Docket #: S21-121

Multi-Regional Human Neural Circuits in Assembloids Derived from Pluripotent Stem Cells

Researchers at Stanford have described, for the first time, the formation of a human neural circuit loop from stem cells in human assembloids. Specifically, they have developed methods for in vitro generation of functional human cortico-striatal-midbrain-thalamic-cortical (CSMTC) spheroids by functionally integrating brain-region specific organoids. Complete CSMTC spheroids are assembled from component cultured cell systems, each designed to provide specific sets of neural cells. These functionally integrated cells interact in a physiologically relevant manner (e.g. forming synapses or neuromuscular junctions, transmitting signals, inducing muscle contractions, forming multicellular structures, etc.). This technology enables reconstruction of a "direct" cortico-basal ganglia pathway in vitro from parts derived from human pluripotent stem cells. The methods generate 3D self-organizing cultures (also known as organoids or spheroids) that resemble the human cerebral cortex, the human diencephalon including thalamus, human midbrain and human striatum, and then integrate them in various combinations and spatial arrangements that allow formation of reciprocal connections and enable loop circuit-like properties.

Currently, researchers have limited access to intact, functional human brain tissue to probe and manipulate CSMTC loop circuits. There remains a great need for human cellular models that can functionally integrate components of the corticospinal tract circuit, allowing screening for new therapies for patients with implicated disorders, including autism spectrum disorder, Parkinson's disease, schizophrenia and obsessive-compulsive disorder (OCD).

Stage of Development

The researchers have demonstrated successful assembly of four-loop assembloids from human cortical spheroids (hCS), human striatum spheroids (hStrS), human

midbrain spheroids (hMbS) and human diencephalic spheroids (hDiS).

Applications

- Biological understanding of human neural circuit assembly
- Modeling of disorders of the CSMTC loop, including OCD, autism spectrum disorder, schizophrenia and Parkinson's disease
- Large scale viral screening for circuit-specific gene therapy
- Large scale small molecule screening in human pluripotent stem cell-derived CSMTC

Advantages

- First preparation fo this kind. Previous in vitro models included one or two of the components with little functionality or maturation.

Publications

- Miura, Yuki, et al. "Generation of human striatal organoids and cortico-striatal assembloids from human pluripotent stem cells." *Nature Biotechnology* 38.12 (2020): 1421-1430.

Patents

- Published Application: WO2022271697
- Published Application: 20240254438

Innovators

- Sergiu Pasca
- Yuki Miura
- Ji-il Kim

Licensing Contact

David Mallin

Licensing Manager, Physical Sciences

Email