Biomimetic collagen tubular constructs for vascular and tracheal grafting

In mammals, vascular tissues such as arteries, capillaries and veins are composed of a precise assembly of specialized muscular and endothelial cells held together by a complex structure composed of proteins such as laminin, elastin and collagens. Arteries in particular, are composed of three layers with different protein compositions, the tunica intima, tunica media and tunica adventitia. The composition of the two latter structures is largely dominated by type I collagen. This protein ensures the mechanical performance of the arteries and hosts smooth muscle cells. Mimicking such layers using the native proteins found in arteries may provide a successful alternative to the synthetic vascular grafts, which use in small-diameter vessels can cause occlusion following surgery. The application of collagen-based materials in tissue engineering requires a precise control over the proteins’ assembly mechanisms to mimic the architecture of native tissues [1]. The recently proposed topotactic fibrillogenesis strategy enables self-assembly of type I collagen into fibrillar constructs and, simultaneously, stabilization of the macroscopic patterns defined by the ice templating technique [2]. This thesis project aims at providing new types of biomimetic tubular materials to serve as models to deepen the fundamental understanding of graft integration and tissue regeneration after implantation. The ultimate goal is to help provide new types of tubular biomaterials as potential grafts to address unmet clinical needs in vascular and thoracic surgery. The ice templating technique actually offers the possibility to adjust the compositional, mechanical and geometrical properties of the relevant materials in order to optimize potential surgical protocols. The fabrication process can be optimized based on structural (TEM, SEM, POM, 2 photon confocal microscopy) and mechanical characterization (tensile testing and radial deformation vs internal pressure). A first research axis will focus on replicating the outer layers of elastic arteries, and to establish the conditions for a proper colonization of the luminal surface by endothelia cells, which is critical to prevent ischemia after implantation. The substrate properties and cellularization process, in particular the interplay between smooth muscle cells and endothelial cells, will be evaluated under static and physiological flow conditions, in collaboration with Prof. A. Barakat (LADHYX, Polytechnique) [3]. The materials will also be assessed by Dr. J. Gaudric (Vascular surgery, Pitié Salpêtrière). A second research axis will focus on selecting the most suitable characteristics for airway transplantation, with iteration of the materials fabrication for tracheal substitution. One type of the prepared tubular constructs will further be implanted in vivo in a large animal model in collaboration with clinical teams (Avicenne Hospital) [4].

(3) E. E Antoine, F. P. Cornat, A. I. Barakat. J. R. Soc. Interface 2016, 13, 20160834
(4) E. Martinod et al., JAMA 2018, 319, 2212-2222