Directed Differentiation of Human Pluripotent Stem Cells into Functional Kidney Cells that Form Nephrons in Kidney Scaffolds

Maxim, Demetri

Chronic kidney disease (CKD) is a significant global health problem that affects over 31 million Americans. Kidney transplantation is an effective treatment for CKD, but is limited by donor shortage and organ rejection. The regeneration of functional kidney tissue or even a full kidney from human pluripotent stem cells (hPSCs) would be an ideal treatment for CKD because hPSCs can be derived from patient skin cells, which would eliminate the risk of rejection. Here I describe a method of differentiating hPSCs into functional kidney cells that can subsequently form nephrons when seeded into kidney scaffolds. HPSCs were first differentiated into nephron progenitor cells through treatment with the WNT signaling pathway activator, CHIR99021, followed by treatment with fibroblast growth factor (FGF) signaling factors. When cultured in the absence of external factors, these nephron progenitors underwent a mesenchymal-to-epithelial transition and differentiated into functional kidney epithelial cells that formed tubules expressing the proximal tubule markers, AQP1, CDH6, LTL, and KSP, the distal tubule markers, PAX2 and CDH1, and the collecting duct markers, LHX1 and PAX2, as well as glomerular structures expressing the podocyte marker, WT1. When seeded into scaffolds of decellularized mouse kidney tissue, this heterogeneous population of functional kidney cells organized into 3-D nephrons. These data show that decellularized mouse kidney tissue can provide the necessary signals to induce nephron formation in vitro and establish a method of generating functional kidney structures from hPSCs. These structures could be used to create functional kidney tissue or potentially a full replacement kidney as a more effective and longer lasting treatment for patients suffering from CKD.

Awards Won:
First Award of $5,000
Intel ISEF Best of Category Award of $5,000