Nanotechnology researchers develop new strategy to deliver chemotherapy to prostate cancer cells

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Honing chemotherapy delivery to cancer cells is a challenge for many researchers. Getting the cancer cells to take the chemotherapy "bait" is a greater challenge. But perhaps such a challenge has not been met with greater success than by the nanotechnology research team of Omid Farokhzad, MD, Brigham and Women's Hospital (BWH) Department of Anesthesiology Perioperative and Pain Medicine and Research.

In their latest study with researchers from Massachusetts Institute of Technology (MIT) and Massachusetts General Hospital, the BWH team created a drug delivery system that is able to effectively deliver a tremendous amount of chemotherapeutic drugs to prostate cancer cells.

The study is electronically published in the January 3, 2012 issue of *ACS Nano*.

The process involved is akin to building and equipping a car with the finest features, adding a passenger (in this case the cancer drug), and sending it off to its destination (in this case the cancer cell).

To design the "vehicle," researchers used a selection strategy developed by Farokhzad's team that allowed them to essentially select for ligands (molecules that bind to the cell surface) that could specifically target prostate cancer cells. The researchers then attached nanoparticles containing chemotherapy, in this case docetaxel, to these hand-picked

ligands.

To understand Farokhzad's selection strategy, one must understand ligand behavior. While most ligands mainly have the ability to bind to cells, the strategy of Farokhzad and his colleagues allowed them to select specific ligands that were not only able to bind to prostate cancer cells, but also possessed two other important features: 1) they were smart enough to distinguish between cancer and non-cancer cells and 2) they were designed to be swallowed by cancer cells.

"Most ligands are engulfed by cells, but not efficiently," said Farokhzad. "We designed one that is intended to be engulfed."

Moreover, the ability for a ligand to intentionally be engulfed by a cell is crucial in drug delivery since it enables a significant amount of drug to enter the cancer cell, as opposed to remaining outside on the cell surface. This is a more effective method for cancer therapy.

Another important aspect of this drug delivery design is that these ligand-nanoparticle components are able to interact with multiple cancer markers (antigens) on the cell surface. Unlike other drug delivery systems, this makes it versatile and potentially more broadly applicable.

According to the study's lead author, Zeyu Xiao, PhD, a researcher in the BWH Laboratory of Nanomedicine and Biomaterials, current strategies for targeting nanoparticles for cancer therapy rely on combining nanoparticles with ligands that can target well-known cancer markers. Such strategies can be difficult to execute since most cancer cells do not have identifiable cell surface markers to distinguish themselves from normal cells.

"In this study, we developed a unique strategy that enables the nanoparticles to specifically target and efficiently be engulfed into any

desired types and sub-types of cancer cells, even if their cancer markers are unknown," said Xiao. "Our strategy simplifies the development process of targeted nanoparticles and broadens their applications in cancer therapy."

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