

Abstract

Joshua Bagley :

“Using brain organoids to study human interneuron migration”

Development of the forebrain involves the migration of GABAergic interneurons over long distances from subcortical into cortical brain regions. Although defects in interneuron migration are implicated in neuropsychiatric diseases such as Epilepsy, Autism, and Schizophrenia, model systems to study this process in humans are currently lacking. To develop a suitable model system, we used a novel 3D cerebral organoid co-culture system to study human interneuron migration. We observed robust long-distance migration of interneurons from ventral into dorsal forebrain regions. These migrating interneurons can produce various interneuron subtypes, and live-imaging analysis shows features consistent with tangential interneuron migration. Moreover, reduced migration through drug-induced inhibition of chemotaxis receptors highlights the utility of this system for drug-screening. Therefore, our results demonstrate that cerebral organoid co-cultures can model complex interactions between different brain regions. Combined with reprogramming technology, this system offers a possibility to analyze complex neurodevelopmental defects using cells from neuropsychiatric disease patients, and to test potential therapeutic compounds.