RESEARCH TOPIC MECM_20

Glial-enriched stem-cell 3D model of smoldering inflammation in multiple sclerosis: towards a drug screening cellular platform

Curriculum
MECM Standard

Research Area
Neuro

Laboratory name
Experimental Neuropathology Lab

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Abstract
In the central nervous system (CNS), the role of macroglia-microglia axis in sustaining self-autonomous inflammation and driving clinical progression in multiple sclerosis (MS) is attracting increasing scientific and pharmacological interest. In absence of clear preclinical animal models of smoldering MS lesion formation and maintenance, here, we propose an experimental platform using 3D hiPSC-derived self-organizing submillimetric forebrain organoids. Our preliminary data support that this in vitro cellular system is responsive to external stimuli such as complex inflammatory pulses and drug-induced oxidative stress, by properly mimicking macroglia-microglia neurodegenerative phenotypes and communication patterns seen in chronic active MS lesions.
The current proposal includes 2 specific aims: (a) to optimize our 3D stem cell-based model to generate reproducible MS-inflamed organoids resembling the chronic inflammatory CNS environment of MS lesions; (b) to expose MS-inflamed organoids to selected compounds, currently under investigation in MS, targeting relevant pathways in critical glial populations to assess their pharmacological potential. The results obtained by this study will pave the way for the implementation of such innovative 3D multilineage cellular model for drug screening of repurposed and/or newly synthesized drugs to counteract smoldering neurodegeneration and inflammation in MS.

Main technical approaches
hiPSC cell culture expertise; Drug screening on cell cultures; Immunostainings

Scientific references
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Type of contract

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