Mechanical and molecular parameters underlying tendon formation

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Tendon is a unique connective tissue that transmits the forces generated by muscle to bone and allow body motion. Tendons are comprised of a dense extracellular matrix of type I collagen fibrils that are arranged parallel to the bone-muscle axis. Tendon development, homeostasis and repair rely on specific combinations of mechanical parameters, transcription factors and growth factors that regulate the production and spatial organisation of type I collagen (reviewed in *Nourissat et al., 2015, Havis and Duprez, 2020*). In contrast to other components of the musculoskeletal system, tendon biology is poorly understood (*Gaut and Duprez, 2016*). With bulk transcriptomic analysis of mouse limb tendon cells, we have listed genes coding for transcription factors, signalling molecules and matrix components involved in tendon cell specification and differentiation during development (*Havis et al., 2014*) and identified EGR1 transcription factor and TGFbeta/SMAD2/3 signalling pathway as being involved in tendon formation (*Guerquin et al., 2013*). The interplay between the mechanical and molecular signals regulating tendon formation remains elusive. We have identified the signalling pathway TGFbeta/SMAD2/3 as acting downstream of muscle contraction to regulate limb tendon development *(Havis et al., 2016)* and transcription factor EGR1 as acting downstream of mechanical input in 3D-engineered tendons and mouse Achilles tendons (*Gaut et al., 2016*). We are currently trying to hierarchize the molecular pathways downstream of mechanical forces that regulate tendon formation. We have generated single-cell RNA-sequencing datasets from limb cells under different mechanical constraints. We are about to identify the molecular signatures in different population of connective tissue cells in normal and immobilisation conditions. We believe that the understanding of the interplay between mechanical and molecular signals involved in tenogenesis will provides insights into tendon repair processes.

References

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