3D colonization of biomimetic tendinous collagen scaffolds

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Tendons connect muscles to bones and transmit forces between them. They are mainly composed of type I collagen fibrils, aligned on average along the bone-muscle axis and arranged in a hierarchical fibrous structure. Collagen fibers fascicles exhibit a periodic waviness, called “crimp”. This supramolecular structure provides tendons with their unique mechanical properties. Tendon injuries are very frequent and standard therapies have a low success rate. For this reason, in vitro tendon engineering represents an important clinical challenge. Furthermore, the complex collagen arrangement in a tendon cannot be reconstituted without the action of specialized cells. We are currently developing a bottom-up approach based on the assembly of a biomimetic collagen scaffold which can be colonized by cells, first on the surface then in the bulk where they can eventually reorganize the matrix.

Concentrated acidic collagen solutions (up to 60 mg/mL) are extruded in a neutralizing buffer which triggers their fibrillation. We thus obtain collagen threads in a reproducible and standardized manner. Extrusion/fibrillation and the subsequent aging result in multiscale surface and bulk structures. A characteristic surface roughness, akin to the “shark skin” pattern exhibited by polymer melts, is observed for the most concentrated solutions. This can be explained owing to their strong viscoelasticity. More unexpectedly, Second Harmonic Generation microscopy reveals that collagen fibrils tend to align at a sharp angle with the thread axis inside a shell of age-dependent thickness, while the core remains isotropic.

Finally, the collagen threads were seeded with mesenchymal stem cells under tension. After two weeks, cells actually colonized the matrix and their morphology showed alignment along the fiber axis (Fig. 1). Our collagen threads constitute a promising in vitro 3D model to study the interplay between the complex supramolecular organization of the scaffold and the cell morphology/differentiation.