Image-guided breast cancer therapy enabled by nanodrug

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By combining an iron oxide nanoparticle, a tumor-targeting peptide, and a therapeutic nucleic acid into one construct, a team of investigators from the Massachusetts General Hospital and Harvard Medical School have created an agent that holds potential as targeted therapy for breast cancer. In addition, this new agent can be easily tracked in the body using standard magnetic resonance imaging (MRI).

Zdravka Medarova led this study. She and her colleagues published their results in the journal Cancer Research.

Dr. Medarova and her collaborators created their nanoparticle to bind to a tumor-specific molecules known as uMUC-1, which is found on the surface of over 90 percent of human breast tumors, and deliver a synthetic small interfering RNA (siRNA) molecule designed to shut down a specific gene - *BIRC5* - that blocks cell death in most tumors and is associated with the development of drug resistance. The investigators also added a fluorescent dye to their nanoparticle to afford them the ability to track the nanoparticle using near-infrared spectroscopy. Because the nanoparticle itself is composed of superparamagnetic iron oxide, it is readily visible in MRI scans.

When added to breast cancer cells growing in culture, this nanoparticle construct had a profound impact on the expression of the *BIRC5* gene, knocking down its expression. Both fluorescence imaging and MRI showed that the nanoparticle was taken up rapidly by the cells. Subsequent experiments showed that this construct had the same positive

effect on both human pancreatic cancer cells and colon cancer cells.

Based on these initial results, the investigators injected the nanoparticles intravenously into mice bearing human breast tumors. The drug was administered on two separate occasions, a week apart. Both MRI and fluorescence imaging scans revealed that the nanoparticle accumulated preferentially in the tumors and that tumor levels remained high over the course of the two week experiment. Very little drug accumulated in muscle tissue surrounding the tumors.

When the tumors themselves were examined, the investigators found that the siRNA payload produced a five-fold increase in cell death compared to when animals were instead treated with a similar construct bearing a nonsense siRNA molecule even though the two nanoparticles accumulated to the same level in the tumors of treated animals. This result shows that the therapeutic effect of the construct is independent of its tumor targeting properties and is instead a result of its therapeutic siRNA payload.

More information: This work is detailed in a paper titled, "Image-Guided Breast Tumor Therapy Using a Small Interfering RNA Nanodrug ."

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