3D Cultures of Parkinson's Disease-Specific Dopaminergic Neurons for High Content Phenotyping and Drug Testing

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Résumé

The human brain is an immensely complex structure, which makes it difficult to recapitulate its development, function and disorders. In the recent years, brain organoids derived from human induced pluripotent stem cells have risen as novel tools to study neurodegenerative diseases such as Parkinson's disease (PD). PD is a multifactorial disorder, with aging, genetics and environmental factors as key etiological elements. Organoids, as complex multicellular tissue proxies, are an ideal tool to study cellular response to genetic mutations as well as to environmental changes. However, with increasing complexity of the system, usage of quantitative tools becomes challenging. This led us to develop an automated high-content image analysis pipeline for image-based cell profiling in the organoid system. Here, we present a human midbrain organoid system that recapitulates features of monogenetic as well as neurotoxin-induced PD, representing a platform for machine-learning-assisted prediction of phenotypes in high-content imaging data. This model is a valuable tool for advanced *in vitro* PD modeling and for the screening of neuroprotective compounds.

Mots-Clés: 3D cultures, dopaminergic neurons, Parkinson

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