PARKINSON INFORMATION

Parkinson Society Canada
Société Parkinson Canada

STEM CELL RESEARCH AND PARKINSON'S DISEASE

This document has been prepared to help you become more informed about stem cell research. It is designed to answer questions about the status of stem cell research in relation to Parkinson's disease and what is currently known about therapies.

Parkinson's disease: symptoms and treatment

Parkinson's is a disorder of the brain. Movement is controlled by dopamine, a chemical that carries signals between nerves in the brain. When cells that produce dopamine die or are damaged, Parkinson's symptoms appear. The loss of dopamine can cause a variety of motor symptoms, including tremor, muscle stiffness, slowness of movement, and impaired balance. Non-motor symptoms also develop, such as constipation, sleep disturbances, bladder urgency, dizziness, fatigue, depression and memory problems. (See PSC Information Sheet on Progression of Parkinson's disease at www.parkinson.ca.)

Currently there is no cure for Parkinson's. Many of the motor symptoms can be treated with medications that either replace the lost dopamine or mimic the action of dopamine in the brain. Medications can alleviate the symptoms, but do not slow the progression of Parkinson's. Some people may benefit from brain surgery (often known as deep brain stimulation, or DBS).

Who discovered stem cells?

The first stem cell discovery was made by Canadian scientists James Till and Ernest McCulloch in 1961. These were stem cells of the blood system, but provided a foundation to understand other stem cells from other tissue, such as the brain.

What are stem cells?

Stem cells are defined by two properties. First, they can 'self-renew,' that is, they can divide and give rise to more stem cells of the same kind. Second, they can mature or 'differentiate' into specialized cells that carry out a specific function.

There are many different types of stem cells. These include embryonic stem cells that exist only at the earliest stages of development; and types of 'tissue-specific' stem cells (referred to as 'adult' or 'somatic' stem cells) that are found in various tissues in our bodies.

What are embryonic stem cells and why are they important?

Embryonic stem cells are *pluripotent*, meaning they are capable of generating most cells in the body. Since *pluripotent* cells self-renew easily in the lab, they have been instrumental in the study of human development and disease modeling.

What are adult stem cells and why are they important?

Adult stem cells are *undifferentiated* cells found in various tissues within the human body. For example, adult stem cells have been found in skin, brain, liver, muscle, and retina. Although adult stem cells have the ability to self-renew, their limitation in therapeutic application is due to the fact that they produce a restricted number of specialized cell types. For some specific diseases, such as leukemia, they are an effective therapeutic tool.

What are induced pluripotent stem cells and why are they important?

In 2007, researchers engineered adult skin cells into a *pluripotent* state. These *induced pluripotent stem (iPS) cells* have characteristics similar, but not identical, to embryonic stem cells – they are able to self-renew and form all cell types in the body. The method of producing *iPS* cells is not yet ideal for the purposes of treatment in humans. Research is continuing to improve the method of creation and to better understand how *iPS* cells can be used in therapies safely and effectively.

Benefits of *iPS* cells are two-fold:

1. The opportunity to obtain the cells directly from a patient, thus potentially reducing the risk of auto-immune reactions following cell therapy; and
2. The ability to model diseases in the lab in order to better understand a disease and identify novel therapeutic approaches.

Why is it important to conduct research for all stem cells?

Continued study using embryonic stem cells, induced pluripotent stem cells and adult stem cells will help determine which cell type will ultimately be the best cell for clinical use and treatment of a particular disease.

Why do researchers study stem cells in neurodegenerative disease like Parkinson's?

While most clinical trials have focused on improved drug therapies, stem cell research has focused on finding ways to regenerate, repair or replace these cells so functioning can be restored. This is called *neurogenesis* and is part of an emerging field called *regenerative medicine.*

What is known about stem cell research in Parkinson's?

Since the motor symptoms of Parkinson's are related to loss of dopamine—one specific chemical—stem cell therapy is theoretically possible. Scientists pursue the principle or hypothesis that stem cells can be successfully transplanted, survive and produce dopamine to improve body function.

How do scientists get stem cells?

For practical reasons, researchers need to identify a stem cell population that can be grown in large supply, maintained indefinitely in the laboratory and differentiated efficiently into dopamine neurons that work when transplanted into Parkinson's patients.

This goal has motivated scientists to study both embryonic and adult stem cells as an alternative source of dopamine-producing neurons. In laboratories, with the right combination of growth factors (chemicals like hormones), undifferentiated stem cells can be cultivated to a point where they can become dopamine neurons, then implanted into the animal's brain to finish maturing.

