Building the kidney from pluripotent stem cells

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Organogenesis generates higher-order structures containing functional subunits, connective components, and progenitor niches. Despite recent advances in organoid-based modeling of tissue development, recapitulating these complex configurations from pluripotent stem cells (PSCs) has remained challenging. The kidney derives from the embryonic metanephros, which develops by the reciprocal interactions between the nephron progenitor and ureteric bud. We previously identified the distinct origins of these two precursor tissues and generated the nephron progenitor from mouse and human PSCs (Taguchi et al. Cell Stem Cell 2014). The induced nephron progenitors readily formed glomeruli and renal tubules in vitro, and upon transplantation, human glomeruli were vascularized with the host mouse endothelial cells (Sharmin et al. J Am Soc Nephrol 2016). We also developed a protocol to expand the nephron progenitors in vitro while retaining their nephron-forming potential (Tanigawa et al. Cell Rep 2016).

More recently, we reported an induction protocol for the ureteric bud from mouse and human PSCs, by studying the developmental processes of this second lineage, which contains epithelial kidney progenitors that undergo branching morphogenesis and thereby plays a central role in orchestrating organ geometry. Importantly, mouse organoids reassembled from the differentially induced ureteric bud and nephron progenitors developed the inherent architectures of the embryonic kidney, including the peripheral progenitor niche and internally differentiated nephrons that were interconnected by a ramified ureteric epithelium (Taguchi et al. Cell Stem Cell 2017). This selective induction and reassembly strategy will be a powerful approach to recapitulate organotypic architecture in PSC-derived organoids.