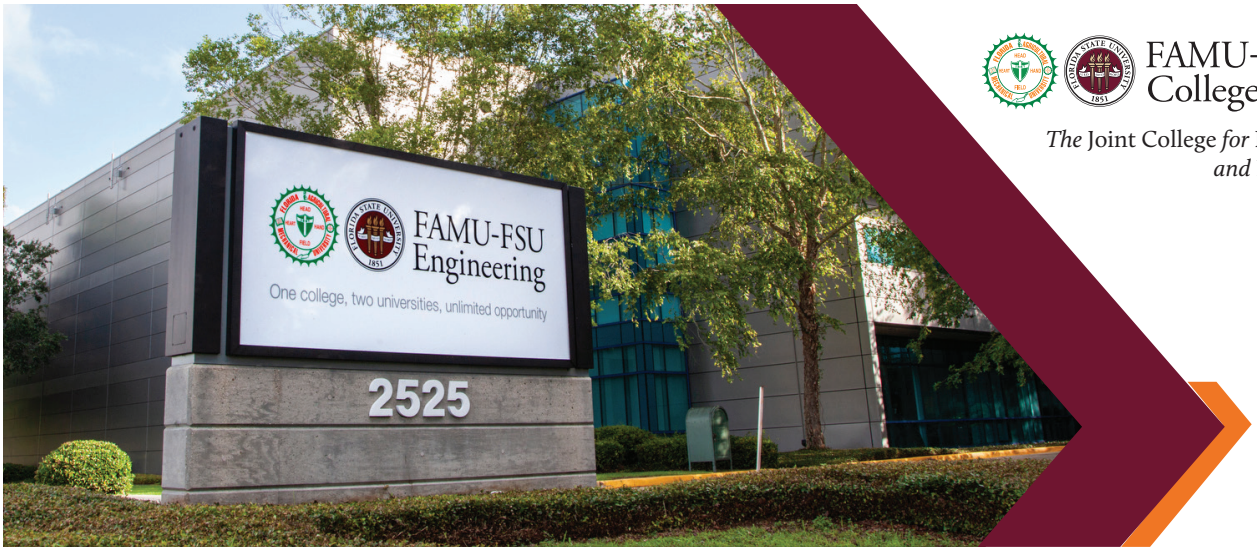

FAMU-FSU College of Engineering

The Joint College *for* Florida A&M Univeristy
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Department of Chemical and Biomedical Engineering

Dissertation Defense

DEPARTMENT OF CHEMICAL & BIOMEDICAL ENGINEERING | FAMU-FSU College of Engineering

By: Ananya Naha (Advisor: Tristan Driscoll)
Date: Monday, September 22, 2025
Time: 1:00pm - 3:00pm
Location: IRCB 1030

Integrin Based Activation of Fibrotic and Inflammatory Pathways in Intervertebral Disc

Abstract: Degenerative disc disease is strongly associated with low back pain, making it a leading cause of disability. With injury and age, cellular remodeling of the disc tissue leads to compositional changes, stiffening, and loss of stress relaxation, particularly in the central gelatinous nucleus pulposus (NP) region of the disc. As part of this extracellular matrix (ECM) remodeling, there is an increase in the deposition of fibronectin, a strongly adhesive integrin ligand that is known to regulate inflammatory signaling. However, it is unclear how these pathological changes in cellular adhesion regulate cell phenotype, and which domains of fibronectin are specifically involved. The goal of this work was to test the effects of fibronectin on disc cell phenotype, mechanosensing, and inflammatory signaling. We identify that fibronectin increases the activation of cellular contractility, the mechanosensitive transcription factor Yes-associated protein (YAP), and the inflammatory transcription factor nuclear factor-κB (NF-κB). This results in decreased production and expression of proteoglycans, which are required to maintain healthy disc function. Next, a dextran vinyl sulfone (DexVS) hydrogel system was employed for presentation of specific fibronectin domains. Fibronectin peptides were found to enhance YAP signaling, inflammatory NF-κB signaling, cellular adhesion, and cellular contractility in NP cells, which leads to a decrease in aggrecan gene expression. Covalent modification of these DexVS hydrogels with bioactive peptides allows for targeted interactions with specific integrin receptors that are involved in healthy or degenerative signaling. In doing so, the integrin binding peptides from fibronectin were identified to activate a contractile phenotype in NP cells. Finally, we developed a disc explant culture system that allowed us to test the efficacy of this material in a native disc environment. This has potential as a therapeutic approach to reverse or slow down intervertebral disc degeneration. Overall, we show that fibronectin is a regulator of phenotypic changes in disc cells, and a potential target for treating disc degeneration at the cellular level. Understanding the role of fibronectin, and its potential as a therapeutic target, could provide new approaches for preventing or reversing disc degeneration.

Key words: Disc Degeneration, Fibronectin, DexVS, Contractility, YAP, NF-κB