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Microglia derived from patient-specific human-induced pluripotent stem cells

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Today, during the 81st American Association of Neurological Surgeons (AANS) Annual Scientific Meeting, researchers announced new findings regarding the development of methods to turn human induced pluripotent stem cells (iPSC) into microglia, which could be used for not only research but potentially in treatments for various diseases of the central nervous system (CNS).

Microglia are the resident inflammatory cells of the CNS and can modulate the outcomes of a wide range of disorders including trauma, infections, stroke, brain tumors, and various degenerative, inflammatory and psychiatric diseases. However, the effective therapeutic use of microglia demonstrated in various animal CNS disease models currently cannot be translated to patients due to the lack of methods for procuring high-purity patient-specific microglia. Developing a method for obtaining these cells would be highly valuable.

In the study "Differentiation of Induced Pluripotent Stem Cells to Microglia for Treatment of CNS Diseases," mouse and human iPSCs were generated and sequentially co-cultured on various cell monolayers and in the presence of added growth factors. The microglial identity of the resulting cells was confirmed using fluorescence activated cell sorting analyses, functional assays, gene expression analyses and brain engraftment ability. The study results will be shared by presenting author John K. Park, MD, PhD, FAANS, from 3:34-3:42 p.m. on Monday, April 29. Co-authors are Michael Shen, BS; Yong Choi, PhD; and Hetal Pandya, PhD.

In the results, researchers found mouse and human iPSCs co-cultured with OP9 cells differentiate into hematopoietic progenitor cells (HPCs). HPCs in turn co-cultured with astrocytes, generate cells that express CD11b, Iba-1 and CX3CR1; secrete the cytokines IL-6, IL-1ß and TNF-a; generate reactive oxygen species; and phagocytose fluorescent particles, all consistent with a microglial phenotype. Gene expression clustering using self-organizing maps indicates that iPSC-derived microglia more closely resemble normal microglia than other inflammatory cell types. The iPSC-derived microglia engraft and migrate to areas of injury within the brain. These finding have led researchers to conclude that iPSC-derived microglia may one day be useful as gene and protein delivery vehicles to the CNS.

"The actual results of our research were not surprising to us, but the overall importance of microglia in a wide variety of brain and spinal cord diseases was surprising. Microglia likely have a role in improving or worsening diseases such as multiple sclerosis, Alzheimer's disease, Parkinson's disease, obsessive compulsive disorder and Rett's syndrome, just to name a few," said John K. Park, MD, PhD, FAANS. "Microglia are the principal immune system cells of the brain and spinal cord, and help fight infections as well as help the healing process after injuries such as trauma and strokes. They also play a poorly understood role in many neurodegenerative and psychiatric diseases. We have developed methods to turn iPSCs into microglia. Because human iPSC can easily be obtained in large numbers, we can now generate large numbers of human microglia not only for use in experiments, but also potentially for use in treatments. The ability to study normal and diseased human microglia will lead to a greater understanding of their roles in healthy brains and various diseases. Diseases that are caused or exacerbated by defective microglia or a paucity of normal microglia may potentially be treated by microglia generated from a patient's iPSC."

More information: 2013 AANS Annual Scientific Meeting: