Investigating Sex-Dependent Differences in Tensional Homeostasis

Team 17: **Diya Desai, Josephine Dunphy, Nourhan El Sherif, Marin Perez, & Sabrina Wilderotter**
Advisors: **Brianne Connizzo, Michael Smith**

Sex-dependent variances in cellular and tissue mechanics are poorly understood despite evidence showing females' increased susceptibility to soft tissue injuries and degenerative diseases compared to males. This project outlines a collaborative effort between the Smith and Connizzo labs to explore sex-specific differences in cellular mechanosensing, focusing on how cells respond to external stimuli to maintain a resting level of mechanical stress (tensional homeostasis) and extracellular matrix (ECM) remodeling. Using traction force microscopy and a novel tissue bioreactor system, the study aims to quantify differences in tensional homeostasis maintenance between male and female tenocytes and investigate strain transfer through the ECM in mouse flexor digitorum longus tendons. The process involves two components: cellular and tissue levels, described as follows. At the cellular level, mouse tenocytes are extracted through digestion, seeded onto polyacrylamide gels, and then imaged to determine the coefficient of variance in traction forces between the sexes. On the tissue level, tendons are stained for their nucleus and cellular membrane, loaded onto a bioreactor, inserted into a confocal microscope, stretched, and imaged. Initial results reveal challenges in cell culture viability, but successful staining protocols for live tissue imaging have been obtained with images from male and female tendons subjected to strains of 0%, 3%, 6%, and 9%. Subsequent image analysis will calculate nuclear and cellular strain differences between the sexes. The ongoing study will provide crucial insights into sex-dependent mechanisms underlying tissue mechanosensing and potential implications for gender-specific therapeutics.