Human Pluripotent Stem Cells (hPSCs)-based Neurological Disease Modeling and Therapeutic Development

Research in neurological diseases harnesses human pluripotent stem cells for innovative disease modeling and therapeutic discovery. Research in the field of neurological diseases leverages human pluripotent stem cells (hPSCs) to model diseases and develop therapeutic interventions. Parkinson's disease (PD), a prominent focus, exemplifies the complexity of age-related neurodegenerative disorders, characterized by dopaminergic neuron degeneration and the formation of Lewy bodies enriched with alpha-synuclein aggregates. PD's classification as a proteinopathy, a disease caused by protein misfolding and aggregation, highlights the challenges faced by traditional models in accurately simulating its progression, especially in reproducing the crucial age-related protein aggregation. One of the intrinsic hurdles in using hPSCs for modeling late-onset diseases like PD is the reset of age-related phenotypes during cell reprogramming. This reset makes it difficult to capture the late-onset characteristics and progression of neurodegenerative diseases. To overcome these obstacles, the development of the OASIS system, an optogenetics-assisted method, has been crucial. It efficiently induces alpha-synuclein aggregation in hiPSC-derived neurons and organoids, aiding in identifying BAG956, a compound that shows potential in reversing PD by promoting the autophagic degradation of pathological aggregates. Concurrently, research using an opto-TMEM106B system investigates TMEM106B in various neurodegenerative conditions, aiming to broaden our understanding of its role across different diseases.

In addition, a key advancement has been made in developing therapies for Neurofibromatosis type 1, focusing on a novel protocol for differentiating hPSCs into functional Schwann cells, critical for the peripheral nervous system. This comprehensive approach underscores the significant progress in neurodegenerative disease research, from understanding basic mechanisms to pioneering new treatments.