Modeling human neurodevelopment using brain organoids

Alysson R. Muotri[1,2]

[1]University of California San Diego, School of Medicine, Department of Pediatrics/Rady Children's Hospital San Diego, La Jolla, California 92093, USA.
[2]University of California San Diego, School of Medicine, Department of Cellular & Molecular Medicine, La Jolla, California 92093, USA.

Structural and transcriptional changes during early brain maturation follow fixed developmental programs defined by genetics. However, whether this is true for functional network activity remains unknown, primarily due to experimental inaccessibility of the initial stages of the living human brain. We developed cortical organoids that spontaneously display periodic and regular oscillatory network events that are dependent on glutamatergic and GABAergic signaling. These nested oscillations exhibit cross-frequency coupling, proposed to coordinate neuronal computation and communication. As evidence of potential network maturation, oscillatory activity subsequently transitioned to more spatiotemporally irregular patterns, capturing features observed in preterm human electroencephalography (EEG). These results show that the development of structured network activity in the human neocortex may follow stable genetic programming, even in the absence of external or subcortical inputs. Our approach provides novel opportunities for investigating and manipulating the role of network activity in the developing human cortex. Applications for neurodevelopmental and neurodegenerative disorders will be discussed.