First-of-its-kind self-assembled nanoparticle for targeted and triggered thermo-chemotherapy

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(Phys.org)—Excitement around the potential for targeted nanoparticles (NPs) that can be controlled by stimulus outside of the body for cancer therapy has been growing over the past few years. More specifically, there has been considerable attention around near-infrared (NIR) light as an ideal method to stimulate nanoparticles from outside the body. NIR is minimally absorbed by skin and tissue, has the ability to penetrate deep tissue in a noninvasive way and the energy from NIR light can be converted to heat by gold nanomaterials for effective thermal ablation of diseased tissue.

In new research from Brigham and Women's Hospital (BWH), researchers describe the design and effectiveness of a first-of-its-kind, self assembled, multi-functional, NIR responsive gold nanorods that can deliver a chemotherapy drug specifically targeted to cancer cells and selectively release the drug in response to an external beam of light while creating heat for synergistic thermo-chemo mediated anti-tumor efficacy. The study is electronically published in Angewandte Chemie International Edition.

"The design of this gold nanorod and its self-assembly was inspired by nature and the ability of complimentary strands of DNA to hybridize on their own without imposing complicated chemical processes on them," explained Omid Farokhzad, MD, an anesthesiologist and Director of the Laboratory of Nanomedicine and Biomaterials at BWH, and senior

author of this study. "Each functionalized DNA strand individually, and the self assembled components as a system, play a distinct yet integrative role resulting in synergistic targeted and triggered thermo-chemotherapy capable of eradicating tumors in our pre-clinical models."

One DNA strand is attached to the gold nanorod and the complementary strand is attached to a stealth layer and a homing molecule that keeps the system under the radar of the immune system while targeting it directly to cancer cells. When the DNA strands come together, the targeted gold nanorod is formed and the double stranded DNA serves as the scaffold for binding the chemotherapy drug, doxorubicin, which can be released in response to NIR light that concurrently results in generation of heat by the gold nanorods.

"This new platform is comprised of three distinct functional components and each plays a role in contributing to the triple punch of triggered thermotherapy, controlled doxorubicin release, and cancer cell targeting," explained Zeyu Xiao, PhD, a postdoctoral fellow at BWH and lead author of this study.

To demonstrate the robust capability of this nanorod system, Farokhzad and colleagues used a pre-clinical model to evaluate the in vivo anti-tumor efficacy in two different tumor models and four different groups with different drug regiments, each group varying in weight and tumor size. Researchers administrated an injection of the novel, self-assembled nanoparticle and then 10 minutes post-injection, the tumors were irradiated using NIR light that activated the nanoparticle using the gold nanorod and created heat. The results showed that this platform successfully delivered heat and anti-cancer drugs and synergistically eradicated tumors.

"Thermal ablation is already commonly used in cancer treatment," said Dr. Farokhzad. "What is extremely exciting about this platform is that

we are able to selectively target cancer cells and then hit the tumor twice: first with a controlled release of a chemotherapy drug and then secondly with triggered induction of heat from the activation of the gold nanorod. And all this can be done noninvasively."

Researchers acknowledge that more research is necessary in other pre-clinical models before testing the safety and efficacy of this platform in human clinical trials.

More information: onlinelibrary.wiley.com/doi/10 … /anie.201204018/full

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