

2020 - \$175,000 matched 1:1 for a \$350,000 investment

Given the impact of COVID-19 pandemic on our research partners and their sincere request for continued support we continued funding the projects initiated in 2019 in 2020. Each institution experienced varying impacts of the pandemic- from research labs turning into COVID testing facilities to clinical trials closing across the country. It is clear the pandemic stalled momentum and set MBC research back. However, our research partners found ways to persevere and continue their important work. And, we were grateful to support the continuation of initiatives outlined below in the 2019 summary.

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Understanding and Treating Breast Cancer Metastasis at Single Cell Resolution

Andrew J. Ewald, Ph.D.

Professor of Cell Biology, Oncology, and Biomedical Engineering

Co-Director, Cancer Invasion & Metastasis Program, Sidney Kimmel Comprehensive Cancer Center
Johns Hopkins University, School of Medicine

Breast cancer is most dangerous when it has spread to distant organs, a process scientists call metastasis. Current treatments are not sufficiently effective for metastatic breast cancer patients, due to an incomplete molecular understanding of the underlying biology. The Ewald Lab, with support from Hope Scarves, has shown that breast tumors contain many different types of cancer cells, that they travel together in groups to distant organs, and that the cancer cells depend on their molecular connections to each other in order to form dangerous metastases. We recently discovered that different cancer cells in the same tumor can metastasize with different strategies, which necessitates understanding metastasis at single cell resolution. Accordingly, we propose to use the latest molecular techniques to isolate cancer cells from breast tumors, profile their molecular features, sort them into categories based on their metastatic ability, and then use techniques from pathology to determine which breast tumors metastasize by which method. The goal is to be able to develop personalized approaches to eliminate breast cancer metastases in patients.

Understanding Estrogen Receptor Loss as a Mechanism of Resistance in ER+ Metastatic Breast Cancer

Nikhil Wagle, MD and Daniel Abravanel, MD PhD

Dana-Farber Cancer Institute

Metastatic breast cancer (MBC) remains troublingly incurable, primarily due to the resistance it develops to treatment. While the majority of breast cancers express the estrogen receptor (ER), some breast cancers that start out as ER+ breast cancer evolve and eventually lose ER, becoming triple negative breast cancer. We do not currently have a good understanding of why or how this occurs. Moreover, once ER loss does occur, treatment options are quite limited. With support from Hope Scarves, we will study the causes and drivers of ER loss, and attempt to identify new therapeutic strategies for patients whose tumors transition from ER+ to triple negative MBC. To our knowledge, this proposed research is the most comprehensive effort to-date aimed at profiling ER loss in MBC, with the ultimate goal of identifying the most effective therapies to combat this incredibly difficult and aggressive disease.

Hope Scarves Fund for Metastatic Breast Cancer Clinical Research

University of Louisville, James Graham Brown Cancer Center

Dr. Beth Riley

This gift will be used to hire additional staff to support the JGBCC Breast Clinic, and Beth Riley, MD, Director of the Breast Clinic and JGBCC Deputy Director for Health Affairs, in efforts to expand clinical trials and clinical research at the JGBCC for metastatic breast cancer patients through three distinct efforts: 1) expand the biorepository at the JGBCC specific to metastatic breast cancer to allow greater access for scientists which will in turn accelerate our understanding of this disease, with a goal of two additional protocols this year for the biorepository; 2) expand the current metastatic trial portfolio to ensure the options available to breast cancer patients in the region is comprehensive and local to minimize need for travel. The goal of this gift is to open trials in 90 days and offer more depth per subtype; 3) increase patient accruals to these trials which in turn will increase the availability and support of early stage innovative trials. Goal is to increase trials open in each subtype of metastatic breast cancer along with increase in phase I/II trials with novel targets, immunotherapy.

