EGCs)*
Possible Benefits	• may form more types of cells than was first speculated • some types can produce an entirely different set of cells depending on their location	• form nearly all types of cells that make up an organism • proliferate for a long period of time in vitro	• do not form tumors as easily as ESCs • proliferate more rapidly than ASCs • proliferates fairly well in vitro
Possible Drawbacks	• no known type of ASC can form as many types of cells as ESCs • rare and difficult to separate from progenitor cells • haven't proliferated well in vitro	• divide rapidly and can form tumors • difficult to control the types of cells they produce	• while they proliferate in vitro, they have not divided for as many generations as ESCs

them and others who share their afflictions by allowing this research to be funded and proceed unhindered. Their emotionally charged messages cloud the present reality of the situation. Celebrities such as Michael J. Fox, Mary Tyler Moore, and Christopher Reeve are not likely to be cured as a result of embryonic stem cell research.

Research exploring the potential of stem cells as treatments for Parkinson's disease, diabetes, and spinal cord injury is still at a very early stage. Animal models of human diseases are currently used, and these animal models are do not precisely mimic human diseases.

It is too early to know for certain if research on embryonic stem cells will lead to any effective treatments. While the only way to uncover these benefits is to keep researching and learning, the present situation should be kept in perspective.

Myth: Embryonic stem cells are the only possible treatments for diseases like diabetes, Alzheimer's disease, and Parkinson's disease.

Stem cells are not the only possible source of future treatments for these diseases. Scientists researching diabetes are looking into new drugs that would "sensitize" people with type 2 diabetes to the insulin that is in their blood. Other drug possibilities are in the works.

Possibilities for preventative treatments for Alzheimer's disease, such as estrogen replacement for women and anti-inflammatories, are currently being researched.

Also, a lineup of drugs for Parkinson's disease is entering phase two clinical trials. While stem cells may offer treatments at a later date, we must not lose focus on other possibilities.

Myth: We can only get stem cells from embryos.

Amidst all the hype about embryonic stem cells, it would be easy to come to this conclusion, and it is simply untrue. As mentioned earlier, there are many sources of stem cells in adult humans.

Myth : We can simply use adult stem cells as substitutes for destroying human embryos for science.

Adult stem cells are not mere substitutes for embryonic stem cells, and vice versa. Each have advantages and disadvantages.
(see chart: Comparison of Human Stem Cell Types)

Adult stem cells may have medical promise, and may turn out to be more effective than embryonic stem cells in treating some diseases, but it is too early to know for certain.

CONCERNS AND A NEED FOR CAUTION

Many people fear that experimentation on human embryos coupled with our knowledge of the human genome will lead us down a dangerous path to modifying the inborn characteristics of children, and thus a new eugenics movement. The more we learn about early human development, the more tempted we may be to attempt to change characteristics. Testing IVF embryos for certain traits, such as sex, is already taking place. Scientists can then implant only the embryos that have the desired trait into a woman's uterus.

The majority of ESC lines have been derived from embryos left over from in vitro fertilization. However, women have also been paid to provide their eggs to biotechnology companies for embryo research. In either case, women are given drugs to increase the number of eggs that develop.

The health risks of these drugs have been largely ignored. There is some evidence of increased risk of breast or ovarian cancer, though the exact risk is unknown as studies are contradictory and incomplete. Health risks to women undergoing egg retrieval need to be taken into account in discussions about embryo research.

Research on embryonic stem cells may not, in fact, lead to any useful treatments. In his August 9th television address, President Bush pointed out that fetal tissue once was hailed as a very promising potential source of treatments, but the research has yielded few

positive results.

A tragic result was reported in the March 8, 2001 *New England Journal of Medicine.* Patients with Parkinson's disease experienced horrible side effects in an experiment that involved the injection of fetal neurons into their brains. The unexpected and extremely unfortunate results showed that we do not know how to control cell growth. Control of the proliferation and differentiation of any implanted cells must be accurate, as the cells cannot be removed once implanted.

POLITICS

In addition to allowing federal funding on 60 embryonic stem cell lines, Mr. Bush has promised to create a new President's Council on Bioethics, chaired by Dr. Leon Kass, an expert in biomedical ethics and a professor at the University of Chicago. The sorely needed Council will study such issues as embryo and stem cell research, assisted reproduction, cloning, genetic screening, gene therapy, euthanasia, psychoactive drugs, and brain implants.

Since President Bush's decision, researchers and politicians have debated about whether there are truly 60 stem cell lines, whether these lines will be made available to public researchers, whether they have been maintained properly, and whether the alleged 60 lines will be enough for basic research. The number of viable stem cell lines and is still unconfirmed. Scientists are also unsure how many will be "needed" to pursue their research.

United States patent 6,200,806, issued by Geron Corporation, makes claims to human embryonic stem cells. Geron has the intellectual property rights to the methods used to isolate human and other primate ESCs. The rights to use human embryonic stem cells can now be bought and sold. Some fear that because of Geron's patent, the cost to work with embryonic stem cell lines will be too high and research in the public sector will be very slow. With or without assistance from public researchers, private research will continue, and it will continue unregulated.

In January 2001, Great Britain became the first country to allow research on embryonic stem cells. It is also legal to clone embryos for research purposes. Since Great Britain has more lenient regulations, some U.S. scientists have threatened to pursue their research overseas.

Although the message underlying President Bush's August 9th announcement was to proceed with caution, the only way scientists can be truly cautious and avoid a "slippery slope" is to enact regulations that reach worldwide and include private biotechnology and pharmaceutical companies. These companies have billions of dollars invested in biomedical research; should we allow bioethical boundaries to be determined and controlled by corporations?

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