STEM CELLS

Budding renal progenitors

Human pluripotent stem cells (PSCs—both embryonic stem cells and induced pluripotent stem cells), differentiated *in vitro* towards a ureteric-bud-committed, renal progenitor-like fate, are able to spontaneously assemble into the cognate three-dimensional (3D) renal structure in organ culture experiments, according to findings just published by researchers at the Salk Institute for Biological Sciences, California, USA. “Our studies ... represent the first report demonstrating the suitability of 3D differentiation and maturation approaches for specifying PSCs into renal-like lineages,” the authors assert in their paper.

Although differentiation of PSCs into renal-like lineages has been reported previously, the derived cells failed to integrate into complex 3D renal structures such as the ureteric bud. To overcome these problems, the researchers developed a 4-day, two-stage renal priming protocol, in which sequential combinations of growth factors were used to direct cells towards a mesodermal renal lineage with

a gene-expression profile characteristic of ureteric bud progenitor cells.

The investigators then tested the ability of the differentiated human cells to aggregate and integrate into complex 3D renal structures by performing re-association organ culture experiments with dissociated and re-aggregated mouse embryonic kidney cells. The differentiated human cells specifically integrated into chimeric ureteric bud structures (bud trunk and tip) with an efficiency of 20–50%, but not into other renal structures. Functionality of the formed chimeric ureteric buds was demonstrated in long-term cultures, by polarization of the ureteric bud tips and subsequent compression of the surrounding mouse metanephric mesoderm, thereby mirroring nephrogenesis processes that occur *in vivo*.

The potential application of the researchers’ protocol for drug discovery studies in disease-related renal lineages was established by the successful ureteric bud formation by *in vitro* differentiated PSCs derived from a

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patient with polycystic kidney disease. As the researchers further speculate, “the possibility to generate human renal lineages able to integrate into complex 3D structures *ex vivo* might facilitate the modelling of kidney disease as well as allow for the advancement of stem cell-based clinical applications for the treatment of renal diseases.”

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Original article Xia, Y. et al. Directed differentiation of human pluripotent cells to ureteric bud kidney progenitor-like cells. *Nat. Cell Biol.* doi:10.1038/ncb2872