Year	Grant Recipient	Research Institute	Abstracts
2007	Chatterjee, Samit PhD	Cold Spring Harbor Laboratory	Dr. Chatterjee, a Molecular Cell Biologist, studied the molecular determinants of cellular polarity. It is thought that dysregulation in cell polarity may be a preamble to formation of early epithelial breast malignancies. This proposal was executed
2007	Oliver, Andrea MD	Dana-Farber Cancer Institute	Dr. Oliver studied molecular pathways conferring Tamoxifin and Herceptin
2007	Mayer, Erica MD, MPH	Dana-Farber Cancer Institute	Dr. Mayer studied the vascular injury and hypertensive liabilities of Avastin which limit its therapeutic potential. Understanding this problem could improve
2007	Lee, Dongjoo PhD	Memorial Sloan Kettering	Dr. Dongjoo Lee, a Clinical Research Oncologist at the Memorial Sloan-Kettering Institute, developed a chemical synthesis of the potent novel carbohydrate-based glycopeptides anticancer vaccine candidate that will be evaluated for
2008	Choudhury, Sibgat PhD.	Dana-Farber Cancer Institute	Dr. Choudhury looked at putative mammary precurser cells that are resistent in breast tissue. Such cells were hoped to provide clues as to the progression of breast cancer.
2008	Fertuck, Kirsten PhD	Dana-Farber Cancer Institute	Dr. Fertuck is a cell biologist studying estrogen receptor signaling in a premier laboratory guided by Myles Brown. Estrogen has a well documented but only partially understood role in etiology of breast cancer even though the activity of several successful drugs are modeled on this important hormone. Dr. Fertuck's project was designed to provide a more precise picture of how estrogen interacts
2008	Irie, Hanna Y MD, PhD.	Mount Sinai School of Medicine	Dr. Irie, a cell biologist, investigated the bais of the resistance of cancer cells to undergo programmed cell death. She sought to understand why certain genes
2009	Bialucha, Carl Uli PhD	Cold Spring Harbor Laboratory	Dr. Bialucha has developed a sophisticated technology that can correctly identify the specific gene deletions that drive breast cancer. Results from these studies could lead to a new generation of therapies and diagnostic tools.
2009	Kutuk, Ozgur MD, PhD	Dana-Farber Cancer Institute	Resistance to chemotherapy is a major problem in the fight against breast cancer. Dr. Kutuk's research involved exploring the pathways of cell death activated by chemotherapeutics in breast cancer cells and the regulation of these pathways by
2009	Bailey, Shannon T. MD	Dana-Farber Cancer Institute	Dr. Bailey's research focuses on how the estrogen receptor influences the cell

2009	Zang, Qing PhD	Dana-Farber Cancer Institute	Normal cells have a remarkable ability to sense oxygen and nutrients in their environment and to respond. Cancer cells possess the same machinery but respond in an unhealthy metastatic manner. Dr Zhang studied one such oxygen sensing system in breast cancer cells that is believed to provoke tumors to grow
2010	Zhou, Penghui MD	Dana-Farber Cancer Institute	It has always been a mystery as to why a person's own immune system doesn't fight off tumors as it does infections. In fact, the immune system's major weapon, the T-cell, does attack tumors, but it quickly gets deactivated in the tumor environment. Dr. Zhou dedicated his research to understanding why this occurs
2010	Kochupurakki, Bose PhD	Dana-Farber Cancer Institute	Specific aims of Dr. Kochupurakki's proposed work were to determine the sub-type specificity of activated NF-kB in tumor samples; analyze the phenotype of mammary epithelial cells expressing constitutively active mutant of NF-kB and screen for drugs that will inhibit cell transformation; and determine the activation
2010	Gajria, Devika, MD	Memorial Sloan Kettering	One of the great frustrations in treating breast cancer results from some patients being resistant to therapies that work successfully in others. Dr. Gajria believes that such resistance can be overcome by combining two novel clinical drugs whose activities could synergize and provide enough potency to overcome such resistance. Dr. Gajria will first find the most appropriate dosing regimen to
2010	Kass, Elizabeth MD	Memorial Sloan Kettering	It would be of great value to understand how breast cancer develops. The research of Dr. Kass probed breast cancer tumorigenesis. Events that occur during the earliest stages of mammary development are believed to alter the lifetime risk of breast cancer. Her research seeks to elucidate how specific developmental changes in mammary epithelium affect the molecular mechanisms by which cells
2011	Li, Yang PhD	Dana-Farber Cancer Institute	A major problem that plagues breast cancer therapy is the resistance that some patients have to drugs that can treat this disease. Dr. li has discovered that patients with high levels of Lysosomal-associated protein transmembrane-4beta (LAPTM4B) are the very patients for whom chemotherapy is unsuccessful. This work alone is valuable in itself because it could be used to predict which patients will benefit from drug treatments and those who won't. Dr. Li advanced this by studying what mechanistic role LAPTM4B is playing in the process. He believes

