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NOVELTIES

From the Lab, a New Weapon Against Cholesterol

By ANNE EISENBERG

The particles that ferry cholesterol through the bloodstream are popularly known as “bad” or “good”: bad if they deposit cholesterol on vessel walls, potentially clogging them; good if they carry the cholesterol on to the liver for excretion.

Now scientists have created tiny particles in the laboratory that mimic those good carriers, scooping up the cholesterol before it can grow into dangerous deposits of plaque. The surfaces of these new particles are coated with fats and proteins so they can bind tightly with the sticky cholesterol to transport it through the bloodstream.

The particles may someday be important in treating cardiovascular disease, said Dr. Andre Nel, chief of the division of nanomedicine and director of the Center for Environmental Implications of Nanotechnology at the University of California, Los Angeles.

“Researchers have endowed these artificial particles with the same properties as natural particles that circulate in the blood,” called high-density lipoproteins, or HDL, he said. The artificial carriers can clean up sites where plaques can otherwise rupture, leading to strokes and heart attacks.

The particles may be useful not only in cardiovascular therapy, but also in diagnosis. The researchers have put gold and other metal cores at the center of the particles, Dr. Nel said, so that they show up well in medical imaging. Such imaging could be used, for example, to monitor plaques as they build up in blood vessels.

At the Chicago campus of Northwestern University, artificial HDL nanoparticles have been designed by Dr. C. Shad Thaxton, an assistant professor in the urology department, and Chad A. Mirkin, a professor and director of the International Institute for Nanotechnology at the university’s Evanston campus They have founded a company, AuraSense, to commercialize the technology.

The Northwestern researchers replaced the fatty core found in natural HDL with gold nanoparticles, Dr. Mirkin said. “The gold core serves as a scaffold for attaching molecules that are the same as those on the surface of naturally occurring HDL,” he said. “We have demonstrated that our synthetic version of HDL binds cholesterol very tightly, not only in the laboratory, but in animals.”

The group has done a pilot study in animals and will soon begin a larger study, also involving animals, Dr. Thaxton said

At the Mount Sinai School of Medicine in Manhattan, Willem J. M. Mulder, an assistant professor of radiology and gene and cell medicine, and his research group have developed HDL-like nanoparticles intended primarily for imaging and diagnosis. The particles have centers of gold or other materials, Dr. Mulder said, depending on the type of imaging to be used.

“One of our interests is in the imaging of the biological processes in atherosclerosis,” the hardening of the arteries caused by plaques, he said.

Gold nanocrystals show up well in one type of imaging, called computed tomography, he said, and iron oxide nanocrystals work well with magnetic resonance imaging.

The research of the Northwestern and Mount Sinai groups may one day benefit people who develop deposits of atherosclerotic plaque, said Dr. Gregory M. Lanza, a professor of medicine at the School of Medicine at Washington University in St. Louis.

“Both of these groups have shown that this HDL mimic can adsorb cholesterol,” he said. One day, the particles like those created by the groups may be included in therapies for heart disease, he said. “They may become part of good anti-atherosclerosis management, along with diet, nonsmoking and statins,” drugs that interfere with the synthesis of cholesterol.

BUT for that to happen, cautioned Dr. Nel at U.C.L.A., more study will be needed. “We will have to find out what happens when the gold nanoparticles accumulate in the body,” he said. “This is a problem for treatment of chronic diseases where you administer materials over a long time.”

Vincent M. Rotello, a professor of chemistry at the University of Massachusetts, Amherst, who does nanoparticle research, agreed. “Right now, nanoparticles are great for diagnostic and acute therapeutics,” he said, but issues lie ahead that must be solved before the particles can be prescribed.

“Gold is nontoxic,” he said. “But it does build up. We don’t know what the effects of the buildup might be.” Smaller particles are excreted, he said. But larger particles may accumulate in the liver. Dr. William O’Neill, executive dean for clinical affairs at the Miller School of Medicine at the University of Miami, welcomed the artificial particles.

“If we can prove they don’t have side effects, we could give them as a drug, causing plaque in the coronary arteries to shrink,” he said. “It could revolutionize cardiology.”

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