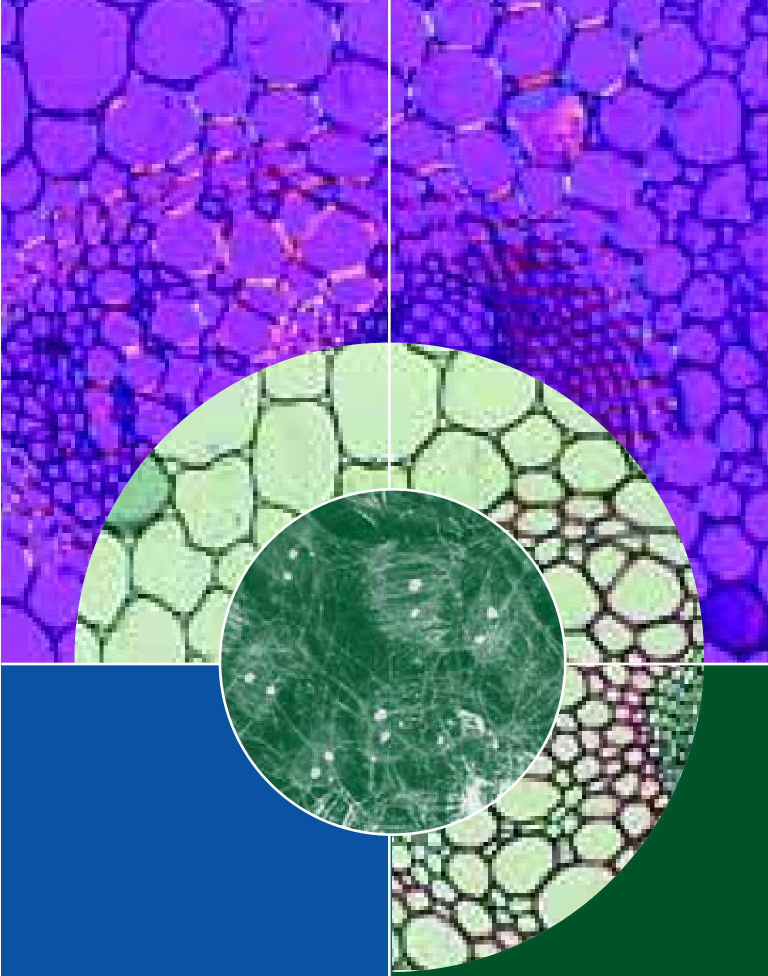


Stem Cell Facts

The next frontier?

ISSCR

International Society for Stem Cell Research

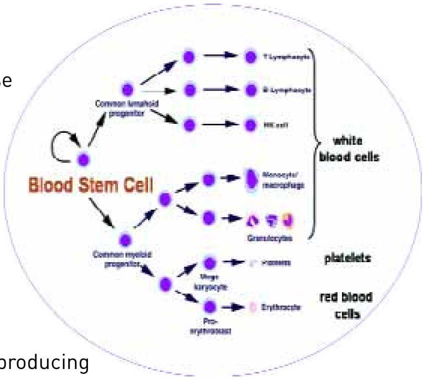
Prepared by the International Society for Stem Cell Research, an independent, nonprofit organization formed to foster the exchange of information on stem cell research.

Stem Cells

Mouse embryonic stem cells were first discovered in 1981. Since then, they have been an invaluable tool of modern biology and medical research. They have provided models to study diseases, they have brought about the discovery of many genes associated with diseases and they have been used to cure certain human disorders in animal models. After 20 years of exciting research, the mouse embryonic stem cell has helped to establish the value of these cells in *regenerative medicine*, which is the creation of cells or organs to replace tissues lost to disease or injury.

The discovery of *human* embryonic stem cells in 1998 triggered important ethical controversy and debate, yet scientists are convinced that they hold enormous potential for clinical applications. Many diseases plaguing the modern world may be improved, or even cured, with therapies using human stem cells. Whether human embryonic stem cells or adult stem cells are used in future therapies will depend on the type of disease or injury. There are specific advantages for each stem cell type. Thanks to the ease of growing them in the laboratory, human embryonic stem cells may one day become the source of artificial organs. Or scientists might one day be able to mobilize one's own adult stem cells to repair tissue damage caused by trauma, disease, and even aging. To reach such goals, both human embryonic and adult stem cells will have to be extensively studied. The complementary information acquired from studying both stem cell types is the key to unlocking their full potential.

What Are Stem Cells?



A stem cell is the base building block of an entire family of cells that make up any organ. A common trait of stem cells is that they can maintain themselves indefinitely in a stem cell state, which is referred to as "self-renewal," while also producing — through division — more specialized cells. For example, the blood stem cell can produce all the cells in the blood, including the red blood cells, white blood cells and platelets.

