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# Synthetic HDL: A mimic of nature's nanomedicine

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Coronary Heart Disease (CHD) affects over 16 million people in US and is the largest killer in the western world. Overwhelming evidence indicates that increasing levels of circulating high-density lipoprotein (HDL) significantly decreases occurrence of coronary artery disease. Atheroprotective properties of HDL result from its ability to efflux excess of cholesterol from macrophages in plaques and transport it to the liver for excretion. Infusion of synthetic HDL (sHDL) nanoparticles to facilitate cholesterol removal from hardened arteries has been proven effective in phase 2 clinical studies. Synthetic HDL is a nanoparticle (~8-12 nm) composed of a lipid membrane-like bilayer wrapped around by a "belt" of amphipathic helices of Apolipoprotein A-I (ApoA-I). Development of sHDL as therapeutic drugs has been difficult owing to the very large doses (~1-8 g) required to attain clinical endpoints. Administration of high doses results in toxicity due to nanoparticle and protein impurities, and further requires manufacture of high quantities of recombinant ApoA-I, which is both technically difficult and costly. The focus of this research is discovery of novel ApoA-I mimic peptides, optimization of lipid composition of sHDL and use of these nanoparticles for atherosclerosis imaging and drug delivery. By understanding of biophysics of ApoA-I peptide binding to lipid membranes we are able to produce highly pure sHDL of homogeneous size, which are capable of mimicking the function of endogenous HDL. We have found that by optimizing lipid composition, the potency of sHDL *in vitro* and *in vivo* could be increased 3-fold. In addition, sHDL composition affected anti-inflammatory properties of nanoparticles and their remodeling in human plasma. Hence, understanding the mechanisms of how composition alters efficacy and safety of sHDL is critical for successful clinical translation of this novel class of cardiovascular drugs to the clinic.

## Biography

Anna Schwendeman received her Bachelor of Science from Moscow Institute of Physics and Technology and PhD in Pharmaceutics from The Ohio State University. From 2000 to 2011 she has worked at Esperion Therapeutics, Pfizer and Cerenis Therapeutics on developing synthetic high-density lipoprotein (sHDL) drugs. She was a part of the team that translated seven different products to clinic and phase II trials. She became Research Assistant Professor at Biointerfaces Institute at the University of Michigan in 2012. Her research focus is on optimization sHDL nanoparticles for treatment of atherosclerosis, sepsis and autoimmune diseases as well as using them for drug delivery purposes.

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