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A full-layer bladder wall patch by mincing both porcine bladder mucosa and detrusor in a natural-synthetic scaffold

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INTRODUCTION: Full layer bladder regeneration has remained a challenge in bladder tissue engineering due to lack of or incomplete regeneration of smooth muscle cells, especially in large area defects [1, 2]. To create a suitable tissue transplant for bladder augmentation, we developed a tissue-engineered construct that includes 1) autologous urothelial cells for good barrier function, 2) autologous smooth muscle cells to regenerate a muscular layer, and 3) a biodegradable support that allows take of the transplant, tissue ingrowth and meets the need of low-pressure high-compliance storage function.

METHODS: An electrospun PLGA sheet with optimized porosity [3] was placed on a semi-gel collagen inside a mold and covered by a second collagen hydrogel followed by distribution of minced detrusor from porcine bladder on top. Thereafter, third collagen hydrogel layer was added and minced mucosa of porcine bladder was seeded on top. The whole construct underwent plastic compression (PC), and was incubated for 1, 2, and 4 weeks *in vitro* for electron microscopy, histology and immunoassay studies.

RESULTS: SEM imaging was performed on both surfaces seeded by minced tissue. Imaging the top collagen surface demonstrated a complete coverage with proliferated urothelial cells after two (confluent) and four (multi- layered) weeks. SEM imaging on the middle-seeded surface also showed that, spindle-shaped smooth muscle cells completely covered the surface after two weeks.

Histology and immunoassays demonstrated that successful proliferation of both urothelial and smooth muscle cells was achieved. It was seen that cells migrated from the minced tissue specimens (either on top or inside the construct), proliferated, reorganized and formed a multilayer epithelium (4 weeks) as well as muscle cells. Furthermore, immunostaining for MNF116 and SMA indicated epithelial cell origin and smooth muscle cells respectively.

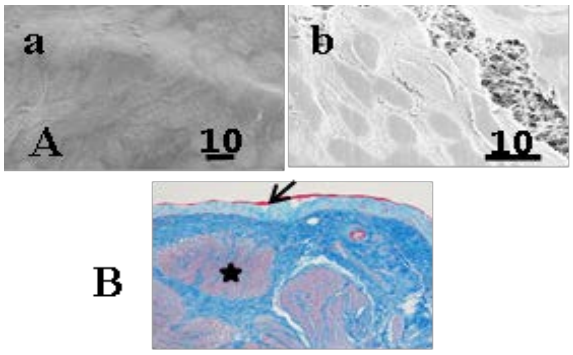

Fig. 1: A) SEM images (a) confluent urothelium, (b) smooth muscle cells and B) Cross-section of PLGA-PC collagen construct seeded with minced mucosa and detrusor after 2 weeks (Trichrome x10 magnification, (arrow) shows urothelium, (*) denotes muscle cells.

DISCUSSION & CONCLUSIONS: With our previous achievements, based on mincing bladder mucosa to regenerate urothelium [3], we continued to develop the technique to regenerate bladder muscle, a tissue that is considered more challenging to expand. We successfully regenerated both urothelium and muscle cells in a hybrid nano-micro, natural-synthetic scaffold of compressed collagen-electrospun PLGA. In a clinical setting the construct is easy to make and all steps: harvesting, mincing and constructing the hybrid scaffold could be performed just before transplantation in a one-stage procedure.

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