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MICROFLUIDIC SPINNING OF TOPOGRAPHICAL HOLLOW FIBERS FOR THE DEVELOPMENT OF A 3D FUNCTIONAL GLOMERULUS IN VITRO

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Most kidney diseases are recognized to begin with the dysfunction of the glomerulus, a major filtration unit of the kidney where blood is filtered to form urine. Considerable efforts have thus been made to build an *in vitro* human glomerulus model to better understand this filtration unit. However, existing glomerulus models have not been able to recapitulate the spatial arrangement of glomerular cells in a 3D configuration due to the complex structure of the native glomerulus, which hinders the physiological relevance of these models. With the development of microfabrication and organ-on-a-chip technologies, many 3D tissues with biomimetic structures have been successfully created. Therefore, this study aimed to develop an engineered 3D glomerulus model with an *in vivo*-like configuration that could mimic the function of the glomerular filtration barrier. Hollow fibers with knots (h-FIBERs) were fabricated by microfluidic spinning where sodium alginate was extruded via a custom-made coaxial needle with calcium chloride to form a long tube with spindle knots by rapid crosslinking. Microconvex topography was incorporated into the knotted fibers via chemically induced inflation to resemble the topography of the native glomerulus. 20 h-FIBER scaffolds were then assembled onto a 96-well plate-based platform such that each h-FIBER spanned three wells and gravity-driven flow was established. Endothelial cells were lined within the perfusable tubular channel (blood side) whereas podocytes were cultured on the external surface of the knot (urine side). Following long-term culture (1 month), a functional filtration barrier was established, measured by the transfer of albumin from the blood vessel side to the urine side. Podocyte interdigitation, often missing in monolayer culture, was observed in the knot region and was further enhanced when the knots were decorated with microtopography. This 3D glomerulus model could be used to study the mechanisms of glomerular diseases and examine the toxicity of new therapeutics such as nanoparticles.

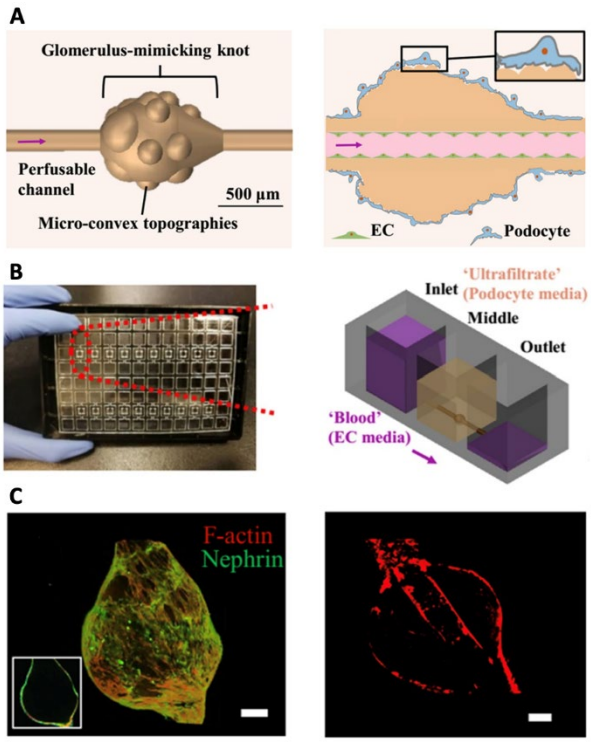

Figure 1 – 3D functional glomerular filtration barrier in vitro. A) Schematic representation of the h-FIBER. B) Assembly of h-FIBER scaffolds onto a 96-well plate-based platform where gravity-driven flow can be established. C) Immunostaining of nephrin (green) and F-actin (red) on the h-FIBER (scale bars: 100 µm).