Immune Function May Predict Breast Cancer Recurrence

By Michelle Perron

No matter how successfully they are treated at the time of diagnosis, every woman affected by breast cancer is at risk for recurrence. The degree of risk varies considerably based on factors such as tumor type, stage at time of diagnosis, inherited risk, and other influences. In recent years, scientists have identified implications for recurrence in the immune cells of breast cancer tumors. But what answers might lie in the blood?

A research team at City of Hope National Medical Center in Duarte, Calif., sought to answer this question in a retrospective study. Their results, published in *Nature Immunology*, suggest that blood biomarkers at diagnosis have the potential to accurately predict whether breast cancer will recur years later (2019; doi: 10.1038/s41590-019-0429-7).

“For more than 20 years, I’ve been interested in how cancer affects the immune system,” said Peter P. Lee, MD, the corresponding author for the study and Chairman of the Department of Immunology at City of Hope, where he is also Co-Leader of the Cancer Immunotherapy Program. “I view the tumor as the front line of the war between cancer and our immune system. Additional information is contained in other parts of the body, such as the blood and lymph nodes. We wanted to find out if there is any altered immune function already present in women newly diagnosed with breast cancer.”

“We found that there are different immune signaling responses in the blood of patients with breast cancer, even at the time of diagnosis,” Lee said. “In some patients, their immune cells cannot sense or respond to certain cytokines properly, leading to abnormal immune response. The presence of these signaling abnormalities at diagnosis predicts relapse 3-5 years later.”

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Immune cells are the “engine” behind a healthy immune system, and the balance of cytokine signaling responses in peripheral blood immune cells is an indicator of overall immune status. By harnessing the signaling data gathered from the blood samples collected from study participants, the City of Hope scientists created a cytokine signaling index that has the potential for widespread use as a predictor of recurrence.

“The most exciting thing about these findings is that we can now measure some aspects of a patient’s immune function at diagnosis and can predict the likelihood of relapse years later,” Lee said. “The key question is, why? How is it that this is the case?”

“I think it’s because at diagnosis, the ability of the immune system to fight off and prevent cancer from coming back in the future has already been determined,” he continued. “If we can confirm and understand this with further research, we can potentially develop new treatments to enhance the immune function and address the abnormal immune signaling at diagnosis in patients who are likely to relapse in the future.”

The Future

In the conclusion to their research article in *Nature Immunology*, Lee and coauthors state that further analyses involving larger cohorts are necessary to develop a prognostic risk score for the clinical setting. Lee noted that this prospective research should involve collaboration among multiple institutions and will require extensive resources. He believes the effort will be worthwhile.

“If we can understand the mechanism by which the signaling is not optimal, we can provide patients with a treatment to make outcomes more optimal,” he said. “We’re not going to stop. We’ll work specifically for patients with recurrence risk. With this blood test, we would be able to identify patients who need to be monitored more carefully and give them more intensive treatment up front.”

Lee predicts that more answers await behind the frontline offense mounted by breast cancer. “The thing I want to emphasize is that we’re not looking at the tumor itself—we’re looking at the host immune response,” he said. “To use a sports analogy, we are focused on the defense. Most of the cancer world is focused on the cancer itself—the circulating tumor DNA and cells. That’s the offense... reflections of the cancer. We’re looking at the defense and how to strengthen it.”

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