Are Personalized Vaccines Part of a New Approach to Treating Melanoma?

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Bracing for cold weather and the threat of runny noses and sore throats, millions of Americans are vaccinated for the flu each year. By priming the immune system, the vaccine reduces the risk of catching the flu and, if not successful at preventing it altogether, reduces both the severity and the duration of symptoms. These are 'one-size-fits-all' vaccines that are useful for all people. But what if each and every person's flu, like each person's melanoma, was unique? You'd need a personalized vaccine that was made and customized for each individual. Patrick Ott, MD, PhD, clinical director of the Melanoma Center at the Dana-Farber Cancer Institute and lead researcher on the BJ's Wholesale Club-MRA Team Science Award, is conducting pioneering research to harness the power of personalized vaccines to combat melanoma.

"If immunotherapy works by releasing the brakes that hold back the immune system, vaccines are like adding more cylinders to the engine," said Ott. But, unlike the flu vaccine which is made in bulk each year, Ott's melanoma vaccines — which he calls NeoVax — are made specifically for each patient over a twelve-week period.

To develop these personalized vaccines, Ott and his team first sequence the genome of each patient's melanoma tumor. Then, they identify the mutated genes in that patient's tumor and select from them the targets most likely to elicit a strong immune response. The selected targets represent the pool of so-called neo-antigens that the NeoVax is aimed at. Because the mutations are only present in the patient's tumor, the immune response is directed only against the tumor and not other, healthy tissues. "The technology needed to do this in time for patients, just didn't exist ten years ago," said Ott. "This is the ultimate form of personalized medicine."

Personalized medicine, sometimes called precision medicine, is based on the idea that every person is unique and that medical interventions should align with or be tailored to the individual patient and their likelihood of responding to a specific treatment approach. At a basic level, doctors have been doing this for centuries, but with the rise of our understanding of the molecular basis of disease — doctors and researchers have a greater insight into individual patient needs than ever before.

In melanoma, personalized medicine isn't new. For example, tumors from half of all patients with

melanoma have a mutation in the BRAF (pronounced bee-raf) gene. Drugs, called targeted therapies, have been developed to exploit this altered BRAF, but before a doctor prescribes one of these medications, they must actually test the patient's tumor for this specific mutation. If the patient's tumor does have a BRAF mutation they are a candidate for the targeted therapy. If not, a doctor would likely turn to other treatment approaches.

Ultraviolet radiation from the sun or tanning equipment is like a proverbial shot gun blast to DNA — and even though DNA tries to repair itself — mistakes are inevitable. In melanoma, as these mistakes add up altered proteins, the neo-antigens, accumulate. These neo-antigens are believed to be critical to help the immune system detect the cancer and can be used to create tumor-targeting, personalized vaccines. Ott and his team will build upon research, published last year in Nature, where they demonstrated not only the safety and feasibility of these custom-made vaccines, but also strong immune responses directed at the neo-antigens contained in each patient's vaccine. This time they will test the vaccines in patients with metastatic melanoma and will introduce protocol refinements to hopefully increase the strength of the vaccine even further. They will also introduce novel technologies to assess these exquisitely specific immune responses in each patient's metastatic tumors over time.

In addition to a personalized vaccine designed to help spur their immune system to identify and attack the cancer, patients enrolled in the trial will also receive the anti-CTLA4 treatment ipilimumab delivered locally to turn up the recognition of tumor neo-antigens, and enhance T cell activity in the lymph node where the T cells first "see" the neoantigens and get activated. Finally, patients will be administered the vaccines along with systemic infusions of the anti-PD-1 drug nivolumab to keep T cells from being turned off by tumor signals. By boosting the immune system in three different ways, Ott and his team hope to generate a strong and durable immune response to melanoma.

While this approach is experimental, it represents a promising avenue of future research for the next iteration of melanoma treatments. Learn more about this and other clinical trials here.

BJ's Wholesale Club, the generous sponsor of this research, hosted their first-ever Melanoma Awareness Campaign in partnership with MRA last year. The campaign featured a reverse of point sale that allowed vendors to be recognized for their donation to MRA. They also developed an extensive promotional plan that included full-page ads and an educational email distributed to their six million members, massive signage in all 225 stores, and social media messaging throughout the month of May. In total, BJ's raised $800,000 that was donated to MRA and used to fund Ott's research. This year, BJ's hopes to raise even more in their Melanoma Awareness Month campaign with MRA.

"As someone who has a family member that was diagnosed with melanoma, I know all too well the effect that skin cancer can have on a family," says BJ's Wholesale Club Executive Vice President and Chief Financial and Administrative Officer Bob Eddy. "I'm thrilled that funds raised through this partnership are making a meaningful contribution to research that helps advance treatments for melanoma and brings us closer to a cure," says Eddy.

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