2011	Gucalp, Ayca MD	Memorial Sloan Kettering	Estrogen receptor and progesterone receptor negative breast cancer is known as “Triple Negative Breast Cancer” (TNBC). TNBC represents 15% of all breast cancers but accounts for a higher proportion of breast cancer related mortality each year. Interestingly, the androgen receptor has also been implicated in breast cancer as it is expressed in 60 – 80% of primary breast tumors. Dr. Gucalp believes that the androgen receptor plays a role in TNBC based on earlier work done at Memorial Sloan-Kettering that showed that an androgen receptor blocker can halt cell proliferation in TNBC cells. She is therefore proposing to do a
2011	Walczak, Maciej MD	Memorial Sloan Kettering	A major challenge in fighting breast cancer is trying to block cancer cell metastasis – the process where cancer cells travel and proliferate into other organs. Japanese scientists have previously isolated a compound called “migrastatin” which is able to inhibit metastasis in vitro. Unfortunately, migrastatin has only modest efficacy and does not have the necessary properties to be a drug. Dr.
2012	Brastianos, Pricilla MD	Dana-Farber Cancer Institute	Dr. Brastianos studied the unique gene mutations that lead to brain metastases which occur in breast cancer patients. Brain metastases occur in up to 30% of patients with metastatic breast cancer. Survival continues to be dismal and ranges from 3 months to 23 months after the diagnosis of a metastasis in the central nervous system. Using a rapid and robust technique called whole-exome
2012	Diab, Adi MD	Memorial Sloan Kettering	Dr. Diab evaluated the safety of two strategies called "cryoablation" and "immune therapy" in early stage breast cancer patients. "Cryoablation" is a procedure in which very cold temperatures are applied to kill the cancer cells. The killed cancer cells can be recognized by a person's immune system. The "immune therapy" in Dr Diab’s study is an FDA approved antibody drug called ipilimumab. It is believed that this combination could provide a new approach for treating
2012	Jhaveri, Komal, MD	Memorial Sloan Kettering	Dr. Jhaveri is evaluating the effect of a potent class of drugs called HSP90 inhibitors in combination with the established standard-or-care therapy, Paclitaxel and Herceptin in patients with metastatic disease. HSP90 is a protein found in some cancers, and helps the cancer cell to divide and change at the alarming rates observed. In addition, Dr. Jhaveri is employing a "personalized"
2013	Anczukow-Camarda, Olga, PhD	Cold Spring Harbor Laboratory	Cancer is a very complex disease in which many cellular processes are deregulated. Understanding cellular processes and molecular interactions is necessary to understand how cancer starts and can be treated. Dr. Anczukow-Camarda works on “splicing”, a critical step in gene expression that determines how genetic instructions in DNA are cut and pasted together as RNA

2013	Vora, Sadhna R. MD	Dana-Farber Cancer Institute	Roughly 30% of breast cancers demonstrate a mutation in the gene PIK3CA, which drives their growth by activation of the PI3K pathway. While these breast cancers may initially respond to drugs that target this pathway, they ultimately grow again by developing ways to overcome the action of the drug. Dr. Vora's work examines how tumors become resistant to these drugs and seeks ways to
2013	Gajria, Devika MD	Memorial Sloan Kettering	One of the great frustrations in treating breast cancer results from some patients being resistant to therapies that work successfully in others. Dr. Gajria believes that such resistance can be overcome by combining two novel clinical drugs whose activities could synergize and provide enough potency to overcome such resistance. Dr. Gajria is searching the most appropriate dosing regimen to
2013	Rossetti, Stephano PhD	Roswell Park Alliance Foundation	Breast cancer cells typically produce more ribosomes, the cellular machines that synthesize proteins, to meet their increased metabolic demand. While increased ribosome production has been used for many years as a diagnostic and prognostic marker of breast cancer, it is currently unknown whether this feature is a cause or a consequence of breast cancer. This project aims to answer this
2014	Carmona, Javier PhD	Memorial Sloan Kettering	The efficacy of targeted therapies in cancer patients is often limited by the emergence of resistance. Anti-HER2 agents, specifically trastuzumab, have significantly improved survival rates in HER2 positive breast cancer patients. However, a considerable number of patients exhibit primary resistance or become refractory after initial responses. Therefore, understanding the mechanisms by which cancer cells escape treatment is mandatory to design better therapeutic strategies. To do so, we will perform targeted exome
2014	Page, David PhD	Memorial Sloan Kettering	The immune system is highly capable of recognizing and killing cancer, but is in constant struggle with cancer's evolving ability to 'escape' the immune response. A new drug called tremelimumab serves to restore the anti-cancer immune response by releasing a natural 'brake' found on a subset of immune cells. Dr. Page is conducting a clinical trial evaluating whether tremelimumab could be
2014	Hofstatter, Erin MD	Smilow Cancer Hospital at Yale New Haven	Age appears to be the single most important risk factor for the development of breast cancer; however, why increasing age is associated with increasing incidence of breast cancer remains incompletely understood. In our study, we will examine epigenetic changes in breast tissue and blood samples from women with breast cancer at young (<45) and older ages (>65), and compare them to samples from age-matched healthy women. We hypothesize that women who