Researchers do not yet know if adult neural stem cells have the same potential as embryonic stem cells or whether this approach will work in humans.

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What are scientists learning about stem cells and Parkinson's?

Scientists are investigating which stem cells (e.g. embryonic, blood, bone marrow, retina, skin cells) are best for a potential therapy for Parkinson's. The researchers are tracking cell markers to learn which stem cells survive, multiply and successfully produce dopamine under what conditions. They are determining the cues that neural stem cells use to differentiate into dopamine-producing cells. They are decoding signals in the brain that allow transplanted cells to survive, integrate and function properly; deciding which areas of the brain and whether transplantation or some other method of delivery (e.g. using genes) would yield the best results.

What are scientists learning about brain repair?

Scientists are investigating how the brain turns on its own mechanism for self-repair, possibly involving adult stem cells that reside in certain parts of the brain. For example, the brain's white matter contains *multipotent progenitor cells* that can multiply and form all the major cell types of the brain, including neurons. These appear to be remnants of stem cells that existed during fetal brain development that might be coaxed into becoming dopamine-producing cells in a patient with Parkinson's.

This capacity to regenerate relies on growth hormones and other signaling molecules that help cells survive and grow. Scientists are beginning to understand what fires up a patient's own stem cells and internal repair mechanism to allow the body to cope with damage from disease or injury. Even transplanted neural cells have a 'homing instinct' that leads them to gravitate to exactly that part of the brain that is injured and needs regeneration.

What is the future for stem cell research?

Research continues in Canada, the US, the UK, Israel, Sweden, and Japan on using stem cells in Parkinson's disease with varying results. Unfortunately, in recent experiments, tumors appeared as a result of transplanting embryonic stem cells in animal models.

Translating success (and failure) from animal models to human trials requires controlling many factors, such as the source and type of stem cell used, the culture in which they are grown, the protocol for injecting them into the brain, the method of activating cell differentiation, and what factors ensure their survival. Long-term studies are also awaited to determine whether the transplanted stem cells will eventually degenerate much like the natural dopamine cells affected by the ongoing Parkinson's process.

Further research is needed to understand the basic science and the various strategies for testing stem cells. Progressing to the next step requires a multi-disciplinary network of scientists, clinicians and laboratories in order to determine whether a safe and effective protocol for transplanting stem cells into the brain is feasible.

If such therapeutic strategies are successful, they may be applied to the treatment of Parkinson's where cell replacement and regeneration might help restore function.

Are there successful stem cell therapies for Parkinson's disease?

No. At the present time, there are no such therapies for Parkinson's. It is still being determined which cells will work best to repair a particular damaged or diseased tissue, and how to get those cells to the right place in the brain.

What about stem cell treatments available on the Internet?

In Canada, stem cell treatments must be approved by Health Canada before use in a medical trial or therapy. Read more at: http://www.hc-sc.gc.ca/dhp-mps/index-eng.php.

A Canadian researcher[1] conducted an independent study concerning the validity of online stem cell clinics marketing directly to consumers. The findings showed that neurological diseases were the most commonly mentioned categories (84%) on stem cell clinics on the Internet. Among the neurological diseases, MS, stroke, Parkinson's, spinal cord injury and Alzheimer's were the most common. The study found that treatments offered on stem cell websites for neurological diseases were generally unsupported by clinical evidence.

The International Society of Stem Cell Research, published *The Patient Handbook* which provides a short list of things to look out for, such as:

1. Claims based on patient testimonials rather than evaluated clinical research.
2. Multiple diseases treated with the same cells. Different diseases, such as Parkinson's and heart disease, would be expected to have very different treatments. You also want to be treated by a doctor who is a specialist in Parkinson's.
3. The source of cells or how the treatment will be done is not clearly documented.
4. Claims that there are no risks.
5. High cost of treatment or hidden costs. It is not customary for someone to pay to be part of a clinical trial.

What is Parkinson Society Canada's position?

Stem cell research holds promise for finding a cure and/or treatments for Parkinson's disease. Parkinson Society Canada is committed to finding a cure for Parkinson's disease and supports stem cell research, including adult, embryonic and skin.

[1] Stem Cell Clinics Online: The Direct-to Consumer Portrayal of Stem Cell Medicine, Prof. Caulfield.

RESOURCES:
Stem Cell Network Canada, www.stemcellnetwork.ca.
McMaster Stem Cell & Cancer Research Institute, www.fhs.mcmaster.ca/SCCRI/
International Society for Stem Cell Research, www.isscr.org.