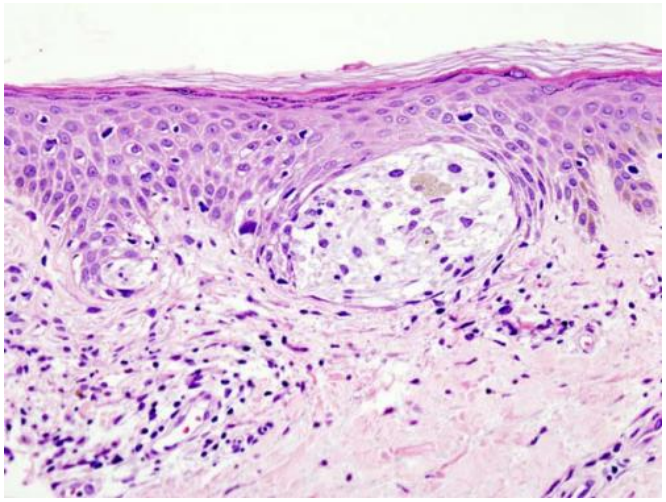
Researchers discover how to boost vaccine designed to prevent melanoma recurrence

16 November 2020



Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

A vaccine created to prevent the recurrence of the deadly skin cancer melanoma is about twice as effective when patients also receive two components that boost the number and effectiveness of immune system cells called dendritic cells, according to phase 2 clinical trial results published in *Nature Cancer* in November.

These results are important because most cancer vaccine trials have failed to show clinical efficacy. These results show that adding two immune-boosting components can boost the immune response for not only melanoma patients but possibly also others whose cancers express a protein called the vaccine antigen, which is common in some cancers.

Researchers at The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, working with colleagues at the National Cancer Institute-funded Cancer Immunotherapy Trials Network (CITN) based at the Fred Hutchinson Cancer Research Center, found that adding the small molecule Flt3L, which increases the number of dendritic cells, boosted the vaccine's effectiveness at producing antibodies and T cells that can later fight melanoma. Adding a second component, called poly-ICLC, also strengthened the dendritic cells' ability to promote antibodies as well as helper and killer T cells.

Sixty patients who had stage 2 or 3 melanoma, and whose cancer was successfully removed via surgery, received the vaccine. Half of the patients received the vaccine alone while the other half received the vaccine with Flt3L and poly-ICLC.

The vaccine is designed to target dendritic cells and is composed of an antigen found in melanoma bound to an antibody to increase the chances of binding with dendritic cells.

The cocktail of the vaccine, Flt3L, and poly-ICLC nearly doubled the vaccine's efficacy, according to analysis of the T cells detected in patients' blood samples after they received four doses over four months. That immune response was seen significantly earlier in the patients who received the cocktail and at much higher levels in many more patients compared to those who received only the vaccine. Researchers found antibodies were still present in blood samples tested 12 weeks after the last dose.

"This is the first randomized clinical trial to show that an immune response to a cancer vaccine can be potentiated by the addition of Flt3L," says Nina Bhardwaj, MD, Ph.D., Director of the Immunotherapy Program at The Tisch Cancer Institute, and first author and a corresponding author on the study. "The response was achieved because Flt3L mobilized dendritic cells, which are the gold standard in promoting cancer immunity, and improved the overall immunogenicity of the vaccine. This may change the approach of

increasing efficacy in other cancer vaccines in the future."

"These positive results are significant not only for improving cancer vaccines, but also potentially for application to other vaccine platforms," reported the study's co-corresponding and senior author Steven Fling, Ph.D., Director of the CITN Laboratory and Senior Staff Scientist in the Vaccine and Infectious Disease Division at the Fred Hutchinson Cancer Research Center, "and we are extremely grateful and indebted to the patients whose unwavering participation made this demanding clinical protocol a success."

These findings also provide a basis for adding immunotherapies called checkpoint inhibitors, which have been successful in treating metastatic melanoma, to vaccines in order to further increase the success in fending off melanoma recurrence. Researchers also plan to follow trial participants over time and measure how many have cancer recurrence to further study the vaccine's efficacy in each group.

"Immunotherapy has already shown great promise for patients with metastatic melanoma who would normally have a difficult, sometimes grave, prognosis," said Philip Friedlander, MD, Ph.D., Director of the Melanoma Medical Oncology Program at The Tisch Cancer Institute at Mount Sinai and site investigator of the trial. "It's important to work toward developing effective cancer vaccines that can prevent cancer on their own or in addition to the drugs already available."

More information: Flt3 ligand augments immune responses to anti-DEC-205-NY-ESO-1 vaccine through expansion of dendritic cell subsets, *Nature Cancer* (2020). DOI: 10.1038/s43018-020-00143-y , www.nature.com/articles/s43018-020-00143-y

Provided by The Mount Sinai Hospital