2022 IMPACT CIRCLE

Project Title: A novel 3-dimensional human tissue model ('*knee in a dish*') to screen for therapeutic interventions for osteoarthritis and to develop optimized treatments"

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Unmet Need/Primary Question:

We are focusing on developing and validating therapeutic interventions for osteoarthritis (OA) using a complex 3D human tissue model ('knee in a dish'). Osteoarthritis is a chronic disease characterized by pain, loss of cartilage, and joint inflammation, and its incidence increases with age. New evidence has emerged for the causative role of senescent cells in the development of posttraumatic and age-related arthritis along with the therapeutic benefit of senescent cell clearance. Interventions will be monitored by measuring proteomic profiles using mass spectrometry to determine changes in protein signatures/biomarkers with treatments.

Novel Hypothesis:

Using a novel model system (3D tissue pellets) that closely mimics what really happens in human diseased or aged joints, and specifically investigating the role of cartilage cells during OA tissue damage, we will discover powerful therapeutic interventions. Cutting-edge mass spectrometry will enable us to tailor drugs, understand how they bolster joint health, and how they actually intervene. This human model may increase the success of future clinical trials in human patients.

Project Proposal:

Human cartilage samples explanted from patients with OA undergoing total knee arthroplasty will be used to build 3D primary tissue pellets. Briefly, cartilage tissue will be cut and 3D pellet cultures of these human chondrocytes will be seeded and formed by centrifugation. After interventions with various senolytic or senomorphic treatments, samples will be prepared for proteomic analysis. The molecular details will provide insights into which interventions are most promising, and which molecular pathways are affected most strongly to refine drug selection.

Description of Potential Impact: This project will provide an excellent platform to screen drugs in these *ex vivo* 3D human tissue models. Proteomics technologies will highlight mechanisms and key components that contribute to OA to refine, optimize, and monitor therapeutic interventions – including future partnering with companies to design novel and more potent drugs.