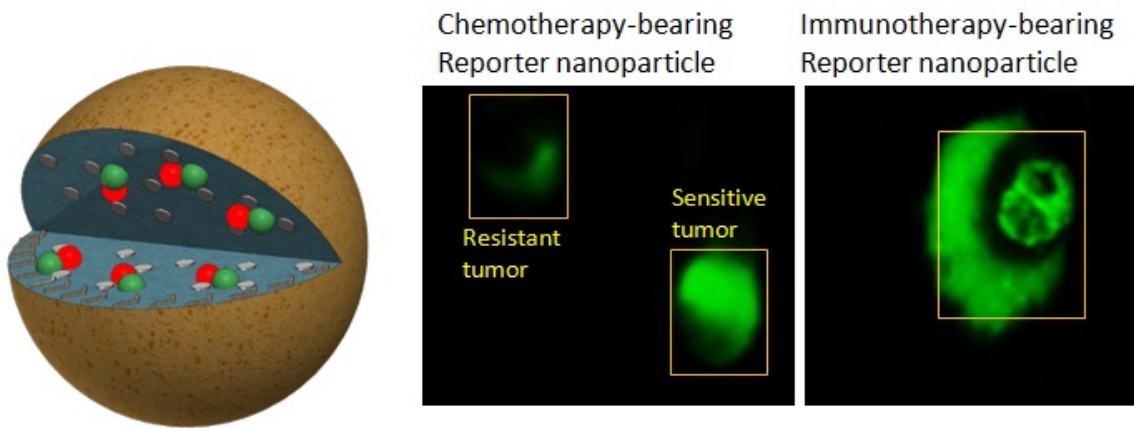


New nanoparticle reveals cancer treatment effectiveness in real time

March 28 2016



Using reporter nanoparticles loaded with either a chemotherapy or immunotherapy, researchers could distinguish between drug-sensitive and drug-resistant tumors in a pre-clinical model of prostate cancer. Credit: Ashish Kulkarni, Brigham and Women's Hospital

Being able to detect early on whether a cancer therapy is working for a patient can influence the course of treatment and improve outcomes and quality of life. However, conventional detection methods—such as PET scans, CT and MRI—usually cannot detect whether a tumor is shrinking until a patient has received multiple cycles of therapy.

A new technique developed in pre-clinical models by investigators at Brigham and Women's Hospital (BWH) offers a new approach and a

read out on the effectiveness of chemotherapy in as few as eight hours after treatment. The technology can also be used for monitoring the effectiveness of immunotherapy. Using a nanoparticle that delivers a drug and then fluoresces green when cancer cells begin dying, researchers were able to visualize whether a tumor is resistant or susceptible to a particular treatment much sooner than currently available clinical methods.

The team's findings are published online this week in *The Proceedings of the National Academy of Sciences*.

"Using this approach, the cells light up the moment a cancer drug starts working. We can determine if a [cancer therapy](#) is effective within hours of treatment," said co-corresponding author Shiladitya Sengupta, PhD, a principal investigator in BWH's Division of Bioengineering. "Our long-term goal is to find a way to monitor outcomes very early so that we don't give a chemotherapy drug to patients who are not responding to it."

The [new technique](#) takes advantage of the fact that when cells die, a particular enzyme known as caspase is activated. The researchers designed a 'reporter element' that, when in the presence of activated caspase, glows green. The team then tested whether they could use the reporter nanoparticles to distinguish between drug-sensitive and drug-resistant tumors. Using nanoparticles loaded with anti-cancer drugs, the team tested a common chemotherapeutic agent, paclitaxel, in a pre-clinical model of prostate cancer and, separately, an immunotherapy that targets PD-L 1 in a pre-clinical model of melanoma. In the tumors that were sensitive to paclitaxel, the team saw an approximately 400 percent increase in fluorescence compared to tumors that were not sensitive to the drug. The team also saw a significant increase in the fluorescent signal in tumors treated with the anti-PD-L1 nanoparticles after five days.

"We've demonstrated that this technique can help us directly visualize and measure the responsiveness of tumors to both types of drugs," said co-corresponding author Ashish Kulkarni, an instructor in the Division of Biomedical Engineering at BWH. "Current techniques, which rely on measurements of the size or metabolic state of the tumor, are sometimes unable to detect the effectiveness of an immunotherapeutic agent as the volume of the tumor may actually increase as immune cells begin to flood in to attack the tumor. Reporter nanoparticles, however, can give us an accurate read out of whether or not [cancer cells](#) are dying."

Researchers now plan to focus on the design of radiotracers that can be used in humans, and tests of both safety and efficacy will be necessary before the current technique can be translated into clinical applications. Sengupta, Kulkarni and their colleagues are actively working on these steps in order to further the lab's goal of improving the management and treatment of [cancer](#) using nanotechnology.

More information: Reporter nanoparticle that monitors its anticancer efficacy in real time, *PNAS*,
www.pnas.org/cgi/doi/10.1073/pnas.1603455113

Provided by Brigham and Women's Hospital

Citation: New nanoparticle reveals cancer treatment effectiveness in real time (2016, March 28) retrieved 29 April 2024 from
<https://phys.org/news/2016-03-nanoparticle-reveals-cancer-treatment-effectiveness.html>

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