

STEM CELL FACTS

ISSCR



INTERNATIONAL SOCIETY
FOR STEM CELL RESEARCH

The ISSCR is an independent, nonprofit organization providing a global forum for stem cell research and regenerative medicine.

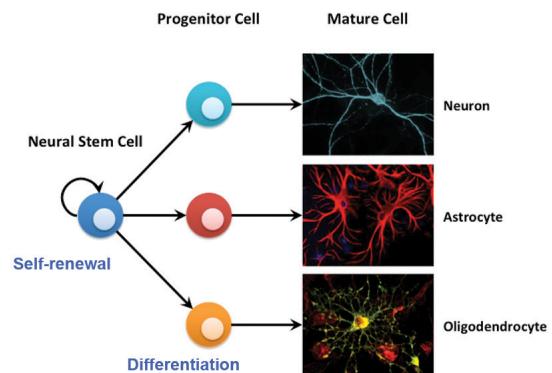
WHAT ARE STEM CELLS?

Stem cells are the foundation cells for every organ and tissue in our bodies. The highly specialized cells that make up these tissues originally came from an initial pool of stem cells formed shortly after fertilization. Throughout our lives, we continue to rely on stem cells to replace injured tissues and cells that are lost every day, such as those in our skin, hair, blood and the lining of our gut. Stem cells have two key properties: 1) the ability to **self-renew**, dividing in a way that makes copies of themselves, and 2) the ability to **differentiate**, giving rise to the mature types of cells that make up our organs and tissues.

TISSUE-SPECIFIC STEM CELLS

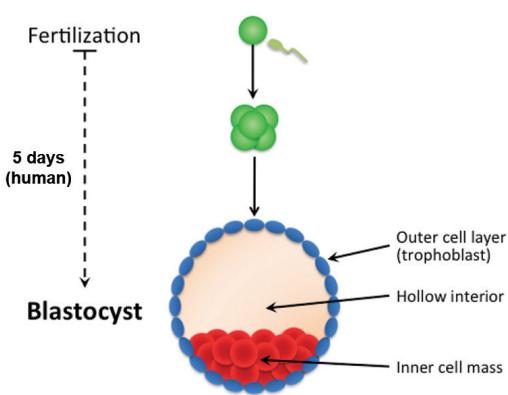
Tissue-specific stem cells, which are sometimes referred to as “**adult**” or “**somatic**” stem cells, are already somewhat specialized and can produce some or all of the mature cell types found within the particular tissue or organ in which they reside. Because of their ability to generate multiple, organ-specific, cell types, they are described as “**multipotent**.” For example, stem cells found within the adult brain are capable of making neurons and two types of glial cells, astrocytes and oligodendrocytes.

Tissue-specific stem cells have been found in several organs that need to continuously replenish themselves, such as the blood, skin and gut and have even been found in other, less regenerative, organs such as the brain. These types of stem cells represent a very small population and are often buried deep within a given tissue, making them difficult to identify, isolate and grow in a laboratory setting.



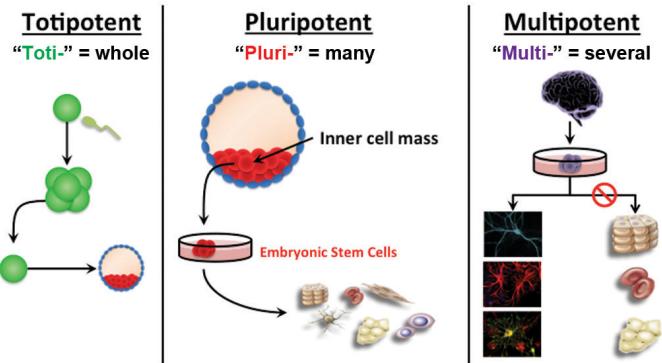
Neuron – Dr. Gerry Shaw, EnCor Biotechnology Inc.
Astrocyte – Abcam Inc.
Oligodendrocyte – Dhaunchak and Nave (2007).
Proc Natl Acad Sci USA 104:17813-8

EMBRYONIC STEM CELLS



Embryonic stem cells have been derived from a variety of species, including humans, and are described as “**pluripotent**,” meaning that they can generate all the different types of cells in the body. Embryonic stem cells can be obtained from the **blastocyst**, a very early stage of development that consists of a mostly hollow ball of approximately 150-200 cells and is barely visible to the naked eye. At this stage, there are no organs, not even blood, just an “inner cell mass” from which embryonic stem cells can be obtained. Human embryonic stem cells are derived primarily from blastocysts that were created by **in vitro fertilization** (IVF) for assisted reproduction but were no longer needed.

