

What are Stem Cells?

Stem cells are a class of undifferentiated cells that are able to differentiate into specialized cell types. Commonly, stem cells come from two main sources:

1. Embryos formed during the blastocyst phase of embryological development (embryonic stem cells) and
2. Adult tissue (adult stem cells).

Both types are generally characterized by their potency, or potential to differentiate into different cell types (such as skin, muscle, bone, etc.).

Adult stem cells

Adult or somatic stem cells exist throughout the body after embryonic development and are found inside of different types of tissue. These stem cells have been found in tissues such as the brain, bone marrow, blood, blood vessels, skeletal muscles, skin, and the liver. They remain in a quiescent or non-dividing state for years until activated by disease or tissue injury.

Adult stem cells can divide or self-renew indefinitely, enabling them to generate a range of cell types from the originating organ or even regenerate the entire original organ. It is generally thought that adult stem cells are limited in their ability to differentiate based on their tissue of origin, but there is some evidence to suggest that they can differentiate to become other cell types.

Embryonic stem cells

Embryonic stem cells are derived from a four- or five-day-old human embryo that is in the blastocyst phase of development. The embryos are usually extras that have been created in IVF (in vitro fertilization) clinics where several eggs are fertilized in a test tube, but only one is implanted into a woman.

Sexual reproduction begins when a male's sperm fertilizes a female's ovum (egg) to form a single cell called a zygote. The single zygote cell then begins a series of divisions, forming 2, 4, 8, 16 cells, etc. After four to six days - before implantation in the uterus - this mass of cells is called a blastocyst. The blastocyst consists of an inner cell mass (embryoblast) and an outer cell mass (trophoblast). The outer cell mass becomes part of the placenta, and the inner cell mass is the group of cells that will differentiate to become all the structures of an adult organism. This latter mass is the source of embryonic stem cells - totipotent cells (cells with total potential to develop into any cell in the body).

In a normal pregnancy, the blastocyst stage continues until implantation of the embryo in the uterus, at which point the embryo is referred to as a fetus. This usually occurs by the end of the 10th week of gestation after all major organs of the body have been created.

However, when extracting embryonic stem cells, the blastocyst stage signals when to isolate stem cells by placing the "inner cell mass" of the blastocyst into a culture dish containing a nutrient-rich broth. Lacking the necessary stimulation to differentiate, they begin to divide and replicate while maintaining their ability to become any cell type in the human body. Eventually, these undifferentiated cells can be stimulated to create specialized cells.

Stem cell cultures

Stem cells are either extracted from adult tissue or from a dividing zygote in a culture dish. Once extracted, scientists place the cells in a controlled culture that prohibits them from further specializing or differentiating but usually allows them to divide and replicate. The process of growing large numbers of embryonic stem cells has been easier than growing large numbers of adult stem cells, but progress is being made for both cell types.

Stem cell lines

Once stem cells have been allowed to divide and propagate in a controlled culture, the collection of healthy, dividing, and undifferentiated cells is called a stem cell line. These stem cell lines are subsequently managed and shared among researchers. Once under control, the stem cells can be stimulated to specialize as directed by a researcher - a process known as directed differentiation. Embryonic stem cells are able to differentiate into more cell types than adult stem cells.

Potency

Stem cells are categorized by their potential to differentiate into other types of cells. Embryonic stem cells are the most potent since they must become every type of cell in the body. The full classification includes:

- Totipotent - the ability to differentiate into all possible cell types. Examples are the zygote formed at egg fertilization and the first few cells that result from the division of the zygote.
- Pluripotent - the ability to differentiate into almost all cell types. Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation.
- Multipotent - the ability to differentiate into a closely related family of cells. Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets.
- Oligopotent - the ability to differentiate into a few cells. Examples include (adult) lymphoid or myeloid stem cells.
- Unipotent - the ability to only produce cells of their own type, but have the property of self-renewal required to be labeled a stem cell. Examples include (adult) muscle stem cells.

Embryonic stem cells are considered pluripotent instead of totipotent because they do not have the ability to become part of the extra-embryonic membranes or the placenta.

Identification of stem cells

Although there is not complete agreement among scientists of how to identify stem cells, most tests are based on making sure that stem cells are undifferentiated and capable of self-renewal. Tests are often conducted in the laboratory to check for these properties.

One way to identify stem cells in a lab, and the standard procedure for testing bone marrow or hematopoietic stem cell (HSC), is by transplanting one cell to save an individual without HSCs. If the stem cell produces new blood and immune cells, it demonstrates its potency.

Clonogenic assays (a laboratory procedure) can also be employed in vitro to test whether single cells can differentiate and self-renew. Researchers may also inspect cells under a microscope to see if they are healthy and undifferentiated or they may examine chromosomes.

To test whether human embryonic stem cells are pluripotent, scientists allow the cells to differentiate spontaneously in cell culture, manipulate the cells so they will differentiate to form specific cell types, or inject the cells into an immunosuppressed mouse to test for the formation of a teratoma (a benign tumor containing a mixture of differentiated cells).

