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森實 隆司 博士

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"Kidney Organoids for Disease Modeling and Kidney Regeneration"

日時：2018年6月6日（水）9:00 ～11:00 AM

場所：JKiC棟 1階会議室

Abstract: We have developed an efficient, chemically defined protocol for differentiating human pluripotent stem cells into multipotent nephron progenitor cells (NPCs) that can form nephron-like structures. By recapitulating metanephric kidney development *in vitro* we generate $SIX2^+SALL1^+WT1^+PAX2^+$ NPCs with 80-90% efficiency within 8-9 days of differentiation. NPCs form kidney organoids containing epithelial nephron-like structures expressing markers of podocytes, proximal tubules, loops of Henle and distal nephrons in an organized, continuous arrangement that resembles the nephron *in vivo*. The organoids express genes reflecting many transporters seen in adult metanephric-derived kidney, enabling assessment of drug nephrotoxicity mediated by drug transporters. Stromal cells are also generated with the presence of $PDGFR\beta^+$ fibroblasts/pericytes, and $CD31^+$ endothelial cells. This kidney differentiation system can be used to study mechanisms of human kidney development. Epithelial toxins can cause stromal cell expansion with characteristics of myofibroblasts, indicating kidney organoids can be used to model kidney fibrosis *in vitro*. Polycystic kidney disease (PKD) patient-derived organoids exhibit cystic phenotypes. Hence the generated kidney organoids are effective tools to study genetic disorders of the kidney as well as mechanisms of kidney injury. Generation of NPCs, when coupled with tissue engineering, may lead the way to generation of functional kidney replacement tissue in the future.

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