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Promoting Podocyte-Endothelial Interactions in Human Kidney Organoids Using Microfluidic Chips

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Objectives: Human kidney organoids are nephron-like structures that can be grown in vitro to study renal disease and develop therapies. A drawback, however, is that organoids are not properly vascularized and lack perfusion. Combining kidney organoids with microfluidic chips has promise to improve organoid maturation and vascularization. Thus, we have developed a protocol to carry out kidney organoid differentiation entirely within a microfluidic device and assessed the resultant structures for evidence of improved vascularization.

Methods: A positive-relief mold was generated using a stereolithography 3D printer to make a PDMS device with multiple channels separated by micro-pillars, which could accommodate a physiological flow rate. Then, we optimized our standard kidney organoid protocol for the microfluidic chip by altering the ECM surface coating, undifferentiated human pluripotent stem cell seeding, and timing of media exchanges to support the much smaller growth environment. Following these modifications, we imaged organoids on day 18 of differentiation by immunofluorescence.

Results: The presence of kidney-specific cells and structures was confirmed by confocal microscopy after fixing and staining for podocyte, proximal tubule, and endothelial cells. The organization of these organoids was comparable to those made in 24-well plates indicating that we have successfully optimized our standard differentiation protocol for a microfluidic platform. Increased endothelial cells were observed in chip-differentiated organoids, compared to 24-well plates. The endothelial cells integrated into organoids in 3D and demonstrated a tendency to interact with the basal membrane of podocytes which was not observed in 24-wells (Fig.1).

Conclusions: Our microfluidic chips provide a stable environment for organoid differentiation. Endothelial cells arise alongside podocytes and can interact with these as they develop. Confined growth or shear stress from media changes promotes podocyte-endothelial cell interactions, compared to static conditions. This provides a strong foundation for future work to study glomerular filtration functions, with potential to enhance bioartificial kidneys.

Endothelial cells invade kidney organoids in microfluidic chips