Who Needs Stem Cells?

Harnessing the power of human stem cells will revolutionize our health, our lives, and our society. In principle, any affliction involving the loss of cells, including many diseases, injuries and even aging, could be treated with stem cells. In the United States alone, more than 100 million people could benefit from therapies derived from stem cell research.

Adult Stem Cells

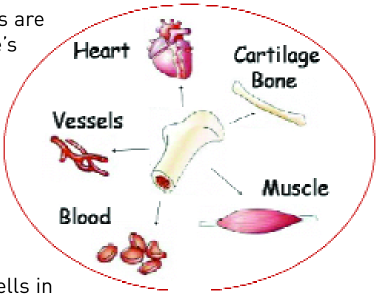
Adult stem cells are more specialized stem cells living in the majority of tissues and organs in our bodies and generate the mature cell types within that tissue or organ. In tissues where adult stem cells have been found, they are extremely rare and very difficult to isolate. Once isolated, adult stem cells grow poorly in culture, and it is difficult to obtain enough of these cells for use in clinical trials. In addition, access to the tissues harboring these cells is problematic since most human tissue is not easily available.

Two readily available sources of human adult stem cells are the bone marrow and the umbilical cord blood. In both these tissues are blood stem cells, as well as other rare types of stem cells, which can produce bone, muscle, blood vessels, heart cells and possibly more.

Adult Stem Cells in the Clinic

The majority of stem cell clinical trials now underway use blood stem cells from the bone marrow or umbilical cord blood to treat blood disorders or diseases, such as leukemia, different types of anemia, systemic lupus, and certain other autoimmune diseases or deficiencies.

A handful of clinical trials are evaluating the use of one's own bone marrow stem cells to repair heart tissue and to improve blood flow or to help to repair bone and cartilage.



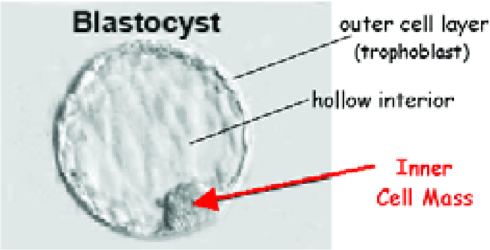
Other adult stem cells being explored for use in the clinic include stem cells in the eye and the skin.

Adult stem cells are also thought to play a role in tissue transplants that have been performed for several years. For example, insulin-producing cells for type I diabetes, fetal neurons for Parkinson's disease, and skin for bladder reconstruction have been transplanted successfully. It is possible that in cases where long-term regeneration has been achieved, stem cells contained in these tissues have contributed to regeneration.

The widespread use of adult stem cell-derived therapies and treatments is complicated by several factors. First, available human tissue is scarce, with only 6000 donors/year for more than 100 million Americans that could benefit from cellular therapy. Second, immune rejection caused by not using one's own cells or tissue is a problem. On the other hand, using one's own cells or tissue may become a problem for older patients, as evidence has been accumulating that adult stem cells age during the life of the body and lose their potential.
Thus, stem cells isolated from a young adult may have a greater potential to produce numerous daughter cells than the cells of an older person.

Embryonic Stem Cells

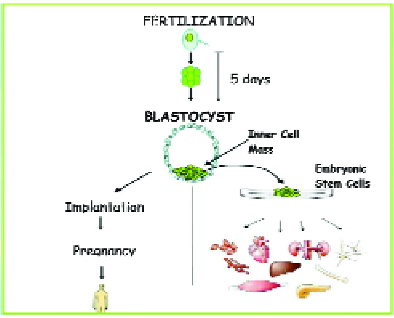
Human embryonic stem cells are like a blank slate and can produce all the cells of the body. They are obtained from the ICM (inner cell mass) of the blastocyst. The blastocyst is a very early stage of human development, which forms about 5 days after fertilization of an egg. It is approximately 1/10 the size of the head of a pin, almost invisible to the eye, and it has not yet implanted into the uterus.



Once the blastocyst has implanted and a normal pregnancy can be detected, it is too late to derive human embryonic stem cells from the embryo.

At the blastocyst stage, organ formation has not started and more specialized cells are not yet present, not even the beginning of the nervous system. To obtain human embryonic stem cells, blastocysts created in culture for *in vitro fertilization* (IVF) treatment by combining sperm and egg in a dish, are used. If they are not implanted into the uterus, the blastocysts are either discarded or frozen for later fertility cycles.

They can also be donated to other patients or to research. If not donated, they will stay in the freezer as long as the storage fees are paid, otherwise they will be discarded.



Because the cells obtained from the blastocyst have not yet specialized, they are considered highly valuable. They can generate cells that go on to form all the body's tissues and organs.

Why Are Embryonic Stem Cells So Valuable?

