

Animal model for human brain development and neuropsychiatric disorders

Researchers from Stanford University have developed an in vivo model of human neural development and disease.

A key challenge in the study of human neurological diseases is the lack of animal models for the human brain and the scarcity of human brain tissue obtained for research. In recent years, organoids of human induced pluripotent stem (hiPS) cells have provided an in vitro model to study brain development and disorders. While self-organized organoids can be generated that resemble different brain regions (such as human cortical organoids, (hCO)), the in vitro models lack the microenvironments or sensory inputs that are present in a living brain. Thus, in vitro organoids fail to provide an understanding of brain function, including neural circuits, behavioral outputs, and neuropsychiatric disease phenotypes.

This technology successfully integrates human organoids into intact, living brains of developing rats to create an in vivo model of human neural development and function (Figure 1). The transplantation is performed several days after birth when the rat brains still have developmental plasticity. Early introduction enables the transplanted organoid (t-hCO) to anatomically and functionally integrate into the rat brain, creating working hybrid neural circuits. The resulting mature t-hCO neurons are able to respond to external sensory stimuli and can drive behavioral responses. The ability to transplant a broad spectrum of hiPS cell derived organoids offers this platform broad application to the study and therapeutic testing for many human neuropsychiatric disorders.

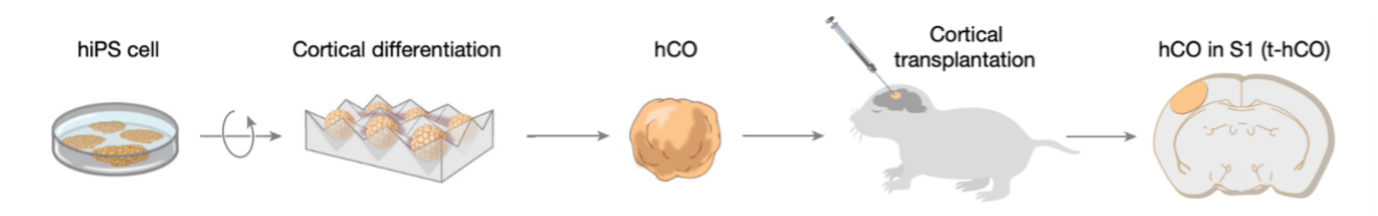


Figure Description: Transplantation of human cortical organoids into the developing rat cortex. (Image Credit: inventors)

Stage of Development

Proof of concept

Applications

- Therapeutic testing for human neuropsychiatric disorders
- Platform for human neural development research

Advantages

- The technology enables the study of brain development and disease in a **functional animal model**
- hCOs are transplanted into rats at an early, plastic developmental stage favoring **functional and anatomical integration of the organoids**
- **MRI monitoring** allows for longitudinal studies
- **Transplantation of intact organoids** (vs. single cell suspension) minimizes disruption to the human cells and enables formation of a human cortical neural cell unit within the rat brain

Publications

- Revah, O., Gore, F., et al. (2022). [Maturation and circuit integration of transplanted human cortical organoids](#). Nature, 610(7931), 319-326.

Patents

- Published Application: [WO2023239483](#)

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