



STEM CELLS AND CEREBRAL PALSY

Cerebral palsy (CP) is an umbrella term which includes several forms and levels of non-progressive brain-related injury, which cause limitations in muscle control, movement and mobility (known as *neuromotor impairment*) and other symptoms that lead to physical disability. CP is caused by many factors, and can include infection before birth, premature birth and lack of oxygen around the time of birth.

It is thought that the major common feature in CP is a lack of blood and oxygen to the brain during fetal development and/or delivery, known as a *hypoxic-ischemic insult*. The cells most vulnerable to this hypoxic-ischemic insult are *oligodendrocytes*, the support cells that wrap nerve cells (or *neurons*) with a protective white fat called *myelin*, hence the term white matter of the brain.

Because of this myelin, neurons can send electrical signals efficiently throughout the body. Once oligodendrocytes die, the neurons are no longer protected and they eventually die. If myelin could be replaced before neurons die, neurons could be spared and motor impairments could be lessened. For this reason, scientists are investigating whether lost oligodendrocytes can be replaced with stem cells.

Stem cells are unspecialized cells which can become specialized cells such as brain cells, heart cells or muscle cells. The process of developing into a specialized cell is known as *differentiation*.

Stem cells can also multiply over and over again, a process known as *proliferation*. During the process of proliferation the stem cell either remains unspecialized or, under the right condition, can become a specialized cell such as a brain cell.

Replacing neurons themselves would be like trying to rewire a giant switchboard with tens of thousands of ports but no labels, where

improper connections could lead to pain. It is for this reason that the aim of many cell transplantation strategies now being tested is to replace lost oligodendrocytes rather than to make and successfully connect new neurons.

Recent decades have seen advances in our knowledge of how to study and use stem cells. It is expected we will develop ways to transplant stem cells into damaged tissues to treat and cure injury and diseases like CP.

From Mice to Humans

Use of neural stem cells resulted in improvement of motor function and injury sparing in *animal models*. Researchers have used these cells to improve the injury environment or to replace lost oligodendrocytes.

Damage to the nervous system is one of the most well studied areas of *Regenerative Medicine*, and each piece learned about the repair of the brain and spinal cord helps to develop approaches to treat other diseases. Even if cell transplantation proves to be impossible, the lessons learned about how to handle stem cells that naturally exist in the body could lend hope that such basic knowledge will translate into useful therapies and drugs. Indeed, current research is investigating how stem cells already in the brain can mobilize and repair tissue in response to drugs or chemicals.

How NeuroDevNet Is Pursuing Stem Cell Treatment for CP

As a joint effort between the laboratory of Dr. Michael Fehlings in Toronto (University of Toronto Neuroscience Program), and Dr. Jerome Yager in Edmonton (University of Alberta), this NeuroDevNet initiative is



investigating stem cells in animal models of CP. By first developing the most reliable and relevant means of creating CP in animal models, NeuroDevNet's researchers aim to restore myelin-producing cells (oligodendrocytes), thereby saving neurons before CP-related damage can occur.

Clinical Trials in Humans

There is a huge leap however, between what can be done in a lab with mice and what should be done in a hospital to humans. Clinical trials are closely monitored tests of potential medical treatments performed on patients.

Based on positive results from work done in cells and animals, a treatment is first tested on a small group of people to make sure it does not cause harm, and then on larger groups to make sure it works.

Developing any new type of therapy carries risk. First of all, clinical trials must prove that a treatment is safe. Treatments that work perfectly in mice will often show no benefit when used in people. Mice used in research have simple, tailor-made injuries, and cannot reject transplanted cells.

Also to inject stem cells in people can be dangerous. There are currently 4 trials evaluating stem cell transplantation

Two of these are being conducted in the United States, and use stem cells taken from the patient's own umbilical cord. Proving that this approach is safe and effective will take several years. In the meantime, research will continue looking into other ways of treatment, including transplantation of other cell types.

Unproven Treatments

No trustworthy stem cell treatment for CP currently exists, and it will take a number of

years for safe and effective therapies to make it to the clinic.

