# Lipid Nanoparticles Enhance Antitumor Vaccine Activity

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Positively charged lipid-based nanoparticles are known to trigger strong immune responses when injected into the body, which can be problematic when attempting to use this type of nanoparticle as a drug delivery vehicle. Now, researchers at Colorado State University, led by Steven Dow, Ph.D., D.V.M., have taken advantage of this effect to boost the activity of a DNA-based anticancer vaccine. This work appears in the journal *Cancer Gene Therapy*.

Cancer vaccines have the promise to harness the body's immune system to kill cancer and to prevent tumors from metastasizing, but the results of human clinical trials for a variety of cancer vaccines have produced mixed results. And while DNA-based vaccines work well in animal models, they have done poorly in humans, particularly at preventing the spread of cancer to the lungs. Some studies suggest that humans, unlike mice, do not produce a strong immune response to DNA-based cancer vaccines.

In previous work, Dow and his co-workers had established that nanoparticles formed from DNA and positively charged liposomes are potent activators of the innate immune system, which involves cells called leukocytes, natural killer cells, and mast cells, among others. The innate immune system acts as a first line of defense against infection. Activation of the innate immune system triggers the more complex adaptive immune response, which is associated with antibody production. Dow and others have also shown that such nanoparticles will trigger the release of cytokines, potent stimulators of the adaptive

immune system.

In this study, the investigators showed that simply mixing the dendrimer with antisense oligodeoxynucleotides triggered a self-assembly process that generated stable nanoparticles. Electron microscopy revealed that these nanoparticles were toroidal in shape, a finding that implies that the dendrimer and oligodeoxynucleotide first zip together to form a single structure that then wrap around themselves to create the final nanoparticle.

To test the hypothesis that such nanoparticles might do a better job than conventional DNA vaccines at killing tumors, the investigators created a DNA plasmid that earlier experiments had shown will elicit some antitumor activity. They then created a lipid-based nanoparticle by mixing this plasmid with a standard cationic liposome. Mice with human colon tumors were then immunized with either the plasmid or the nanoparticle.

Within two weeks of immunization, it was clear that the nanoparticles had triggered a much stronger immune response, which was translating into a more potent antitumor effect. In addition, the investigators found that immunization with the nanoparticles increased the survival rate in animals with established lung metastases

The investigators found that they could tie this enhanced response to a boost in the production of a specific type of T cell, known as CD8(+), as well as to a boost in the production of several cytokines. More importantly, the CD8(+ )cells produced in response to nanoparticle vaccination were more active than those produced in response to vaccination with plasmid DNA. The researchers also found that nanoparticle vaccination boosted activation of the adaptive immune system.

This work, which was supported by the National Cancer Institute, is detailed in a paper titled, “Vaccination with liposome – DNA complexes elicits enhanced antitumor immunity.” An investigator from the National Jewish Medical and Research Center also participated in this study. An abstract of this paper is available through PubMed.

Source: National Cancer Institute