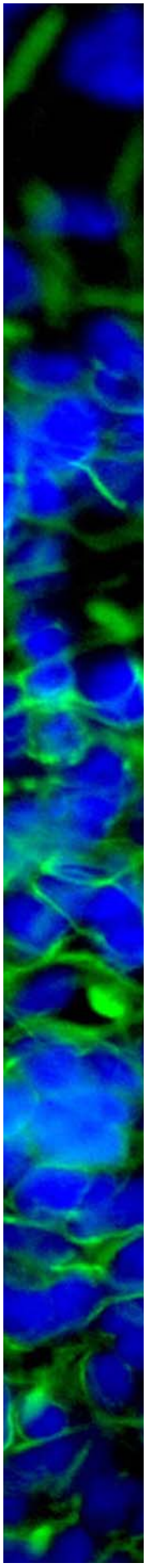
Australian Stem Cell Centre



Fact Sheet

Types of Stem Cells

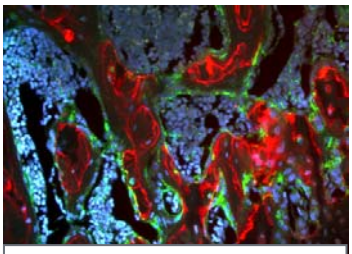
The body is made up of about 200 different kinds of specialised cells such as muscle cells, nerve cells, fat cells and skin cells. All specialised cells originate from stem cells. A stem cell is a cell that is not yet specialised. The process of specialisation is called differentiation and once the differentiation pathway of a stem cell has been decided, it can no longer become another type of cell. A stem cell that can become every type of cell in the body is called pluripotent whilst a stem cell that can become only some types of cells is called multipotent. Stem cells are found in the early embryo, the fetus, placenta, umbilical cord, and in many different tissues of the adult body.

Stem cells are often divided into two groups: adult stem cells and embryonic stem cells. Adult stem cells are derived from, or resident in, fetal or adult tissue, and can usually only give rise to the cells of that tissue, thus they are considered multipotent. Embryonic stem cells, derived from a small group of cells within the very early embryo, and their new counterpart induced pluripotent stem (iPS) cells are considered pluripotent as they can become every type of cell in the body.

Adult Stem Cells

Adult stem cells are undifferentiated cells found in the tissues and organs of the body. They are capable of self-renewal. Their differentiation is mainly restricted to forming the cell types of that tissue or organ. The chief role of adult stem cells is to maintain and repair the tissue in which they are found. Skin stem cells, for example, give rise to new skin cells, ensuring that old or damaged skin cells are replenished.

It now appears that all tissues probably contain adult stem cells, but only in very small numbers. In each tissue, they are used to produce new mature cells as old ones die in the natural processes of senescence. They may also remain dormant until activated by disease or injury. Their small numbers make adult stem cells difficult to isolate but they have been successfully isolated from the brain, bone marrow, blood, muscle, skin, pancreas and liver. Most research has been carried out on haematopoietic (blood forming) stem cells isolated from bone marrow and blood.

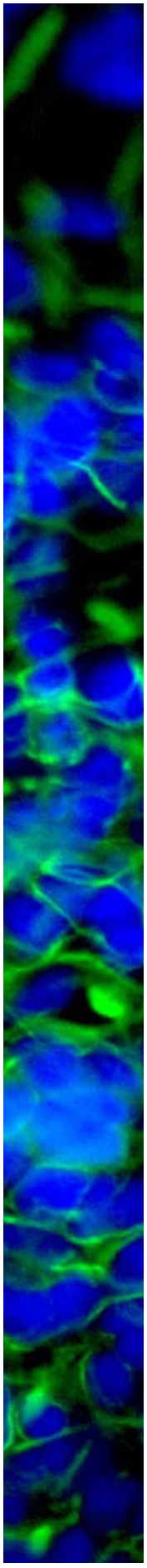


Adult mouse bone marrow

Within the body, adult stem cells normally only generate the cell types of the tissue in which they are found. Haematopoietic stem cells, for example, are found in the bone marrow and give rise to the many types of cells found in the blood, including red and white blood cells and platelets. The existence of these types of stem cells has been known for a long time and bone marrow transplants containing such cells have been used for over 50 years to treat people with a variety of life-threatening disorders such as lymphomas, leukaemia and thalassemia.

