

OVERVIEW ABOUT STEM CELLS AND TREATMENT

Stem cells are cells that divide to replace their own numbers and can give rise to two or more specialized cell types. There are different kinds of stem cells: pluripotent, adult, and fetal.

- There are many different types of stem cells (e.g. bone marrow stem cells, embryonic stem cells, adult stem cells, umbilical cord stem cells, mesenchymal stem cells, induced pluripotent stem cells, etc.)
- What differentiates one stem cell type from another is how many cell types they can become.
- Based on this feature **we can categorize all stem cell types as either multipotent or pluripotent**
- **Multipotent stem cells** can become two or more cell types in the body but NOT all cell types in the body
- **Pluripotent stem cells** can become ALL types of cells in the body

WHAT IS A STEM CELL?

Pluripotent Stem Cells:

Pluripotent stem cells (PSCs) self-renew and can become all cell types in the body. These cells are either derived by reprogramming from adult cells (induced pluripotent stem cells or iPSCs) or generated from 5-day old embryos that are produced by in vitro fertilization or parthenogenetic activation of oocytes (embryonic stem cells). Pluripotent stem cells can be expanded and later used to make specific types of cells. Pluripotent stem cells exist only in laboratories, not in our bodies.

- Pluripotent means “very many powers”.
- Human embryonic stem cells (hESCs) are generated from 5-day old embryos that are produced by in vitro fertilization. A version of hESCs, parthenogenetic hESCs, are produced from unfertilized artificially activated oocytes.
- Induced pluripotent stem cells (iPSCs) are generated in the laboratory from adult somatic (body) cells through a process called “reprogramming”.
- PSCs exist only in the laboratory, and can live forever.

Multipotent or Adult Stem Cells:

Multipotent Stem Cells exist in many organs and have limited ability to become mature cell types. Multipotent stem cells **cannot** become dopaminergic neurons, the cell type lost in Parkinson’s disease.

- Multipotent means “many powers”. Some types can develop into several, but not all, cell types.
- Senescent in the body and in the laboratory (will eventually die)

Examples of adult stem cells:

- Hematopoietic stem cells in bone marrow or blood can make blood cells but not cells of the brain or any other organ. HSCs are the only FDA-approved stem cell therapy, for use in treatment of blood cancers like leukemia.
- Umbilical cord stem cells are a type of hematopoietic stem cells isolated from the blood vessels in the umbilical cord. They are used to treat children with blood cancers.
- Neural stem cells are rare in the brain and have only limited ability to replace some nerve cells and supportive cells
- Mesenchymal stem cells (also known as “mesenchymal stromal cells”) are found in connective tissues. MSCs have narrow differentiation abilities, with some sources able to make cartilage, bone, and fat. Some but not all mesenchymal stem cell preparations may transiently reduce inflammation, and are approved outside the US for treatment of graft versus host disease, a condition associated with some organ transplants.
- Adipose stem cells are derived from body fat. These cells are often used in unregulated clinics *claiming* to treat a large range of diseases and conditions. There are no FDA approved uses for these cells.

Fetal Stem Cells:

During fetal development, while organs are still developing, cells exist in some locations that can be harvested, expanded in cell culture, and sometimes retain the ability to make several different cell types. A fetal tissue-derived cell line called HEK293 is used in many labs to grow viruses for making vaccines and antibodies. Notably, fetal neural stem cells have been used in unregulated clinics promising treatments for stroke and neurodegenerative diseases. No one has successfully made fetal neural stem cells that can be directed into becoming dopamine neurons, so fetal neural stem cells are not a good source of the dopamine neurons needed in PD.

WHAT IS DIFFERENTIATION?

Differentiation is the process by which cells change from relatively generalized to specialized kinds of cells during embryonic development.

Summit scientists can differentiate induced pluripotent stem cells into dopamine neurons for cell replacement therapy for Parkinson's disease.

TYPES OF STEM CELLS AND THEIR CHARACTERISTICS:

Stem cell type	Cell source	Multipotent	Pluripotent	Does it make dopaminergic neurons?
Embryonic stem cells (ESCs)	Fertilized embryos Assisted reproduction (in vitro)		✓	Yes
Induced pluripotent stem cells (iPSCs)	Adult tissue often skin or blood		✓	Yes
Parthenogenic stem cells	Unfertilized embryos		✓	Yes
Adipose stem cells	Fat	✓		NO
Hematopoietic stem cells (tissue specific stem cells)	Bone marrow, blood	✓		NO
Neural stem cells (tissue specific stem cell)	Fetal brain	✓		Unlikely
Mesenchymal stem cells	Adult tissues	✓		NO

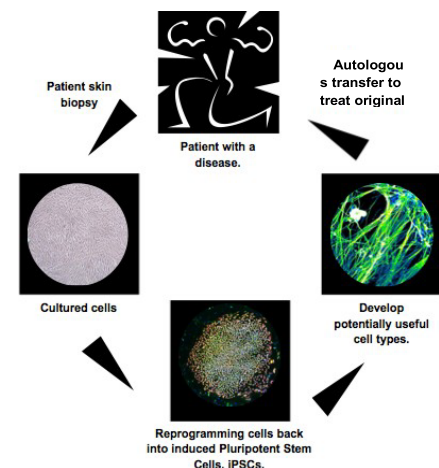
WHY CELL REPLACEMENT THERAPY? ...& PARTICULARLY FOR PARKINSON'S?

Summit supports of all types of evidence-based research investigating the causes, prevention, and treatment of Parkinson's disease and other neurodegenerative conditions. It is an unfortunate reality that by the time PD is diagnosed, many of a person's dopamine-producing neurons have already been lost. This means all therapeutic approaches are vital: early detection, protection of the remaining dopamine neurons, AND replacement of lost neurons.