2015	Dhimolea, Eugen PhD	Dana-Farber Cancer Institute	Most breast cancer patients are Estrogen Receptor (ER)-positive and are treated with antiestrogens after the surgical removal of the mammary tumor. Nonetheless approximately 1/3 of the patients develop metastases, frequently in the bone, that do not respond to treatment. The preference of breast cancer for dissemination to specific tissues (organotropism) indicates a favorable local microenvironment in these organs. While the antiestrogen resistance of ER+ metastatic tumors has been mainly attributed to acquisition of mutations, the role of the metastatic microenvironment in the emergence of these mutations
2015	Ilic, Nina PhD	Dana-Farber Cancer Institute	Activating mutations in the PIK3CA gene are found in approximately 30% of breast cancers and promote growth of these tumors. Despite extensive efforts, direct pharmacologic inhibition of this mutant lesion has shown limited patient benefit in recent clinical trials. Therefore, to provide novel personalized treatment options for breast cancer patients, it is critical that we identify alternative gene vulnerabilities that can be targeted for therapy. To discover such mutant PIK3CA-specific vulnerabilities, we interrogated genome-wide genetic
2015	Pavlova, Natalya PhD	Memorial Sloan Kettering	Dr. Pavlova's 2015 Terri Brodeur Breast Cancer Foundation fellowship award focuses on the investigation of metabolic adaptations which drive breast cancer metastasis. Cancer-specific metabolic alterations and their functional contribution to tumorigenesis have been under intense investigation in the recent years. However, we still lack a clear picture of how these alterations align with the multistep nature of tumorigenesis. In particular, relatively little is known about metabolic adaptations which distinguish metastatic cancer cells from their non-metastatic counterparts. As preliminary data indicate, metastatic isolates from triple negative breast cancer cells display distinct alterations in the
2016	Albrengues, Jean PhD	Cold Spring Harbor Laboratory	Dr. Albrengues' 2016 Terri Brodeur Breast Cancer Foundation fellowship award focuses on the regulation of breast cancer dormancy by the tumor microenvironment. Metastatic breast cancer relapse occurring years after a seemingly successful treatment is preceded by an interlude, termed dormancy, when the cancer remains non-proliferative and undetected at a secondary site. Unfortunately, these dormant tumor cells appear to be refractory to available therapies and the cues mediating their reawakening are largely unknown. Dr. Albrengues' hypothesized that dormant cells are awakened by signals from inflammatory immune cells, which also provide cues for aggressive behavior of cancer cells in the primary tumor. To test this hypothesis, he will use newly developed in vitro and in vivo models of dormancy and reawakening. To visualize the interactions with the surroundings, the survival, and the proliferation of

2016	Karaayvaz, Mihriban PhD	Mass General Hospital Cancer Center	Making a major impact on the incidence and lethality of breast cancer will require a detailed understanding of the early events in breast cancer development, particularly in women who are at the highest risk of developing these cancers such as those who carry mutations in the BRCA1/2 genes. Unfortunately, few breast cancer studies are focused on these early events and on breast cancer prevention. We have established a method to analyze distinct cell populations from healthy mastectomy tissues of BRCA1/2 carriers and from tissues of patients undergoing reduction mammoplasty (non-carrier controls). Through detailed molecular analysis of these tissues, we will determine the key functional
2016	Stover, Daniel MD	Dana-Farber Cancer Institute	The host immune system is critical in the control and elimination of tumors in many cancer types. In breast cancer, tumor infiltrating immune cells have been associated with both response to chemotherapy and overall outcome for patients. Understanding what immune cell populations infiltrate tumors may help guide which patients are likely to benefit from chemotherapy and provide targets to improve the efficacy of chemo- and other therapies. Within breast cancer, estrogen receptor (ER)-positive breast cancers comprise the majority of all breast cancers but the role of immune cells remains less well-understood relative to other breast cancer subtypes. We developed evidence that immune cells play a critical role in response to chemotherapy in a subset of patients with ER-positive breast cancers. As a Terri Brodeur Fellow, Dr. Stover will integrate large, publicly
2016	Toska, Eneda PhD	Memorial Sloan Kettering	Mutations in the PIK3CA gene are the most frequent genomic alterations in estrogen receptor (ER)-positive breast cancers. One treatment strategy is the use of drugs that inhibit the gene's signaling pathway—however, many patients eventually become resistant to this type of therapy. Further, PI3K signaling pathway inhibition has been show to increase ER activity, which then increases cells' dependency on ER and estrogen—fueling growth. However, very little is known about the molecular basis of the crosstalk between the PI3K pathway and ER function. To better understand this relationship, we have identified genes that both contribute to PI3K inhibition resistance and are necessary for the ER-PI3K
2017	Li, JI PhD	Dana-Farber Cancer Institute	Basal-like breast tumors comprise a heterogeneous group that accounts for about 15% of all breast cancers. They are highly aggressive and generally fail to respond to targeted therapies. Thus, there is a great need to identify novel vulnerabilities and develop novel therapies for this aggressive breast tumor type. The epithelial-to-mesenchymal transition (EMT) is often reactivated during tumor formation. Compared to other breast cancer subtypes, basal-like breast cancers display the highest degree of mesenchymal and stem-like features, which are responsible for tumor initiation, metastasis and therapeutic resistance. We have recently identified genes that regulate EMT in breast cancer using a genome scale screen and identified several RNA splicing factors that are upregulated in basal-like