Although adult stem cells are less versatile than embryonic stem cells, their use in research is less topical as it does not involve the destruction of embryos. Their potential use for cell-based therapies is also attractive as it may be possible to use a patient's own stem cells to generate tissue for transplantation, thus avoiding problems with immune rejection.

One of the potential hurdles for the use of adult stem cells for transplants is their limited ability to generate different cell types. Recent experiments, however, have revealed that, under some experimental conditions, certain types of adult stem cells from one tissue may be able to colonise a completely different tissue. This phenomenon is called plasticity and some researchers believe



that adult stem cells may, in the future, may be as useful as embryonic stem cells in generating tissue for transplants. A major focus of current research is the investigation of factors and conditions that control the differentiation of adult stem cells in the laboratory.

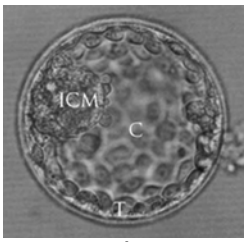
Umbilical Cord Blood Stem Cells

Umbilical cord blood stem cells are a type of adult stem cell. Blood can be collected from the umbilical cord of a newborn baby shortly after birth. This blood is rich in blood stem cells that can be used to generate red blood cells and cells of the immune system. Cord blood stem cells may be used to treat a range of blood disorders and immune system conditions such as leukaemia, anaemia and autoimmune diseases. Once collected, cord blood can be stored in a cord blood bank for future use as a potential source of stem cells for transplant.

Embryonic Stem Cells

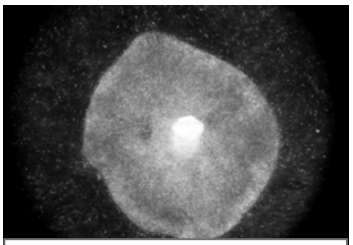
Embryonic stem cells can replicate and generate every cell type of the body.

Human embryonic stem cells are derived from human blastocysts (early stage embryos) that are five to seven days old. These blastocysts are donated with consent from patients who have completed their infertility treatment specifically for research. At this stage of development the blastocyst is a hollow ball of about 150 cells and no bigger than a pinhead. Within the blastocyst, next to a large internal cavity (C), is a small group of approximately 30 cells called the inner cell mass (ICM). The outer layer is the trophectoderm (T).



Human Blastocyst

The ICM cells are able to develop into any type of cell in our body and can contribute to all the cells and tissues of the adult organism. These types of cells are called pluripotent and it is this pluripotency that makes them of interest to researchers. Embryonic stem cells are isolated from the blastocyst when the inner cell mass is removed and cultured in the laboratory. During this process the blastocyst is destroyed.

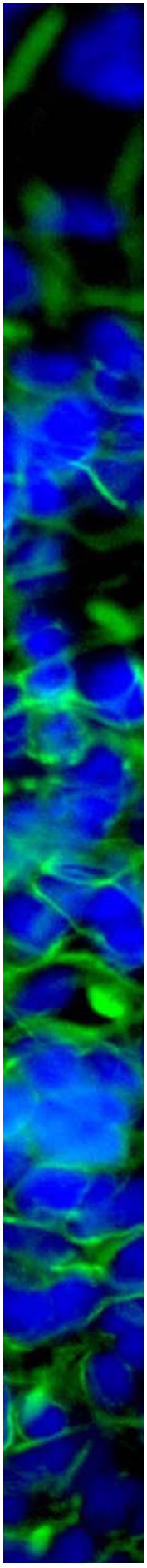

Human embryonic stem cell colony

Once the cells have been isolated they can be grown continuously in a laboratory culture dish that contains a nutrient-rich culture medium. As the stem cells divide and spread over the surface of the dish some are removed to populate fresh subcultures to form a stem cell line. Because these cells have the ability to keep dividing (self-renewing), large numbers of embryonic stem cells can be grown in the laboratory and also frozen for future use. Therefore, established HESC lines can be maintained in laboratories for research, shared between researchers and ultimately used in cell-based therapies.