Research with stem cells

Scientists and researchers are interested in stem cells for several reasons. Although stem cells do not serve any one function, many have the capacity to serve any function after they are instructed to specialize. Every cell in the body, for example, is derived from first few stem cells formed in the early stages of embryological development. Therefore, stem cells extracted from embryos can be induced to become any desired cell type. This property makes stem cells powerful enough to regenerate damaged tissue under the right conditions.

Organ and tissue regeneration

Tissue regeneration is probably the most important possible application of stem cell research. Currently, organs must be donated and transplanted, but the demand for organs far exceeds supply. Stem cells could potentially be used to grow a particular type of tissue or organ if directed to differentiate in a certain way. Stem cells that lie just beneath the skin, for example, have been used to engineer new skin tissue that can be grafted on to burn victims.

Brain disease treatment

Additionally, replacement cells and tissues may be used to treat brain disease such as Parkinson's and Alzheimer's by replenishing damaged tissue, bringing back the specialized brain cells that keep unneeded muscles from moving. Embryonic stem cells have recently been directed to differentiate into these types of cells, and so treatments are promising.

Cell deficiency therapy

Healthy heart cells developed in a laboratory may one day be transplanted into patients with heart disease, repopulating the heart with healthy tissue. Similarly, people with type I diabetes may receive pancreatic cells to replace the insulin-producing cells that have been lost or destroyed by the patient's own immune system. The only current therapy is a pancreatic transplant, and it is unlikely to occur due to a small supply of pancreases available for transplant.

Blood disease treatments

Adult hematopoietic stem cells found in blood and bone marrow have been used for years to treat diseases such as leukemia, sickle cell anemia, and other immunodeficiencies. These cells are capable of producing all blood cell types, such as red blood cells that carry oxygen to white blood cells that fight disease. Difficulties arise in the extraction of these cells through the use of invasive bone marrow transplants. However hematopoietic stem cells have also been found in the umbilical cord and placenta. This has led some scientists to call for an umbilical cord blood bank to make these powerful cells more easily obtainable and to decrease the chances of a body's rejecting therapy.

General scientific discovery

Stem cell research is also useful for learning about human development. Undifferentiated stem cells eventually differentiate partly because a particular gene is turned on or off. Stem

cell researchers may help to clarify the role that genes play in determining what genetic traits or mutations we receive. Cancer and other birth defects are also affected by abnormal cell division and differentiation. New therapies for diseases may be developed if we better understand how these agents attack the human body.

Another reason why stem cell research is being pursued is to develop new drugs. Scientists could measure a drug's effect on healthy, normal tissue by testing the drug on tissue grown from stem cells rather than testing the drug on human volunteers.

Stem cell controversy

The debates surrounding stem cell research primarily are driven by methods concerning embryonic stem cell research. It was only in 1998 that researchers from the University of Wisconsin-Madison extracted the first human embryonic stem cells that were able to be kept alive in the laboratory. The main critique of this research is that it required the destruction of a human blastocyst. That is, a fertilized egg was not given the chance to develop into a fully-developed human.

When does life begin? The core of this debate - similar to debates about abortion, for example - centers on the question, "When does life begin?" Many assert that life begins at conception, when the egg is fertilized. It is often argued that the embryo deserves the same status as any other full grown human. Therefore, destroying it (removing the blastocyst to extract stem cells) is akin to murder. Others, in contrast, have identified different points in gestational development that mark the beginning of life - after the development of certain organs or after a certain time period.

People also take issue with the creation of chimeras. A chimera is an organism that has both human and animal cells or tissues. Often in stem cell research, human cells are inserted into animals (like mice or rats) and allowed to develop. This creates the opportunity for researchers to see what happens when stem cells are implanted. Many people, however, object to the creation of an organism that is "part human".

The stem cell debate has risen to the highest level of courts in several countries. Production of embryonic stem cell lines is illegal in Austria, Denmark, France, Germany, and Ireland, but permitted in Finland, Greece, the Netherlands, Sweden, and the UK. In the United States, it is not illegal to work with or create embryonic stem cell lines. However, the debate in the US is about funding, and it is in fact illegal for federal funds to be used to research stem cell lines that were created after August 2001.

Questions

1. Where do stem cells originate from (2)? What property defines both as stem cells?
2. What does the term quiescent mean?
3. What role do adult stem cells have in the body?
4. What is a blastocyst? Where are stem cells located within the blastocyst?
5. How can a cell's differentiation be directed?
6. Describe the 5 different classes of potency that cells can acquire.
7. What are the 2 criteria that are commonly accepted to define a stem cell?
8. For each of the following situation describe how stem cells could be used to help
 - a. Organ and tissue regeneration
 - b. Brain disease
 - c. Cell deficiency
 - d. Blood disease
9. Describe why stem cell research has been controversial over the years.