A Multilayered Urethral Construct with Functional Tissue Engineered Vasculature and Epithelial Barrier

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INTRODUCTION

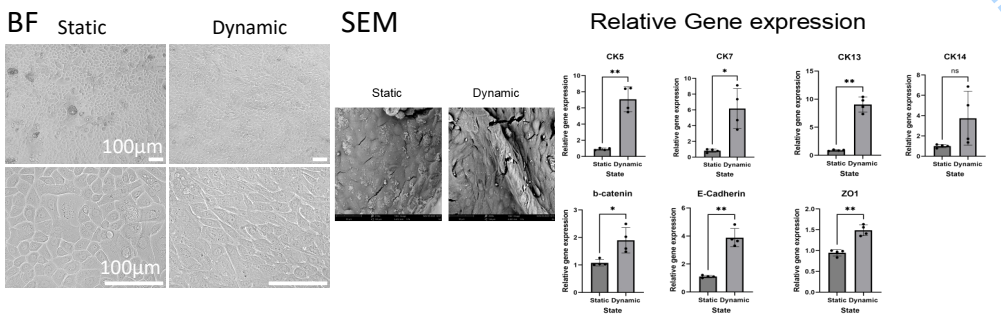
Urethral stricture remains a major reconstructive challenge because current grafts often lack durable integration and vascular support. To address this, we engineered a multilayered urethral construct, combining a functional epithelial barrier with a prevascularized stromal layer, to better mimic native urethral anatomical structure and biological function.

METHODS

Human umbilical vein endothelial cells (HUVECs) and pericytes were encapsulated in collagen I/fibrin hydrogels to generate a prevascularized stromal layer. Vascular functionality was assessed by rhodamine transport and perfusion assays. Human oral mucosal epithelial cells (HOMCs) were expanded, cultured under optimized dynamic conditions, and harvested as intact epithelial sheets using temperature-responsive plates. Melt electrowriting (MEW) was used to fabricate hexagonal poly-ε-caprolactone scaffolds to provide mechanical support. The epithelial patch was then integrated with the vascularized hydrogel to form a multilayered construct, followed by evaluation of morphology, transepithelial electrical resistance, and macromolecular permeability.

RESULTS

-HOMCs



-Cell Sheet, PCL Scaffold and Cell Patch

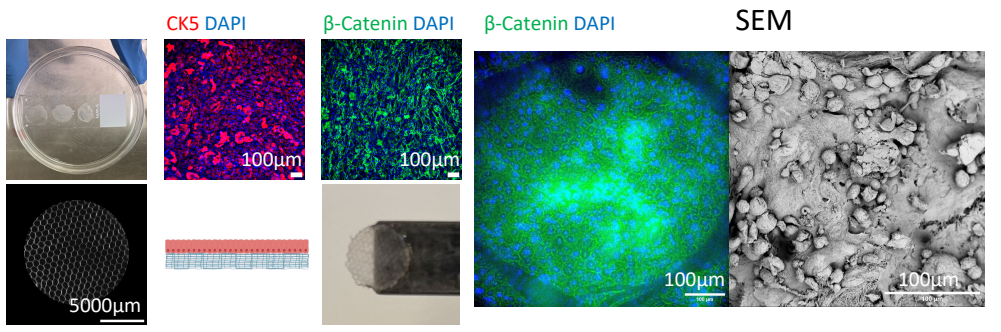
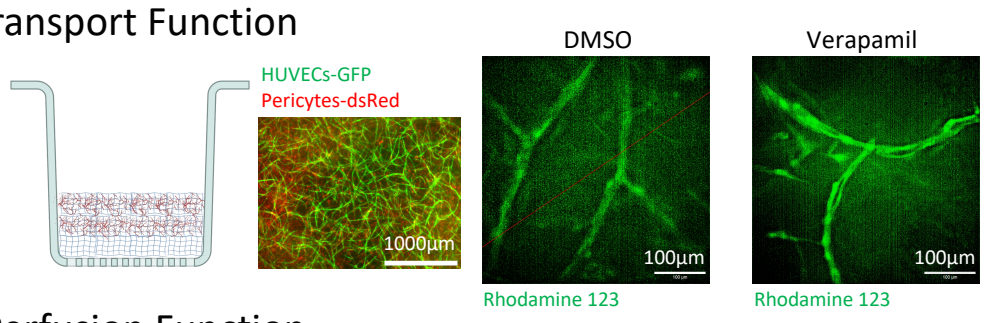


Figure 1. Epithelial Patch: Fabrication and characterization of oral mucosa epithelial cell based epithelial patches using cell sheet reinforced with melt electrowriting (MEW) scaffold.

