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Reconstructing Midbrain Organoid Neural Networks with Light-Sheet Microscopy to Investigate Parkinson's Disease

Human midbrain organoids (hMOs) have recently emerged as 3D in vitro systems capable of self-organizing in complex structures. They can recapitulate key features of the human midbrain, providing a physiologically and pathologically relevant model to investigate Parkinson's disease (PD). This study aimed to compare the morphology of the dopaminergic neuronal network in midbrain organoids derived from healthy individuals and from PD patients carrying a genetic mutation for the protein MIRO1, associated with an increased risk of developing the disorder. The combination of light-sheet fluorescence microscopy (LSFM) on optically cleared organoids with AI-based image analysis enabled high-resolution three-dimensional reconstruction of neuronal networks. This approach provides an insight on structural organization, network complexity, and patterns of neuronal connectivity, ultimately leading to the understanding of how alterations in network architecture may relate to functional changes observed in PD.

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