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## **Generation of 3D kidney from pluripotent stem cells**

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The kidney has a higher order structure: multiple branched collecting ducts connected to nephrons located at the periphery. Recapitulating such an organotypic structure in vitro is a major challenge in developmental biology and regenerative medicine. The kidney develops through the triad interactions of nephron progenitor, ureteric bud and stromal progenitor. We have previously established the induction protocols for the first two from mouse and human pluripotent stem cells (PSCs) (Cell Stem Cell 2014&2017). These protocols have been successfully applied to model inherited kidney diseases, including congenital nephrotic syndrome and autosomal polycystic kidney disease (Stem Cell Reports 2018, J Am Soc Nephrol 2020). We have recently established an in vitro induction protocol for stromal progenitors from mouse PSCs by elucidating the in vivo molecular features of the renal stromal lineage at the single-cell resolution level. When the induced stromal progenitors are assembled with two differentially induced parenchymal progenitors (nephron progenitors and ureteric buds), the fully PSC-derived organoids reproduce the higher-order kidney structure: branched collecting ducts connected to multiple nephrons with stromal cells distributed between the epithelia (Nat Commun 2022). Thus, integration of PSC-derived lineage-specific stroma into parenchymal organoids will pave the way for recapitulation of organotypic architecture and functions.