Human induced pluripotent stem cells-derived neural models for translational research in neurogenomic era

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ABSTRACT

The advent of human induced pluripotent stem cells (hiPSCs) has revolutionized translational neuroscience, offering unprecedented opportunities to model neurodevelopmental and neurodegenerative disorders in vitro. Patient-derived hiPSCs for disease modelling allow the recapitulation of patient-specific genetic backgrounds and cellular phenotypes during disease onset and development. By reprogramming somatic cells into a pluripotent state, hiPSCs can be differentiated into various neural lineages, including neurons, astrocytes, and oligodendrocytes, faithfully representing the complexity of the human brain. HiPSC-derived 3D cerebral organoids or mini-brains in a dish have been proven beneficial to model more complex neurological disorders such as neurodegenerative and neuropsychiatric diseases in elucidating the pathogenic mechanisms underlying neurodevelopmental basis of Alzheimer's disease, bipolar disorder, and Down syndrome. These models recapitulate disease-specific phenotypes, such as protein aggregation, mitochondrial dysfunction, and synaptic loss, enabling screening potential disease-modifying therapies and personalized medicine approaches. Integrating hiPSC-derived neural models with cutting-edge genomic technologies, such as CRISPR/Cas9 genome editing and single-cell/bulk RNA sequencing, can unravel the genetic architecture of complex neurological traits and identify disease-associated genetic variants. In conclusion, hiPSC-derived neural models represent a powerful tool for translational research in the neurogenomic era, offering unprecedented opportunities to dissect the molecular and cellular mechanisms underlying neurological disorders and accelerate the development of precision therapies.