

# 2-PREVENT TRANSLATIONAL CENTER OF EXCELLENCE (TCE)

A COMPREHENSIVE APPROACH TO ADDRESS  
BREAST CANCER RECURRENCE AND  
METASTATIC DISEASE

## **AN UPDATE ON YOUR IMPACT**

March 2022

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# 2-PREVENT TRANSLATIONAL CENTER OF EXCELLENCE (TCE) PROGRESS REPORT

## A COMPREHENSIVE APPROACH TO ADDRESS RECURRENCE AND METASTATIC DISEASE

For nearly a decade, the 2-PREVENT TCE has grown as a national and international leader for advanced and recurrent breast cancer research and care. Today, **our mission is twofold: to reduce the burden of recurrent breast cancer and improve survival and quality of life after primary treatment, while developing improved treatment methods for locally advanced and metastatic disease.** Built to evolve with advances in research, the TCE calls on experts across Penn Medicine to join together to fully integrate basic and clinical studies that are paving the way for the future of breast cancer treatment and care.

The TCE takes a comprehensive approach, integrating the best science, newest therapies and patient centered care to create a research program that addresses each stage in the continuum of breast cancer treatment.



## EARLY RECURRENCE AND SURVEILLANCE

The high rate of relapse and metastatic disease among breast cancer survivors remains one of the greatest challenges for breast cancer researchers. The 2-PREVENT TCE is working to understand the biology of recurrence and develop screening tools to help identify patients at risk.

### *Understanding the Biology of Breast Cancer Recurrence*

Today, as a result of research from the 2-PREVENT TCE, we understand that breast cancer can recur when Disseminated Tumor Cells (DTC); cancer cell “seeds” escape the primary tumor before surgery and remain dormant and undetected in the body. For reasons still unknown, these DTCs can be reactivated and begin growing again.

Dr. Lewis A. Chodosh and his team are focused on understanding the biology of these cells to enhance our ability to prevent and treat recurrent disease. Using animal models to study DTCs, this work seeks to answer three critical questions:

1. How do dormant cancer cells survive?
2. Why do some DTCs “wake up” and recur in some patients?
3. Can we prevent breast cancer recurrence by targeting DTC survival mechanisms to eradicate these cancer cells?

### *Finding Dormant “Sleeper” Cells*

The Chodosh lab has also developed a new test to detect DTCs in patients and provide crucial information on the unique properties of these cells. The test, called “DTC-Flow” is significantly more sensitive than traditional methods, with the ability to detect a single DTC ‘hiding’ among 5 million normal cells. This process also allows researchers to analyze these cancer cells in order to identify the precise properties of the cancer cells that each patient might harbor.

DTC-Flow technology has the potential to transform breast cancer treatment, giving doctors the information they need to offer personalized treatment options designed to defeat a patient’s specific cancer.

### *Surveillance Testing for “Minimal Residual Disease” (MRD)*

Research continues to study markers in the blood or bone marrow that could help us predict which patients are at increased risk of their cancer returning and in doing so, identify those who would benefit from additional targeted treatments. These markers are collectively called “minimal residual disease” or “MRD”. These terms refer to cells that remain in the body after patients have completed all of their treatment and have the potential to lead to metastatic breast cancer. The key is to find MRD that is destined to cause metastasis and kill these cells before they can cause harm

Dr. Angela M. DeMichele and her team continue their work on the SURMOUNT screening platform, which looks for the presence of DTCs and other measures of MRD in patient’s blood or bone marrow. To date, the study has enrolled over 200 patients, and has expanded from one site at Penn to eight sites across the country.

If DTCs are present, patients are offered enrollment onto a one of several clinical trials that are targeting these cells to prevent breast cancer recurrence and metastasis. These trials use a variety of approaches to try to turn these cells off, keep them from waking up, or starve them, using different combinations of drugs to find the most effective line of attack. In addition, we are now studying how the immune system may play a role in controlling MRD and working on ways new treatments to activate the immune system to “seek and destroy” these cells.

### **LATE RECURRENCE**

In recent years, researchers have also begun to focus on the differences in patients who recur more than 5 years after their initial diagnosis and treatment. This work is especially critical for women with hormone receptor positive disease (otherwise known as “ER+ breast cancer”), as they have an ongoing risk of recurrence for the rest of their lives.

The 2-Prevent TCE is investing resources in this work to understand how late recurrence differs from early recurrence with the ultimate goal of finding more effective, targeted methods of prevention and treatment.

### *Leading a National Coalition Focused On Late Recurrence*

Dr. DeMichele is leading a new collaboration in North America focused on designing and implementing clinical trials to address this problem. The REFINE-BRCA Coalition is made up of investigators from five collaborative breast cancer research groups located across the United States and Canada.

Their first trial, called AMMbER, is a national trial open to women who are receiving endocrine therapy and are 4-8 years from their initial diagnosis. The trial will look for circulating tumor DNA in the blood of over 1000 patients and will generate preliminary data to feed into a larger clinical trial.

### *Harnessing the Power of the Immune System to Create Living Drugs*

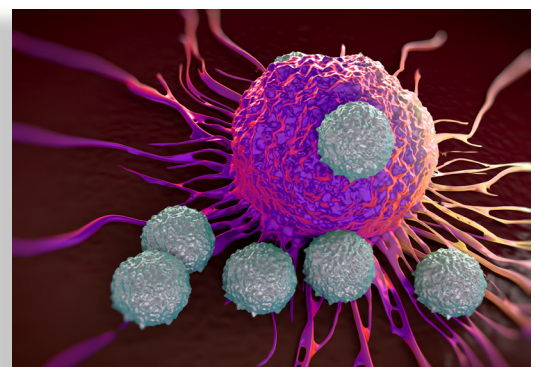
The Chodosh lab is working to understand the immune system’s role in detecting and fighting dormant cancer cells. Understanding the ‘invisibility cloak’ that prevents dormant cancer cells from being recognized and eliminated by immune cells is a major scientific challenge, whose solution would enable new therapies that harness the incredible power of the immune system to prevent cancer recurrence.

