NYSCF MICROGLIA PROTOCOL

NYSCF The New York Stem Cell Foundation Research Institute

MICROGLIA DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

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

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15/449,519 (U.S.)
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NYSCF PAPER

Directed Differentiation of Human Pluripotent Stem Cells to Microglia.

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partnering@NYSCF.org

Overview

Microglia, the immune cells of the brain, are crucial to the proper development and maintenance of the central nervous system and are involved in numerous neurological diseases and disorders. Dysfunctional microglia have been linked to amyotrophic lateral sclerosis (ALS) and Alzheimer's disease (AD), chronic activation of microglial cells is a possible trigger to the progression of multiple sclerosis (MS) and Parkinson's disease (PD), while defective phagocytosis and synaptic pruning – essential microglia functions – have been implicated in the pathogenesis of schizophrenia and autism spectrum disorders. Combined, these patient populations total roughly 14 million in the United States and exceed 200 million worldwide.

Most knowledge regarding microglia derives from rodent studies. However, there are major differences between rodent and human microglial cells, such as in their proliferation rates, adhesive properties, and expression of critical receptors. Direct analysis of primary human microglial cells has been severely hampered by the limited availability of human brain specimens, creating a need for efficient and reproducible methods of generating human microglial cells.

Technology Summary

The present technology provides various new and improved methods for the generation of human microglia from pluripotent stem cells (PSCs), using chemically defined media. The disclosed methods are used to generate microglial progenitors from both embryonic and induced pluripotent stem cells. Such microglial progenitors typically appear within 25-30 days and continue to produce until around day 50. The methods further enable the differentiation of such microglial progenitors to ramified microglia that have highly motile processes, express many typical microglial markers, release cytokines, have phagocytotic activity, and respond to adenosine diphosphate by producing intracellular Ca2+ transients. These methods are highly reproducible across different PSCs, providing a new source of human microglial cells.

Inventor Profiles

Working across multiple disease areas and disciplines, co-inventors, Dr. Scott Noggle, Ph.D. and Dr. Valentina Fossati, Ph.D. have used their knowledge and experience to accelerate work in this critical field. Dr. Noggle and Dr. Fossati share an interest in the derivation and the use of human stem cells to better understand human development and disease. Dr. Noggle, Senior VP of Research at the NYSCF Research Institute, oversees the Institute's stem cell research programs and is focused on the creation of human models of neurodegenerative diseases, such as AD and PD, to discover new disease targets and to understand how genetics impact disease susceptibility. Dr. Fossati, Senior Research Investigator at the NYSCF Research Institute, oversees the Institute's MS research program and is focused on discovering novel treatments for progressive forms of MS. Dr. Fossati's group is currently developing co-culture systems including iPSC-derived neurons, oligodendrocytes, astrocytes and microglia to dissect each cell type's role in the progression of MS.