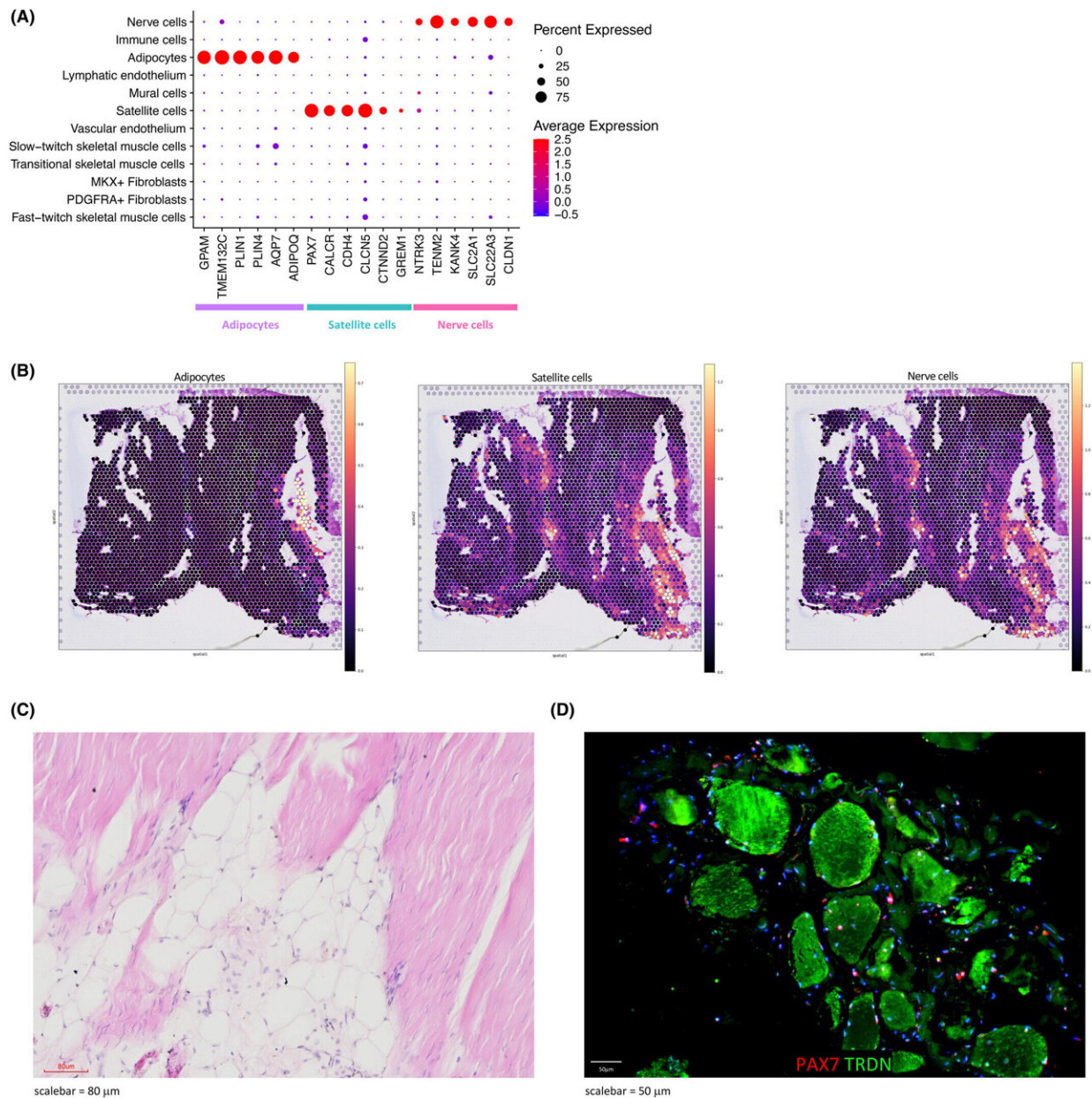


Researchers uncover the cellular secrets of healthy tendons

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(A) Expression of differentially expressed genes in adipocytes, satellite cells, and nerve cells. (B) Cell2location analysis predicted location of adipocytes, satellite cells, and nerve cells. (C) Histology (hematoxylin and eosin staining) clearly showing the presence of adipocytes in healthy hamstring tendon tissue. (D) Representative image of immunofluorescence staining for PAX7 (red) and triadin (TRDN, green) reveals that satellite cells are present in close proximity to muscle fibers in hamstring tendon tissue. Credit: *The FASEB Journal* (2024). DOI: 10.1096/fj.202300601RRR

Research has unveiled the intricate cellular landscape of healthy human hamstring tendons, shedding new light on this vital yet often overlooked component of our musculoskeletal system.

Tendons are the tough, fibrous tissues that connect our muscles to our bones, allowing for smooth, coordinated movement and the transfer of forces generated by our muscles. While tendons are critical for our mobility, their underlying biology has remained poorly understood, particularly in healthy human tissues.

"Tendons are absolutely essential for musculoskeletal function, yet we still have so much to learn about their basic biology, even in a healthy state," said senior author Associate Professor Sarah Snelling of NDORMS, University of Oxford.

"By mapping the cellular makeup of healthy tendons, we can start to unravel the [complex networks](#) that maintain [tendon](#) health and identify potential targets for treating tendon disorders like tendinopathy and tears, which are all too common, especially as we age."

Published in *FASEB Journal*, the [study](#) used single-nuclei and spatial transcriptomic techniques to profile the different [cell types](#) present in

healthy hamstring tendons.

The research team analyzed more than 10,000 individual cell nuclei from four healthy human donors, revealing a surprisingly diverse array of cell types. In addition to the well-known tendon cells, called [fibroblasts](#), the team identified the presence of endothelial cells (which line blood vessels), [immune cells](#), and unexpected cell types previously unreported in tendons, including different skeletal muscle cells, satellite cells, adipocytes (fat cells), and even some cells from the nervous system.

Importantly, the researchers found two distinct subsets of fibroblasts, which appear to play a central role in maintaining tendon health. These fibroblasts are responsible for producing and organizing the tendon's extracellular matrix, the flexible, fibrous scaffold that gives tendons their strength. The fibroblasts were found to have the highest number of potential interactions with other cell types, suggesting they act as key coordinators within the tendon's cellular ecosystem.

"Fibroblasts seem to play a central coordinating role in healthy tendon function," explains lead author, Dr. Jolet Mimpén of NDORMS, University of Oxford. "Not only do they produce the essential building blocks of the tendon, but they also appear to orchestrate complex signaling networks with other cell types. This highlights their crucial role as master regulators of tendon homeostasis."

The study also uncovered the spatial distribution of these cell types within the tendon. This revealed the intricate organization of the tendon, with the two [fibroblast](#) subsets occupying distinct niches and interacting with their neighboring cells in unique ways.

"This study represents a significant step forward in our understanding of tendon biology," says Jolet. "By creating a comprehensive reference atlas

of healthy human [tendons](#), we can start to identify the critical pathways and interactions that are disrupted in disease. This could ultimately lead to new treatments that address the root causes of tendon problems, rather than just managing the symptoms."

More information: Jolet Y. Mimpen et al, Single nucleus and spatial transcriptomic profiling of healthy human hamstring tendon, *The FASEB Journal* (2024). [DOI: 10.1096/fj.202300601RRR](https://doi.org/10.1096/fj.202300601RRR)

Provided by University of Oxford

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