

New Discoveries, New Possibility

Fueling world-changing advances in breast cancer research

Breast cancer can take several forms, depending on its molecular makeup. And that means clinicians need just as many methods for treating it. Thanks to our donor community, cancer researchers at Fred Hutch Cancer Center and UW Medicine continue to break new ground in understanding the various drivers of breast cancer and uncovering new approaches to overcome them.

Generous philanthropic support continues to fuel innovative research throughout our labs that may one day improve outcomes for the more than 300,000 people who are diagnosed with breast cancer every year. From identifying links between obesity, recurrence, and metastasis to improving the effectiveness of immunotherapies, our researchers are making life-changing discoveries.



As we mark our 50th Anniversary in 2025, Fred Hutch is looking beyond what's possible today to a new era of discovery. With your partnership, our Campaign for Fred Hutch will transform the pace and scale of innovation so we can redefine cancer and infectious disease for generations to come.

Assessing Additional Risks for Patients with Metabolic Syndrome



Dr. Christopher Li res

Metabolic syndrome, or MetS, is a combination of conditions such as obesity and high blood pressure that can lead to heart disease and diabetes. We've learned in recent years that it's also associated with poor outcomes for patients with breast cancer, but researchers had yet to investigate

which subtypes of the disease are affected.

Now, thanks to recent discoveries from Fred Hutch and UW Medicine researchers led by **Christopher Li, MD, PhD,** we're starting to gather more detailed information about MetS and breast cancer. And that insight could help us determine who's at greater risk and one day know how to adjust treatment accordingly.

Dr. Li, who holds the Helen G. Edson Endowed Chair for Breast Cancer Research and specializes in identifying breast cancer risk factors, set out to investigate the relationship between MetS and cancer recurrence and mortality across four subtypes of the disease. His team's conclusions may be most notable for the connections they *didn't* find: With one exception, MetS does not appear to increase a patient's risk of recurrence or dying specifically from breast cancer.

That exception, though, is a potentially serious one. Patients with MetS and the less-common HR-/HER2+ breast cancer have a *three times* greater risk of recurrence. Although the first-line treatment for this subtype, trastuzumab, is very effective, it is also associated with serious cardiac side effects, particularly for individuals with hypertension, diabetes, and obesity. Unfortunately, but predictably, when these patients are taken off of trastuzumab because of those side effects, their risks of recurrence and death increase.

While the results are just an early step in better understanding the relationship between MetS and breast cancer, they highlight the ongoing importance of managing other health conditions during breast cancer treatment.

Fred Hutch is an independent, nonprofit organization that also serves as the cancer program for UW Medicine. Fred Hutch is proud to raise funds that fuel the adult oncology program on behalf of both Fred Hutch and UW Medicine.

UW Medicine

Sparing Patients Unnecessary Treatment

In addition to the more than 300,000 people who will be diagnosed with invasive breast cancer this year, another 50,000 will be diagnosed with a precursor condition called DCIS. And although less than half of those with DCIS would progress to invasive breast cancer, national guidelines call for treating all of them as if they will.

In other words, this year more than 25,000 people will undergo unnecessary, potentially life-altering breast cancer treatment, up to and including mastectomy. Researchers led by surgeon **Sara Javid**, **MD**, and radiologist **Habib Rahbar**, **MD** — both of Fred Hutch and UW Medicine — are working to spare them that experience.

The pair have been investigating noninvasive methods for spotting early signs that DCIS will progress to invasive breast cancer so they can determine who needs more aggressive treatment. And earlier this year, they published the results of a six-year study that shows MRI has potential for doing just that.

The study was small, with just 56 participants. But its enrollment criteria were less strict than similar studies conducted elsewhere, allowing for a potentially more representative cross-section of patients with DCIS — and therefore stronger data. Drs. Javid and Rahbar are pursuing multiple follow-up trials to further examine MRI's effectiveness for identifying cases of DCIS more likely to progress and ultimately equip oncologists everywhere with tools to head off unnecessary treatment.

Exploring Treatments for Rare Breast Cancer

Although immunotherapies called ICIs have been transformative for some cancers, their benefits for other tumor types, including breast cancer, have been more limited. However, recent research has shown that ICIs have potential as a treatment for metaplastic breast cancer (MpBC), which is rare, highly aggressive, and difficult to treat. Before we can explore that further, though, we need to identify genomic vulnerabilities within these tumors.

Shaveta Vinayak, MD, a UW Medicine researcher, and **Jennifer Specht, MD,** a breast oncologist at Fred Hutch and UW Medicine, may be closing in on a few. The pair recently examined tumors — as well as the surrounding immune cells that they corrupt and recruit for defense — from 13,500 patients with breast cancer.

And last December they reported that the immune environment around the tumors from patients with MpBC are well equipped to shut down *other* immune cells that could attack the cancer cells. However, they also identified genomic changes in the tumors that are different from patients with non-MpBC, including a handful that could be targeted with ICIs to overcome that immune suppression. These provocative findings could lead to future trials with immunotherapies and offer new treatments for patients with this most aggressive form of breast cancer.

"Over the last 50 years, we've seen a 58% decrease in breast cancer mortality thanks to the inroads we've made in understanding the pathways that drive breast cancer. And that understanding has led to new, more precise interventions. Philanthropy drives those discoveries. Donor support is more important than ever for fueling early-stage research with the potential to change lives."



 Nancy Davidson, MD, medical oncologist, executive vice president of Clinical Affairs, and Raisbeck Endowed Chair for Collaborative Research, Fred Hutch

Philanthropic support advances early-stage research that can lead to treatment-defining breakthroughs. To learn more about discoveries like these, **please contact Mallory Smith**, **PhD at 206.667.5265** or **msmith8@fredhutch.org**.