POSTER

EXPLORING NEUROTROPHIN-MEDIATED MECHANISMS IN ISCHEMIC CEREBRAL ORGANOIDS THROUGH INTEGRATED MULTI-OMICS ANALYSIS

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Ischemic stroke is a complex and heterogeneous neurological condition representing a major global cause of mortality and long-term disability. Beyond its functional consequences stroke is frequently associated with cognitive impairment, significantly contributing to the clinical and socioeconomic burden of the disease. Neurotrophins play a critical role in promoting neuronal survival, neuroprotection and neuroplasticity following such injuries. Human brain organoids—3D cellular models that recapitulate the brain's architecture and composition—offer a highly valuable platform for studying these dynamics. In this work, we used a multi-omics framework to dissect the molecular effects of neurotrophin treatment within a cerebral organoid-based model of ischemic stroke. This integrated strategy facilitates the identification of condition-specific molecular signatures and pathways underlying both the ischemic injury and neurotrophin-mediated recovery mechanisms. Cerebral organoids were generated from human induced pluripotent stem cells and characterized over time using specific maturation markers. To establish the stroke model, organoids were exposed to varying durations of oxygen-glucose deprivation followed by reperfusion, allowing us to define a sublethal baseline suitable for evaluating neurotrophin efficacy. We further characterized organoid-based stroke model through Western blotting, immunofluorescence, digital PCR and electrophysiological analyses. Furthermore, to investigate the molecular networks modulated by neurotrophins, transcriptomic profiling was performed using Ion Torrent, while protein-level alterations were assessed via Orbitrap-proteomics. The integration of these datasets maps the molecular signatures and biological pathways associated with both the ischemic insult and the subsequent neurotrophin treatment. Overall, this multi-omics study yields novel insights into the neuroprotective dynamics of neurotrophins in a human 3D model of ischemic stroke.

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