# Nanoparticles Assembled Inside Tumors Trap Drugs and Imaging Agents

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(PhysOrg.com) -- Virtually every study that uses nanoparticles to deliver drugs and imaging agents to tumors starts by loading the clinical payload into the nanoparticle and then injecting the resulting delivery agent into the body. While effective at reducing clearance from the body and improving drug or imaging agent retention in a tumor, the nanoparticles do move relatively slowly from the circulation into the heart of the tumor.

Now, a pair of investigators from the University of Toronto have shown that a system that assembles itself into a nanoparticle, complete with drug or imaging agent, once it gets inside a tumor can dramatically increase the rate at which clinically important molecules get into tumors and still trap those molecules inside the tumor. Warren Chan and postdoctoral fellow Steven Perrault conducted the study and published the results of their work in the Proceedings of the National Academy of Sciences.

The goal of this project was to develop a nanoparticle system that would combine the fast “in” rate for small molecule drugs or imaging agents with the glacial “out” rate associated with nanoparticles. This would allow as much drug or imaging agent to get into and stay in tumors while allowing the body to excrete rapidly any of the active material that remained in the blood stream or that happened to get inside of non-targeted tissue. To create a system that would marry these two seemingly incompatible characteristics, Drs. Chan and Perrault first inject 30 nanometer diameter gold nanoparticles coated with a biotin terminated

polymer; the polmer keeps the particles from sticking to one another and the biotin allows for later conjugation to imaging agents or drugs. Over the course of the next 24 hours, many of the gold nanoparticles accumulate in tumors, while the rest are excreted from the body.

Next, the researchers inject the active substance linked to streptavidin, a molecule that binds tightly and specifically to biotin. This small molecule construct readily enters tumors, as well as other tissues, but once in the tumors it sticks in an almost irreversible manner to the gold nanoparticles, greatly reducing the rate at which the active molecule will exit the tumor.

Using a fluorescent dye as the active molecule linked to streptavidin, Drs. Chan and Perrault were able to track the kinetics of drug accumulation in tumor. The results were remarkable: the active molecule accumulated nearly 200-fold increase in the rate at which drug accumulated in tumors compared to animals that did not receive the biotin-coated gold nanoparticles. In addition, pretreated tumors accumulated five times more of the fluorescent probe than did the control animals.

This work is detailed in a paper titled, “In vivo assembly of nanoparticle components to improve targeted cancer imaging.” An abstract of this paper is available at the journal’s Web site.

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