How the extracellular matrix affects the cells within us

All animals, including humans, are affected by the environment in which they live—the cells within our bodies are no different. Cells live in a dynamic fibrous and fluid network that contains many biopolymers that provide structural support for tissues in the human body. This network, termed the "extracellular matrix (ECM)," plays important roles in both normal development and disease progression in many organs (e.g., bone, tendon, heart, muscle, liver, brain) due to its interaction with embedded cells.

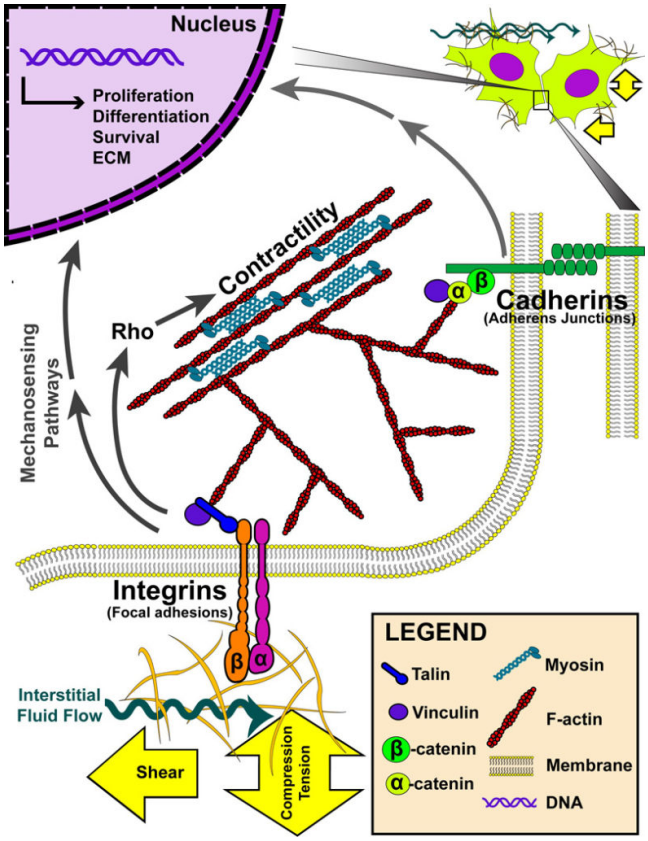

Fig. 1. Model of cell–ECM and cell-cell mechanotransduction.

Through interaction between the ECM and the cells of a tissue, external mechanical stimuli and biochemical cues are converted into signals within the cells. This process is called "mechanotransduction" and helps control cell morphology and function, including cellular processes that remodel the ECM, resulting in complex feedback between the properties of the ECM and the cells within it. In this review, we focus on the role of mechanotransduction in two distinct tissues: tendons, as part of the musculoskeletal system, and the heart, as part of the cardiac system.

The resident cells of our tendons and heart sense ECM stiffness, one of the most profound and well-studied mechanical properties influencing cell behavior, via cell-ECM attachments mediated by cell surface receptors. In particular, integrins, which are a type of adhesion protein that couples the ECM to the cytoskeleton inside of cells, play an important role in force transmission, force balance, and signal transduction of the cells. Tendon and heart tissues have different compositions and functions that demonstrate changes in their ECM during normal homeostasis and disease progression. Despite the fact that the ECMs in diseased tendon and heart are altered mechanically, structurally, and compositionally in dramatically different ways in response to their respective sources of disease onset, cells in these two tissues respond to changes in their environment using similar mechanotransduction machinery. Whereas a wealth of experimental data exists documenting the central interaction between the ECM and cell mechanotransduction, current clinical treatments ameliorating dysfunctional ECM and cell mechanosensing are limited. In addition to continued work using traditional human and animal model systems, new animal models that present unique ECM recovery may inspire innovative treatments. Given that altered matrix stiffness often underlies tendon and heart diseases including tendinopathy and heart failure, understanding how ECM can be remodeled and regenerated biochemically and mechanically may lead to novel therapeutic strategies for targeting the dysfunctional ECM.

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Publication

The (dys)functional extracellular matrix.
Freedman BR, Bade ND, Riggin CN, Zhang S, Haines PG, Ong KL, Janmey PA
Biochim Biophys Acta. 2015 Nov