Recent Advances in Mechanotransduction and Where We Stand in Tendon.

[1,2,3] Banes, AJ., Qi, J., [1,3] Sumanasinghe, R., [3] Tsuzaki, M, [4] Banes, A,N., [5] Dmochowski, J., and [3] Wall, M. Joint Department of Biomedical Engineering[1] UNC, NCSU, Chapel Hill, NC, Curriculum of Applied Sciences and Engineering[2], UNC, Chapel Hill, NC, Flexcell Intl. Corp[3], Hillsborough, NC., College of Veterinary Medicine[4] NCSU, Raleigh, NC, School of Medicine[5], Chapel Hill, NC.

The field of cytomechanics and elucidation of the mechanisms of mechanotransduction have evolved greatly in the past 5 years. Strong support for Ingber's theory of tensegrity has emerged. Na and Wang have shown that mechanical forces can drive COS cell signaling and Src activation much faster than can a ligand such as EGF. There are competing data from Tzima to support the idea that shear stress may activate endothelial cells differently than substrate strain through Pecam-1 and VEGF. The lack of primary cilia in the etiology of polycystic kidney disease by Nauli and the lack of response to shear stress in osteoblasts without primary cilia by Malone and Jacobs point to the idea that cells require the primary cilium but have multiple mechanisms to respond to physical forces. Recent reports by Farnum, Poole and Qi and Banes show that tenocytes have primary cilia that are needed for a proper mechanical stimulus response. Tenocytes respond to substrate strain and shear stress by signaling, activating pathways and strengthening their matrix. Butler's group has shown the relevance of stem cell addition to matrix mechanically conditioned in vitro then returned to the patellar tendon in vivo. However, the magnitude of strain can have adverse affects or act in a positive manner as has been shown for chondrocytes, tenocytes and endothelial cells. Effector ligands such as cytokines, anabolic steroids, norepinephrine and even ATP can modulate tenocyte response to strain. There are likely differences in overall cell responses to strain that depend on the level of cell-cell connectivity and individual vs group, ie syncytial responses. Are cell-cell connections of greater importance than matrix-integrin connections in responses? There is a need to define better markers for tendon cell expression, recognize the multiple cell types in various tendons as well as the contribution from pericytes, stem cells, the vasculature and innervation in these responses.