The fertilized egg and the cells that immediately arise in the first few divisions are **“totipotent.”** This means that, under the right conditions, they can generate a viable embryo (including support tissues such as the placenta). Within a matter of days, however, these cells transition to become pluripotent. None of the currently studied embryonic stem **cell lines** are alone capable of generating a viable embryo (i.e., they are pluripotent, not totipotent).



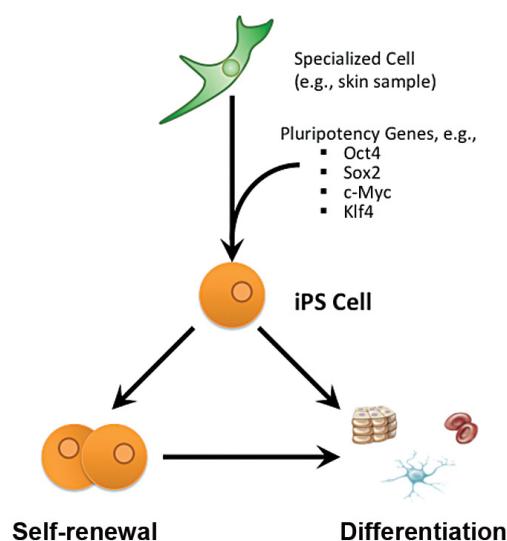
WHY ARE EMBRYONIC STEM CELLS SO VALUABLE?

Unlike tissue-specific (adult) stem cells, embryonic stem cells have the potential to generate every cell type found in the body. Just as importantly, these cells can, under the right conditions, be grown and expanded indefinitely in this unspecialized or “undifferentiated” state. These cells help researchers learn about early human developmental processes that are otherwise inaccessible, study diseases and establish strategies that could ultimately lead to therapies designed to replace or restore damaged tissues.

INDUCED PLURIPOTENT STEM CELLS

One of the hottest topics in stem cell research today is the study of induced pluripotent stem cells (iPS cells). These are adult cells (e.g., skin cells) that are engineered, or “reprogrammed,” to become pluripotent, i.e., behave like an embryonic stem cell. While these iPS cells share many of the same characteristics of embryonic stem cells, including the ability to give rise to all the cell types in the body, it is important to understand that they are not identical.

The original iPS cells were produced by using viruses to insert extra copies of three to four genes known to be important in embryonic stem cells into the specialized cell. It is not yet completely understood how these three to four “reprogramming” genes are able to induce pluripotency; this question is the focus of ongoing research. In addition, recent studies have focused on alternative ways of reprogramming cells using methods that are safer for use in clinical settings.



DISEASE-OR PATIENT-SPECIFIC PLURIPOTENT STEM CELLS

One of the major advantages of iPS cells, and one of the reasons that researchers are very interested in studying them, is that they are a very good way to make pluripotent stem cell lines that are specific to a disease or even to an individual patient. Disease-specific stem cells are powerful tools for studying the cause of a particular disease and then for testing drugs or discovering other approaches to treat or cure that disease. The development of patient-specific stem cells is also very attractive for cell therapy, as these cell lines are from the patient themselves and may minimize some of the serious complications of rejection and immunosuppression that can occur following

MOVING STEM CELLS INTO THE CLINIC

Clinical translation is the process used to turn scientific knowledge into real world medical treatments. Researchers take what they have learned about how a tissue usually works and what goes wrong in a particular disease or injury and use this information to develop new ways to diagnose, stop or fix what goes wrong. Before being marketed or adopted as standard of care, most treatments are tested through clinical trials. Sometimes, in attempting new surgical techniques or where the disease or condition is rare and does not have a large enough group of people to form a clinical trial, certain treatments might be tried on one or two people, a form of testing sometimes referred to as **innovative medicine**.

For more information on how science becomes medicine, please visit www.closerlookatstemcells.org.

