Influence of polyacrylamide hydrogel stiffness on podocyte morphology, phenotype and mechanical properties

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Chronic kidney disease (CKD) is characterized by a gradual decline in renal function that progresses toward end-stage renal disease (ESRD). Podocytes are highly specialized glomerular epithelial cells, which form with the glomerular basement membrane (GBM) and capillary endothelium, the glomerular filtration barrier (GFB). GBM is an extracellular matrix (ECM) that acts as a mechanical support and provides biophysical signals that control normal podocytes behavior in the process of glomerular filtration. Thus, the modulus of elasticity E or stiffness of "ECM" represents an essential characteristic that controls podocyte functions. The biophysical properties of hydrolyzed Polyacrylamide (PAAm) gels resemble to in vivo ECM and thus provide an opportunity to be applied as ECM-like membranes to study cellular behaviors. Therefore, hydrolyzed PAAm hydrogels were investigated for their potential use as new ECM-like constructs to engineer a basement membrane that form with cultured human podocytes a functional glomerular-like filtration barrier. Such ECM-like polyacrylamide hydrogel construct will provide the unique opportunity of understanding in an in vivo-like setting podocyte cells biological responses by controlling the physical properties of the PAAm membranes. In this work, several PAAm hydrogel layers were prepared by changing the crosslinker concentration. The macromolecular microstructure and stiffness were evaluated by Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM) techniques respectively. Accordingly, the mechanical properties and the polymeric network porosity can be effectively controlled by modulating the crosslinker concentration as well as the swelling degree. Moreover, modulating gel stiffness significantly influenced podocyte behavior including morphology, actin cytoskeleton reorganization. In conclusion, podocytes response to the variation of the mechanical properties of the membranes correlated with the hydrogel's stiffness. This work addresses the complexity of podocytes behavior which will further enhance our knowledge to develop a kidney-on-chip model much needed to study kidney function in both health and disease states.

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