There is great deal of evidence-based research being performed around the world for Parkinson's disease (PD). Many studies are researching biomarkers that can be used to diagnose PD and to determine whether treatments are effective. Summit supports the Cincinnati Cohort Biomarker Study, which is analyzing thousands of DNA samples in an effort identify subtypes of Parkinson's disease that might benefit from some treatments but not others.

Summit's flagship project, dopamine neuron replacement therapy, is aimed at providing lasting symptomatic relief for the physical symptoms of PD. Summit launched the project by providing funding to the laboratory of Dr. Jeanne Loring at the Scripps Research Institute, in 2011. Since then, the project has progressed from a research phase to a preclinical phase, and moved from academics to industry with the founding of Aspen Neuroscience. The company is supported by venture capital investment and plans to launch the first clinical trial in about a year.

The plan is to transplant *dopamine neurons*, **not** stem cells. The neurons are autologous, generated from patient-specific induced pluripotent stem cells, so that they match each person; this will avoid the side effects of the immune suppression that will be necessary if unmatched cells were used.



WHAT YOU NEED TO KNOW ABOUT ADVERTISED “STEM CELL” CLINICS

People who have unmet medical needs search for alternative treatments for their condition. As an example, approved medications for the symptoms of Parkinson’s disease work by enhancing the abilities of the remaining dopamine neurons. These drugs do not prevent the continuing death of dopamine neurons that is a characteristic of PD. Similarly, other conditions like arthritis, Alzheimer’s disease, diabetes, and stroke could benefit from evidence-based regenerative therapies.

Warning: only FDA or other regulatory agency-approved regenerative therapies have been shown to be safe and effective. Unapproved treatments are not based in science, are unlikely to have any benefit, and may cause harm.

The FDA warns: “...patients seeking cures and remedies may be misled by information about products that are illegally marketed, have not been shown to be safe or effective, and, in some cases, may have significant safety issues that put patients at risk...” <https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/consumer-alert-regenerative-medicine-products-including-stem-cells-and-exosomes>

Summit’s educational program provides anyone seeking regenerative medical treatments with an understanding of stem cells and their potential. Summit strives to empower patients with evidence-based information from leading experts in the field of regenerative medicine.

Before participation in any therapy, treatment or clinical trial using stem cells, Summit’s scientific advisors suggest that the following 7 questions MUST be answered:

1. What is being transplanted, and how do the transplanted cells act to reduce symptoms?
2. If you are in the United States, is the study/therapy/treatment FDA *approved*? <https://clinicaltrials.gov/ct2/home>
 - a) If you’re in another country, is the study/therapy/treatment approved by that country’s medical regulatory agency?
3. What are the pre-clinical safety and efficacy data supporting the use of the proposed cells?
4. Is the study/trial evidence-based?
5. Do you have concerns about the source of the tissue?
6. What is being claimed– better control of symptoms or a cure?
7. Is the study guided by input from experts in the field?

REFERENCES:

- (1) <https://www.sciencedaily.com/releases/2016/03/160329113350.html>
- (2) <http://www.nature.com/articles/npjparkd201517>
- (3) <http://www.journalofparkinsonsdisease.com/are-stem-cell-therapies-parkinson%E2%80%99s-disease-ready-clinical-trials>
Note: The 6 questions are based on the GForce-PD questions.
- (4) Bratt-Leal, Andrés M., and Jeanne F. Loring. "Stem Cells for Parkinson's Disease." *Translational Neuroscience*. Springer US, 2016. 187-201.
- (5) <http://www.nature.com/nrneurol/journal/v11/n9/full/nrneurol.2015.123.html#1990s-onwards-mdash-other-cell-sources>

ABOUT SUMMIT:

Summit for Stem Cell Foundation's mission is to support, educate and raise awareness about the development of today's and tomorrow's evidence-based regenerative medical therapies focused on Parkinson's disease and other neurodegenerative disorders. It is our goal to empower patients and caregivers with information to elevate their understanding in order to manage their healthcare.

We feel that knowledge is a necessary tool for those wishing to explore treatment/therapy options. Knowledge will aid in making choices – especially when considering regenerative medicine therapies and regenerative medical clinical trials. This document's intent is to provide information and questions to ask regarding alternative regenerative medicine -based therapies.

Summit was founded in 2011 as a grass roots volunteer organization comprised of patients, medical and scientific professionals, and community members with a desire to raise funds for a stem cell-based solution to Parkinson's disease. The body of science for the *autologous dopamine neuron replacement therapy for Parkinson's disease* has been transferred to Aspen Neurosciences and is currently completing the last few required studies.

Today, the therapy is on a hastened path towards FDA approved clinical trials. Summit has grown into a large organization with supporters around the globe. The organization is a 501(c)(3) charitable organization that is dependent on contributions to support its 3 programs:

- (1) Research Program: Support for innovative evidence-based research looking at “old” questions with a new focus.
- Patient Support Program:
 - a) Provide current & reliable information to patients.
 - b) Fundraising campaign for the Center for Parkinson's Health and Wellness Capital Campaign.
- Educational Program: Dedicated to bridging the informational gap between evidence-based science and the patient & medical communities.
 - a) Live educational webinars for medical professionals with world-class leaders in regenerative medicine as presenters.
 - b) Reliable information empowering patients with the ability to separate stem cell hope from hype and to safely navigate stem cell therapies.

Summit continues with a passionate dedication for persons living with Parkinson's disease and other neurodegenerative conditions by supporting evidence-based regenerative medical research.

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