



Parkinson's
Disease Society

Stem Cell Research

What are stem cells and where do you find them?

Stem cells are unspecialised cells that can divide to produce copies of themselves and they also have the ability to develop into different types of cells, for example skin, blood, brain and bone, by a process known as differentiation. Stem cells are found at many different sites in the developing and adult body and brain. They also have the ability to renew themselves for long periods and, because they are so versatile, could potentially be used to repair and renew cells in the body and brain.

Stem cells can be derived from several sources, including the very earliest stages of embryo formation, aborted fetuses, blood cells taken from the umbilical cord at birth, bone marrow, and even the adult brain.

The cells derived from the early embryo, known as embryonic stem cells (or ES cells), are of particular interest to researchers because they have the ability to develop into all cell types found in the human body. These are one of the main types of stem cell that Parkinson's disease research is concentrating on.

In the UK, human ES cells can be collected from surplus embryos produced as part of In vitro fertilisation (IVF) programmes. This can only be done legally under strict UK guidelines issued by the Human Fertilisation and Embryology Authority (HFEA).

These ES cells, while showing great promise for the treatment of Parkinson's, also carry with them a risk of uncontrolled growth, which could lead to problems such as the formation of tumours. Much more research is therefore needed in order for scientists to understand how stem cells work and how they can be used to produce a viable treatment for Parkinson's and many other medical conditions.

An alternative source of stem cells is from the developing foetus, including the brain. These cells divide easily but do not like to form dopamine-producing nerve cells (the cells in short supply in the brains of people with Parkinson's), so before they can be useful for Parkinson's, detailed research is being carried out in order to identify the factors that stimulate this

transformation. It is important to note that these cells are different from those used in foetal brain cell implant surgery. Further information on brain implants is provided later in this information sheet.

Although adult stem cells exist, these are currently not as useful for research purposes because they are only found in relatively small numbers in certain parts of the body and do not replicate rapidly. However, some treatments using adult stem cells do exist to treat some conditions, such as bone marrow transplants to treat leukaemia. It may be that adult brain stem cells can be activated to form nerve cells and if so, then they may be of use in Parkinson's treatments.

What is the difference between therapeutic cloning and reproductive cloning?

Cloning means the production of a genetically identical copy. In mammals, including humans, this is achieved by replacing the DNA in an unfertilised egg with DNA from an adult cell. There are two key types of cloning:

Therapeutic cloning, which is also referred to as cell nuclear replacement (CNR), is the type used in Parkinson's research. This involves the transfer of genetic material from the potential recipient to an unfertilised egg. This aims to produce embryonic stem cells that could be used to repair or to treat diseased or damaged tissue.

The cloned embryos are not implanted in a womb but are grown in the laboratory to serve as a source of embryonic stem cells. The advantage of producing embryonic stem cells by cloning is that they should be genetically identical to the patient's own cells and should therefore avoid rejection when transplanted.

Reproductive cloning is where the aim is to create a plant or animal that has exactly the same genetic make-up as another. The cloned embryo is implanted in the womb and allowed to continue its development until birth. An example in animals of reproductive cloning is Dolly the sheep. In the UK, only animal reproductive cloning is legal, and human reproductive cloning is illegal.



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Why is stem cell research important for Parkinson's?

There is currently no known cure for Parkinson's and while modern medicines can help manage the symptoms, they may only be effective for a relatively short time, as there may be significant side effects from these drugs. Surgical interventions can offer some relief from symptoms in some cases, but there are risks involved with brain surgery. It is also unknown for how long these treatments will be effective and what side effects they may produce. Furthermore, Parkinson's currently cannot be halted and will continue to progress despite drug therapy or surgical intervention.

Stem cell research aims to understand more about how an organism develops from a single cell and how healthy cells can replace damaged cells in the adult. The hope is that eventually, through this research, the dopamine-producing cells that are lost in the brains of people with Parkinson's can be replaced with new healthy dopamine-producing cells derived from stem cells grown in the laboratory. If this were possible, stem cell therapy could be the first treatment to eventually offer an effective cure for Parkinson's.

Dopamine-producing cells generated from stem cells could also be used to develop and test new drug treatments.

How would stem cell therapy work?

The aim of stem cell research into Parkinson's is to find a way of inducing the unspecified stem cells to become dopamine-producing cells. In order to do this, we need to determine how stem cells remain unspecialised and discover what conditions cause stem cells to become specialised into different types of cell.

