Stem Cells

Stem cells are cells present in all multicellular organisms that can multiply (self-renew) and differentiate. In humans, stem cells have the capacity to become every cell within an adult human being, for example, skin cells, brain cells, and blood cells.

In a developing embryo, stem cells can differentiate into all of the specialized embryonic tissues. In adult humans, stem and progenitor cells act as a repair system for the body, replenishing specialized cells.

Stem cell research has been active for over 50 years, because stem cells have a unique ability to divide and replicate repeatedly. In addition, their unspecialized nature allows them to become a wide variety of tissue types, which gives them enormous potential for use in regenerative medicine.

Several broad categories of stem cells exist, including:

• Embryonic Stem Cells (ESCs) – This is the only controversial stem cell type. ESCs are derived from blastocysts, a stage in the developing embryo. They can become any cell type within the human body.

• Perinatal Stem Cells – These cells are obtained during the period immediately before and after birth. Collection of these cell types does not impact the development of the fetus or newborn, so they are non-controversial.

• Adult Stem Cells – These are non-controversial cells found in living adults. Everyone has stem cells present in their bone marrow, fat (adipose tissue), and many other sites.

• Induced Pluripotent Stem Cells (iPS Cells) – iPS cells were discovered in 2006. They are non-controversial, because they are adult cells that are genetically reprogrammed in a lab. Like embryonic stem cells, they can become any cell within the body.

• Cancer Stem Cells (CSCs) – Cancer stem cells are a type of stem cell that biotech and pharma companies are exploring, because they play a role in facilitating the formation of tumors. Companies exploring CSCs are interested to discover how be manage and prevent cancer.

To make things simple, apply these definitions to classify stem cells by when they are collected during the human lifecycle:

• Embryonic stem cells– Stem cells derived from embryos (controversial)

• Pre-natal stem cells– Stem cells derived from the fetus or supporting structures (non-controversial)

• Post-natal stem cells– Stem cells derived from a recent newborn (noncontroversial)

• Adult stem cells– Stem cells derived from living humans (non-controversial). Common adult stem cell types include mesenchymal stem cells (MSCs), hematopoietic stem cells (HSCs), and neural stem cells (NSCs), among others.

Totipotent vs. Pluripotent vs. Multipotent

To understand the functional potential of each stem cell type, scientists like to describe to what degree each stem cell type can differentiate into other cell types. When assessing the functional potential of stem cells, you may use the following definitions:

• Totipotent stem cells– Cells that have the capacity to form an entire organism

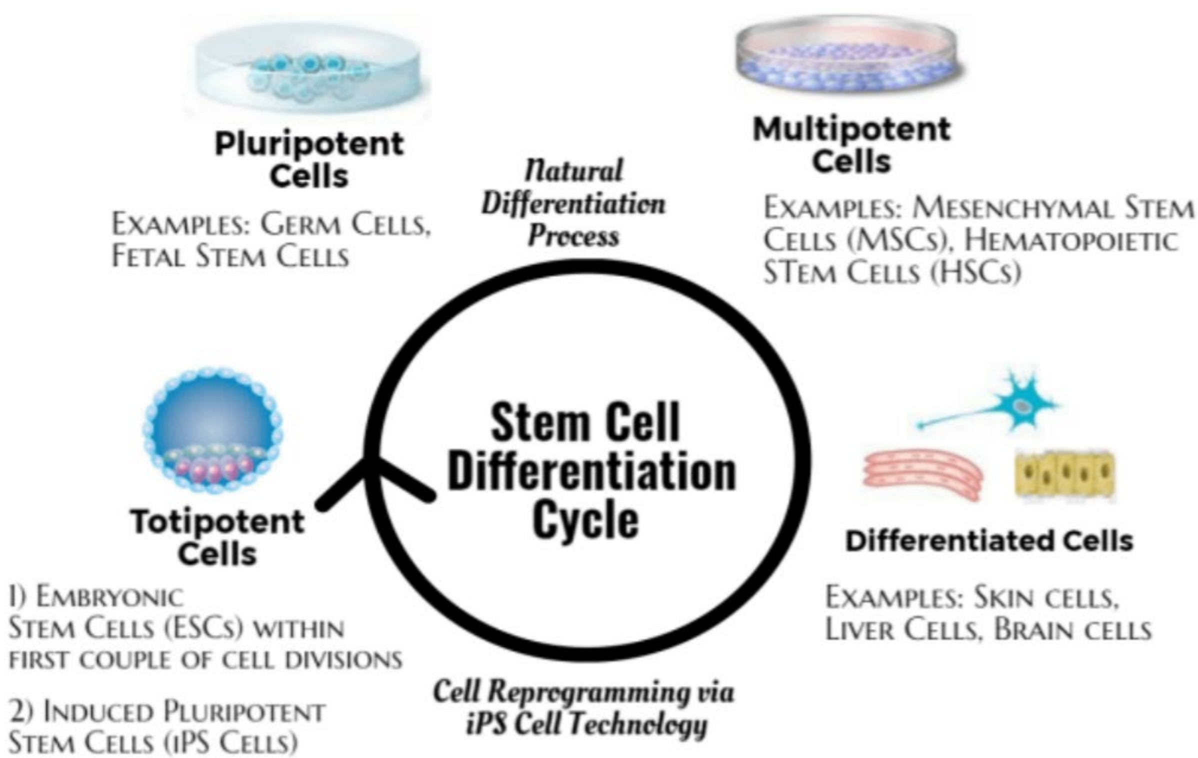
• Pluripotent stem cells – Can give rise to most, but not all, tissues within an organism

