Department of Materials Science and Engineering,

PhD Defense

March 19th at 1:00pm
PISB 107

Cartilage Molecular Engineering Using Biomimetic Proteoglycans

Name: Evan Phillips
Advisor: Dr. Marcolongo

Abstract

Osteoarthritis is among the leading causes of disability, affecting more than 30.8 million people in the United States, and is associated with a high economic burden that will continue to increase with the aging population. Osteoarthritis is a progressive disease characterized by the degeneration of collagen and the loss of proteoglycans such as aggrecan. The loss of proteoglycans cause a decrease in hydration, load bearing support, and lubrication of the articular cartilage. The goal of this thesis was to evaluate the use of a novel family of biomimetic proteoglycans as a treatment during the early stages of osteoarthritis and to examine the molecular engineering of the cartilage matrix by biomimetic proteoglycans. Biomimetic proteoglycans synthesized by our lab have similar composition, structure, and hydrating capabilities as natural proteoglycans that are lost during osteoarthritis, but resist enzymatic degradation from the hostile environment caused by osteoarthritis. Here, we investigated the effects of biomimetic proteoglycans injected into the intra-articular space in an in vivo osteoarthritic rabbit knee model and evaluated the histological response, joint friction, and the distribution and retention of biomimetic proteoglycans. Our findings showed that biomimetic proteoglycans were well tolerated by the cartilage for the mild osteoarthritic state that was generated and that the molecules were able to diffuse into the cartilage and remain there for at least five

days. We also examined the diffusion characteristics of biomimetic proteoglycans through cartilage with the use of an in vitro cartilage diffusion model in both normal bovine and human osteoarthritic cartilage explants. The molecular diffusion was shown to be size and concentration dependent. Steady state diffusion coefficients for biomimetic proteoglycans were found to be comparable to other large molecule diffusion in cartilage despite the difference in charge. In both bovine and osteoarthritic human cartilage, biomimetic proteoglycans were found localized around the chondrocytes in the pericellular matrix, the region around a chondrocyte which modulates mechanical and chemical signals. This is a first look into the use of biomimetic proteoglycans to molecularly engineer articular cartilage as a way to restore the proteoglycans lost during osteoarthritis.