Research Week 2020

Single-Cell Transcriptomics and Epigenomics Analysis of Tendon Development

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Keywords

single-cell, transcriptomics, epigenomics, tendons, development

Abstract

Despite tremendous advances in knowledge of most of the organs in our bodies, tendons largely remain a mystery. Yet tendons are implicated in a number of disorders, including over 400 that are characterized by congenital joint contractures—a condition known as arthrogryposis multiplex congenita. To investigate tendons and how they develop, I am performing single-cell transcriptomics analysis of tendon tissues taken from mouse limbs at eight different stages of development. I also plan to supplement this analysis with investigation of single-cell epigenomics data. The aim of this research is to gain insight into various aspects of tendon biology and development, including how tendons can molecularly be distinguished from other tissues, what the distinct stages of tendon development are, how tendon progenitors transition from one developmental stage to the next, and what distinct cell populations exist in the tendon. The tendons come from standard Black6 mice, as well as Scx-GFP mice, which are mice on a Black6 background that express GFP whenever the tendon biomarker Scleraxis (Scx) is expressed. This exogenous Scx-GFP is expressed at a very high level, dwarfing the expression of endogenous Scx. As a result, the level of endogenous Scx is unclear, so an additional aim is to quantify the natural level of Scx in the tendon at each stage. While bioinformatics cannot definitively answer all of these questions on its own, it can inform hypotheses that can then be tested in the wet lab. Ultimately, by improving our understanding of normal tendon development, we can also begin to understand what happens during abnormal development. Furthermore, this new insight could suggest ways to utilize developmental pathways to lengthen tendons, reducing and perhaps eliminating joint contractures.