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Dana-Farber Cancer Center at Harvard University: One of the main projects of the Wagle Lab is the utilization of molecular and genomic studies to improve our understanding of resistant ER+ metastatic breast cancer. The group hypothesizes that intrinsic and acquired resistance to therapies that target the estrogen receptor will involve genomic and/or molecular alterations that result in different cell states that indicate sensitivity or resistance to therapies. To test this, and with support from Hope Scarves, the Wagle Lab is developing a Resistance Atlas in ER+ MBC. Once completed, this project should bring new insights about pathways and dependencies in resistant ER+ metastatic breast cancers. Long-term, it is hoped that the Resistance Atlas will lead to the development of new therapeutic strategies in breast cancer, including clinical trials and targeted drug combinations, designed to overcome resistance mechanisms and ultimately achieve cure or disease control for the many women and men suffering from ER+ breast cancer.

The Johns Hopkins Kimmel Cancer Center: The main focus of the Ewald Lab is on understanding how breast cancer cells build new tumors in distant organs during metastasis. They have shown previously that breast cancer cells spread through the body in groups, attached to each other with molecular Velcro. The protein responsible for these attachments, E-cadherin, is expressed in 90% of breast tumors. With funding from Hope Scarves, the lab showed that E-cadherin was helping breast cancer cells survive during metastasis. Then they developed new experimental methods to model the process of metastatic growth in the lungs. Currently they are using these new approaches to identify systematically new drugs that can prevent metastases. Finally, they showed that breast cancer cells can corrupt cells of the immune system in order to promote metastatic growth and identified therapeutic strategies to restore the ability of the immune system to attack the tumor. [Watch](#) Dr. Ewald explain his work.

"Support from Hope Scarves has been critical to our ability to move our best ideas rapidly towards patient impact."

University of Louisville James Graham Brown Cancer Center:

- Expand the biorepository at the JGBCC specific to metastatic breast cancer to allow greater access for scientists which will in turn accelerate our understanding of this disease, with a goal of two additional protocols this year for the biorepository.
- Expand the current metastatic trial portfolio to ensure the options available to breast cancer patients in the region is comprehensive and local to minimize need for travel. The goal of this gift is to open trials in 90 days and offer more depth per subtype.

- Increase patient accruals to these trials which in turn will increase the availability and support of early stage innovative trials. The Goal is to increase trials open in each subtype of metastatic breast cancer along with increase in phase I/II trials with novel targets, immunotherapy.

Collaboration with Metavivor in memory of Laura Williams funded two projects:

- Wei Tao, PhD -The Brigham and Women's Hospital/Harvard University - Multi-staged delivery system overcoming the physiological barriers for metastatic breast cancer (MBC) therapy -(HER2+ MBC focus – small biologic drug conjugates on nanoparticles for targeted treatment of mets)
- Ana Castro-Garrido, MD - Dana-Farber Cancer Institute Identifying predictive biomarkers of response to PD-1 inhibition in metastatic triple-negative breast cancer - (TNBC focus – looking at biomarkers for response to immunotherapy)

2017 - \$200,000 matched 1:1 for a \$400,000 investment

- Memorial Sloan Kettering Cancer Center– Looking specifically at a new class of MBC drugs called CDK 4/6 inhibitors with the tools of DNA and RNA sequencing to understand and overcome resistance mechanisms.
- Dana-Farber Cancer Center at Harvard University– Researchers there are working to create a “Resistance Atlas” for ER-positive metastatic breast cancer, which should help inform treatment decisions for individual patients and propel the development of new combination treatment strategies. [The MBC Project](#), which Hope Scarves is an Advocate Partner, is a vital part of this ongoing work, providing access to an unprecedented database of genetic information from patients with MBC.

2016 - Hope Scarves' Metastatic Breast Cancer Research Fund established.

We spent this year understanding the landscape of MBC Research and formalizing our Metastatic Breast Cancer Research Fund to ensure we were funding research that would make the biggest impact for MBC patients.

2015- \$50,000

Our first donation of \$50,000 was presented to [James Graham Brown Cancer Center at University of Louisville](#) in December 2015. This gift supported Dr. Yoannis Imbert-Fernandez work to determine the effects of simultaneous suppression of estrogen signaling and a key metabolic enzyme known as PFKFB3 on sugar metabolism, growth and survival of metastatic breast cancer.