



Neuroengineering Brain Organoids to Investigate Neurological Diseases

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Abstract: Access to human brain tissue for scientific investigation has traditionally been limited, creating obstacles in understanding brain disorders and developing new treatments. To overcome this barrier, our research team has engineered and validated three-dimensional brain organoids generated from induced pluripotent stem cells (iPSCs), providing biologically relevant models for studying neurological conditions. We employ a structured, multi-phase differentiation process that starts with forming the ectodermal layer, advances through neural progenitor cell generation, and culminates in fully developed cerebral organoids. After six months of maturation, these organoids exhibit strong expression of cortical biomarkers such as MAP2, CTIP2, SATB2, and GFAP.

Applying schizophrenia as our disease framework, we performed extensive transcriptomic comparisons between organoids derived from affected individuals and healthy donors. The analysis identified substantial differences in gene expression within pathways governing synaptic transmission, GABA production, and oxidative phosphorylation. We validated these findings functionally by measuring oxygen consumption rates and conducting multi-electrode array (MEA) electrophysiology, which revealed disease-characteristic metabolic patterns and neural connectivity profiles. A key innovation in our work involves novel computational methodologies employing source-sink connectivity analysis.

This approach successfully differentiated between control, schizophrenia, and bipolar disorder organoids with 83.3% accuracy under baseline conditions, which increased to 91.6% accuracy after electrical stimulation. These electrophysiological patterns hold potential for clinical translation, possibly connecting laboratory-based disease models with patient EEG diagnostic markers. Our research validates cerebral organoids as robust tools for modeling neurological diseases, screening therapeutic compounds, and identifying biomarkers. This work opens new pathways for investigating brain disorders and expediting the development of treatments for neuropsychiatric diseases.

Friday, November 7th | 2:00pm-3:15pm | Science Hall 126 & Zoom

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