Nanoparticles harvest invisible cancer biomarkers

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(PhysOrg.com) -- Cancer biologists have long presumed that tumor cells shed telltale markers into the blood and that finding these blood-borne biomarkers could provide an early indicator that cancer is developing somewhere in the body. While there has been some progress in finding such markers, researchers have been largely stymied in this pursuit by the fact that such proteins are present in trace amounts that are cloaked by the few proteins present in far larger amounts, such as albumin and antibodies.

Now, a research team at the George Mason University has shown that they can fish out the "invisible" proteins masked by albumin and other high concentration proteins using porous nanoparticles decorated with a series of chemical baits, each designed to harvest specific types of trace proteins from body fluids. Better yet, hooking these proteins onto the baits, which are buried within the pores of the nanoparticles, protects them from degradation until they can be released and analyzed using mass spectroscopy.

Alessandra Luchini led the international team of investigators that designed and tested the bait-laden core-shell nanoparticles. The investigators published their work in the Journal of the American Chemical Society.

Core-shell hydrogel nanoparticles have been touted as potential protein drug delivery vehicles that would sequester these drugs from the action of protein degrading enzymes in blood until they reach their targets in

the body. Luchini and her collaborators turned this paradigm on its head, choosing to use them to instead remove proteins from the blood until they can be safely collected. The key was identifying a set of 17 molecules that the researchers could attach inside the cavity structures that exist in hydrogels. These cavities are large enough to let most proteins in, but are too small for the relatively gigantic proteins that are overwhelmingly prevalent in blood and other biological fluids. To prevent smaller fragments of albumin, which are also a major blood component, from entering the nanoparticles, the investigators added to the outer shell the chemical vinylsulfonic acid, or VSA, that actively excludes albumin fragments of all sizes.

For bait molecules, Luchini and her colleagues started with a few dye molecules that biochemists have used as protein binding agents and inhibitors of protein-protein interactions in chromatography experiments. Working from the chemical structures of these molecules, the investigators created a set of dyes that they could then react with their core-shell hydrogel nanoparticles. They then mix the resulting nanoparticles with a biological fluid - whole blood, urine, and sweat, for example - and incubated for 15 minutes. The particles are collected using a centrifuge, and the captured proteins are washed out for analysis using a set of buffers.

Luchini's team showed that the nanoparticles enabled a 10,000-fold effective amplification of protein levels in the wash fluid compared to their concentration in blood. As a result, they were able to use mass spectrometry to identify a variety of proteins that were previously undetectable in blood using any type of method that would be clinically useful.

This work, which was supported in part by the National Cancer Institute, is detailed in a paper titled, "Multifunctional Core-Shell Nanoparticles: Discovery of Previously Invisible Biomarkers." Investigators from

Stockholm University in Sweden, the Instituto Superiore di Sanità in Rome, Italy, and the University of Turin in Italy also participated in this study.

More information: View abstract

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