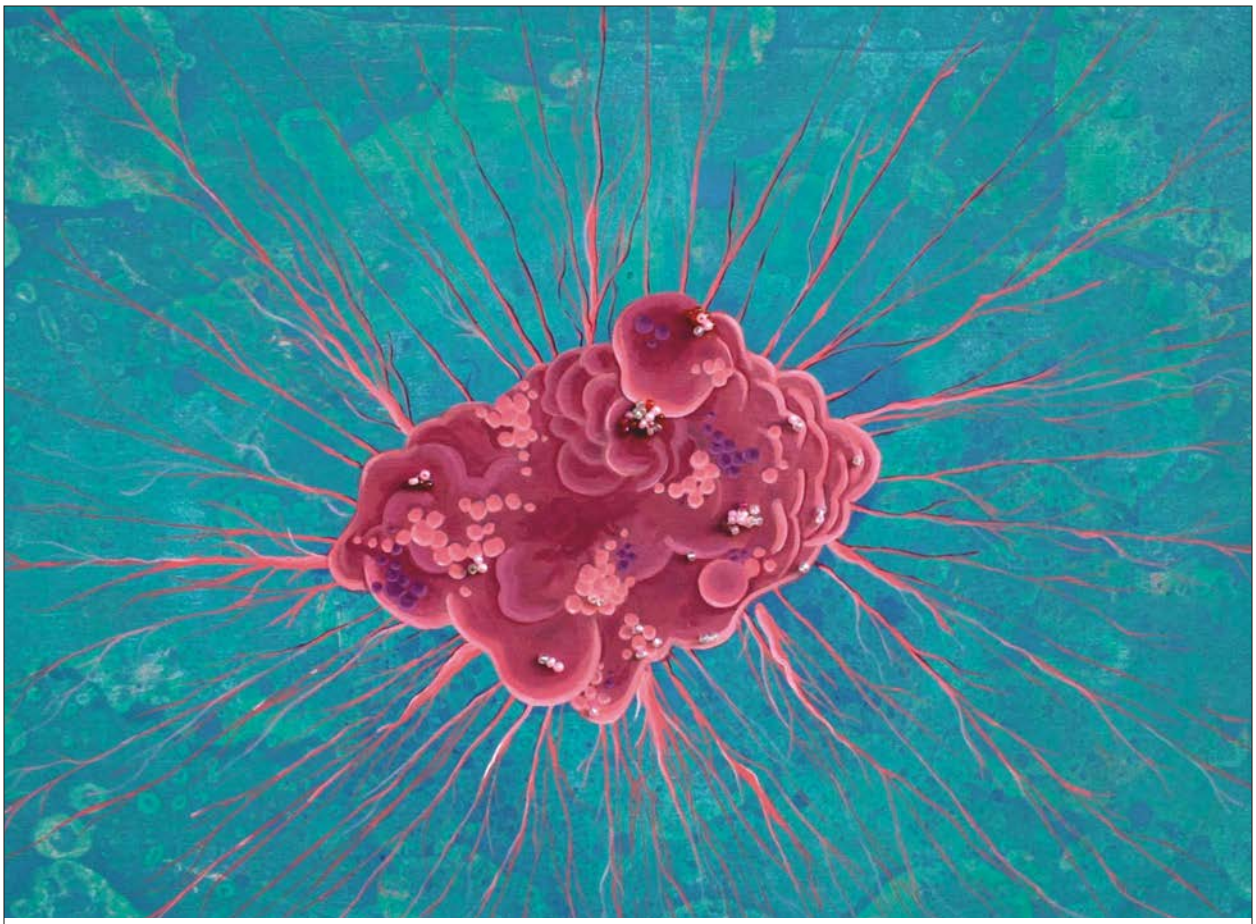

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Scientists Discover Potential Strategy to Improve Cancer Vaccines

The promise of vaccines targeted against various types of cancer has raised the hopes of patients and their families. The reality, however, is that these promising treatments are difficult to develop. One of the challenges is identifying a discrete cellular target to stop cancer growth without inactivating the immune system. Scientists at UNC Lineberger Comprehensive Cancer Center report a laboratory finding that has the potential to increase the effectiveness of therapeutic cancer vaccines.

The team found that the absence of the function of a protein called NLRP3 can result in a four-fold increase in a tumor's response to a therapeutic cancer vaccine. If this finding proves consistent, it may be a key to making cancer vaccines a realistic treatment option. Their findings were published in the Dec. 15, 2010 issue of the journal Cancer Research.

Jonathan Serody, MD, a study author, explains, "This finding suggests an unexpected role for NLRP3 in vaccine development and gives us a potentially pharmacologic target to increase vaccine efficacy."

The research team was headed by co-leaders of the UNC Lineberger Immunology Program: Serody, MD, an expert in tumor immunology, and Jenny Ting, PhD, a pioneer in understanding the NLR family of proteins. Serody is the Elizabeth Thomas Professor of Hematology and Oncology. Ting is UNC Alumni Distinguished Professor of Microbiology and Immunology and director of the Inflammation Center at UNC.

The team discovered that deleting the NLRP3 proteins reduced the supply of a tumor-associated cell called myeloid-derived suppressors, making them five times less effective in reaching the site of tumor growth. Researchers working with Serody had previously shown that these myeloid cells are critically important as they allow the tumor to evade a beneficial immune response. This finding is the first to link immature myeloid cells, NLRP3, and the response to cancer vaccines.

Serody says, "We had originally thought inactivating the NLRP3 protein would decrease the immune system's ability to respond to cancer because NLRP3 is important in alerting immune cells to changes in the environment the immune response to cancer. Instead what we found was that by inactivating these proteins, the tumor vaccine was made more effective because fewer myeloid-derived suppressor cells were available to promote tumor growth and reduce the efficacy of the vaccine."

At present, there is only one FDA-approved cancer vaccine called Provenge, used to treat advanced prostate cancer. Provenge has been shown to extend survival by three to four months.

Vaccines are difficult to make. Because a vaccine is person-specific, made with the individual's immune cells, the production process requires that the individual's cells are isolated and shipped to the company for vaccine production. As a result, the vaccines are expensive. Provenge costs approximately $100,000 for three treatments.

"A vaccine is not like a pill that can be manufactured in bulk," Serody explains. "And, it's not like developing a vaccine against a virus such as polio or smallpox. Cancer cells look a lot like regular cells, so it is hard to trick the body into thinking cancer cells are 'foreign.' Our hope is that our findings and future work in this area will enable us to develop more effective vaccines against many types of cancer. "

Other UNC authors are Hendrik W. van Deventer, MD, assistant professor of medicine; Joseph E. Burgents, former UNC graduate student, now a postdoctoral fellow at the National Institute of Environmental Health Sciences; Qing Ping Wu, research specialist; Rita-Marie T. Woodford, research assistant in the UNC School of Dentistry; W. June Brickey, research assistant professor of microbiology and immunology; Irving C. Allen, Ph.D, postdoctoral fellow, UNC Lineberger; and Erin McElvania-Tekippe, former UNC graduate student, now a postdoctoral fellow at Washington University in St. Louis.

Hendrik W. Van Deventer, Joseph E. Burgents, Qing Ping Wu, Rita-Marie T. Woodford, W. June Brickey, Irving C. Allen, Erin Mcelvania-Tekippe, Jonathan S. Serody, and Jenny P.-Y. Ting. The Inflammasome Component Nlrp3 Impairs Antitumor Vaccine by Enhancing the Accumulation of Tumor-Associated Myeloid-Derived Suppressor Cells. Cancer Research, 2010; DOI: 10.1158/0008-5472.CAN-10-1921