Defining the Design Rules for Targeted Nanoparticles Used To Image Tumors

February 19 2010

One of the challenges of using nanoparticles for imaging tumors during surgery is that there needs to be a tradeoff between the number of nanoparticles that target a tumor and the rapid clearance of any unbound nanoparticles from the body. A large number of nanoparticles sticking tightly to a tumor will provide a bright signal that can help a surgeon spot the edges of the malignant tissue, but only if the background signal from unbound nanoparticles - the ones circulating freely through the body - is not too high.

Now, a team of investigators has developed a set of design rules that can optimize that tradeoff, producing nanoparticles that have the best chance of binding to a tumor but that will clear rapidly through the kidneys when they do not find their target. The team, led by John Frangioni, from the Beth Israel Deaconess Medical Center, and Moungi Bawendi, of the Massachusetts Institute of Technology and a member of the MIT-Harvard Center of Cancer Nanotechnology Excellence, published the results of their work in the journal *Nature Nanotechnology*.

In earlier work, the investigators had found that the kidneys efficiently filter out of the blood stream nanoparticles of approximately 5.5 nanometers (nm) in diameter and that are zwitterionic, that is they have both positive and negative charges on their surface. The researchers also developed ultrasmall, zwitterionic, brightly fluorescent nanoparticles consisting of a zinc-cadmium sulfide core surrounded by a cadmium selenide shell and a cysteine coating.

In this study, the investigators linked one of two tumor targeting agents to the cysteine coating and tested the ability of the two formulations to target tumors and yet be cleared from circulation. While the usual approach to developing targeted nanoparticles has been to add as large a number of targeting molecules as possible in order to increase the probability of sticking to the targeted tissue, the investigators found that they could only add between five and ten targeting molecules without increasing the overall size of the nanoparticle above the 5.5 nm cutoff. Of equal importance, they also found that nanoparticles prepared in this manner did not bind to blood stream proteins, which would have had the effect of increasing the overall size of the nanoparticles.

Tests in animals using cultured cells showed that using even relatively low numbers of targeting molecules produced nanoparticles capable of binding tightly to targeted tumor cells. Biodistribution studies showed that the nanoparticles accumulated in targeted tumors, where they could be imaged, but not in the liver, spleen, and lungs, tissues that often accumulate circulating nanoparticles. Unbound nanoparticles were excreted through the kidneys, as predicted, within 4 hours. Four-hour clearance is important because it means that in practice, a patient scheduled for tumor-removing surgery could receive a dose of the nanoparticles when first arriving at the hospital and that background levels of unbound nanoparticles would be close to zero by the time the surgeon needed to image labeled tumors.

This work, which is detailed in a paper titled "Design considerations for tumour-targeted nanoparticles," was supported in part by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. An abstract of this paper is available at the journal's website.

Citation: Defining the Design Rules for Targeted Nanoparticles Used To Image Tumors (2010, February 19) retrieved 20 March 2024 from https://phys.org/news/2010-02-nanoparticles-image-tumors.html