CURRENT THERAPIES

Blood stem cells are currently the most frequently used stem cells for therapy. For more than 50 years, doctors have been using bone marrow transplants to transfer blood stem cells to patients, and more advanced techniques for collecting blood stem cells are now being used to treat leukemia, lymphoma and several inherited blood disorders. Umbilical cord blood, like bone marrow, is often collected as a source of blood stem cells and in certain cases is being used as an alternative to bone marrow transplantation.

Additionally, some bone, skin and corneal diseases or injuries can be treated by grafting tissues that are derived from or maintained by stem cells. These therapies have also been shown to be safe and effective.

POTENTIAL THERAPIES

Other stem cell treatments, while promising, are still at very early experimental stages. For example, the **mesenchymal stem cell**, found throughout the body including in the bone marrow, can be directed to become bone, cartilage, fat and possibly even muscle. In certain experimental models, these cells also have some ability to modify immune functions. These abilities have created considerable interest in developing ways of using mesenchymal stem cells to treat a range of musculoskeletal abnormalities, cardiac disease and some immune abnormalities such as graft-versus-host disease following bone marrow transplant.

REMAINING CHALLENGES

Despite the successes we have seen so far, there are several major challenges that must be addressed before stem cells can be used as cell therapies to treat a wider range of diseases.

First, we need to identify an abundant source of stem cells. Identifying, isolating and growing the right kind of stem cell, particularly in the case of rare adult stem cells, are painstaking and difficult processes. Pluripotent stem cells, such as embryonic stem cells, can be grown indefinitely in the lab and have the advantage of having the potential to become any cell in the body, but these processes are again very complex and must be tightly controlled. iPS cells, while promising, are also limited by these concerns. In both cases, considerable work remains to be done to ensure that these cells can be isolated and used safely and routinely.

Second, as with organ transplants, it is very important to have a close match between the donor tissue and the recipient; the more closely the tissue matches the recipient, the lower the risk of rejection. Being able to avoid the life-long use of immunosuppressants would also be preferable. The discovery of iPS cells has opened the door to developing patient-specific pluripotent stem **cell lines** that can later be developed into a needed cell type without the problems of rejection and immunosuppression that occur from transplants from unrelated donors.

Third, a system for delivering the cells to the right part of the body must be developed. Once in the right location, the new cells must then be encouraged to integrate and function together with the body's other cells.

GLOSSARY

Blastocyst

A very early embryo that has the shape of a ball and consists of approximately 150-200 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 a dish outside of the body.

Clinical translation

The process of using scientific knowledge to design, develop and apply new ways to diagnose, stop or fix what goes wrong in a particular disease or injury.

Differentiation

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

Embryo

The early developing organism; this term denotes the period of development between the fertilized egg and the fetal stage.

Embryonic stem cell

Cells derived from very early in development, usually the inner cell mass of a developing blastocyst. These cells are self-renewing (can replicate themselves) and pluripotent (can form all cell types found in the body).

Induced pluripotent stem (iPS) cell

Induced pluripotent cells (iPS cells) are stem cells that were engineered ("induced") from non-pluripotent cells to become pluripotent. In other words, a cell with a specialized function (for example, a skin cell) that has been "reprogrammed" to an unspecialized state similar to that of an embryonic stem cell.

Innovative medicine

Treatments that are performed on a small number of people and are designed to test a novel technique or treat a rare disease. These are done outside of a typical clinical trial framework.

In vitro fertilization

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

Mesenchymal stem cells

Mesenchymal stem cells were originally discovered in the bone marrow, but have since been found throughout the body and can give rise to a large number of connective tissue types such as bone, cartilage and fat.

Multipotent stem cells

Stem cells that can give rise to several different types of specialized cells, but in contrast to a pluripotent stem cell, are restricted to a certain organ or tissue types. For example, blood stem cells are multipotent cells that can produce all the different cell types that make up the blood but not the cells of other organs such as the liver or brain.

Pluripotent stem cells

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

Self-renewal

The process by which a cell divides to generate another cell that has the same potential.

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.

Tissue-specific stem cells

(also known as adult or somatic stem cells)

Stem cells found in different tissues of the body that can give rise to some or all of the mature cell types found within the particular tissue or organ from which they came, i.e., blood stem cells can give rise to all the cells that make up the blood, but not the cells of organs such as the liver or brain.

Totipotent stem cells

Stem cells that, under the right conditions, are wholly capable of generating a viable embryo (including the placenta) and, for humans, exist until about four days after fertilization, prior to the blastocyst stage from which embryonic stem cells are derived.