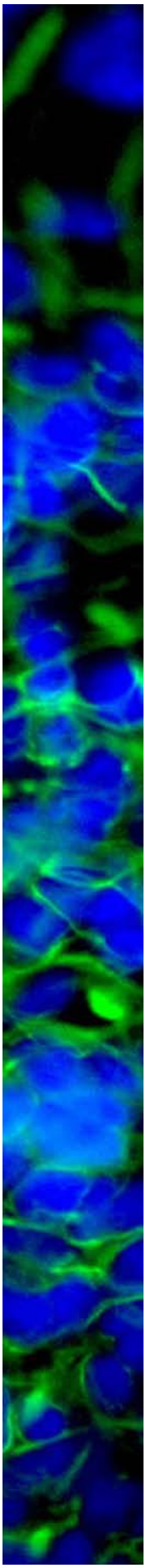


Fact Sheet 2

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: tissue specific stem cells (often referred to as adult stem cells) and pluripotent stem cells (including embryonic stem cells and induced pluripotent stem cells). Tissue specific 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.

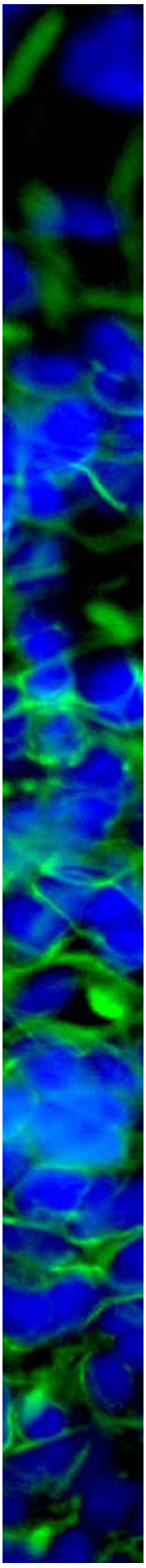
Tissue Specific Stem Cells

Tissue specific 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 tissue specific 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. Most tissues contain only tiny numbers of stem cells. The exception is bone marrow and umbilical cord blood which contains relatively high numbers of stem cells. In each tissue, adult stem cells are used to produce new mature cells as old ones die in the natural processes of ageing. They may also be activated by disease or injury. Due to their small numbers isolation of adult stem cells is difficult but they have been successfully isolated from the brain, bone marrow, blood, muscle, skin, lung, pancreas and liver. To date the majority of research has been carried out on haematopoietic stem cells isolated from bone marrow and umbilical cord blood and on mesenchymal stem cells which can also be sourced from the bone marrow and some other tissues. Mesenchymal stem cells are the stem cells that form our fat, muscle, bone and cartilage and they can also differentiate into nerve cells.

Haematopoietic stem cells are the stem cells from which all blood cells and many of the cells of our adult immune system are derived. These are the stem cells with the longest history of clinical use in treating disorders such as leukaemia via bone marrow transplants. There has recently been much interest in whether haematopoietic stem cells can be caused to differentiate into non blood cells, such as heart muscle cells or even nerve cells.

Mesenchymal stem cells can be found in the bone marrow but are also found in several other sites in the body such as the placenta. Mesenchymal stem cells are particularly interesting to researchers because in addition to their capacity to differentiate into the multiple cell types listed above, they also have anti-inflammatory and immune-suppressing properties. This means that mesenchymal stem cells could be useful as therapies for diseases caused by immune attack on specific tissues.



Umbilical cord blood stem cells are a type of tissue specific stem cell. Blood can be collected from the umbilical cord of a newborn baby shortly after birth. This blood is rich in haematopoietic stem cells that can be used to generate 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.

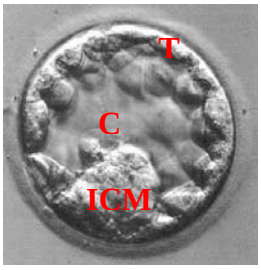
Pluripotent Stem Cells

Embryonic Stem Cells

Discovered in 1998, human embryonic stem cells (hESCs) are the most primitive type of stem cell and can replicate and generate every cell type of the human body.

Human embryonic stem cells are derived from human blastocysts (early stage embryos) that are five to seven days old. In Australia these blastocysts are donated for research with consent from patients who have completed treatment for infertility, and have surplus embryos. At this stage of development the blastocyst is a hollow ball of about 150 cells and no bigger than a pinhead. Figure 1 demonstrates the different parts of the blastocyst, showing that 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). The inner cell mass is what ultimately becomes the embryo, and the trophectoderm becomes the placenta.

Figure 1: Human Blastocyst



The inner cell mass 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 research and therapy. 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.

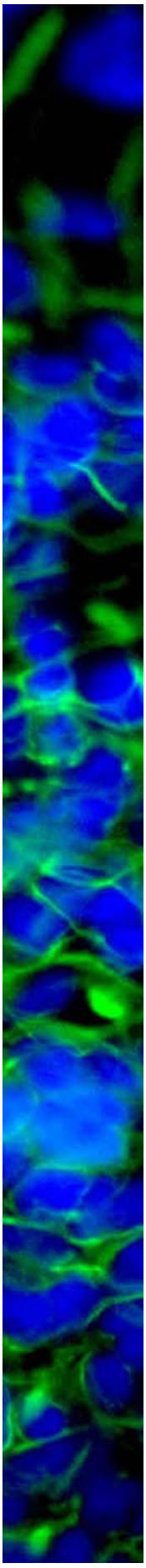
Once the cells have been isolated they can be grown continuously in a laboratory culture dish that contains a nutrient-rich culture medium. As the stem cells divide and spread over the surface of the dish some are removed to populate fresh subcultures to form a stem cell line. Because these cells have 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 maybe 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 entity 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.

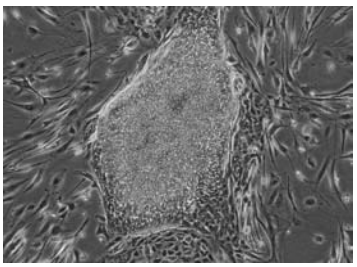


Figure 2: Human iPS Cells

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 offering 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, however there is much to be understood before this could be achieved.

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.