'Theranostic' imaging offers means of killing prostate cancer cells

August 10 2012

(Phys.org) -- Experimenting with human prostate cancer cells and mice, cancer imaging experts at Johns Hopkins say they have developed a method for finding and killing malignant cells while sparing healthy ones.

The method, called theranostic imaging, targets and tracks potent drug therapies directly and only to cancer cells. It relies on binding an originally inactive form of drug chemotherapy, with an enzyme, to specific proteins on tumor cell surfaces and detecting the drug's absorption into the tumor. The binding of the highly specific drug-protein complex, or nanoplex, to the cell surface allows it to get inside the cancerous cell, where the enzyme slowly activates the tumor-killing drug.

Researchers say their findings, published in the journal *ACS Nano* online Aug. 6, are believed to be the first to show that chemotherapies can be precisely controlled at the molecular level to maximize their effectiveness against tumors, while also minimizing their side effects.

Senior study investigator Zaver Bhujwalla, Ph.D., a professor at the Johns Hopkins University School of Medicine and its Kimmel Cancer Center, notes that a persistent problem with current chemotherapy is that it attacks all kinds of cells and tissues, not just cancerous ones.

In the theranostic imaging experiments, overseen by Bhujwalla and study co-investigator Martin Pomper, M.D., Ph.D., investigators directed drugs

only to cancer cells, specifically those with prostate-specific membrane antigen, or PSMA cell surface proteins.

"Our results show a non-invasive imaging approach to following and delivering targeted therapy to any cancer that expresses PSMA," says Bhujwalla, who also serves as director of the Johns Hopkins In Vivo Cellular and Molecular Imaging Center (ICMIC), where the theranostic imaging studies were developed.

Bhujwalla says the new technique potentially will work against any cancer in which tumors elevate production of certain cell surface proteins. Examples would include breast cancers with HER-2/neu and CXCR4 proteins, and some liver, lung and kidney cancers also known to express particular proteins. She notes that PSMA is expressed in the vessels of most solid tumors, suggesting that the nanoplex reported in the latest study could be used in general to image and treat a variety of cancers.

In their latest series of experiments, primarily in mice injected with human prostate tumor cells, Bhujwalla and the Johns Hopkins team tested their ability to track with imaging devices the delivery of anti-cancer drugs directly to tumors. Some of the tumors were comprised of cells with PSMA, while other so-called control tumors had none. Included in the drug nanoplex were small strands of RNA, cell construction acids that can be used instead to block and turn down production of a well-known enzyme, choline kinase, whose levels usually rise with tumor growth. All nanoplex components were imaged inside the tumor, in addition to dropping choline kinase production, which decreased by 80 percent within 48 hours of nanoplex absorption into cells with ample PSMA. When researchers used antibodies to block the action of PSMA, down went the level of nanoplex uptake and drug activation in cancerous cells as measured by dimming of the image.

Different concentrations of the drug nanoplex, tagged with radioactive and fluorescent molecules, were mixed in the lab with prostate cancer tissue cells, some of which had extra PSMA and others which had none. Only those cells with extra PSMA showed nanoplex uptake, as measured by image intensity, which later decreased when PSMA-blocking chemicals were added (back to levels seen in cells with almost no PSMA).

Additional experiments involving injections of three different concentrations of the drug nanoplex showed no damage to other vital mouse organs, such as the kidney and liver, nor any uptick in the mouse immune system response.

"Our theranostic imaging approach shows how the best methods of detection and treatment can be combined to form highly specialized, more potent and safer forms of chemotherapy," says Pomper, a professor at Johns Hopkins, who also serves as an associate director at ICMIC.

He says that an important goal for theranostic imaging is to move it beyond standard chemotherapy that attacks one target molecule at a time. "With theranostic imaging, we can attack multiple tumor targets, making it harder for the tumor to evade drug treatment," says Pomper, who is already working with colleagues at Johns Hopkins to identify other molecular targets.

Provided by Johns Hopkins University