Study identifies biomarker for breast cancer response to immunotherapy

27 July 2021

Credit: Unsplash/CC0 Public Domain

A biomarker that has proven to be a predictor for response to immunotherapies in melanoma patients also has clinical relevance for breast cancer patients, according to a new study published in *Clinical Cancer Research*.

The study demonstrated that this biomarker, a molecule called the Major Histocompatibility Complex Class II protein (MHC-II), has the potential to be a predictor of immunotherapy benefit with two types of breast cancer—early-stage, triple negative breast cancer (TNBC) and high-risk, estrogen receptor-positive breast cancer (HR+) when expressed on breast cancer cells. Although immunotherapies are likely to soon be prescribed along with chemotherapies for these breast cancers before surgery, most patients don't require the addition of immunotherapy to achieve treatment response. Without an optimal biomarker, clinicians don't have a reliable way to discern which patients need immunotherapy and which ones don't.

Clinical tests for MHC-II expression could shield breast cancer patients who don't need the immunotherapy from possible treatment complications and additional costs. Immunotherapies are expensive and associated with significant toxicity.

Justin Balko, PharmD, Ph.D., associate professor of Medicine and Pathology, Microbiology and Immunology, conceived and designed the study.

"These findings are particularly exciting for us, because if validated, they could provide a better way to personalize therapy for breast cancer patients. So far, the typical biomarkers like PD-L1 expression and the numbers of immune cells in the tumor have not done a good job of identifying patients who need immunotherapy," said Balko, the study's senior author.

Paula Gonzalez Ericsson, the study lead author, added, "the test can be easily performed on patient's tissue samples obtained for diagnosis without the need of additional intervention."

Balko and colleagues analyzed tissue samples donated by three cohorts of patients:

- patients with non-immunotherapy-treated breast cancers
- patients with TNBC treated with the immunotherapy durvalumab and standard chemotherapy
- patients with HER2-negative breast cancer treated with either standard chemotherapy or the standard chemotherapy plus the immunotherapy pembrolizumab.

They determined that MHC-II is expressed in a subgroup of primary TNBC and HR+ breast cancers, and that tumor MHC-II expression is associated with response to standard chemotherapy plus durvalumab or pembrolizumab, but not to standard neoadjuvant chemotherapy alone.

"The findings of the association with response in early-stage high-risk HR+ patients suggests that MHC-II may be a useful tool in a broader context for breast cancer and this area would benefit from further study," said co-senior author, Kim Blenman, Ph.D., MS, assistant professor of Medicine at Yale University.

The study is believed to be the first to evaluate and demonstrate the predictive capacity of tumor MHC-II for immunotherapy-specific benefit in patients with breast cancer. The researchers also noted that MHC-II has the potential to be a pan-cancer biomarker predictor for anti-PD-1 or anti-PD-L1 immunotherapies since its clinical relevance has been demonstrated with melanoma, breast cancer and Hodgkin's lymphoma in this study and previous studies. However, they call for a large, randomized controlled trial to validate their findings with breast cancer, which was based on a retrospective tissue-based analysis.

More information: Paula I Gonzalez-Ericsson et al, Tumor-specific major histocompatibility-II expression predicts benefit to anti-PD-1/L1 therapy in patients with HER2-negative primary breast cancer, *Clinical Cancer Research* (2021). DOI: 10.1158/1078-0432.CCR-21-0607