Clarkson
SCHOOL OF ARTS & SCIENCES

Department of Biology
Interdisciplinary Biosciences & Biotechnology
PhD Dissertation Defense

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will present

"Moving toward treatment of degenerative disc disease: From single-cell level characterization to post-injection leakage assessment"

Abstract:

Degenerative disc disease (DDD) is a leading cause of chronic low back pain (LBP), which results in serious disability and causes a substantial global economic burden. Intervertebral disc (IVD) degeneration (IVDD) alters disc structure and spine biomechanics resulting in a positive feedback loop of degenerative changes. At the cellular and molecular aspect of degenerative changes, cellular senescence accrues in IVDD as does catabolic metabolism. The ability to identify RNA transcript and protein distribution in tissue or cells within a heterogeneous population, such as that of the IVD, at the single cell level while retaining environmental cues can provide immense opportunity to discern different cell types and functions, elucidate clues of pathogenesis, and monitor efficacy of therapies. Challenges exist to accomplish this identification with cost of antibodies, their limited availability or potential incompatibility to the model organism being used, length of probes, insufficient labelling intensity, and inability to label non-coding RNA among other things. This dissertation introduces a detailed, flexible, and economic tool set employing a PCR-tailored RNA *in situ* hybridization in combination with immunohistochemistry protocol that addresses the existing challenges and can be tailored to any gene of interest.

At the macro and clinical aspect, current treatments of LBP due to DDD include conservative treatments (e.g., medications, physiotherapy) and surgical treatments (e.g., discectomy, spinal fusion) that focus on treating the symptoms, not fixing the root problem by repairing or regenerating the disc and its functionality. Although the precise pathogenesis of IVDD remains elusive and controverted, there has been a large movement of research to address the treatment gap by developing and examining the effectiveness of various biological therapeutic approaches (e.g., stem cells, molecular therapies, biomaterials). The avascular nature of the IVD leaves needle injection as the primary means of delivery for these therapeutic agents. However, needle puncture of the disc's annulus fibrosus (AF) has been shown to result in significant disruption of the tissue structure, as the needle must pass through the AF to deposit the injectate into the nucleus pulposus. This disruption provides a ready pathway for injectate to leak out of the disc following needle retraction, decreasing the efficiency of the treatment, and increasing the risk of side effects. Prior studies of post-injection leakage have depended on an *a priori* selection of injection parameters by assessment of evidence of either leakage or the presence or absence of retained injectate. However, there currently exists no experimental framework for rapidly screening injection protocol parameters for leakage risk. This dissertation establishes a protocol for quantifying post-injection leakage and testing its sensitivity to factors believed to affect needle track geometry (i.e., needle size, axial load, and movement) employing a through-puncture defect model we created and validated. The methods described in this dissertation show great promise as tools of detection, assessment, and analysis in various aspects of scientific research moving toward the treatment of DDD.

FRIDAY, APRIL 15TH, 2022

10:15 a.m.

Bertrand H. Snell Hall 112

DISSERTATION COMMITTEE:

Co-Advisors: Drs. Thomas Lufkin (IBB Director), Shantanu Sur (Biology Dept.), Arthur Michalek (MAE Dept.)

Dr. Michelle Yoo, Clarkson University (Biology Dept.)

Dr. Fadi Bou-Abdallah, SUNY Potsdam (Chemistry Dept.)