There is an increasing trend of people travelling to foreign countries to receive stem cell injections. Clinics offering "Stem Cell Tourism" are located in China, India, Germany, and Central America and operate outside medical or scientific supervision.

These clinics commonly inject patient-specific bone marrow, or banked umbilical cord cells. Adult bone marrow cells do not turn into mature neurons or oligodendrocytes within the brain, and banked cord blood cells are killed by the patient's immune system.

The improvements that are reported for muscle tone, etc., are most probably a result of placebo effects, the child's natural aging and development, and ongoing rehabilitation. Reports of successful treatments create demands for new procedures or therapies to become available before they can be properly tested.

Patients and their families deserve evidence showing that treatments offered are safe. Stem Cell Tourism requires that families:

- ✓ Are critical and informed reviewers of these clinics
- ✓ Look beyond amazing and unbelievable stories or videos of how their clients have had major recovery
- ✓ Critically examine the information and look for total clients treated, detailed methods of treatment, detailed information about the results of treatment, comparison to similar patients who do not receive treatment and long-term follow-up.

Without clear, controlled evidence, patient testimonials cannot be trusted.

It is difficult and time-consuming for researchers to prove that using stem cells is safe. It is even

Stem Cell Treatments for Cerebral Palsy

Factsheet for patients and families

Crystal Ruff,* Jared Wilcox,* Michael Fehlings



more difficult to prove that it is also effective.. It is best to be patient and wait for proof that these treatments work. Once stem cells are put in, they cannot be taken out.

Selected References

Stem Cell Facts: Where to Look

Several organizations have excellent up-to-date information on stem cells and CP:

International Society for Stem Cell Research (ISSCR)

A world leader for stem cell research with 2600+ scientific members, the ISSCR produced several educational materials on stem cells, including a handbook on experimental stem cell therapies, and will contact companies on your behalf:

<http://www.isscr.org/public>

<http://www.closerlookatstemcells.org/>

Canadian Institutes of Health Research

The CIHR Stem Cell Research page provides up-to-date information on stem cell governance and legislature in Canada.

<http://www.cihr-irsc.gc.ca/e/15255.html>

National Institutes of Health Research

For a superb overview on diagnosis, additional symptoms, associated health concerns, treatments and research on cerebral palsy:

http://www.ninds.nih.gov/disorders/cerebral_palsy/detail_cerebral_palsy.htm

The NIH also runs a Government sponsored initiative providing up-to-date information on stem cells in regenerative medicine:

<http://stemcells.nih.gov/>

Clinical Trials

Current information on registered clinical trials:

<http://clinicaltrials.gov/ct2/results?term=cerebral+palsy+AND+stem+cells>

Glossary

Animal Model: a living, non-human animal that can be used in medical research to study a

human condition. Using these models, scientists can gain understanding of the underlying causes for numerous conditions, and can create viable treatment options as a result.

Placebo effect: improvement in the condition of a patient that happens in response to treatment, but cannot be considered caused by the specific treatment used

Neurons: nerve cells which make up the basic signaling units of the brain. They consist of three main parts: dendrites, which receive electrical signals from other neurons; the cell body, which acts as a processing centre, and; axons, which send electrical signals over long distances throughout the body.

Oligodendrocytes: small supporting cells for the brain and nervous system, with few branches. They provide the myelin wrapping for the neurons

Myelin: a soft white material of fat and protein that is secreted by oligodendrocytes (and Schwann cells), and forms a thick sheath around axons (fibers which extend from neurons)

Hypoxic-ischemic insult: injury to the body caused by a lack of oxygen (hypoxic) and blood (ischemic) to the tissues

Neuromotor impairment: damage to nerve impulses that stimulate muscle movement, causing movement restriction

Regenerative medicine: a discipline of medicine that focuses on the renewal, regrowth, or restoration of a body or a bodily part, tissue, or substance after injury or as a normal bodily process

Transplantation: the removal of tissue from one part of the body or from one individual and its implantation or insertion in another especially (by injection or surgery)

*Authors contributed equally to this factsheet