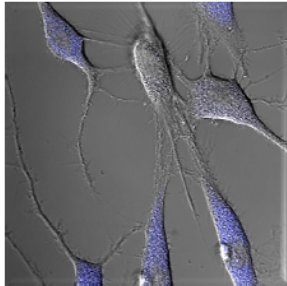
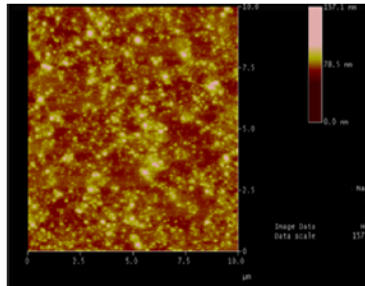


Polysaccharide-Based Carrier Systems for Targeted Drug Delivery in Rheumatoid Arthritis

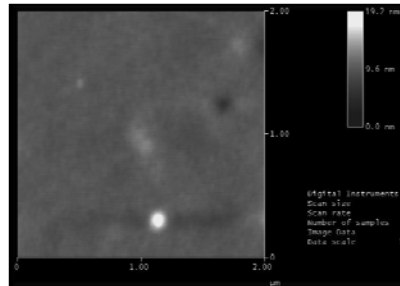
Adverse side effects associated with common therapeutics for rheumatoid arthritis are often a result of non-specific organ toxicity and unpredictable pharmacokinetics. We have several projects aimed at exploiting the properties of biodegradable, natural polymers, particularly polysaccharides, as drug delivery systems to increase the therapeutic efficacy of the so-called disease modifying anti-rheumatic drugs (DMARDs). Polysaccharide-based carriers with large radii to reduce renal filtration and increase circulation time are designed to passively accumulate within joint tissue as a result of the leaky vasculature that characterizes the diseased region. The targeting ability of the drug delivery systems is increased by modification of the carrier system surface with functional groups specific to receptors selectively expressed within inflamed tissue. Furthermore, some of the selected polysaccharides act as active targeting agents by themselves.



Cellular uptake of DMARD-polysaccharide conjugates



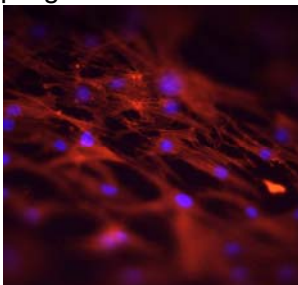
Polysaccharide-based nanoparticles



Polysaccharide-based micelles

The Role of Mechanical Stimuli in the Pathogenesis of Rheumatoid Arthritis

The exact cause of rheumatoid arthritis has not yet been identified, and consequently treatment methods have not been optimally effective. Dynamic exercise therapy is often prescribed to maintain muscle strength and improve the stability and range of motion of joints in patients with rheumatoid arthritis. However, despite the effectiveness of physical activity at increasing muscle strength and fitness, the impact upon disease progression remains unclear. The aim of this project is to use 2D and 3D models based upon rheumatoid arthritis synovial fibroblasts (RASFs) to study the impact of biomechanical factors on rheumatoid arthritis progression.



3D model of rheumatoid arthritis with RASFs



2D and 3D models are subjected to tension using the FlexCell device

Optimization of the Treatment of Rheumatoid Arthritis with an iPod-Size Therapeutic Ultrasound Device

Our collaborator at Cornell University, George Lewis, has created and tested successfully the world's smallest long duration low-intensity therapeutic ultrasound (LITUS) device as a pharmaceutical free approach to osteoarthritis management. However, the potential for LITUS to reduce the symptoms and pharmaceutical needs of RA patients has not been explored. The aim of this project is to use 3D models to gather a greater understanding how the rheumatoid arthritis disease state is altered by long duration ultrasonic stimulation in order to optimize ultrasonic treatment parameters, including wave mode, intensity, and frequency.



The iPod-sized LITUS device



Application of ultrasound to a 3D model