# Advancing the applications of human pluripotent stem cell-derived kidney organoids.

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The development of protocols for the differentiation of human pluripotent cells to complex multicellular organoids provides novel opportunities for stem cell medicine. We have developed a protocol for the generation of multicellular human kidney organoids from human pluripotent stem cells (Takasato et al, Nature, 2015; Nature Protocols, 2016). The application of kidney organoids for disease modelling, drug screening or tissue therapy options will require evidence that kidney organoids are an accurate model of the developing human kidney tissue and that the protocols for generation of such tissue are robust, transferable, able to be scaled and can result in a functional tissue. Using CRISPR/Cas9 gene edited iPSC lines, we are comprehensively examining both the lineage relationships of the cell types within kidney organoids and the identity of the component cells and comparing these to what is known in both developing mouse and human fetal tissues. Via single cell transcriptional profiling, we have examined the cellular complexity of kidney organoids, identifying the underlying sources of batch variation and the identity of potential off target cell types. Using changes in culture format, we are developing approaches for the scale up of tissue generation and automate the production of organoids. Transplantation of these human pluripotent stem cell-derived kidney organoids has revealed evidence for vascularisation and maturation, as evidenced by improved ultrastructure. Altogether, these advances are moving us closer to the application of patient-derived kidney organoids for tissue regeneration.