

Faculty Mentor: Dr. Aaron Stoker, Orthopaedic Surgery

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Metabolic Responses of ACL Explants to Estradiol and Pro-inflammatory Cytokine Stimulation

Nicholas Choma, Richard Ma, James Cook, and Aaron Stoker

INTRODUCTION: Anterior cruciate ligament (ACL) injury in females are almost ten times more common than in males. Estrogen levels present during the menstrual cycle have been associated with increased ACL injury rates. Therefore, this study was designed to assess the responses of ACL explants to estrogen and pro-inflammatory cytokine stimulation. It was hypothesized that 17- β estradiol and IL-1 β stimulation, individually or in combination, will significantly increase production of inflammatory biomarkers when compared to controls.

METHODS: With ACUC approval, the ACL was collected from female dogs (n=12). Four 6mm-explants were taken from each ACL. Explants (n=12/group) were randomly assigned to groups: (1) Control (ACL-N), (2) IL-1 β (1ng/ml) stimulated (ACL-I), (3) Estrogen (300ng/mL) stimulated (ACL-E), or (4) Cytokine and estrogen stimulated (ACL-IE). The explants were cultured for 12 days with consistent media changes. Media were assessed for inflammatory biomarkers using commercially available assays.

RESULTS: The ACL-I and ACL-IE groups produced significantly higher inflammatory biomarkers compared to the ACL-N and ACL-E groups across time points. There were no significant differences between the ACL-I and ACL-IE groups or the ACL-N and ACL-E groups.

CONCLUSION: The data from this study indicate that estrogen does not have direct inflammatory or degradative effects on the ACL even in the presence of a pro-inflammatory stimulus. Our laboratory is working to better understand sex disparities with ACL injury and treatment failure.