



Michael J. Fox Foundation Supports Two Engineered Stem Cell Research Projects for Parkinson's Therapeutic Development and Disease Investigation

- Harvard Teaching Hospitals funded to develop dopamine neuron replacement treatment
- Parkinson's Progression Markers Initiative making iPSCs available to broad research community
- Dopamine neurons engineered from iPSCs may hold utility as therapeutics and research tools

NEW YORK (May 25, 2016) — The Michael J. Fox Foundation for Parkinson's Research (MJFF) announced funding for two projects leveraging the promise of engineered stem cells to speed new therapies and deeper understanding of Parkinson's disease.

Advances in technology are allowing scientists to engineer dopamine neurons, which degenerate and die in Parkinson's disease, from skin and blood cells. Researchers are attempting to use these neurons to replace what is lost in Parkinson's and restore motor function. In addition, the cells can serve as research tools for exploration into the disease process and impact of therapeutic intervention.

"The complexity and mystery of brain diseases make them incredibly difficult to understand and to treat," says MJFF CEO Todd Sherer, PhD. "Stem cell technologies may offer a more sophisticated dopamine replacement approach and provide the opportunity to study the influence of disease and of interventions on these vulnerable cells."

Therapy Replacing Machinery, Not Only Product

Dopamine loss causes Parkinson's motor symptoms including tremor, rigidity and slowness and may play a role in some non-motor symptoms. Replacing dopamine neurons may provide a regulated stream of dopamine that would alleviate motor symptoms.

The Michael J. Fox Foundation and the National Stem Cell Foundation (NSCF) are partnering to fund Ole Isacson, MD, director of the Neuroregeneration Research Institute at McLean Hospital and principal faculty at Harvard Stem Cell Institute, to further study implantation of dopamine neurons made from induced pluripotent stem cells (iPSCs) in the brains of non-human primates. In 2015, Dr. Isacson published that implanted iPSC-derived dopamine neurons survived and that the therapy was associated with motor improvement. In 2010, Dr. Isacson and colleagues published the first evidence of iPSC protocols, showing the function of human midbrain dopamine neurons. Read more about this project from NSCF and MJFF.

"The restoration of the dopamine supply system would be a significant step forward in our treatment of Parkinson's disease," said Dr. Isacson. "This project brings us closer to realizing such a therapy, though there is still much work to be done."

MJFF also is funding a project led by Lorenz Studer, MD, at Memorial Sloan Kettering Cancer Center, investigating transplantation of dopamine neurons derived from embryonic stem cells drawn from existing cell lines. Dr. Studer has received multiple grants from the Foundation to study the potential of

embryonic stem cells to treat Parkinson's, and was part of the team that first successfully developed dopamine neurons from human embryonic stem cells.

Tools Lay Groundwork for Insight into Disease Process and Therapeutic Impact

In addition to breeding a direct therapy, iPSCs are used to develop and test other treatments. Dopamine neurons engineered from iPSCs provide an unparalleled model to mimic the Parkinson's disease process in laboratory experiments. Scientists can use this resource to, for example, investigate the impact of causal factors such as genetic mutations and environmental exposures and the pathogenic role of cellular processes including mitochondrial dysfunction and oxidative stress. Furthermore, researchers can introduce drug compounds and assess the impact on maintenance or restoration of dopamine function.

To further these investigations, the MJFF-sponsored Parkinson's Progression Markers Initiative (PPMI) is making iPSCs available at no cost to the researcher community. PPMI is following a diverse population of people with Parkinson's, with risk factors of the disease and control volunteers for more than five years across 33 clinical sites. Robust clinical, imaging and biological data from PPMI (also available to all qualified researchers) increases the value of the study's iPSCs.

"PPMI builds the infrastructure off which the greater research community can drive discovery, validation and replication," said Mark Frasier, PhD, MJFF Senior Vice President of Research Programs. "The 'disease in a dish' model provided by iPSCs is an asset in the development and testing of new treatments, and streamlined access to these well characterized tools will speed progress."

The Golub Capital iPSC PPMI Sub-study has two phases. The first — a partnership with the New York Stem Cell Foundation (NYSCF) Research Institute funded by Lawrence E. Golub and Karen L. Finerman, a member of the MJFF Board of Directors — created iPSC lines and fibroblasts from skin samples of 20 people with Parkinson's disease and five control volunteers. This extensive collection of Parkinson's and control participant iPSCs with complementary clinical information is now available to interested researchers at <http://www.ppmi-info.org/cell-lines/>.

The second phase — funded by nationally recognized credit asset management firm Golub Capital, led by Lawrence and David Golub, also a member of the MJFF Board of Directors — contracts Cellular Dynamics International to make available iPSCs derived from blood samples from 85 PPMI participants. This cohort includes volunteers recently diagnosed with Parkinson's, those with genetic mutations associated with the disease, people with a clinical risk factor of hyposmia or REM sleep behavior disorder, and control volunteers. This diverse population and number of samples will increase the scope and scale of investigation with these resources, and those iPSCs will be available later this year.

Cells Reborn with New Direction

Stem cells form a more specialized type of cell (e.g., muscle or red blood cell). There are two natural categories of these cells: Embryonic stem cells (also called pluripotent) are found in fertilized eggs and can become any type of cell. Adult stem cells are found among specialized cells in a tissue or organ and can differentiate only into the cell types found in that tissue or organ. In the brain, regions involved in memory formation and smell function contain pockets of adult stem cells that help those systems replace neurons. Research to this point has shown other regions — including the substantia nigra (site of Parkinson's degenerating dopamine neurons) — do not contain stem cells and therefore do not renew.

In 2007, researchers realized another category. With genetic manipulation, scientists engineered embryonic stem cells from an adult fibroblast (cell found in connective tissue). The creation of these induced pluripotent stem cells has transformed medical research. iPSCs are easier to access and may be the source of a personalized therapy that the body is less likely to reject (i.e., dopamine neurons made from one's own blood or skin cell).

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About The Michael J. Fox Foundation for Parkinson's Research

As the world's largest nonprofit funder of Parkinson's research, The Michael J. Fox Foundation is dedicated to accelerating a cure for Parkinson's disease and improved therapies for those living with the condition today. The Foundation pursues its goals through an aggressively funded, highly targeted research program coupled with active global engagement of scientists, Parkinson's patients, business leaders, clinical trial participants, donors and volunteers. In addition to funding more than \$600 million in research to date, the Foundation has fundamentally altered the trajectory of progress toward a cure. Operating at the hub of worldwide Parkinson's research, the Foundation forges groundbreaking collaborations with industry leaders, academic scientists and government research funders; increases the flow of participants into Parkinson's disease clinical trials with its online tool, Fox Trial Finder; promotes Parkinson's awareness through high-profile advocacy, events and outreach; and coordinates the grassroots involvement of thousands of Team Fox members around the world.

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