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Technology Offer

Neuro-epithelial stem cells (NESCs) capable of forming both central nervous system (CNS) and peripheral nervous system (PNS) neurons

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(linked to MI-1012-5677-LI-ZE describing the generation of human neural microtissues from NECS cells)

Max-Planck-Innovation GmbH
Amalienstr. 33
80799 Munich
Germany

Phone: +49 (89) 29 09 19 - 0
Fax: +49 (89) 29 09 19 - 99
info@max-planck-innovation.de
www.max-planck-innovation.de

Contact:
Dr. Dieter Link
Tel.: 089 / 290919-28
Dieter.link@max-planck-innovation.de

Background

Human pluripotent stem cells (hPSCs) are able to differentiate into all somatic cell types and into the germ line. As such, hPSCs have significant potential to improve medicine. In principle, hPSCs could replace tissue lost through disease or injury, and significantly improve drug discovery through the use of in vitro models of human physiology. However, for these applications to become reality, it is necessary to faithfully establish large numbers of homogenous cells that belong to a defined lineage. Unfortunately, many specialized cell types, such as neurons, are post-mitotic and cannot be expanded in culture. Therefore, a major challenge in hPSC research is to derive precursor populations that are expandable in culture and committed to the neural lineage while retaining the ability to be differentiated into broadly different neuronal subtypes.

Technology

Researchers from the Max-Planck-Institute of Molecular Biomedicine in Münster developed a method to differentiate hPSCs into a new precursor population named neuro-epithelial stem cells (NESCs)(1). Importantly, NESCs can be differentiated into neurons from both central nervous system (CNS) and peripheral nervous system (PNS).

Our scientists discovered, that combination of WNT and HEDGEHOG signals specifies self-renewal of NESCs by maintaining a neural plate border-like identity. Removal of HEDGEHOG signals increased expression of neural crest markers, leading to the formation of Peripherin-positive PNS neurons. In contrast, HEDGEHOG signals inhibit the upregulation of Peripherin, leading to the formation of CNS cell types, including, but not limited to midbrain dopaminergic neurons, motor neurons, oligodendrocytes and astrocytes. In addition, since the cells are already specified to the neural lineage, they form electrophysiologically functional neurons more quickly than protocols starting with hPSCs.

NESCs are a valuable source of material for disease model studies (1). They can be derived from hPSCs including patient-specific induced iPSCs, without need of manual selection steps. Importantly, the method described here cultures the cells under chemically defined conditions in which proteins are substituted for small molecules. This reduces batch-to batch variability inherent to purified protein preparations and considerably reduces expense. The efficient expansion and broad differentiation profile are compatible with automation, making them highly convenient for large-scale production of disease models for applications such as high-throughput drug discovery (1).

Patent Information: A European priority application has been filed in 2012.

We offer this technology on a co-exclusive basis to interested licensees.

References: 1) Reinhard et al. PLoS One (2013), doi: 10.1371/journal.pone.0059252