Can scientists predict which cancer markers are likely to trigger an immune response?

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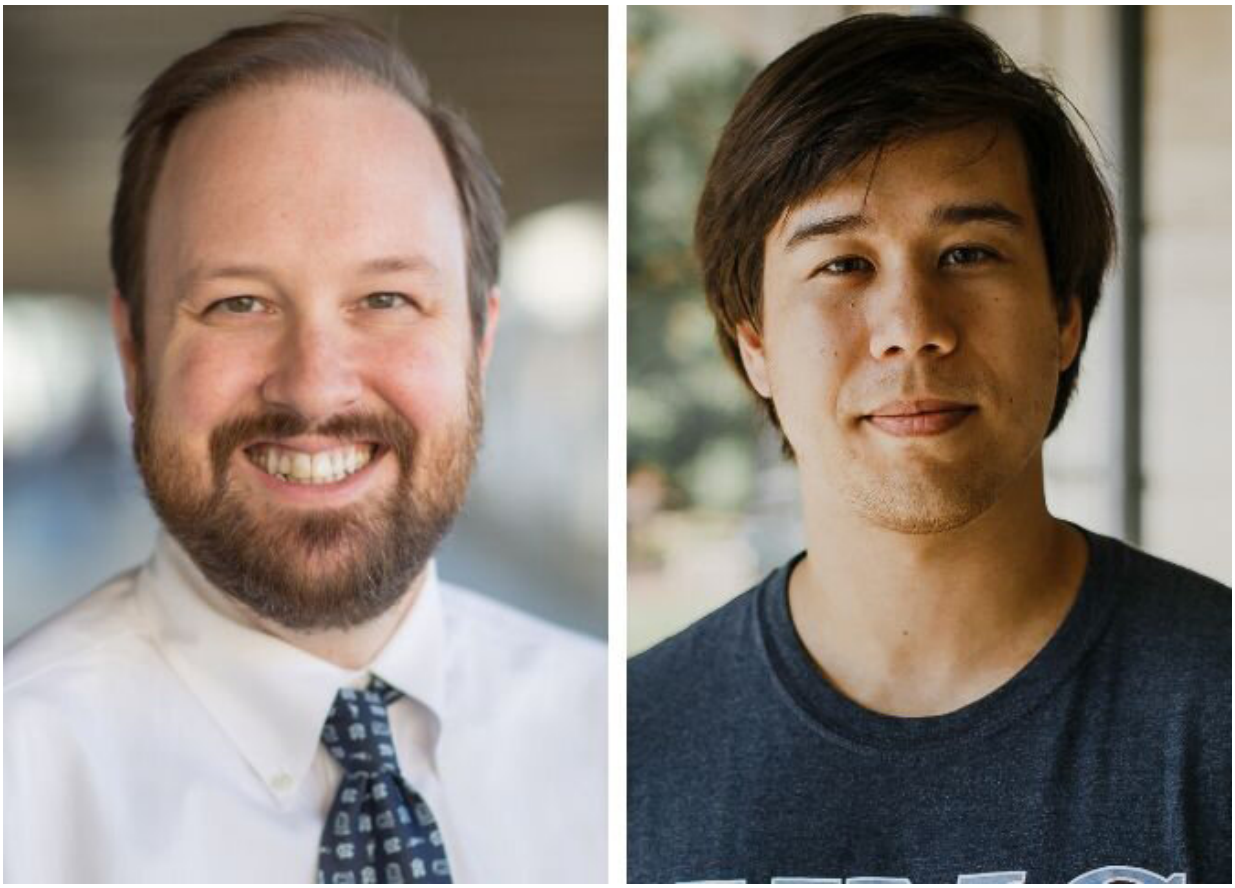
Scientists at the University of North Carolina Lineberger Comprehensive Cancer Center have designed and validated a model for predicting what might make an effective cancer vaccine against a patient's tumor. This finding could help overcome a significant obstacle in the development of personalized cancer vaccines.

In a study published in the journal *Cancer Immunology Research*, UNC Lineberger scientists reported on the discovery of a method for predicting whether abnormal proteins produced by cancer cells could trigger an immune response. This is important because not all so-called "neo-antigens" created by cancer cells will trigger the body's immune system to fight the cancer.

"While the field of therapeutic tumor vaccines is rapidly advancing, a major challenge is identifying which targets will provide the best anti-cancer effects," said UNC Lineberger's Benjamin Vincent, MD, assistant professor in the UNC School of Medicine Division of Hematology/Oncology and the corresponding author of the study. "This study provides a new method to tackle this challenge: predicting the efficacy of a tumor vaccine target prior to treating the patient and allowing for treatment with an optimized set of robust vaccine targets."

The work is part of an effort by researchers to study whether they can scan the genome of a cancer cell to find clues to the presence of irregularities produced by the cancer—irregular proteins called neo-antigens, or new antigens, that might appear on the cancer cell's surface. Then, based on those findings, they want to use those neo-antigens to trigger an immune response to the cancer, but not against normal, healthy cells.



Benjamin G. Vincent, MD, and Christof Smith, PhD. Credit: University of North Carolina at Chapel Hill School of Medicine

"One of the obstacles to cancer vaccine research is that you can have vaccine targets that aren't able to generate a good response," said Christof Smith, Ph.D., an MD/Ph.D. student at the UNC School of Medicine. "To address this problem, we designed and validated a new machine-learning algorithm to predict for the ability of a particular, tumor-specific antigen to produce an immune response."

There already exist methods capable of predicting potential neo-antigen expression and presentation by the tumor, but Smith said they tell "only

half the story." While existing methods focus on how well a particular abnormal cancer marker might be packaged and presented on the surface of a tumor cell, Smith said their method further looks at how well an immune cell might recognize that marker and respond.

"Current methods for ranking the efficacy of neo-antigens rely on prediction of how well that neo-antigen will be presented in the body," Vincent said. "The problem with this method is that it does not account for how well the neo-antigen can actually activate the immune system. As such, our algorithm can further improve the accuracy of predicted neo-antigens capable of generating robust immune responses."

In their method, researchers used laboratory models to analyze the immune response to hundreds of different predicted neo-antigens. Then they used machine learning to analyze the data to glean which antigens might best produce an immune response.

"In essence, we're designing a software product that can directly predict how immunogenic a particular target is, which is really needed in the field," Smith said.

More information: Christof C. Smith et al. Machine-Learning Prediction of Tumor Antigen Immunogenicity in the Selection of Therapeutic Epitopes, *Cancer Immunology Research* (2019). DOI: 10.1158/2326-6066.CIR-19-0155

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