Researchers develop synthetic HDL cholesterol nanoparticles

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(Phys.org) —Atherosclerosis, a buildup of cellular plaque in the arteries, remains one of the leading causes of death globally. While high-density lipoprotein, or HDL, the so-called good cholesterol, is transferred to the liver for processing, low-density lipoprotein, or LDL, builds up in the arteries in the form of plaque.

Early detection of cellular components in the plaque that rupture and block arteries have long been held as potentially effective detection for heart diseases and their link to atherosclerosis.

A new study by University of Georgia researchers in the Franklin College of Arts and Sciences department of chemistry, published online May 13 in the *Proceedings of the National Academy of Sciences*,

documents a technological breakthrough: Synthetic high density lipoprotein nanoparticles. A completely biodegradable synthetic version of the so-called good cholesterol, the nanoparticles represent a potential new detection and therapy regimen for atherosclerosis.

In the process of developing a nanoparticle sensor to detect unstable cellular components in atherosclerotic lesions, study coauthors assistant professor Shanta Dhar and graduate student Sean Marrache constructed the lipoprotein nanoparticle in Dhar's NanoTherapeutics Research Laboratory. In bench-scale animal trials, the synthetic HDL-mimicking nanoparticle showed significant reductions in total cholesterol and triglycerides.

"In creating all the processes for the nanoparticle to mimic the natural HDL and carry a signaling output, we were able to demonstrate excellent biocompatibility," Dhar said. "If we simply leave out the sensor, we have a very promising therapy for triglyceride reduction in the bloodstream."

High-density-lipoprotein-mimicking nanoparticles have been created previously, though in published reports particles have been reconstituted from human blood. Though successful, these particles face many challenges in reproduction and scale-up for manufacturing, including variability in immune responses.

"Researchers have used reconstituted versions of HDL from blood, which will always have its drawbacks," Marrache said. "By creating this particle from scratch, we are able to bypass many of the drawbacks while accomplishing all of the positive aspects of HDL delivery."

Dhar's synthetic HDL nanoparticle is a polymer lipid hybrid, requiring fewer amino acids and thus better suited for potential scale-up. The researchers used an FDA-approved biodegradable polymer as a matrix and mixed it with cholesterol ester, a component in natural HDL, to

create the high-density lipoprotein core. They introduced a mimetic peptide that adheres to the nanoparticle with the precision of natural HDL.

"Chemists always seek to make things more synthetic, and, with me, the goal is always to make the product biodegradable," she said. "That was the unique combination that led us to come up with these technologies that hold promise for translational tools that could aid in early diagnosis and prevent vulnerable plaque progression."

Her department head agrees. "Professor Dhar has quickly built a research program in nanomaterial-based therapeutics during her three years at UGA and achieved remarkable success in a short period of time," said Jonathan Amster, who also is a chemistry professor at UGA.

More information:
www.pnas.org/content/early/2013/05/09/1301929110

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