Engineering self-assembled 3D bladder models using FN-silk scaffolds and micrografts structural and transcriptomic characterization

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Introduction & objective

Micrografting is a regenerative strategy in which small tissue fragments promote cell outgrowth and tissue repair. In vitro, similar principles can be applied to generate tissue models from explant-derived micrograft. Recombinant spider silk is an attractive scaffold material due to its favorable biomechanics' properties and biocompatibility.

Research question

Can bladder-derived micrograft combined with recombinant spider silk scaffolds generate physiologically relevant urinary bladder 3D-models?

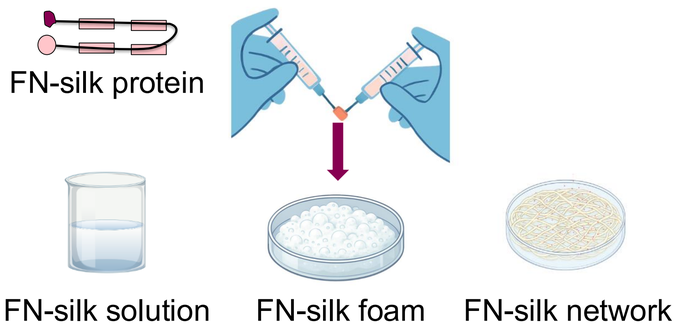
Aims

-To establish a 3D culture system using bladder-derived micrograft integrated into recombinant silk microfibers.

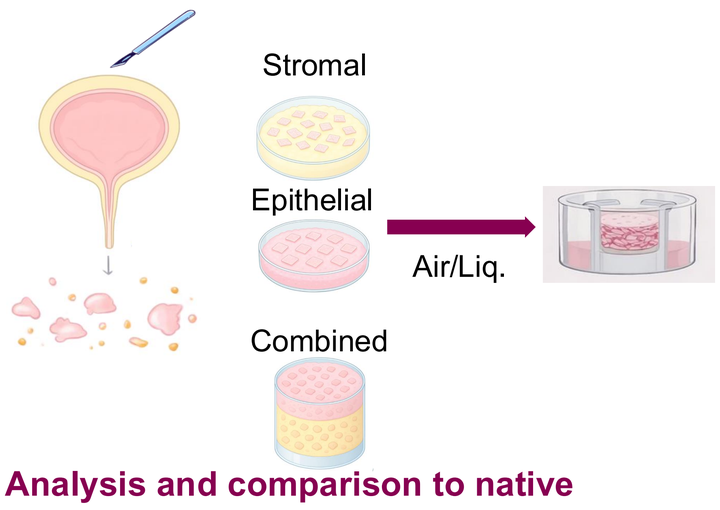
-To evaluate the generated constructs by structural and transcriptomic analyses in comparison with native urinary bladder tissue.