While grown in a dish, human embryonic stem cells can maintain their *"stem-cellness"* and provide an unlimited supply of more stem cells, as well as specialized cells that can be used for experiments and for the development of therapies. Apart from their potential to treat or cure diseases, human embryonic stem cells also provide a model to study very early human development and some of the disorders that lead to birth defects and childhood cancers. Many of these disorders develop in early pregnancy and are impossible to study in humans.Also, human embryonic stem cells also can be used to examine the genes that are turned "on" or "off" as stem cells generate more specialized cell types, permitting a unique understanding of the genetics of human development. The specialized cells derived from human embryonic stem cells also can be used to study the effectiveness of potential new drugs to treat diseases. This provides a human cellular model and can reduce animal experimentation and drug development costs.

Additionally, embryonic stem cells can be derived from human blastocysts with specific genetic abnormalities. These types of blastocysts are identified through genetic diagnosis during IVF treatment, to screen out genetically abnormal blastocysts, and are usually discarded. The stem cells from them can provide a unique resource to understand genetic diseases and to develop cures.

Human embryonic stem cells also could be used to understand the origin or causes of various diseases such as Alzheimer's disease or Parkinson's disease, which are currently unknown. Stem cells derived through *nuclear transfer* (more info below) from patients with such afflictions would provide special tools to study these diseases and possibly develop drugs for treatments.

Embryonic Stem Cells in the Clinic

Embryonic stem cells have not yet been used in treating humans. But numerous animal studies have shown that many of the specialized cells derived from them can indeed integrate into damaged tissues and function properly. Thus, diseases such as myocardial infarction, severe immune deficiency, diabetes, Parkinson's disease, spinal cord injury, and demyelination have been successfully treated in animal models. But the pathway from animal models to the clinic is still complex and burdened with obstacles to be overcome.

- First, not all specialized cells derived from human embryonic stem cells have been shown to integrate into animal tissue and function properly. This can be due to the poor quality of the specialized cells derived in culture, or to a lack of adequate communication between the human cells and the animal environment in which they are placed.
- Then there is the problem of scaling up to yield enough of the specialized cells to treat a human, since this requires many more cells than to treat a tiny mouse. Such cells will have to be produced under specific conditions to ensure safety for use in patients. Most human embryonic stem cells are still grown on a layer of mouse feeder cells, a potential source of contamination.
- Last, there's the problem of immune rejection by the patient. While the drugs used in the organ transplantation field to suppress immune rejection have been improved over the years, rejection is still a major problem.

Human Embryonic Stem Cells

From Animal Models to Patients

- **Transplanted Cells Must Function Properly**
- **Need Many Cells to Transplant**
- **Transplanted Cells Must Be Safe**
- **Must Avoid Immune Rejection**

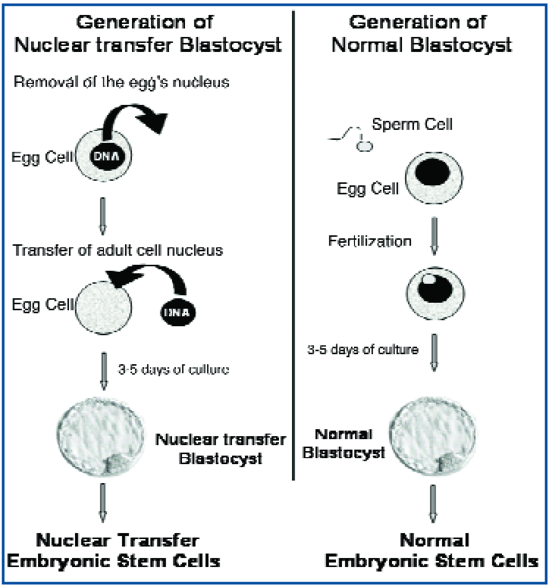
Nuclear Transfer to Generate Stem Cells

Immune rejection of transplanted stem cells could be avoided if the therapeutic cells derived from the human embryonic stem cells express a patient's own genes and proteins. A method to generate these types of stem cells is by *nuclear transfer*.

The nuclear transfer technique is similar to the process of generating a blastocyst from the fertilization of an egg by a sperm cell; however, in this process the DNA in an egg is exchanged for the DNA from a cell of the patient. The egg is then coaxed to divide in a culture dish into a blastocyst. The human embryonic stem cells derived from this blastocyst will be an identical genetic match to the patient and can provide "customized" replacement cells for any disorder.

As long as the blastocyst is not implanted into a uterus, it CANNOT develop further into a living clone of the patient.

If the blastocyst is implanted, it is possible that a live offspring could be born (so-called *reproductive cloning*). But based on animal models of reproductive cloning, the procedure is very inefficient; over 95% of the clones die before birth, and those that do survive have serious genetic and biological problems. Thus, medically it is irresponsible to consider reproductive cloning for humans. It is also morally and ethically unacceptable.