These are complicated questions but if they can be answered, in the future it may be possible to develop a treatment whereby stem cells that have been induced to become dopamine-producing cells could be implanted into the brains of people with Parkinson's to replace the missing dopamine-producing nerve cells.

What sort of time frame is involved?

Although stem cell research is progressing steadily in the UK, it will be at least five to ten years before clinical trials using stem cell therapy will be considered. While therapeutic cloning has been carried out successfully in some animals, it has not yet proved possible in humans.

What is the legal position of stem cell research in the UK?

In January 2001, Parliament agreed to allow research for therapeutic purposes on cells derived from human embryos under the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. The therapeutic purposes for which research using this material can be used are:

- increasing knowledge about the development of embryos
- increasing knowledge about serious disease
- enabling any such knowledge to be applied in developing treatments for serious disease

In December 2001, the Human Reproductive Cloning Act 2001 was put in place. This Act prohibits using a human embryo for the purposes of reproductive human cloning.

The HFEA can provide more information on the legal aspects of stem cell research in the UK

Human Fertilisation and Embryology Authority

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What is the PDS's position on stem cell research?

The Society firmly supports stem cell research and has warmly welcomed the 2001 Regulations which allow embryonic stem cell research for serious conditions in the UK. In adopting its position, the PDS was advised by its Research Advisory Panel that stem cell research has great potential and may lead to new treatments



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for several serious conditions, including Parkinson's. The PDS's Board of Trustees (the majority of whom are elected by the Society's members) decided unanimously to support this research. In doing so, they clearly resolved that the PDS respects the views of those who take a different position on moral or ethical grounds and also expressed opposition to human reproductive cloning.

It should be noted that embryos that can be used in stem cell research were created originally for use in IVF treatments and would otherwise be destroyed. Also, embryos can only be used for research with the informed consent of the donors.

The PDS believes that research using embryonic stem cells as well as research using other types of stem cell are necessary at present, as it is still unclear which route will prove to be most effective in producing pliable and versatile cells that can be adapted for medical use with patients.

At the same time, along with leading members of the research community, the Society believes that it is necessary to explore the potential of 'therapeutic cloning'. This experimental approach may allow the development of embryonic stem cells that are compatible with the person's immune system and overcome possible immunological rejection by the body following transplantation of cells.

The PDS believes that the HFEA provides a strong regulatory presence and ensures that research is carried out within the existing legislation. The HFEA has to approve each individual research licence, be satisfied that the research cannot be conducted using an alternative method, and has an inspection and enforcement role. Further, any work that involves patients requires ethical approval.

I have heard the term 'stem cell lines' mentioned, particularly in reference to the USA where they talk about having cell lines they can use. What are cell lines?

These are stem cells that have been manipulated in a laboratory so that they can continue to divide almost

indefinitely. By developing these cell lines, the need to extract stem cells from other sources such as fresh embryonic tissue will be lessened. It is, however, essential that the cells can be made to stop dividing at some point in order to generate specific cell types such as nerve cells. Therefore, through developing these lines, researchers hope to discover how to control the differentiation process of stem cells so that large quantities of cells can be developed to use for transplant purposes in the future.

In the USA, research using a few existing stem cell lines has been permitted because they had already been created as a result of IVF research.

Are brain implants using foetal brain material a type of stem cell research?

No. Brain implants using foetal material and stem cell research are both types of neural replacement therapy, but the material used and the techniques are different.

Brain implants using foetal material involve taking developing cells directly from aborted fetuses. The foetal material contains cells that are already committed to becoming dopamine cells. The aim of brain implants using foetal dopamine cells is that these cells will connect with other cells in the region of the brain in which they have been implanted and start producing enough dopamine to correct the problems that result from a shortage of this neurotransmitter. Results for this type of neural transplant have been mixed, partly because it has been impossible to standardise the foetal cell material that is used for the implants. Furthermore, it is not possible to control accurately the amount of dopamine released by the cells, and this may result in side effects such as uncontrolled movements (termed dyskinesia). Using stem cells may overcome this obstacle, since it should be possible to produce large amounts of pure, quality-controlled dopamine-producing nerve cells from stem cells, which could then be implanted into the brain.

Another type of neural transplant of interest in Parkinson's research is xenografts. This involves transplanting tissue from one species to another,



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and research into Parkinson's using this method has concentrated on using pig foetal dopamine cells. There are problems associated with this technique, including tissue rejection and the potential transmission of harmful viruses between species.

