NYSCF OLIGODENDROCYTE PROTOCOL

NYSCF The New York Stem Cell Foundation Research Institute

OLIGODENDROCYTES DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

FUNCTIONAL OLIGODENDROCYTES DERIVED FROM PLURIPOTENT STEM CELLS AND METHODS OF MAKING AND USING THE SAME

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*patented

NYSCF PAPER

Generation and isolation of oligodendrocyte progenitor cells from human pluripotent stem cells.

Nature Protocols. 2015.

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Overview

Oligodendrocytes are central nervous system cells that produce myelin to create defined segments of electrical insulation, maximizing the speed of neuronal signaling. Studies have shown that even small changes affecting oligodendrocyte metabolism can lead to neurodegeneration. Disorders such as multiple sclerosis (MS), adrenoleukodystrophy (ALD), vanishing white matter disease (VWM), Pelizaeus-Merzbacher disease (PMD), and leukodystrophies all exhibit demyelination, the loss or destruction of myelin. Increasingly, the scientific community's understanding of oligodendrocytes' critical role in many other conditions, including amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), Alzheimer's disease (AD), and schizophrenia is emerging. Patient populations impacted by these disorders exceed 10 million in the United States and represent over 125 million worldwide.

However, there remains a need for efficient and reproducible methods for the generation of human oligodendrocyte progenitor cells (OPCs) to develop *in vitro* myelination assays, to screen for myelinating compounds, and to ultimately become a source for autologous cell replacement therapies for impacted patients.

Technology Summary

The present invention provides for the improved generation of OLIG2+, O4+, and OPCs from pluripotent stem cells (PSCs) that is significantly quicker and more efficient than previous protocols (40% to 70% of O4+ OPCs within 75 days compared to 4% to 47% of O4+ OPCs within 120 days). Furthermore, O4+ OPCs generated using the present methods are able to differentiate into MBP+ mature oligodendrocytes *in vitro*, and to myelinate axons *in vivo* when injected into immuno-compromised Shiverer mice, providing proof of concept that transplantation of PSC-derived cells for remyelination is technically feasible. NYSCF researchers have validated the protocol using over nine PSC lines, whereas previous protocols were optimized using only one or two lines.

Inventor Profile

Dr. Valentina Fossati, Ph.D., is a Senior Research Investigator at the NYSCF Research Institute. Dr. Fossati oversees the MS research program and is focused on novel treatments for progressive forms of MS. Dr. Fossati obtained her Ph.D. in 2008 from the University of Bologna after relocating to New York, at Mount Sinai School of Medicine, as a visiting student and NYSCF-Druckenmiller postdoctoral fellow during her Ph.D. Bringing stem cell expertise to the MS field, Dr. Fossati developed a research plan focused on modeling MS with human induced pluripotent stem cell (iPSC) derived cell types, understanding genetic susceptibility by studying patient-specific cells and, ultimately, drug discovery and cell replacement therapies to promote neuroprotection and remyelination. Dr. Fossati's group has generated iPSC lines from MS patients and is currently developing co-culture systems including neurons, oligodendrocytes, astrocytes and microglia to dissect the role of each cell type in the progression of the disease.