New 'nanoburrs' could add to arsenal of therapies against heart disease

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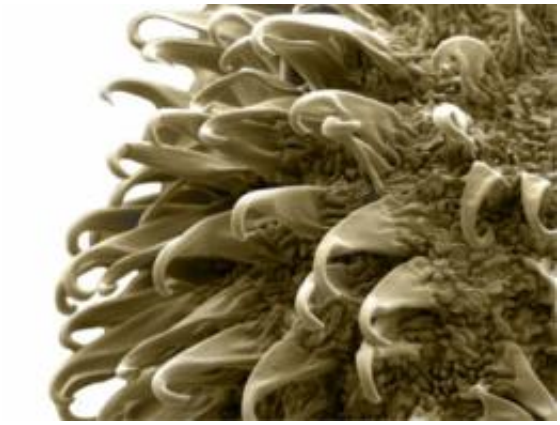

(PhysOrg.com) -- Researchers at MIT and Harvard Medical School have built targeted nanoparticles that can cling to artery walls and slowly release medicine, an advance that potentially provides an alternative to drug-releasing stents in some patients with cardiovascular disease.

Building on their previous work delivering cancer drugs with nanoparticles, MIT and Harvard researchers have turned their attention to cardiovascular disease, designing new particles that can cling to damaged artery walls and slowly release medicine.

The particles, dubbed “nanoburrs,” are coated with tiny protein fragments that allow them to stick to damaged arterial walls. Once stuck,

they can release drugs such paclitaxel, which inhibits cell division and helps prevent growth of scar tissue that can clog arteries.

“This is a very exciting example of nanotechnology and cell targeting in action that I hope will have broad ramifications,” says MIT Institute Professor Langer, senior author of a paper describing the nanoparticles in this week’s issue of the *Proceedings of the National Academy of Sciences.*

Langer and Omid Farokhzad, associate professor at Harvard Medical School and another senior author of the paper, have previously developed nanoparticles that seek out and destroy tumors. Their nanoburrs, however, are among the first particles that can zero in on damaged vascular tissue.

Mark Davis, professor of chemical engineering at Caltech, says the work is a promising step towards new treatments for cardiovascular and other diseases. “If they could do this in patients — target particles to injured areas — that could open up all kinds of new opportunities,” says Davis, who was not involved in this research.

On target

Currently, one of the standard ways to treat clogged and damaged arteries is by implanting a vascular stent, which holds the artery open and releases drugs such as paclitaxel. The researchers hope that their new nanoburrs could be used alongside such stents — or in lieu of them — to treat damage located in areas not well suited to stents, such as near a fork in the artery.

The nanoburrs are targeted to a structure known as the basement membrane, which lines the arterial walls but is only exposed when those walls are damaged. To build their nanoparticles, the team screened a

library of short peptide sequences to find one that binds most effectively to molecules on the surface of the basement membrane. They used the most successful, a seven-amino-acid sequence called C11, to coat the outer layer of their nanoparticles.

The inner core of the 60-nanometer-diameter particles carries the drug, which is bound to a polymer chain called PLA. A middle layer of soybean lecithin, a fatty material, lies between the core and the outer shell, which consists of a polymer called PEG that protects the particles as they travel through the bloodstream.

The drug can only be released when it detaches from the PLA polymer chain, which occurs gradually by a reaction called ester hydrolysis. The longer the polymer chain, the longer this process takes, so the researchers can control the timing of the drug's release by altering the chain length. So far, they have achieved drug release over 12 days, in tests in cultured cells.

Uday Kompella, professor of pharmaceutical sciences at the University of Colorado, says the nanoburr's structure could make it easier to manufacture, because the targeted peptides are attached to an outer shell and not directly to the drug-carrying core, which would require a more complicated chemical reaction. The design also reduces the risk of the nanoparticles bursting and releasing drugs prematurely, says Kompella, who was not involved in this research.

Another advantage of the nanoburrs is that they can be injected intravenously at a site distant from the damaged tissue. In tests in rats, the researchers showed that nanoburrs injected near the tail are able to reach their intended target — walls of the injured carotid artery but not normal carotid artery. The burrs bound to the damaged walls at twice the rate of nontargeted nanoparticles.

Because the particles can deliver drugs over a longer period of time, and can be injected intravenously, patients would not have to endure repeated and surgically invasive injections directly into the area that requires treatment, says Juliana Chan, a graduate student in Langer's lab and lead author of the paper.

The team is now testing the nanoburrs in rats over a two-week period to determine the most effective dose for treating damaged vascular tissue. The particles may also prove useful in delivering drugs to tumors. "This technology could have broad applications across other important diseases, including cancer and inflammatory diseases where vascular permeability or vascular damage is commonly observed," says Farokhzad.

More information: "Spatiotemporal controlled delivery of nanoparticles to injured vasculature," Juliana Chan, Liangfang Zhang, Rong Tong, Debuyati Ghosh, Weiwei Gao, Grace Liao, Kai Yuet, David Gray, June-Wha Rhee, Jianjun Cheng, Gershon Golomb, Peter Libby, Robert Langer, Omid Farokhzad. Proceedings of the National Academy of Sciences, week of Jan. 18, 2010.

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