POSTER

MODELING THE COMPLEXITY OF THE CENTRAL NERVOUS SYSTEM WITH PATIENT IPSC-DERIVED CEREBRAL ORGANOIDS

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2D cultures poorly model tissue complexity. This study aims to develop a patient-iPSC-derived 3D model of the central nervous system - integrating neuronal and immune components - to study neurodegenerative diseases, specifically amyotrophic lateral sclerosis (ALS). ALS patients and healthy control fibroblasts were reprogrammed into iPSCs to generate liquid-cultured brain organoids (BOs), maintained for 50, 70, 80 and 100 days. To improve model complexity, BOs were stimulated with specific growth factors to induce oligodendrocytes differentiation. Microglial cells (generated from matched patient-derived iPSCs) were integrated. Morphometric analysis showed regular growth of both CTRL and ALS BOs over time, suggesting morphological stability. Immunofluorescence and gene expression analyses confirmed correct neuronal differentiation and spatial organization in both groups. Motor neurons and oligodendrocytes were detected. Microglia were effectively integrated into both CTRL and ALS BOs, displaying an amoeboid morphology in the latter group, suggesting a more activated state compared with CTRL BOs. This study establishes an optimized protocol for modeling a 3D platform suitable for investigating ALS.

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