# Neuronal Organoid Ref.

## with R&D systems Protein

### Modeling G2019S-LRRK2 Sporadic Parkinson's Disease in 3D Midbrain Organoids

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generate isogenic 3D midbrain organoids with or without a Parkinson's disease-associated LRRK2 G2019S mutation to study the pathogenic mechanisms associated with LRRK2 mutation. We demonstrate that these organoids can recapitulate the 3D pathological hallmarks observed in patients with LRRK2-associated sporadic Parkinson's disease. Importantly, analysis of the protein-protein interaction network in mutant organoids revealed that TXNIP, a thiol-oxidoreductase, is functionally important in the development of LRRK2-associated Parkinson's disease in a 3D environment. These results provide proof of principle for the utility of 3D organoid-based modeling of sporadic Parkinson's disease in advancing therapeutic discovery.

### Vincristine Impairs Microtubules and Causes Neurotoxicity in Cerebral Organoids

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Vincristine is commonly administered as an effective anti-brain tumor drug. It is known to act by interfering with microtubule dynamics, but models for detailed elucidation of its mechanism of neurotoxicity are limited. Here we generated cerebral organoids using human-induced pluripotent stem cells (iPSCs) for evaluation of neurotoxic mechanisms. Cerebral organoids were treated with different concentrations of vincristine for 48 h and their expansion was measured. We also assayed various cell markers, microtubule associated proteins, and matrix metalloproteinases (MMP) in cerebral organoids. After treatment for 48 h, we observed dosedependent neurotoxicity, including reduced neuron and astrocyte numbers at high concentration. Vincristine treatment also impaired the microtubule-associated protein tubulin, and fibronectin, and downregulated MMP10 activity. Further analysis using the STRING database found that, both MMP10 and fibronectin bind with MMP9 experimentally, and text-mining indicated an interaction between MMP10 and fibronectin. Our organoid model system allowed quantitative investigation of the effects of vincristine treatment. Our findings indicated vincristine exhibited dose-dependent neurotoxicity, inhibited fibronectin, tubulin, and MMP10 expression in cerebral organoids.