Research into the potential use of stem cells in Parkinson's generally uses material from the very early embryo (ES cells), which is at a much earlier stage of development than material derived from a foetus. Foetal stem cells are also being researched, although these have not been used in clinical trials of foetal brain cell implant surgery. These have used dopamine-producing cells taken from the brain of an aborted foetus.

Is keeping the blood from an umbilical cord to be used as a source of stem cells in the future a good idea? A member of my family is due to give birth shortly and I understand we could pay a cord bank to preserve it for us.

Cord blood banking can be useful for the treatment of blood diseases. However, there is insufficient evidence to support the use of umbilical cord blood as a source of stem cells to repair the brains of people with Parkinson's. We would not recommend that people pay for this, given the current position with stem cell technology. Getting stem cells derived from the brain at any stage of its development to turn into dopamine-producing cells is a huge challenge for stem cell researchers, let alone trying to do this with sources of non-nervous tissue cells.

What is the status of stem cell research at the moment?

Research on stem cells relating to the brain and Parkinson's has been taking place for about ten years. During this time, much progress has been made. However, the scale of the problem in developing this type of therapy has at the same time become apparent. In particular, the growth and differentiation of stem cells needs to be better understood and controlled, with predictable outcomes established. At the moment there are problems with the reliability of producing sufficient numbers of dopamine-producing cells.

Only when this is achieved would the therapy be ready for the clinic. Some research groups and companies feel they are close to that stage. However, researchers connected with the PDS feel that a move into human trials is premature and runs the risk of producing negative results and possibly even side effects. This, in the long term, would do more harm than good, not least because it may erroneously appear to remove the hope of a cure.

What research is the PDS funding?

The PDS currently provides financial support for a number of stem cell research projects. The Society has also worked closely with the Medical Research Council and others to set up the UK Stem Cell Bank. This is Europe's first centralised stem cell resource, providing researchers with shared access to research on a variety of different human stem cells.

The Society currently funds research projects in several leading laboratories in the UK looking at the area of stem cells. For more information see the PDS research magazine *Progress*.

While the PDS gives broad support to stem cell research, it should be noted that the Society recognises that support is needed for other complementary avenues of research to further our understanding of Parkinson's, and to identify other potential treatment strategies.

Each year the PDS funds research into many different areas, including genetics, surgery and developing therapies, and has also established and supports the PDS Brain Tissue Bank based at Imperial College London. Since its conception, the Society has spent over £35million on research with £4.2million being committed in 2007 alone.

Where can I get more information?

The following websites contain further information on stem cells, and have been used as references in compiling this information sheet.



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UK sites

Human Fertilisation and Embryology Authority – www.hfea.gov.uk

Medical Research Council – www.mrc.ac.uk

The Royal Society – www.royalsoc.ac.uk/cloning

The Wellcome Trust – www.wellcome.ac.uk

BBC – the Science section of its website has a useful section on genetics and issues to do with cloning – www.bbc.co.uk/science/genes/gene_safari/

US sites

US National Institutes of Health – <http://stemcells.nih.gov/>

Further information can also be obtained from the PDS's Research Department (research@parkinsons.org.uk).

Glossary

Adult stem cells – stem cells derived from 'mature' adult tissue sources.

Differentiation – the process by which unspecialised stem cells develop into specific types of cells, e.g. dopamine-producing nerve cells.

DNA – stands for deoxyribonucleic acid. DNA is a large, ladder-like molecule in humans and other living organisms that contains the instructions needed for growth and function.

Embryo – stage in the development of a human being from implantation to about 8–12 weeks after conception.

Embryonic stem cells – cells derived from the very earliest stages of embryo development. Such cells have the capacity to form any cell in the body, including dopamine-producing nerve cells.

Foetus – stage in the development of a human being usually from 8–12 weeks after conception.

IVF (in vitro fertilisation) treatment – fertility treatment involving fertilisation outside the body in a laboratory.

Neural transplant – transplanting neural material into the brains of people with conditions like Parkinson's, to replace lost or damaged cells and restore normal function.

Precursor or progenitor cells – cells that can divide but have a limited potential to turn into different types of cells. This typically represents a stage between stem cells and their differentiated product (e.g. neuron).

Stem cell – unspecialised cells that have the ability to maintain themselves and also to develop into specialised types of cells within the body tissues, e.g. skin, blood, intestine.

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