Nanoscale gene 'ignition switch' may help spot and treat cancer

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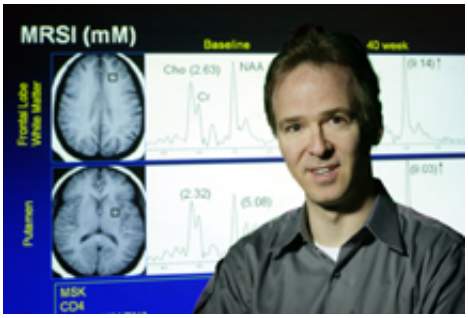

Martin Pomper, M.D., Ph.D.

(PhysOrg.com) -- In a proof of principal study in mice, scientists at Johns Hopkins and the Virginia Commonwealth University (VCU) have shown that a set of genetic instructions encased in a nanoparticle can be used as an "ignition switch" to rev up gene activity that aids cancer detection and treatment.

The switch, called a promoter, is a set of chemical letters that interacts with DNA to turn on gene activity. In this case, the scientists used a promoter called PEG-Prom, cloned by VCU researcher Paul Fisher, Ph.D. PEG-Prom is activated only when inside cancer cells, not in normal ones.

"With current imaging devices like CT and PET, we can tell if something is wrong in a patient, but we don't have definitive tools to

distinguish cancer from inflammation or infection," says Martin Pomper, M.D., Ph.D., professor of radiology at Johns Hopkins. "It generally takes at least one month after giving patients certain cancer treatments before existing imaging tools can measure the patient's response to the therapy."

To differentiate cancer cells from normal cells, Johns Hopkins scientists connected PEG-Prom to either a gene that produces firefly luciferase, the substance that make fireflies glow, or a gene called HSV1tk, which initiates a chemical reaction with radioactive labels inside the cell that can be detected by imaging devices. Once inside a cancer cell, the PEG-Prom switch is turned on, and it activates either the luciferase or HSV1tk gene.

Then, they stuffed the PEG-Prom/gene combination into tiny spheres – about 50,000 times smaller than the head of a pin – and intravenously injected the nanoparticles into mice with either metastatic breast cancer or melanoma.

The findings, reported in the December 12 online edition of *Nature Medicine*, reveal a 30-fold difference in identifying cancer cells containing luciferase and normal cells that did not contain the substance. Similar results were observed in cancer cells filled with the radioactive labels and normal ones that were not.

"This type of imaging technique has the potential to add to existing tools with more specificity in identifying the problem," says Pomper.

Pomper says that the technique could likely be used in any cancer, and the nanoparticle and HSV1tk gene used in the current study have been tested previously in clinical studies unrelated to Pomper's work.

In addition to diagnostic and monitoring tools, the technique could be

designed to deliver therapies to the heart of cancer cells. One approach, he says is to use radioactive isotopes to make cancer cells radioactive from the inside, instead of delivering radiation to the patient externally.

Still, Pomper says, such a technique would be limited to identifying tumors that are two millimeters or larger, amounting to millions of cells, because current imaging devices cannot detect anything smaller. He also says that certain doses of nanoparticles could be toxic, so his team is conducting tests to find the best nanoparticle.

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