Antigen-encapsulated chitosan particles improve immune response, study finds

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Bhanu Koppolu uses a flow cytometer to identify changes in immune cell populations.

(Phys.org) —Biomedical engineering researchers at the University of Arkansas have encapsulated two types of protein antigens in chitosan and demonstrated that the combined material enables or improves three important immune responses.

The researchers – Bhanu Koppolu, a doctoral student and senior research

assistant, and David Zaharoff, assistant professor of biomedical engineering – have worked with chitosan for many years and continue to demonstrate its effectiveness as potential biomaterial for the targeted delivery of vaccines and immunotherapy.

"A great deal of effort has been spent developing delivery systems capable of enhancing vaccine responses with specific antigens," Koppolu said. "We believe we have developed a system that will accomplish this. In all tests, our material outperformed soluble antigen. The encapsulation of antigens in chitosan particles enhanced uptake, activation and presentation by antigen-presenting cells."

The researchers' study was published in the journal Biomaterials.

Vaccine development over the past several decades has shifted toward antigens, which are toxins or other foreign substances that induce an immune response, specifically the production of antibodies. Before this shift, vaccine development had focused on developing whole pathogens, which are bacteria and viruses that cause minor versions of diseases for the purpose of immune response.

With this goal, medical researchers have focused on encapsulating polypeptide antigens in nano- and micro-particles as a strategy to enhance immune response. Packaging antigens in these particles has several advantages. The particles prevent antigen degradation, facilitate ingestion of chemical agents into antigen-presenting cells and can be engineered to carry adjuvants, which are substances in addition to the primary antigen or drug.

One particle material that Zaharoff and other researchers have focused on is chitosan, which is a natural polysaccharide derived primarily from the exoskeletons of crustaceans. Chitosan-based vaccine delivery systems have many advantages, Zaharoff said. The particles are easy to

produce, and polypeptides can be encapsulated during particle formation or absorbed into particle surfaces after formation.

Most importantly, chitosan's muco-adhesiveness and ability to loosen gaps between layers of tissue make it an excellent vehicle for delivering vaccine agents.

For their study, Koppolu and Zaharoff focused solely on the function of so-called antigen-presenting cells –macrophages and dendritic cells – which play a critical role in the production of antibodies that fight bacteria, viruses and other foreign substances.

Macrophage cells are phagocytic, meaning they are capable of engulfing and absorbing bacteria and other small cells and particles. Macrophage cells exist in stationary form in tissues or as a mobile white blood cell, especially at sites of infection. Dendritic cells are other types of immune cells that process antigen material. They are short, branch-like extensions of nerve cells.

The researchers' in vitro experiments demonstrated that antigens encapsulated in chitosan enhanced activation of antigen-presenting cells. The combined material also increased the release of cytokines – proteins that produce an immune response – and caused a proliferation of antigen-specific T cells, or lymphocytes, which also actively participate in immune response. The researchers discovered that uptake of antigen encapsulated in chitosan by dendritic cells and macrophages depended on particle size, antigen concentration and exposure time.

Zaharoff has investigated chitosan for several years, going back to his time (2004-2008) at the National Cancer Institute's Laboratory of Tumor Immunology and Biology. In 2009, after coming to the University of Arkansas and setting up the Laboratory of Vaccine and Immunotherapy Delivery, Zaharoff presented results of a major study of the effects of

chitosan combined with Interleukin-12, a powerful cytokine.

The combined material eradicated bladder tumors in mice. Zaharoff is currently in discussions with clinical investigators at the University of Arkansas for Medical Sciences to translate the bladder cancer immunotherapy into human trials.

Provided by University of Arkansas

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