# Photo-immunotherapy boosts nanoparticle delivery to tumors

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(Phys.org)—One of the main reasons that nanoparticles can boost the effectiveness of an anticancer drug while decreasing its toxicity is that they are able to accumulate at cancerous sites in the body through the abnormally leaky blood vessels that surround most solid tumors. While enhanced permeability and retention (EPR) phenomenon is effective, it is inefficient and the vast majority of an injected dose of nanoparticle-entrapped drug is excreted from the body without ever reaching its intended target. Now, however, a team of investigators from the National Cancer Institute (NCI) has found a way of markedly enhancing the EPR effect and boosting nanoparticle accumulation in tumors by more than 20 fold.

Hisataka Kobayashi and his colleagues at NCI's Center for Cancer Research employed a technique they call photo-immunotherapy, which uses an antibody linked to a light-sensitive compound or photosensitizer, to increase the leakiness of tumor-associated blood vessels. The resulting super-enhanced permeability and retention (SUPR) not only increased the amount of drug-loaded nanoparticles that accumulated in sensitized tumors, but more importantly, significantly reduced the size of treated tumors. The investigators report their work in the journal *ACS Nano*.

To create their photo-immunotherapy agent, the NCI team linked an FDA-approved monoclonal antibody, panitumumab, that targets the EGFR receptor variant, ErbB1, that is over-expressed on some solid tumors to a photosensitizing agent known as IR700. One day after injecting this agent into tumor-bearing mice, the investigators used a

single dose of near-infrared light to activate the agent. They then injected panitumumab with a fluorescent label which could be imaged and found that the antibody rapidly accumulated only in the tumors that had been sensitized by irradiation and not in those that had not been sensitized.

Subsequent experiments showed that the irradiated antibody-linked photosensitizer damages the first layer of tumor cells that sits next to the leaky blood vessels. When these cells are damaged, it changes the pressure around the blood vessels, causing them to expand, which increases their leakiness. The investigators demonstrated that the SUPR effect increases the permeability of these blood vessels to particles as large as 200 nanometers.

In a final set of experiments, the researchers then administered commercially available liposome-encapsulated daunorubicin one hour after irradiation. Thirty days after 10 animals were treated, seven of the mice were still alive, compared to only one animal that was treated with liposomal daunorubicin alone.

This work is detailed in a paper titled, "Markedly enhanced permeability and retention effects induced by photo-immunotherapy of tumors." An abstract of this paper is available at the journal's website.

**More information:** View abstract.

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