Tubular Hybrid Scaffolds for Ureter Tissue Engineering: A Dynamic Culture within a Tissue Bioreactor

Eva-Maria Engelhardt1, Lionel Micol1, Jöns Hilborn2, Jeffrey Hubbell1, Peter Frey1,3
Corresponding Author: peter.frey@epfl.ch
1Laboratory for Regenerative Medicine and Pharmacobiology, EPFL, Lausanne, Switzerland
2Department of Materials Chemistry, Polymer Chemistry, University of Uppsala, Sweden
3Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Introduction
Cystoplasty for urinary tract reconstruction, using intestinal or gastric segments is the common treatment for congenital malformations. To overcome complications associated with this treatment (i.e. metabolic disturbances), successful cell-based approaches in cystoplasty have been reported.
We are interested in the regeneration of ureteral tissue. For this purpose, we designed a bioreactor for the culture of tubular scaffolds under dynamic conditions. The mechanical stimuli mimic the dynamic of the ureter. Furthermore, it is known that such a stimulus favours the contractile smooth muscle cell phenotype [1]. As scaffold material we opted for a hybrid matrix made of collagen and a tubular-shaped polycaprolactone mesh. The combination of synthetic and natural materials allows fabricating scaffolds with appropriate mechanical strength and excellent physiological activity.

Materials and Methods
Scaffold fabrication was carried out by a modified technique described previously [2]. A collagen gel made of neutralized rat-tail collagen I solution was polymerized around a tubular polycaprolactone mesh followed by a step of plastic compression. The removal of excess water from the gel enhances the mechanical properties of the scaffold. Human bladder smooth muscle cells (SMCs) were seeded inside the gel by mixing them into the neutralized collagen solution prior to polymerization. Human bladder urothelial cells (UCs) were seeded in the inner lumen of the scaffold. This co-culture represents the histology of ureteral tissue. Cell-seeded tubular scaffolds were placed inside a medium-filled tissue bioreactor. A controlled medium flow through the inner scaffold lumen generates mechanical stimulations, which were analyzed by manometer measurements and stereomicroscopy.

Cell-seeded scaffolds were cultured for 2 weeks and analyzed with the AlamarBlue assay, Live/Dead stain, and immunohistochemistry.

Results
So far, human bladder cells were only grown on hybrid scaffolds under static conditions. Cells showed excellent cell viability. After 2 weeks of culture the scaffold surface was covered with a layer of UCs, and SMCs had proliferated within the scaffold. In a next step cell-seeded scaffolds are cultured in the bioreactor under dynamic conditions and results will be compared with those of static cultures.
The developed tissue bioreactor allows generating pressure waves throughout the scaffold in the same range as in the ureter (5 – 15 cm H2O). A flow gradient from 0 mL/min to 1000 mL/min generated a pressure increase from 3±0.2 cm H2O to 14.4±0.7 cmH2O.

Discussion and Conclusions
Hybrid scaffolds were identified to be excellent scaffolds for human urinary tract cells. Their potential to be shaped into tubular matrices makes them ideal scaffolds for ureter tissue engineering. The designed bioreactor allows engineering an ureteral tissue under conditions that are very similar to natural ones, thus resulting in an implantable, cell-seeded scaffold material.

References