



# CDB SEMINAR

## Minoru Takasato

Murdoch Childrens Research Institute, Melbourne, Australia

Thursday, December 3, 2015

10:00~11:00 Seminar Room A7F

### Regulating mesoderm regionalization generates kidney organoids from human pluripotent stem cells

#### Summary

The human kidney contains up to 2 million nephrons responsible for blood filtration, excretion, the regulation of pH and electrolyte and fluid balance. As there is no postnatal progenitor cell in the kidney, nephrons are never renewed spontaneously once they are lost or severely damaged. This irreversible progression of kidney damage causes the continuous 7% rising of the end-stage renal disease per annum globally and \$1.1 trillion in medical cost of dialysis over this decade. Therefore, there is an urgent need for renal regenerative strategies generating kidney tissues artificially. One approach is the recreation of the kidney via directed differentiation of human pluripotent stem cells (hPSCs). Directing differentiation to kidney is challenging as the adult kidney comprises >25 distinct cell types, derived from 4 progenitors, including ureteric, nephron, vascular and stromal progenitors. Here we utilized the developmental mechanism regulating mesoderm regionalization for the preferential induction of collecting duct versus kidney mesenchyme progenitors. This enabled us to generate kidney organoids that contain nephrons associated with a collecting duct network surrounded by renal interstitium and endothelial cells. When transcription profiles of kidney organoids were compared to human fetal tissues, they showed highest congruence with first trimester human kidney. Furthermore, the proximal tubules revealed reabsorption functionality and differentially apoptose in response to cisplatin, a nephrotoxicant. Such kidney organoids represent powerful models of the human organ for future applications, including nephrotoxicity screening, disease modelling and as a source of cells for therapy.

Takasato, M. et al. Kidney organoids from human iPSC cells contain multiple lineages and model human nephrogenesis. *Nature* 526, 564–8 (2015).

Takasato, M. & Little, M. H. The origin of the mammalian kidney: implications for recreating the kidney in vitro. *Development* 142, 1937–1947 (2015). Review article

Takasato, M. et al. Directing human embryonic stem cell differentiation towards a renal lineage generates a self-organizing kidney. *Nat. Cell Biol.* 16, 118–26 (2014).

#### Host:

Hironobu  
Fujiwara

Tissue  
microenvironment,  
CDB  
[hfujiwara@cdb.riken.jp](mailto:hfujiwara@cdb.riken.jp)  
Tel:078-306-3171  
(ext:1511)

RIKEN CENTER for DEVELOPMENTAL BIOLOGY (CDB)