

Tendon cells behavior and functions are highly primed by the biophysical and biochemical cues of their microenvironment. The rich signaling stemming from cell-ECM interactions and crosstalk between different cell populations govern multiple mechanisms of tissue homeostasis, the onset and progression of tendinopathy, as well as its following repair outcomes. All these factors with many interdependent feedback responses play key roles on tendon physiology and pathophysiology. A better understanding of the complex tendon niche and its cellular crosstalk is thus critical for decoding the healing mechanisms in tendon injuries and to find new therapies for tendinopathy. However, the lack of representative in vitro tendon models has been a major barrier hindering consistent progress in this field. During the last few years we have leveraged on the lessons learned from combining different types of scaffold systems, cell sources and biofabrication technologies developed for engineering artificial tendon tissues to establish a new generation of bioengineered 3D microphysiological systems recreating specific aspects of its niche. During this journey, we have developed different fibrous systems recreating the intricate hierarchical structure of tendon tissue and have demonstrated how the biochemical context of the system can be explored to guide cell fate into different healthy or diseased phenotypes. By exploring innovative bioprinting concepts, we now can recreate tendon mimetic constructs applying automated and highthroughput sample arraying technologies, allowing to fabricate freeform multicellular tendon microphysiological systems embedded within its own chip device. This toolbox is complemented with synthetic protein binding partners capable of modulating selected biological cues and interfacing with cell surface receptors. This talk will highlight how we have been exploring this toolbox to address unanswered question of tendon physiology and pathophysiology, and demonstrate its potential as in vitro platform for uncovering these complex mechanisms.