Self-organized formation of human pluripotent stem cell-derived hippocampal, spinal cord, and cerebral organoids, and a novel method for its functional analysis

Summary
The cerebrum is the basis of human neural function including higher brain function, and the hippocampus is the basis of memory formation and learning. Because several neurological and neuropsychiatric disorders are attributed to cerebral and hippocampal dysfunction, knowing the fundamental aspects of formation of these neural tissues and its function is important.

The neural organoids, which are three-dimensional (3D) neural tissues generated from pluripotent or tissue stem cells, are attractive models of human neural development. The developing 3D neural organoids enable to approach the active and complexed human neural tissues that has been difficult to approach by previous research materials. Using the pioneering method for the induction of neural organoids called SFEBq (serum-free floating culture of embryoid body like aggregates with quick reaggregation), we have investigated organoids of several neural regions such as cerebral cortex, medial pallium (future hippocampus), choroid plexus, and spinal cord, by modulating the culture conditions based on the developmental information of each region. And using cerebral organoids, we investigated self-organized and complex human neural network activities that include synchronized and non-synchronized patterns. The spontaneous individual and synchronized activity of the network was measured via calcium imaging, and subsequent novel analysis enabled the examination of detailed cell activity patterns, providing simultaneous raster plots, cluster analyses, and cell distribution data.
Thus, by providing several types of human neural tissues and detailed analysis method for human neural activities, our research achievement will contribute for furthering future regenerative medicine and drug discovery for complexed neural disorders.