Somatic Cell Nuclear Transfer (SCNT) or Therapeutic Cloning

SCNT refers to the removal of a nucleus, which contains the genetic material or DNA, from virtually any cell of the body and its transfer by injection into an unfertilised egg (oocyte) from which the nucleus has also been removed. The newly reconstituted egg is then stimulated to start dividing. After 5-7 days in culture, embryonic stem cells can then be removed and used to create many embryonic stem cells in culture. These embryonic stem cell lines are genetically identical to the cell from which the DNA was originally removed.

SCNT may have applications in the creation of embryonic stem cells which can then be used for the development of patient- and disease-specific cell-based therapies as well as the production of stem cells with specific disease characteristics for research purposes. The use of a patient's

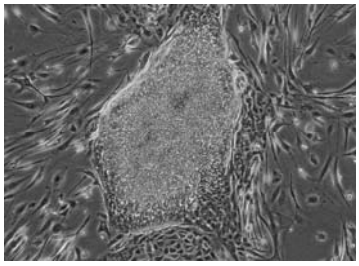


own cells for tissue replacement through SCNT may overcome the problem of immune rejection that is a major complication of tissue or organ transplantation today.

SCNT is commonly referred to as therapeutic cloning. The word 'cloning' often conjures up images of cloning an individual (reproductive cloning) such as the process used to create Dolly the sheep. Using SCNT to create a human embryo to implant into a uterus is illegal in Australia and many parts of the world. The scientific community overwhelmingly rejects reproductive cloning, but SCNT may provide an invaluable tool for basic research. However, whilst the technology has been proven in many species it has yet to produce a stem cell line in humans. A major breakthrough occurred in November 2007 when a group of scientists reported that they had successfully extracted stem cells from monkey embryos generated by SCNT.

Induced Pluripotent Stem Cells (iPS)

In November 2007, a significant development occurred when scientists announced they had developed a new technology to cause mature human cells to resemble pluripotent stem cells similar in many ways to hESCs. These reprogrammed cells are referred to as induced pluripotent stem (iPS) cells.



Human iPS Cells

Initially iPS cells were generated using viruses to genetically engineer mature cells to achieve a pluripotent status. The purpose of the virus was to insert reprogramming genes into a cell such as a skin cell and then culture the cells in the laboratory for 4-5 weeks after which a small number of iPS cells begin to appear. However technologies for reprogramming cells are moving very quickly and researchers are now investigating the use of new methods that do not remain in the cells causing permanent and potentially harmful changes. These new technologies currently utilise different types of non-integrating viruses and chemicals and small molecules.

Similar to SCNT, this technology allows scientists a new method of creating diseased cells for research by using mature cells from a patient with a genetic disease, such as Huntington's disease, and turning those cells into iPS cells. Such disease-specific stem cells may enable disease investigation and drug development offer a unique opportunity to recreate both normal and diseased human tissue formation in the laboratory. iPS technology also has the potential to produce genetically identical "patient specific" embryonic stem cell-like lines that would be recognised as "self" and not rejected by the patient they were made from.

Whilst the discovery of iPS cells is a significant breakthrough in the field of reprogramming, the use of iPS cells in the clinic is many years away - if it occurs at all - as several significant hurdles need to be overcome. It is still unclear how genetically stable or safe iPS cells will be for potential clinical use. More research needs to be done into induced pluripotent stem cells to discover if they will offer the same equivalent research value as embryonic stem cells. Having only recently discovered these cells, scientist are yet to confirm if iPS cells have the ability to divide and remain chromosomally stable like embryonic stem cells over a long period of time.