NANO HIGHLIGHT
Synthetic HDL Nanoparticles: Toward New Therapies for Heart Disease

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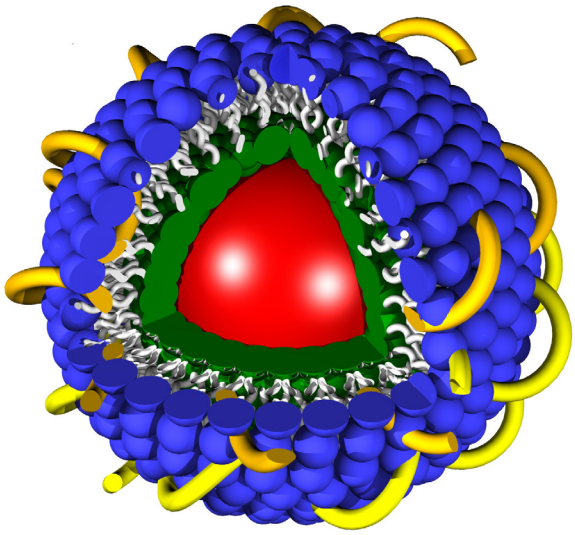
Heart disease is the most common cause of death in men and women in the United States. In order to address the substantial burden of disease, a more thorough understanding of how heart disease develops and then how new treatments can be realized is urgently needed. One intriguing possibility for the development of novel therapies for heart disease is through high density lipoproteins, or HDLs. HDLs are naturally occurring nanoparticles that solubilize "good" cholesterol for transfer and transport in the human body. Cholesterol carried in the context of HDL is believed to be "good" because of its direction of transport. HDL transports cholesterol in a "reverse" direction—that is, from developing plaque lesions within arteries to the liver where it can be excreted. This process of "reverse cholesterol transport" is believed to be the reason why higher HDL levels are associated with a reduced risk of cardiovascular disease.



The spherical HDL particle is synthesized using a gold nanoparticle (5 nm diameter, red) upon which phospholipids (green, blue) and protein (apolipoprotein A-I, yellow) are assembled.

Credit: C. Shad Thaxton, Northwestern University.

This research group has taken a unique approach to mature spherical forms of HDL and view it as a synthetic target. Thus, they have blended nanotechnology with biology, and synthesized functional nanoparticles that are "bio-mimics" of natural HDLs. Their research demonstrates the synthesis of a nanoparticle version of HDL built from the bottom-up using a gold nanoparticle, 5 nanometers in diameter, as a scaffold to assemble the lipid and protein components of natural HDL. Ultimately, by mimicking the size, shape, and surface chemistry of natural HDL species, our work shows that nanoparticle HDL binds cholesterol similarly to natural HDL. Furthermore, work in human cells demonstrates that biological functional is adequately maintained by nanoparticle HDL—they remove cholesterol from cultured cells that model those in diseased arteries. Finally, our data demonstrate that cholesterol removal is optimal when the size of nanoparticle HDL most closely matches that of natural HDL. Overall, this work demonstrates the ability to fabricate a functional nanoparticle that mimics the size, shape, surface chemistry, and in vitro biological function of mature spherical human HDL. Future work will focus on the in vivo biological activity of these, and other, nanoparticle HDLs with regard to preventing and reversing the cellular processes responsible for cardiovascular disease.

[1] C. Shad Thaxton, Weston L. Daniel, David A. Giljohann, Audrey D. Thomas and Chad A. Mirkin, *J. Am. Chem. Soc.*, **131** (4), 2009.