Research Report from Drs. Yeung and Specht at Fred Hutch Cancer Center

Made possible with support from The Judith A. Lese Breast Cancer Foundation

Discovering new biomarkers in breast cancer

The first line of treatment for triple-negative breast cancer (TNBC) is typically chemotherapy, which helps shrink the tumor prior to surgery. If the tumor is completely removed, the prognosis is generally excellent. However, if the tumor can't be fully removed, patients face a worse prognosis, and the cancer often does not respond well to other forms of treatment.

Researchers now know that the immune system plays an important role in how TNBC responds to treatment. Two key factors are:

1. The tumor immune microenvironment (TIME) – how immune cells are arranged and behave inside and around the tumor.

2. Tumor infiltrating lymphocytes (TILs) – immune cells that have entered the tumor and may help fight the caner.

Our goal is to better understand which immune cells are involved when TNBC resists treatment. To do this, we use an experimental technique called "spatial proteomics." This cutting-edge technology allows us to look at many proteins in the cancer tissue at the same time. It helps us see how cancer cells and immune cells interact with each other inside the tumor and then use this information to improve treatments.

Using this approach, we created detailed images of breast cancer tissue. In these images, cancer cells appear dark blue, while different types of immune cells appear in colors such as orange, yellow, cyan and red (Figure 1). An artificial intelligence (AI) program helps identify each cell type and assign it a color. This novel data gives us a clearer picture of how immune cells behave in tumors that remain after treatment. We are now analyzing this data to understand how these immune patterns relate to patient outcomes, including survival.

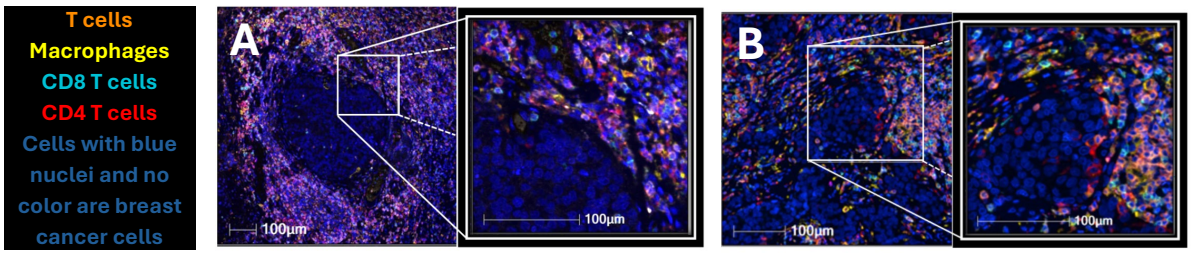

Figure 1. Breast cancer tissue under a microscope which has been categorized and color-coded by cell types. The white boxes in the left are enlarged and presented as the panels on the right for better visualization of the different immune cells that interact with the tumor. The legend indicates the color coding for the different immune cell types. Each image (A, B) represents a different patient breast cancer we tested. Patient A has minimal infiltration of immune cells in the tumor (no brightly colors cells in the tumor). In contrast, patient B shows a tumor with several immune cells that have infiltrated into the tumor.

Developing new assays to understand immunotherapy side effects

Immunotherapy has revolutionized cancer treatment for many patients, but it does not work equally well for everyone. Immunotherapies work by taking a patient's own immune cells, modifying them in a lab so they can better recognize cancer, and then putting those engineered immune cells back into the patient's body. We are trying to better understand why some patients respond well, while others see little effect or experience serious side effects. To answer these questions, we developed three lab tests (assays) that can detect the engineered immune cells in patient tissue samples. These tests allow us to see where the cells travel in the body and whether they are the cause of side effects.

We are currently optimizing one of these lab tests for use in the clinic. It is called the WPRE digital PCR assay (Figure 2). Over the past year, we improved the accuracy of this teach so it is easier to compare results across patients. This means a doctor can better monitor whether the engineered immune cells are reaching the tumor, whether they may be causing side effects, or whether the cells are growing in numbers or disappearing over time.

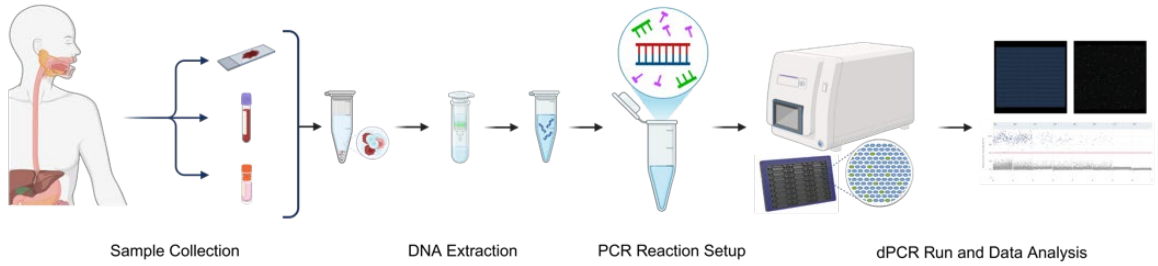

Figure 2. The WPRE digital PCR assay for testing patients' tumor tissue samples. Samples can be from fresh blood/liquid biopsy, fresh surgical tissue, archived biopsy tissue, or cryopreserved cells.

Generous funding from the Judith A. Lese Breast Cancer Research Foundation has helped move us closer to solving one of the biggest challenges in breast cancer: why some tumors resist treatment. By understanding how cancer fights back, we can develop more effective therapies that improve and save lives.

Meet the Researchers

Jennifer Specht, MD, is a board-certified medical oncologist who specializes in all stages of breast cancer with expertise in triple-negative breast cancer. She leads the Phase 1 Breast Cancer Program at Fred Hutch and is Clinical Research Director, Breast Oncology, at UW Medicine. Her research interests include breast cancer genetics, immunotherapy, and molecular imaging to better understand breast cancer biology. She holds the Jill D. Bennett Endowed Professorship in Breast Cancer at UW Medicine.

Cecilia Yeung, MD, is a clinical pathologist, professor, and medical director of Clinical Testing Labs at Fred Hutch and an associate professor in the Department of Laboratory Medicine and Pathology at UW Medicine. Her expertise in molecular pathology has led to novel molecular diagnostic platforms that improve the speed, accuracy and cost of diagnostic tools.

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