

Brett Askins

Mentor: Shanta Dhar

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Synthetic Iron Oxide Containing HDL Nanoparticles for Atherosclerosis

Authors: Brett Askins

Atherosclerosis is one of the world's most aggressive diseases, claiming over 17.5 million lives per year. This disease is often caused by high amounts of lipoproteins circulating in the blood stream, which leads to plaque formation. Ultimately these plaques can undergo thrombosis and cause heart damage. A major contributor to these vulnerable plaques is macrophage apoptosis. Development of sub cellular vehicles that carry contrast and therapeutic agents to the mitochondria within these apoptotic macrophages is attractive for the treatment of atherosclerosis. Previously, our lab reported construction of a biodegradable, synthetic HDL nanoparticle (NP) system that is capable of detecting vulnerable plaques by mitochondrial membrane potential collapse, which occurs during apoptosis. This platform contains a core of poly(lactic-co-glycolic acid) and cholesteryl oleate, with similar hydrophobicity as found in natural HDL. Surrounding this core is a phospholipid layer comprised of 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, along with stearyl-triphenylphosphonium (TPP) cations for detection of mitochondrial membrane potential collapse. On the surface of this lipid layer is an apoA-I mimetic 4F peptide capable of binding cholesterol and participating in reverse cholesterol transport (RCT). A Magnetic Resonance Imaging (MRI) iron oxide-based probe, mitomagneto, was encapsulated within the HDL NPs for potential use in therapeutic monitoring of atherosclerosis by MRI. This platform displays excellent composition, stability, and physiochemical properties required for encapsulation inside the core of the HDL-NPs. Characterization of the potential therapeutic and imaging abilities of these IONP-based HDL-NPs in atherosclerosis can be completed upon conduction of studies to further understand bioimaging, biocompatibility, toxicity, cholesterol efflux properties, and immunogenicity.