Research Theme
Developmental Biology and Regenerative Medicine

Research Project Title
Differentiate Human Pluripotent Stem Cells into Functional 3D Kidney Organoid

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Project Description

Kidneys are bilateral organ playing a critical homeostatic role in regulating body fluid composition, waste excretion, and hormone secretion. Adult mammalian kidney parenchyma is comprised of approximately 30 different types of cells, making it one of the most complicated organs inside our body. Given that the number of people suffering from end-stage renal disease (ESRD), a consequence of many conditions including genetic defects, diabetes, cardiovascular diseases, and hypertension, is increasing rapidly, alternative therapeutic methods other than dialysis and kidney transplantation are urgently needed.

The ultimate goal of regenerative medicine is to replace lost or damaged cells, which potentially could be achieved by extrinsic cell/tissue compensation. The establishment of methodology to reprogram somatic cells into a induced pluripotency status has rekindled our enthusiasm in organ regeneration. The induced pluripotent stem cells (iPSCs), in theory, are capable of differentiating into all cell types inside our body, representing an unlimited cellular resource for regenerative medicine. Kidney development entails a reciprocal induction between two progenitor populations, Metanephric Mesenchyme (MM) and Ureteric Bud (UB), both of which were originated from a thing strip of mesoderm termed intermediate mesoderm. Mouse genetic studies showed that MM develop into podocytes, proximal tubular, loop of Henle, distal tubular, and distal connecting tubular plumbing into the collecting system, which is entirely derived from UB. Vascular progenitors invade into the S-shape stage developing nephron to elaborate the renal vasculature system.

Recent studies have developed protocols to generate kidney organoids from human pluripotent stem cells. However, these organoids resemble more mesonephros, which is a transient embryonic kidney population, instead of metanephros giving rise to functional adult kidney. The ultimate goal of this project is to establish methodologies to differentiate human pluripotent stem cells into 3D kidney organoids, which resemble metanephric kidney. To do this, we will develop multidisciplinary approaches combining a 3D differentiation method with organ scaffolding technology. To evaluate the functionality of the derived kidney organoid in a more stringent manner, we will adopt multiple approaches, including cellular biology, transcriptome/epigenome profiling, chimeric complementation in neonatal mice, and etc. Subsequently, kidney disease modeling will be performed by applying this differentiation method to patient-specific iPSCs baring genetic defects, which dispose the patients to end-stage renal diseases.
Contact Us

If you have questions regarding this project, please email the Principal Investigator.

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