Stem Cell Glossary

Adult stem cells

Stem cells found in different tissues of the developed, adult organism that remain in an undifferentiated, or unspecialized, state. These stem cells can give rise to specialized cell types of the tissue from which they came, i.e., a heart stem cell can give rise to a functional heart muscle cell, but it is still unclear whether they can give rise to all different cell types of the body.

Blastocyst

A very early embryo consisting of approximately 150 cells. It contains the inner cell mass, from which embryonic stem cells are derived, and an outer layer of cells called the trophoblast that forms the placenta.

Cell line

Cells that can be maintained and grown in culture and display an immortal or indefinite life span.

Differentiation

The process of development with an increase in the level of organization or complexity of a cell or tissue, accompanied with a more specialized function.

Embryo

The product of a fertilized egg, from the zygote until the fetal stage.

Embryonic stem cell

Also called ES cells, embryonic stem cells are cells derived from the inner cell mass of developing blastocysts. An ES cell is self-renewing (can replicate itself), pluripotent (can form all cell types found in the body) and theoretically is immortal.

In vitro fertilization

A procedure where an egg cell and sperm cells are brought together in a dish so that a sperm cell can fertilize the egg. The resulting fertilized egg, called a zygote, will start dividing and after a several divisions, forms the embryo that can be implanted into the womb of a woman and give rise to pregnancy.

Mesenchymal stem cell

Also known as bone marrow stromal cells, mesenchymal stem cells are rare cells, mainly found in the bone marrow, which can give rise to a large number of tissue types such as bone, cartilage, fat tissue, and connective tissue.

Multipotent stem cells

Stem cells whose progeny are of multiple differentiated cell types, but all within a particular tissue, organ, or physiological system. For example, blood-forming (hematopoietic) stem cells are single multipotent cells that can produce all cell types that are normal components of the blood.

Nucleus

A part of the cell, situated more or less in the middle of the cell, which is surrounded by a specialized membrane and contains the DNA of the cell, which is the genetic, inherited material of cells.

Plasticity

A phenomenon used to describe a cell that is capable of becoming a specialized cell type of different tissue.

Pluripotent stem cells

Stem cells that can become all the cell types that are found in an implanted embryo, fetus, or developed organism.

Progenitor cell

An early descendant of a stem cell that can differentiate, but cannot renew itself. By contrast, a stem cell can renew itself (make more stem cells by cell division) or differentiate (divide and with each cell division evolve more and more into different types of cells).

Regenerative medicine

Medical interventions that aim to repair damaged organs, most often by using stem cells to replace cells and tissues damaged by aging and by disease.

Reproductive cloning
Somatic cell nuclear transfer used for the production of a fetus and delivery of a live offspring that is genetically identical the donor of the somatic cell DNA.

Somatic cells
All the cells within the developing or developed organism with the exception of germline (egg and sperm) cells.

Stem cells
Cells that have both the capacity to self-renew (make more stem cells by cell division) and to differentiate into mature, specialized cells.

Therapeutic cloning
Somatic cell nuclear transfer for the isolation of embryonic stem cells. The embryonic stem cells are derived from the blastocyst (before it becomes a fetus) and can be instructed to form particular cell types (e.g. heart muscle) to be implanted into damaged tissue (e.g. heart) to restore its function. If the stem cells are placed back into the individual who gave the DNA for the somatic cell nuclear transfer, the embryonic stem cells and their derivatives are genetically identical and thus immunocompatible (they will not be rejected).

Transdifferentiation
The ability of a particular cell of one tissue, organ or system, including stem or progenitor cells, to differentiate into a cell type characteristic of another tissue, organ, or system; e.g., blood stem cells changing to liver cells.

Transplantation biology
The science that studies the transplantation of organs and cells. Transplantation biologists investigate scientific questions to understand why foreign tissues and organs are rejected, the way transplanted organs function in the recipient, how this function can be maintained or improved, and how the organ to be transplanted should be handled to obtain optimal results.

Umbilical cord stem cells
Hematopoietic stem cells are present in the blood of the umbilical cord during and shortly after delivery. These stem cells are in the blood at the time of delivery, because they move from the liver, where blood-formation takes place during fetal life, to the bone marrow, where blood is made after birth. Umbilical cord stem cells are similar to stem cells that reside in bone marrow, and can be used for the treatment of leukemia, and other diseases of the blood. Efforts are now being undertaken to collect these cells and store them in freezers for later use.

Zygote
The cell that results from the union of sperm and egg during fertilization. Cell division begins after the zygote forms.

For more information go to: http://www.isscr.org/public

ISSCR
International Society for Stem Cell Research

International Society for Stem Cell Research
111 Deer Lake Road, Suite 100 | Deerfield, IL 60015 | USA
isscr@isscr.org | www.isscr.org