Methods

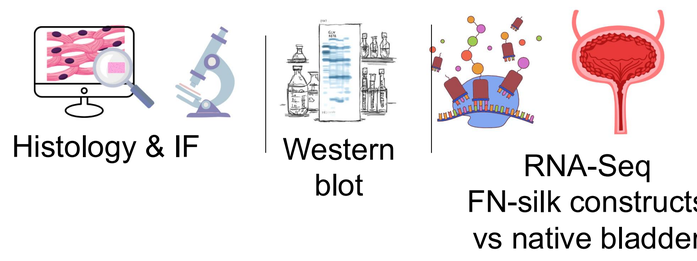
1 FN-silk scaffold preparation



2 Seeding on bladder-derived micrograft and in vitro culture



3 Analysis and comparison to native bladder



Results

1.Structural findings

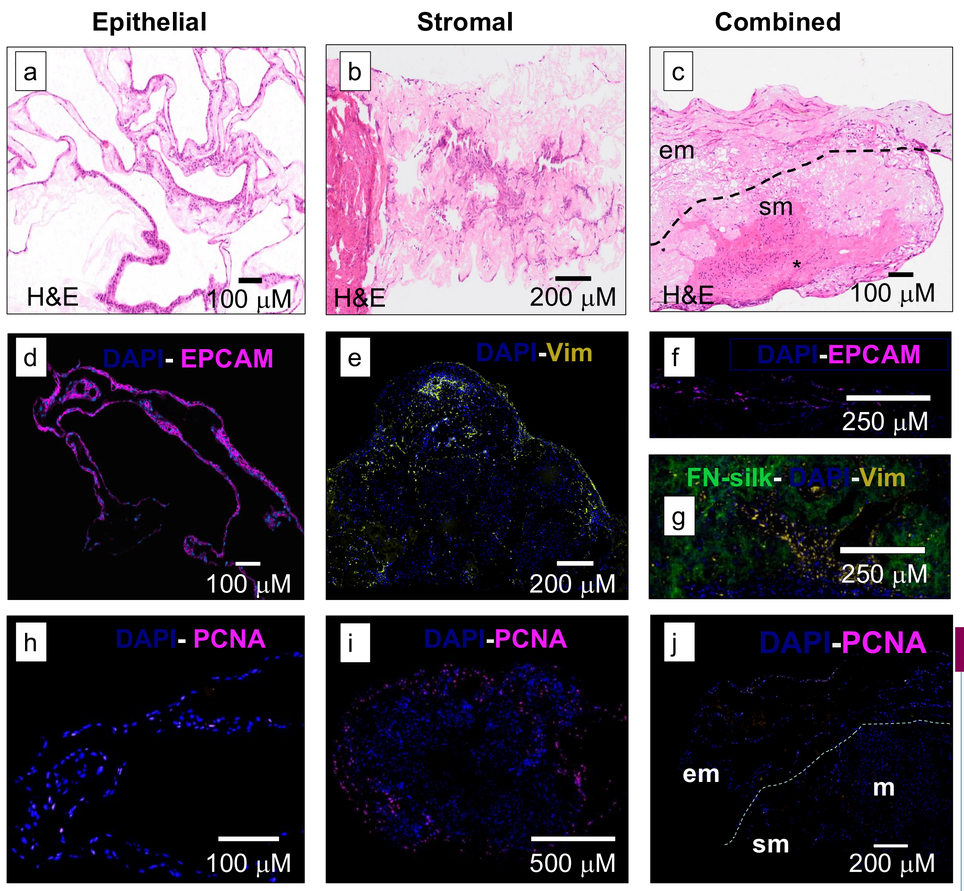


Figure 1. FN-silk micrograft-based bladder constructs and structural characterization. (a–c) Representative H&E staining of epithelial, stromal, and combined constructs, demonstrating tissue organization. (d–g) Immunofluorescence staining showing epithelial marker EPCAM and stromal marker Vimentin. (g) FN-silk scaffold visualization (488) with stromal integration. (h–j) PCNA staining highlights proliferative activity within constructs. (j) Combined constructs display distinct epithelial (em), stromal (sm) compartments, indicating spatial organization and tissue-like architecture. m indicates native micrograft.

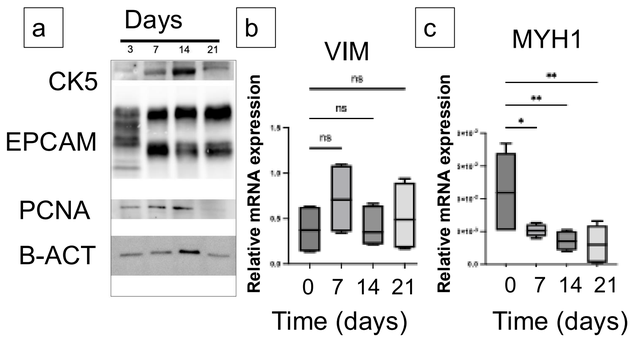


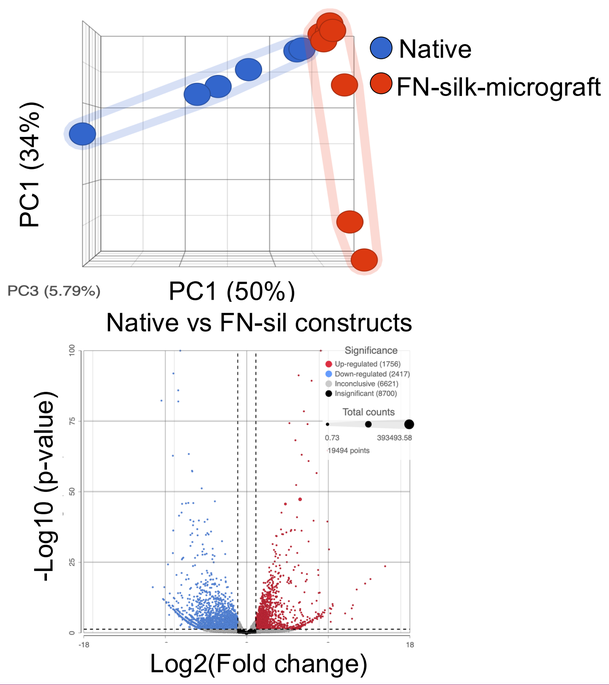
Figure 2. FN-silk micrograft-based constructs expressed epithelial and stromal markers at the protein (a) and mRNA level (b-c).

Key findings

- Highly porous, biocompatible scaffold supporting tissue integration
- Epithelial constructs showed early stratification, proliferative activity, and epithelial marker expression.
- Stromal constructs display cell migration, ECM remodeling, and fibroblast activation.
- Combined constructs formed clear epithelial–stromal layering.

2.Transcriptomic profiling

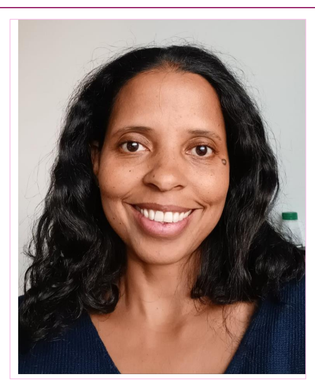
FN-silk constructs display distinct gene-expression profile compared to native micrograft



Biological Pathways	Key marker	Biological interpretation
Inflammation	IL6, C5,S100A8, ARG1, CSF2, S100A12, PTGS2, CXCL8	Mimic early Immune activation
ECM remodeling	MMP1, MMP9, COL1A1,CTSK	Active wound repair and tissue remodeling Cell migration, tissue plasticity
Hypoxia &metabolism	SPARCL1,LUM HK2, PGK1	Glycolysis and HIF1A signaling
Stem/progenitor	SOX9, CD44	Activation of stem cells or Metabolic stress

3.Take-home message & conclusion

- FN-silk scaffolds combined with bladder-derived micrograft supported the formation of biologically active 3D bladder constructs.
- The constructs displayed distinct gene expression profiles compared with native bladder tissue and recapitulated key features of early tissue repair.
- These models may serve as translational platforms for regenerative urology, drug screening, and host–tissue interaction studies.
- FN-silk constructs promote epithelial tissue formation and exhibit wound-associated transcriptional activity, but remain distinct from native tissue and show incomplete smooth muscle maturation



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