PRINTed nanoparticles deliver multiple punches to treat prostate cancer

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Using technologies common to the semiconductor industry, a team of investigators at the University of North Carolina at Chapel Hill and Liquidia Technologies has created a polymer nanoparticle that can encapsulate large loads of therapeutic molecules that may have use in treating prostate cancer. The research, led by Joseph DeSimone, co-principal investigator of the Carolina Center for Cancer Nanotechnology, was published in the journal *Nano Letters*.

Dr. DeSimone and his colleagues developed their nanoparticles to deliver small interfering RNA (siRNA) molecules to tumors. siRNAs block or greatly reduce a cell's production of specific proteins by binding to the messenger RNA (mRNA) molecules that translate information from DNA into proteins. Because of their specificity for specific proteins, siRNAs are thought to hold promise as anticancer agents, but only if techniques can be developed to deliver large quantities of siRNAs to tumor cells.

With an eye on commercialization, the Carolina team created an siRNA delivery vehicle using the PRINT process, which was invented in Dr. DeSimone's laboratory and is now being developed for biomedical applications by Liquidia Technologies. PRINT uses soft lithography to mass produce polymeric nanoparticles under mild conditions suitable for use with biologically compatible materials. In this project, the team created nanoparticles consisting of a polymer core that safely encapsulates siRNA molecules and a lipid shell that promotes cell uptake.

Initial tests with cells engineered to produce a fluorescent protein and a nanoparticle containing an siRNA agent that would block production of this protein, the investigators showed that these particles were readily taken up by the cells. Once inside the cells, the polymeric nanoparticles released their siRNA payload, blocking production of the fluorescent protein.

Next, the investigators created a nanoparticle containing an siRNA designed to interfere with the production of a protein known as KIF11, which plays a role in prostate tumor growth. They then dosed three different prostate cancer cell lines with this formulation and found that all three cell lines experienced a dramatic drop in KIF11 levels, which in turn triggered cell death in all three cell lines. The researchers note that they are now performing animal studies with PRINTed nanoparticles loaded with siRNAs targeted to key tumor proteins.

This work, which is detailed in a paper titled, "Delivery of multiple siRNAs using lipid-coated PLGA nanoparticles for treatment of prostate cancer," was supported in part by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. An abstract of this paper is available at the journal's website.

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