# Boosting immune therapy for cancer with nanoparticles

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(Phys.org) —Activating the body's immune system to attack cancer and prevent it from recurring is one of the Holy Grails of cancer research because of its ability to specifically target cancer and to search almost anywhere in the body for rogue tumors. While the field has made some progress, and immune therapy for malignant melanoma and prostate cancer is proving its value in the treatment of human disease, it appears that no one general approach is going to work in all types of cancer. Two recent papers show how nanoparticles could become important tools for stimulating the immune system to respond to cancer.

Work from Rebekah Drezek's group at the Baylor College of Medicine, for example, is demonstrating that gold nanoparticles can efficiently deliver large amounts of immune system-stimulating nucleic acids into macrophages, activating scavenger cells and enabling them to attack tumors in animals. This work was reported in the journal *PLoS ONE*.

The BCM team has been working with short pieces of synthetic nucleic acids containing repeated segments of cytosine-phosphate-guanine (CpG) that are known to reduce the immune suppressing activity of tumors. To be effective, however, these molecules have to be administered at high doses, raising toxicity concerns. Dr. Drezek reasoned, though, that since nanoparticles are naturally taken up by macrophages and other immune stimulating cells known as dendritic cells, they might prove useful as targeted delivery agents that could enhance the immune response associated with CpG nucleic acids without the associated side effects.

Experiments in mice appear to show just that. When administered to tumor-bearing mice, gold nanoparticles coated with a layer of CpG nucleic acids produced a marked immune response that inhibited tumor growth and increased survival of the treated animals. The researchers showed that nanoparticle-CpG treatment boosted immune cell movement into tumors without producing elevated levels of powerful signaling molecules known as cytokines that can cause unwanted toxicities. Based on these results, Dr. Drezek's group plans to explore if this approach can work synergistically with other types of therapy and in models of metastatic disease.

Researchers at the Sanford Burnham Medical Research Institute are taking a different approach, using modified carbon nanotubes as delivery vehicles of agents that will turn off cells known as T-regulatory (T-reg) cells. When present, these cells suppress the immune system. By targeting T-reg cells found specifically in tumors, Massimo Bottini and his colleagues hope to boost the effect of a wide range of cancer immunotherapies, including the type that Dr. Drezek's group is developing. Dr. Bottinis group published the results of their studies in the journal *Bioconjugate Chemistry*.

This recent work has highlighted the importance of T-reg cells found in tumors in suppressing the immune systems ability to destroy tumors. It has also been shown that these tumor associated cells overexpress a molecule known as the glucocorticoid-induced TNFR-related receptor (GITR) where T-reg cells found in the rest of the body do not. In an important first step, Dr. Bottini and his collaborators showed that attaching a GITR-targeting molecule to carbon nanotubes triggers a dramatic increase in uptake of this construct by T-reg cells within tumors, but not by those in other parts of the body. The researchers note that this achievement represents the first selective intratumor targeting of T-reg cells. "We hope it will pave the way to novel oncologic immunotherapies based on T-reg-selective functional manipulation,"

wrote the investigators.

The work with gold nanoparticle delivery of DNA, which was supported in part by the National Cancer Institute, is detailed in a paper titled, "Gold nanoparticle delivery of modified CpG stimulates macrophages and inhibits tumor growth for enhanced immunotherapy." The full paper is available free at the journal's website.

The work with carbon nanotubes is described in a paper titled,"In vivo targeting of intratumor regulatory T cell using PEG-modified single-walled carbon nanotubes." An abstract of this paper is available at the journals website. View abstract

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