Docket #: S16-009

Genome Editing of Human Neuronal Stem Cells (NSCs) to Treat Genetic Diseases of the CNS, Neural Injury, and Neurodegenerative Diseases

The blood-brain barrier is a huge challenge when it comes to the delivery of therapeutic proteins to treat genetic diseases, injury, and neurodegenerative diseases. By directly editing neuronal stem cells (NSCs), we can create a cell-based therapy that can deliver therapeutic proteins into the CNS in a precise fashion. This occurs by using cells that have the biologic property of turning into multiple CNS cell types and migrating to broad areas of the CNS. The unique and transformative method can be used to treat a variety of both rare and common diseases.

The Porteus Lab at Stanford has developed a completely novel therapeutic method of delivering precise proteins to the CNS. Human NSCs are modified by delivering an engineered nuclease and a donor DNA fragment by electroporation to primary neuronal stem cells. After homologous recombination, the NSCs will have a transgene precisely and permanently inserted into a specific genomic location where it will be expressed in a sustained and regular fashion. The genetically modified NSCs can be purified and transplanted into the CNS where they will differentiate into different CNS lineages thus giving rise to cells in the CNS that express the transgene. Current enzyme replacement therapy does not deliver proteins to the CNS because of the bloodbrain barrier. This is the first invention using gene editing in primary human NSCs and can be used to create cells that can be administered to a patient to treat a disease.

Applications

- Treatments for the CNS and Neurological diseases

- Drug delivery
- Gene editing

Advantages

- Safely modified NSCs for transplantation
- Stable long-term transgene expression not found using other mechanisms of genetic modification
- First invention using gene editing in primary human NSCs

Publications

- Dever, D. P., Scharenberg, S. G., Camarena, J., Kildebeck, E. J., Clark, J. T., Martin, R. M., ... & Porteus, M. H. (2019). " CRISPR/Cas9 genome engineering in engraftable human brain-derived neural stem cells." Iscience, 15, 524-535.

Patents

- Published Application: 20170298348
- Published Application: WO2017180926
- Published Application: 20230250423

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