Stimulating Collateral Arterial Growth Using Acellular, Growth-Factor Free Hydrogels for the Treatment of Critical Limb Ischemia

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Abstract

Critical Limb Ischemia (CLI) affects millions of people worldwide as a comorbidity of diabetes and smoking. CLI occurs when a severe blockage in the arteries, caused by a buildup of plaque, significantly reduces blood flow to lower extremities like the legs. The lack of blood flow causes the surrounding tissue to become necrotic, thus requiring amputation. As of now, CLI lacks robust treatment options. In the past, clinical trials have attempted to stimulate arterial growth using growth-factor encapsulated hydrogels. Unfortunately, these clinical trials have failed to appreciably improve patient outcomes. We propose an alternative method that uses acellular, growth factor-free hydrogels to stimulate arteriogenesis. This methodology is twofold: (1) to further develop and characterize a previously studied GelCad hydrogel (gelatin-based hydrogel with Cadherin peptides attached) and synthesize this GelCad hydrogel into microspheres, and (2) to implement a cell-responsive siRNA release strategy that will trigger arteriogenesis through macrophage polarization. Preliminary results suggest GelCad microspheres can be synthesized using both a 4-Arm PEG SG (negative control) and 3,3′-Dithiodipropionic acid di(N-hydroxysuccinimide ester) (positive control) crosslinkers. 3,3′-Dithiodipropionic acid di(N-hydroxysuccinimide ester) is a reactive oxygen species or ROS active and is capable of macrophage polarization. To test this polarization strategy, RAW 264.7 macrophages will be cultured and embedded in the microgels and the release of FITC Dextran from the microgels will be measured. Recent developments in the literature have ongoing studies using additive manufacturing techniques to design porosity imaging devices. We hope to characterize these microgels by particle size, deformation, and porosity.

Biography of Presenter

Raey Hunde is a rising senior chemical engineering student at the University of Maryland, Baltimore County. She has conducted research in biomedical and chemical engineering at the following institutions: FDA: CBER, Laboratory of Virology, University of Minnesota: Twin Cities, University of Maryland, Baltimore County, Purdue University, and Vanderbilt University. Raey is a Meyerhoff and U-RISE scholar at the University of Maryland, Baltimore County, and aspires to obtain her Ph.D. in chemical engineering after graduation and explore the field of biomaterials further. After obtaining her Ph.D., Raey hopes to apply to the AAAS Science and Policy Fellowship and continue her STEM journey at the intersection of science and policy. Raey also has a huge devotion to diversity and inclusion of STEM and seeks to foster and encourage participation in research and STEM through the Meyerhoff program was well as her school's student chapter of AIChE (the American Institute of Chemical Engineers).