

Evaluation of the Relationship Between Collagen Matrix Damage and Proteoglycan Activity Following Submaximal Fatigue Loading

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Background and Hypothesis:

Previous research indicated that fatigue loading of the anterior cruciate ligament (ACL) leads to disruption and unraveling of the collagen triple helix structure. Using a novel in vivo murine model, we have spectroscopically shown that collagen unraveling at the molecular level is associated with an increase in proteoglycan activity. Moreover, we found an increase in tissue compliance within these damaged tissue domains. We hypothesize that the increase in proteoglycan activity is largely responsible for this mechanical change. To investigate this, we first need to identify the proteoglycan(s) responsible for our biochemical spectra that indicated an elevation in activity associated with unraveled collagen domains. For this pilot project, we histomorphometrically investigated the proteoglycan activity of two potential protein candidates (decorin, versican) following sub-maximal ACL fatigue loading.

Experimental Design or Project Methods:

The right knees of 20 mice underwent 5,000 cycles of moderate or strenuous fatigue loading. Left knees served as a control. Samples were collected 1 and 72 hours after loading. Immunohistochemistry was performed to detect decorin and versican activity in the ACLs.

Results:

A greater area of the ACL was stained with decorin relative to versican in ACLs that underwent moderate fatiguing after 1-hour rest ($p = 0.02$) and 72-hour rest ($p < 0.01$). Similar differences were found in ACLs after strenuous fatiguing and 72-hour rest ($p < 0.01$). No significant temporal differences were found in versican ($p = 0.76$) or decorin ($p = 0.53$) activity in fatigued ACLs relative to controls.

Conclusion and Potential Impact:

These preliminary findings suggest that versican nor decorin are the proteoglycans colocalizing with unraveled collagen. We are currently investigating aggrecan, lumican, and biglycan as other potential proteoglycan candidates to explain our spectroscopic data.