• Multipotent stem cells – Undifferentiated cells that are limited to giving rise to specific populations of cells

Human embryonic stem cells (hESCs) are totipotent cells that are derived from embryos that have been created in vitro at fertility clinics with informed donor consent. Embryonic stem cells are typically collected shortly after fertilization (within 4-5 days). At 5-6 days post-fertilization, embryonic stem cells begin to specialize, at which point they become pluripotent or multipotent cells.

Pluripotent and multipotent stem cells have a more limited differentiation capacity than totipotent stem cells. For example, multipotent blood stem cells can differentiate into red cells, white cells and platelets in the blood, but they cannot become any cell type.

The precise point at which a stem cell switches from a totipotent stem cell to a pluripotent or multipotent stem cell is often unclear. Furthermore, iPS cell technology allows us to reverse mature cell types back into a totipotent state. iPS cells are totipotent, so stem cells can now be collected at any point of the human lifecycle.



What are stem cell lines and why do researchers want to use them?

A stem cell line is a group of cells that all descend from a single original stem cell and are grown in a lab. Cells in a stem cell line keep growing but don't differentiate into specialized cells. Ideally, they remain free of genetic defects and continue to create more stem cells. Clusters of cells can be taken from a stem cell line and frozen for storage or shared with other researchers.

Stem Cell Risk:

One of the risks of totipotent stem cells (embryonic stem cells and iPS cells) is that they have the potential to produce uncontrolled proliferation. The biggest concern surrounding the clinical application of these cells is their tendency to form tumors. Pluripotent and multipotent stem cells have a lower risk of producing tumor formation, but can potentially create growth of the wrong tissue type for a given location within the human body. Additionally, iPS cells are artificially manipulated in a laboratory process, so there is the possibility that the cells can act in unexpected ways.

Because many of these risks can be mitigated and monitored, stem cells are currently being investigated in hundreds of clinical trials worldwide. The majority of these clinical trials involve the use of mesenchymal stem cells (MSCs) and hematopoietic stem cells (HSCs). You can view approximately three-quarters of active stem cell trials worldwide by visiting ClinicalTrials.gov.

Stem Cell Research

*The National Institutes of Health Guidelines for Human Stem Cell Research (*Guidelines*)* pertain to extramural NIH-funded stem cell research. These *Guidelines* establish policy and procedures under which the NIH will fund research involving human embryonic stem cells (hESCs) and certain uses of human induced pluripotent stem cells (iPSCs) and work to ensure such research is ethically responsible, scientifically worthy and conducted in accordance with applicable law.

The University of Massachusetts Amherst is responsible for ensuring that all stem cell research conducted at or sponsored by the University complies with the Guidelines. Compliance authority on campus is placed with the Institutional Biosafety Committee (IBC). The IBC reviews stem cell research and approves those projects in conformity with the *Guidelines* and in accordance with the general principles expressed in the Guidelines for Human Embryonic Stem Cell Research (National Academies' of Science, 2005) and its subsequent amendments.

Researchers at the University of Massachusetts Amherst must be in compliance with the *Guidelines*, irrespective of the source of funding.

Eligibility of Human Embryonic Stem Cells for Research

The eligibility of hESCs for research purposes is governed by the NIH. Researchers may use hESCs that are posted on the NIH Registry or they may establish eligibility for NIH Funding by submitting a compliance of assurance with Section II (A) of the Guidelines. The Institutional Review Board (IRB) will review the compliance of assurance and any part of a research project that meets the federal definitions of human subject research and/or clinical investigation.

Stem Cell Research Registration

Principal investigators (PIs) involved in stem cell research are responsible for:

- Reviewing the Guidelines.
- Completing an IBC protocol in eProtocol.

The University of Massachusetts Amherst follows the procedures and policies as outlined in the Guidelines and expressed in the Guidelines for Human Embryonic Stem Cell Research and its subsequent amendments. These policies and procedures, and the review procedures of the IBC, are summarized in IBC's Policy and Procedures.

Resources:

National Institutes of Health Guidelines for Human Stem Cell Research

NIH Human Embryonic Stem Cell Registry