Department of Health

What are stem cells and where are they found?

Stem cells occur in the early embryo (five days old) when it is a tiny ball of about 100 cells before it implants in the uterus. These are known as embryonic stem cells or ES cells.

Embryonic stem cells can be found in embryos created by in vitro fertilisation technique. In vitro or 'test tube' fertilisation occurs when an egg and a sperm are mixed together in the laboratory and fertilisation occurs outside the body.

Embryonic stem cells can be obtained from embryos that are not needed for infertility treatment or created specifically for research. They can also be found in early embryos created by inserting the nucleus from an adult cell into an egg with its nucleus removed - a technique known as cell nuclear replacement (sometimes called "cloning").

Other stem cells also occur in significant numbers in fetal tissue and in cord blood at birth. They can also be found in small numbers in adults and children, although these are harder to isolate. For example, we all have blood stem cells, which are found in the bone marrow, and continuously replenish the body's red blood cells, white blood cells, and platelets.

Why are they so important?

Scientists want to make use of stem cells' ability to grow into any kind of cell to develop new cell-based treatments. It is hoped that stem cells can be grown to substitute dead or diseased cells in a number of organs.

This would mean treatment for potentially hundreds of thousands of people suffering from currently incurable degenerative diseases such as Parkinson's, Alzheimer's and diabetes. In theory, stem cells could be collected, grown and stored to provide a plentiful supply of healthy replacement tissue for transplantation into any part of the body using much less invasive surgery than conventional treatments.

Stem cells can also potentially be used to develop new skin for burns patients, in the culture of tissue to repair diseased organs, and to provide new healthy bone marrow cells for cancer patients.

The successful application of stem cell research will depend upon:

- whether stem cells can be successfully isolated and grown in the laboratory;
- whether stem cells grown in the laboratory can be influenced to turn into specific cell types;
- whether stem cells that have formed particular cell types could be used to treat patients whose tissue was disease or damaged through injury;
- whether tissue grown in this way would develop normally or whether there might be risks to the patient.

Possible use of tissue derived from stem cells to treat disease

Cell type	Target disease
Neural (nerve) cells	Stroke, Parkinson's, Alzheimer's, spinal cord injury, MS
Heart muscle cells	Heart attacks, congestive heart failure,

Insulin producing cells	Diabetes
Cartiledge cells	Osteoarthritis
Blood cells	Cancer, immunodeficiencies, inherited blood diseases, leukamia
Liver cells	Hepatitis, cirrhosis
Skin cells	Burns, Wound healing
Bone cells	Osteoporosis
Retinal cells	Macular degeneration
Skeletal muscle cells	Muscular dystrophy

Is stem cell research new?

Stem cell research began as early as the 1950s, when scientists began experimenting with mice. Mouse ES cells were first isolated and successfully cultivated in 1981 by a group led by Martin Evans at the University of Cambridge.

Adult stem cells are already an important element in medical care. Bone marrow transplantation depends on the presence of stem cells in the bone marrow, which naturally re-populate the white and red blood cells and blood platelets. This is particularly crucial after cancer chemotherapy.

A recent breakthrough

In July 2002, a leukaemia sufferer become **the first adult in the UK to undergo a stem cell transplant using blood from a baby's umbilical cord.** Stephen Knox, 31, underwent the treatment - previously only performed in the UK on children - after being given just months to live. His cancer went into remission.

Professor Stephen Proctor, of the University of Newcastle, used stem cell blood from discarded placentas and umbilical cords. Previously this type of procedure had been carried out in Spain and Canada.

It is too early to say whether this type of treatment will be successful for other patients. In Spain, the results have varied with the survival rate after two years at 44 per cent. NHS cord blood banks are currently very small - there are about only 5,000 cords stored in total.

Embryonic stem cell research is but one strand of stem cell research. **Adult, fetal and cord blood cells have been available to researchers for longer, and the bulk of research being published at the moment is based on these rather than ES cells.** No one can predict exactly where breakthroughs will come.

The Government's position is that stem cell research is not a matter of one type versus another. The Government wishes to see responsible, ethical and high quality research using all sources of stem cells because this will offer the best chance of developing life saving treatments.

First ES cells cultivated

In 1996 James Thomson of the University of Wisconsin was the first to culture ES cells from non-human primates. His group followed this in 1998 by successfully culturing human ES cells using embryos that had been donated for research.

