BDR SEMINAR (Kobe & online hybrid)

András Lakatos

Department of Clinical Neurosciences, University of Cambridge

Monday, July 1, 2024

11:00-12:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom

Zoom meeting URL will be announced on the event day by e-mail.

※This seminar is open only to BDR members.

3D human neural organoid models for interrogating mechanisms and therapeutics in neurodegeneration

Summary

Animal models and two-dimensional human stem cell-derived culture platforms provided major insights into neurodegeneration-related molecular disturbances, highlighting potential therapeutic targets. However, these models do not faithfully recapitulate the human-specific aspects of cell diversity, complex cell interactions or pathobiology, which may have hampered therapeutic advances. This is especially pertinent to amyotrophic lateral sclerosis (ALS), the most common motor neurone disease, which is invariably fatal and untreatable. To help overcome these issues, we developed an ALS patient-specific three-dimensional neural organoid slice culture system, a complementary human model that mimics cortical tissue architecture and captures early pathological hallmarks. Using a combination of single-cell RNA-sequencing and biological assays, we revealed early and distinct proteostasis, transcriptional, DNA repair and biophysical disturbances in various cortical cell types. Our findings provide mechanistic explanations for the initial steps in synaptic disturbances and cell death, offering a human translational ALS research platform.

In my talk, I will provide proof-of-principle examples of our novel approach for precise target identification and pre-clinical drug testing and discuss its potential broader implications in neurodegeneration research.

Host: Minoru Takasato

Laboratory for Human Organogenesis, BDR

Contact: minoru.takasato@riken.jp

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