### **Recurrence Prevention Trials**

**CLEVER:** examining HydroxyChLoroquine and EVErolimus

**PALAVY:** examining HydroxyChLoroquine and Avelumab

**ABBY:** examining ABemacicliB and HydroxyChLoroquine



### *Exploring Combination Therapies to Prevent Recurrence in Patients with Triple-Negative Breast Cancer*

A new multi-center grant from Stand Up 2 Cancer (SU2C) is advancing research focused on ways to prevent recurrence in patients with triple-negative breast cancer. Triple-negative breast cancer (TNBC) is a tumor type in which cancer cells lack hormone epidermal growth factor receptor 2 (HER-2), estrogen receptors (ER), and progesterone receptors (PR). Because the cancer cells test negative for all three receptors, hormone therapies and drugs that target the receptors are not effective treatments. TNBC is aggressive and can spread after treatment with radiation, chemotherapy, or surgery.

Dr. DeMichele will work with team leader Elizabeth A. Mittendorf, MD, PhD, director of the breast immuno-oncology program at Dana-Farber/Brigham and Women's Cancer Center in Boston, on this project. The ASPRIA trial is now open and enrolling patients. The ASPRIA trial will utilize a blood test called liquid biopsy to detect the spread of the disease before it can gain a foothold in distant organs. When cancer cells are detected, patients would receive a combination of drugs. One drug is sacituzumab, a new type of drug that combines an antibody and a chemotherapy molecule to directly target chemotherapy to cancer cells. The second drug is atezolizumab, which is a PD-L1 inhibitor that enables the immune system to recognize and attack breast cancer cells.

### **UNDERSTANDING METASTATIC DISEASE**

For patients who recur and go on to develop metastatic disease, treatment is often based on the biology of the primary tumor. However, research suggests that some recurrent cancers are different from the primary tumor and may respond better to different therapies. Through the METAMORPH study, the 2-Prevent TCE is working to evaluate a more comprehensive approach to assessing and treating recurrent disease. The goal of the study is to examine markers in blood, bone marrow and tumor tissue to better understand and track the molecular and genetic changes that occur as an individual's disease progresses.

Using the results of this study, researchers can generate a unique "fingerprint" of a patient's metastatic tumor to help understand the unique features that allow a patient's tumor to grow and travel throughout the body. This fingerprint consists of gene changes within cells that can turn on different pathways that in turn send signals instructing the cells to grow and spread. By targeting specific gene changes and pathways, our goal is to stop the metastatic tumor cells, which can lead to better clinical responses and prolonged survival.

Drs. Chodosh and DeMichele recent published preliminary results of the METAMORPH trial in the Journal of Clinical Investigation, identifying several changes that are unique to metastatic disease. They believe these changes may provide a new set of direct targets to more effectively treat metastatic disease.

### *The Penn Metastatic Breast Cancer Collaborative*

The connection between the research bench and the clinic has been a key element in our progress in treating and preventing recurrent breast cancer. The 2-Prevent TCE is now looking to use the same approach to tackle the challenge of metastatic disease, building a bridge from the bench to the clinic inform and enhance our understanding, while also bring these breakthroughs to patients as quickly as possible.

The Penn Metastatic Breast Cancer Collaborative (MBCC) brings together Penn breast cancer experts from across the Health System to collaborate on difficult cases, share information on new treatments, and identify patients for Penn clinical trials.



In addition, the MBCC is working to increase access to new therapies for patients with metastatic disease across the Philadelphia region by:

1. Establishing the Breast Cancer Clinical Trial Navigation Program as a single point-of-contact for providers and patients to learn about and be evaluated for participation in clinical trials at Penn Medicine, and around the region.
2. Utilizing telemedicine visits for trial evaluation to reduce the burden of travel for patients interested in a clinical trial.
3. Bringing trials to outlying Health System sites, expanding access to this critical research.

This approach gets to the heart of the mission of the 2-Prevent TCE, to reach more patients and provide better treatment options for patients and their families.

## **A BRIGHTER FUTURE AHEAD**

As we approach to 10-year anniversary of the 2-Prevent TCE, we are grateful to our community of supporters, who have fueled our progress. The energy and excitement that were born with the establishment of the TCE have grown into a thriving and robust research engine. We are making tangible progress in both our understanding of how breast cancer spreads, and how we can prevent recurrence and metastasis—research that holds the potential to transform the treatment landscape for patients and their families.

Yet, we know our work is not done until recurrent metastatic disease is a thing of the past. With your support, that future is in reach. Thank you.



“The 2-Prevent TCE utilizes a multi-pronged approach to emphasize personalized risk-assessment and monitoring, and is developing novel targeted therapies designed to prevent and treat recurrent breast cancer. The team is making measurable gains to stop recurrent breast cancer before it starts. ”

– Robert H. Vonderheide, MD, DPhil  
Director, Abramson Cancer Center

John H. Glick, MD Abramson Cancer Center Director’s Professor



## PENN MEDICINE **MISSION**

Penn Medicine, a non-profit organization, is a world-renowned institution dedicated to discoveries that will advance science and patient care throughout the world, and to the education of the physicians and scientists of tomorrow to carry on our legacy of excellence.

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