

Collagen-based bilayered biomimetic tubular materials for airway applications

Airway transplantation remains a major biological and clinical challenge. Recently, the group led by Pr. Martinod, from Avicenne Hospital and H&P laboratory, demonstrated that airway bioengineering using cryopreserved and stented aortic allografts was feasible for complex airway reconstruction, with *de novo* generation of cartilage and regeneration of a mixed neoeepithelium. Still, lack of donor tissue prevents this strategy from a wider dissemination. Also, late stent removal (average time 18 months) remains problematic for patients' outcome, causing granulomas, obstruction, and infections. There is a strong need for relevant off-the shelf biomimetic materials.

The LCMCP has developed a materials processing strategy based on ice-templating followed by topotactic fibrillogenesis that enables the formation of highly concentrated tubular collagen materials in non-denaturing conditions. More recently H&P and LCMCP have improved upon this strategy by adding an inner non porous collagen lining to tubes matching the tracheal dimensions. Both human stromal cells and bronchial epithelial cells colonized and differentiated in each relevant layer, and primary cells originating from a fresh sheep bronchus migrated and differentiated in the tubes.

In this doctoral project, we hypothesize that biomimetic collagen-based constructs enriched with relevant growth factors and matrix components can serve as a controlled platform for airway regeneration, and provide grafts with improved mechanical strength, able to accelerate tracheal repair and secure stent removal post-surgery. Optimized compositions will be assessed based on structural, mechanical and *in vitro* analysis, especially chondrogenesis and functional epithelium formation. Materials recapitulating the tracheal architecture with organized annular cartilage rings will also be investigated, and *ex vivo* experiments will enable to mimic *in vivo* regeneration. Implantation of optimized materials in sheep are also planned for long term preclinical evaluation.