

# Homing nanoparticles pack multiple assault on tumors

January 8 2007

---

A collaborative team led by Erkki Ruoslahti, M.D., Ph.D., of the Burnham Institute for Medical Research at UC Santa Barbara (Burnham) has developed nanoparticles that seek out tumors and bind to their blood vessels, and then attract more nanoparticles to the tumor target. Using this system the team demonstrated that the homing nanoparticle could be used to deliver a "payload" of an imaging compound, and in the process act as a clotting agent, obstructing as much as 20% of the tumor blood vessels.

These findings are pending publication in the *Proceedings of the National Academy of Sciences* and will be made available at the journal's website during the week of January 8, 2007.

The promise of nanomedicine is based on the fact that a particle can perform more functions than a drug. Multifunctionality is demonstrated in the current study, in which researchers from Burnham, UC San Diego, and Massachusetts Institute of Technology designed a nanoparticle that combined tumor-homing, self-amplification of the homing, obstructing tumor blood flow, and imaging.

Using a screening technique developed previously in Ruoslahti's laboratory, the group identified a peptide that homed to the blood vessels, or vasculature, inside breast cancer tumors growing in mice. The peptide was comprised of five amino acids: Cysteine-Arginine-Glutamic acid-Lysine-Alanine, abbreviated CREKA.

The researchers then demonstrated that the CREKA peptide recognizes clotted blood, which is present in the lining of tumor vessels but not in vessels of normal tissues. They used a special mouse strain that lacks fibrinogen, the main protein component of blood clots, to show this: tumors growing in these fibrinogen-deficient mice did not attract the CREKA peptide, whereas the peptide was detected in the tumors of a control group of normal littermates.

Having confirmed clotted blood as the binding site for CREKA, the team constructed nanoparticles from superparamagnetic amino dextran-coated iron oxide (SPIO); such particles are used in the clinic to enhance MRI imaging. They coupled the CREKA peptide to the SPIO particles to give the particles a tumor-homing function and programmed an additional enhanced imaging functionality into their nanoparticle by making it fluorescent.

Initially, CREKA-SPIO's tumor homing ability was impeded by a natural defense response, which activates the reticuloendothelial system (RES)--white blood cells which together with the liver and spleen comprise a protective screening network in mice (and humans). The investigators devised "decoy" molecules of liposomes coated with nickel, which diverted the RES response that would have otherwise been directed toward CREKA-SPIO. The use of decoy molecules extended the half-life of CREKA-SPIO in circulating blood five-fold, which greatly increased the nanoparticle's ability to home to tumors.

The CREKA-SPIO that accumulated in the tumor enhanced blood clotting in tumor vessels, creating additional binding sites for the nanoparticles. This "self amplification" of the tumor homing greatly enhanced the investigators' ability to image the tumors. It also contributed to blocking as much as 20% of the blood vessels in the tumor. While occluding 20% of tumor vessels was not sufficient to reduce the rate of tumor growth, it is a promising target for future

studies.

"Having identified the principle of self-amplification, we are now optimizing the process, hoping to obtain a more complete shut-down of blood flow into the tumor to strangle it," says Ruoslahti. "We are also in the process of adding a drug delivery function to the particles. These two approaches are synergistic; the more particles we bring into the tumor, the greater the obstruction of the blood flow and more of the drug is delivered into the tumor."

Source: Burnham Institute

Citation: Homing nanoparticles pack multiple assault on tumors (2007, January 8) retrieved 1 May 2024 from <https://phys.org/news/2007-01-homing-nanoparticles-multiple-assault-tumors.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--