Because embryonic stem cells are the precursor cells to all other cell types in the human body, this research has set the stage for a revolution in medicine and basic biology.

Adult stem cells

Many adult stem cells are difficult to isolate. Those found in adult tissue are called multipotent because their function is to replace cells that are lost due to depletion or damage. For example, adult stem cells found in bone marrow work to replace different types of blood cells.

To date, it has been generally thought that adult stem cells are more limited in the type of cell they may go on to form. It is also much harder to control their differentiation into their desired end cell-types.

New research

Two recent research papers highlight the importance of pursuing research using all sources of stem cells.

Ron McKay and colleagues at the National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, generated a specific class of neurons from cultured mouse ES cells and used the neurons to reverse symptoms of Parkinson's Disease in rats. In other words, the team showed that cells derived from ES cell lines could be used for therapeutic treatment in animals.

Meanwhile, a team from the University of Minnesota Stem Cell Institute, led by Dr Catherine Verfaillie, derived one particular type of cell from the bone marrow of adult mice and rats that appears to be more versatile. It remains to be seen whether these stem cells have the equivalent treatment potential of embryonic stem cells such as that demonstrated by McKay.

Both studies highlight the need for ongoing research making use of both adult and embryonic stem cells to ensure that effective, safe cell-based therapies can be developed.

The research was published in Nature magazine, June 2002

Where do scientists get embryonic stem cells for research purposes?

Until recently the main source of ES cells was from embryos that have not been used during fertility treatment (IVF). These embryos are created in vitro ('test tube') from egg and sperm. Over 50,000 embryos were donated for research purposes between 1991 and 1999 in the UK under the terms of the 1990 Human Fertilisation and Embryology Act.

Where does cloning fit into all this?

In the future, a second source of ES cells could be from embryos created using the **cell nuclear replacement technique (CNR)**. This technique was used to create Dolly the sheep in 1997 and it proved that embryos could be created without the use of sperm.

It is important to be clear that this does not permit a cloned baby to be created.

The fertilised egg may be kept for a maximum of 14 days. Cell nuclear replacement involves inserting the nucleus of a cell from one of the body's organs into an unfertilised egg (oocyte) which has had its nucleus removed. This process is often referred to as cloning.

If the cell nuclear replacement process is stopped after five to six days, embryonic stem cells can be extracted and it is hoped that these cells will have the same potential as ES cells derived from embryos produced by egg and sperm. This is known as therapeutic cloning.

This technique could potentially be used to clone a patient's DNA, harvest the stem cells, and then grow them into the type of tissue needed. It is hoped that tissue cultivated in this way would have the advantage of being free from rejection because it would be genetically compatible with the person being treated. It would also provide a steady supply of stem cells for human research.

Mitochondrial Disease - preventing serious handicap

A different kind of cell nuclear replacement could be used to help women avoid the birth of a child with inherited mitochondrial disease. Maternally inherited defective mitochondrial genes can have very serious consequences, including blindness, deafness, epilepsy and infant death. Mitochondria are components of the cell inherited from the mother's egg; they carry their own genes and are crucial to fundamental processes in all the body's cells.

Theoretically if the nucleus from the mother's egg was inserted into a donor egg, which had both healthy mitochondrial DNA and its nucleus removed, the defective genes should not be passed on. The new egg could then be fertilised by the sperm of the woman's partner by in vitro ('test tube') fertilisation techniques.

This would be the only way for a woman to have a child genetically related but free from mitochondrial disorders. The child would be a new genetic individual and would not be a clone. Brazilian scientists reported they had created an embryo using this procedure, known as oocyte nucleus transfer, in May 2003.

Are there safety issues to consider?

Any new treatments require extensive development and testing before they can be used for humans. Stem cell therapies do raise several safety issues. There is risk of tumour formation if cells are inappropriately or incompletely differentiated. There is concern that stem cells cultivated using the cell nuclear replacement technique may age at different rates to normal cells.

There is also the question of rejection. As discussed above, if stem cells are not exactly identical genetically (due to the presence of mitochondria), what implications does this have for any patients receiving stem cell transplants?

Essential work still has to be done to establish the long term safety of the technique.

DH Department of Health