Onsite!! & Zoom

IMEG Seminar Series

The road to global science

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Human kidney organoids as novel models of developmental and cell biology

This seminar series is open to all students and researchers in Kumamoto University.
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We have developed a simple, commercially available method to differentiate human pluripotent stem cells into intricately patterned, multi-segment organoids that resemble kidney tissues. These organoids form via a developmental pathway that induces the nephron progenitor cell, which gives rise to podocytes, parietal cells, proximal tubules, and distal tubules along a proximal-to-distal axis. Each of these cell types exhibits a unique morphology and gene expression profile. They also exhibit unique functional characteristics, which can be assessed in a growing list of physiology assays and mutant phenotypes. For instance, only proximal tubular cells, which express ACE2, can be infected with COVID-19, whereas only podocytes can recruit vascular cells after implantation to form glomerulus-like structures. The organoid developmental trajectory requires modulation of hedgehog signaling through primary cilia, thus cilia knockout stem cells fail to efficiently differentiate into organoids. Mutations associated with polycystic kidney disease or cilia knockout cause organoid tubules to swell thousands of times in size, producing large, fluid-filled cysts of centimeter diameters. Mutations in cystinosin, a lysosomal cystine transporter, result in cystine accumulation and nephron disintegration, similar to the human pediatric disorder, nephropathic cystinosis. These disease models are currently being used to test innovative therapeutics and disease-specific mechanisms. The combination of CRISPR gene editing with organoid differentiation enables new types of cell and developmental biology experiments, with high relevance for human kidney disease and regenerative medicine.

Host: Ryuichi Nishinakamura (IMEG, Kidney Development)
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