Fibroblast Cytoskeletal Remodeling Contributes to Viscoelastic Response of Areolar Connective Tissue Under Uniaxial Tension

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BACKGROUND: The normal viscoelastic behavior of connective tissue under tension is generally attributed to the material properties of the extracellular matrix (e.g. stiffness, damping) rather than to cellular activity (e.g. contraction, relaxation). A notable exception is healing wounds in which fibroblasts differentiate into myofibroblasts that can generate measurable increases in connective tissue tension over long time periods (hours to days). So far, however, the role of connective tissue fibroblasts in contributing to the viscoelastic behavior of connective tissue under normal physiological conditions remains unknown. We have previously shown that fibroblasts within areolar "loose" connective tissue exhibit pronounced, dynamic cytoskeletal remodeling, spreading and lamellipodia formation within minutes in response to tissue stretch both *ex vivo* and *in vivo*. We also showed that colchicine (inhibitor of microtubule polymerization) abolishes these cytoskeletal responses in response to tissue stretch.
STUDY AIM AND HYPOTHESIS: The goal of this study was to examine the active contribution of fibroblast cytoskeletal remodeling to the viscoelastic behavior of mouse areolar connective tissue *ex vivo*. We hypothesized that colchicine decreases the tissue relaxation time in response to static uniaxial stretch.
METHODS: Areolar connective tissue samples 5 mm by 4 mm and 1 mm thick were dissected from the back of 37 mice immediately after death. Samples were mounted in aluminum clips connected to a tissue stretching device in HEPES physiological saline at 37ºC with/without 100 μM colchicine (randomized). Samples were stretched at 1.0 mm/sec until a load of 4.4 mN was registered, then incubated at that length for 50 minutes while continuously recording tissue load (% tissue elongation 53 ± 5.5%).
RESULTS: In preliminary data analyses, mean ± SE tissue relaxation times were 1170 ± 92 sec and 971 ± 36 sec with and without colchicine respectively ($p < 0.05$). Further analyses of these data will include implementation of a multiparameter viscoelastic model.
CONCLUSION: Inhibition of fibroblast microtubule polymerization with colchicine altered the relaxation response to connective tissue to static stretch. These preliminary data support the hypothesis that fibroblasts actively regulate connective tissue tension under normal physiological conditions.

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