-Transport Function



- Perfusion Function

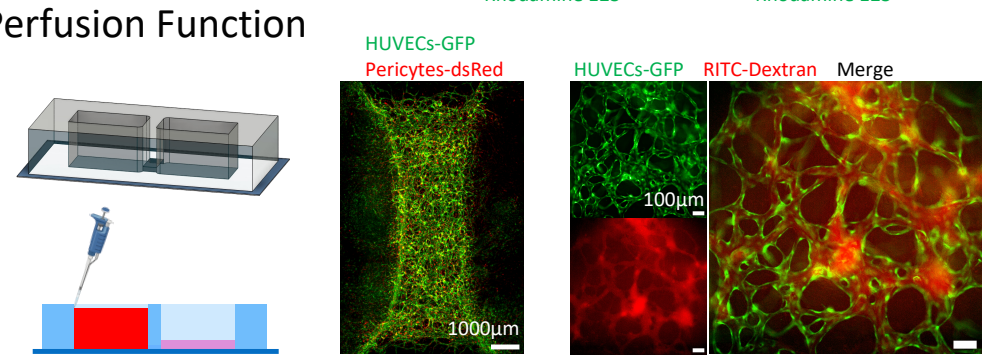
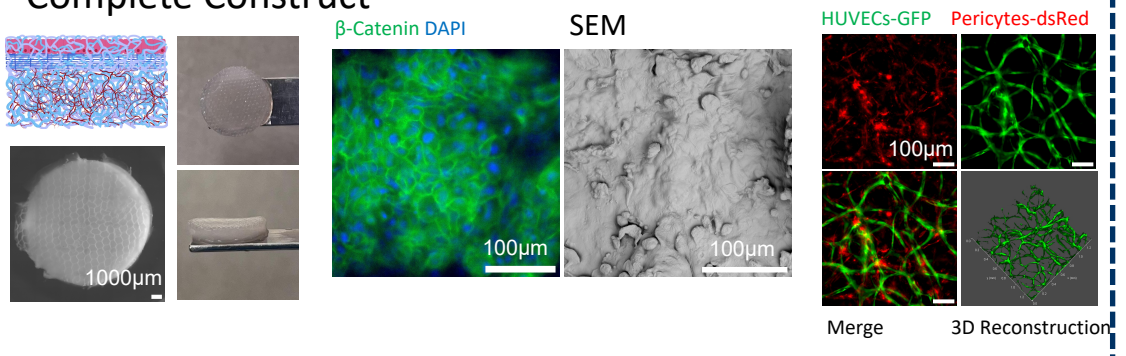


Figure 2. Vascular Construct: Evaluation of angiogenic performance of HUVECs and pericytes in different hydrogel compositions and functionality evaluation.

-Complete Construct



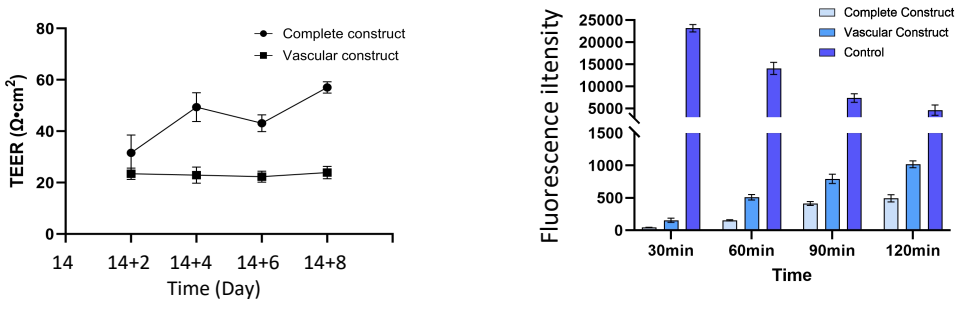


Figure 3. Complete Construct: Assembly and interation of the multilayered urethral-like construct and barrier functional characterization of the complete construct.

CONCLUSIONS

We developed a multilayered urethral construct that integrates a prevascularized stromal compartment with a mature epithelial barrier, thereby reproducing key structural and functional features of native urethral tissue. The vascular layer formed perfusable capillary networks with transport capacity, while the MEW-supported epithelial layer established dense coverage and effective barrier function. By combining vascular support with epithelial integrity, this platform addresses major limitations of current urethral grafts. It therefore represents a promising step toward regenerative urethral reconstruction and also provides a physiologically relevant in vitro model for studying urethral disease mechanisms and evaluating therapeutic candidates.

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