Alterations in Cytoskeletal Gene Expression in Normal and Degenerate Human Tendon Cells following Cyclic Strain

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Summary:
For the study, primary tendon cells were cultured from healthy and tendinopathic human tendon tissue. Cyclic strain, which is a simulated application of a mechanical load to cells in vitro, was tested on tenocytes. This load caused cells to differ significantly in their expression of matrix degrading enzymes, and production of certain components of the extracellular matrix.

Abstract:

Introduction
The purpose of this study is to determine if changes in the cytoskeletal tensional homeostasis of human tendon cells occur as a result of the control of gene expression and to compare the ability of tendon cells cultured from normal and diseased tissue to re-establish their cytoskeletal tensional homeostasis in response to a changing mechanical environment.

Methods
Tendon specimens were harvested from patients undergoing surgical treatment of posterior tibial tendinopathy or Achilles tendinopathy. Various regimens of cyclic strain were applied to normal and diseased tendon cells using Flexcell® Tension Plus™ System (Flexcell International, Hillsborough, NC). RNA was isolated and gene expression analysis was performed on the extracted RNA using a PCR Array or gene specific primer assays, Reverse Transcription Polymerase Chain Reaction (RT-PCR) and Real-Time PCR. We observed gene expression from the normal and diseased samples which would provide evidence of up/down regulation of inflammatory cytokines, matrix-degrading enzymes, and extracellular matrix (ECM) network components in diseased tissue.

Results
The cells derived from diseased tendon subjected to 15 minutes of stretching showed enhanced expression of MMPs (7,8,9,10,11,13) and down regulation of cadherin, contactin, collagen (type 4, 7, 8), ADAMTS1, and TIMP3, compared to the group of cells derived from normal tendon. After 60 minutes of stretching, MMP7 and KAL1 gene levels were significantly decreased. However, there were no significant differences in up-regulated gene expression seen between the normal and diseased derived tendon cells after 60 minutes of stretching.

Discussion
This study demonstrates that cyclic strain can directly alter gene expression which may drive the response of tendon cells to their mechanical environment and also may explain key differences in how normal and diseased tendon cells respond to mechanical stress differently. We suggest that regulation of gene expression may be an alternative mechanism of tendon degeneration in vivo.