2017	Meyer, Aaron, PhD		Metastatic spread drives the majority of breast cancer mortality and, to do so, requires tumor cells to both disseminate and avoid clearance by the immune system. Inhibiting TAM receptors has shown promising results in models of breast cancer by blocking tumor cell dissemination, preventing resistance to existing therapies, and relieving immune suppression. Based on these results, the first therapies targeting these receptors are now in early clinical studies. However, a better understanding of when and where these receptors drive breast cancer progression is needed to identify which patients will benefit from these therapies. As a Terri Brodeur Fellow, Dr. Meyer will use a computational model to direct design of new inhibitors for the TAM receptors. Using these well-characterized
2017	Parsons, Heather, MD	Dana-Farber Cancer Institute	This year, breast cancer will claim the lives of more than 500,000 people worldwide. Most of these will be women in whom the disease has spread to the rest of the body, known as metastatic breast cancer. Women living with metastatic breast cancer typically receive ongoing, single-agent treatments that are effective for a while, but at some point, the disease develops resistance, evading a previously effective therapy and growing again. HER2-overexpressing (HER2-positive) breast cancer is a subtype that accounts for 20-25% of breast cancers, and is associated with faster growing tumors, higher rates of recurrence, and higher rates of brain metastases. Though we have effective treatments for HER2-positive metastatic breast cancer, inevitably the disease develops resistance and progresses. Understanding how and why metastatic breast cancer develops resistance is difficult, but is critical to the development of better treatments for women with this disease. Evidence increasingly suggests that tumors evolve genomically over time and in the face of ongoing systemic therapies. A major obstacle to understanding treatment resistance is access to metastatic tumor tissue, as patients with metastatic breast cancer do not typically undergo multiple, sequential biopsies. Both tumor and normal cells shed DNA into the circulation, and even a small amount of circulating tumor DNA (ctDNA) is

2018	Dasgupta, Arko, PhD	Fred Hutchinson Cancer Research Center	Breast cancer is a major killer in the United States and metastases are the primary cause of breast cancer-related deaths. Approximately 30% of breast cancer patients will develop metastases during their lifetime. Few prognostic factors predict metastases as well as the presence of dormant disseminated tumor cells (DTCs) – cells that have escaped from the primary breast tumor early in the disease and exist in a dormant state in distant organs until they develop in some patients as overt metastases. Clinical evidence suggests that eradication of DTCs would prevent metastasis, however, currently no therapies specifically target these metastases-initiating cells. Indeed, DTCs are resistant to chemotherapy and other targeted therapies, and very little is known about what enables DTC survival despite multiple rounds of chemotherapy. Breast DTCs reside in a perivascular niche (PVN) – areas within a tissue that are occupied by blood vessels – of distant tissues such as lung, bone marrow, brain, liver and lymph
2018	Sun, Sheng, PhD	Mass General Hospital Cancer Center	The majority of breast cancers express hormone receptors, and therapies that antagonize hormonal signaling via these receptors are the most effective treatments for hormone receptor-positive metastatic breast cancer (HR+ MBC). Unfortunately, for the vast majority of patients with hormonal therapy-refractory MBC, the mechanisms of resistance remain poorly understood. Thus, identifying new mechanisms of hormonal therapy resistance and understanding how to overcome them will have direct and immediate relevance to the therapy of patients with MBC. We have identified novel gene fusions in 14% of patients with HR+ MBC and provided strong evidence that these tumor-specific genetic rearrangements are powerful drivers of treatment resistance and poor outcomes. Successfully tracking and therapeutically targeting these fusions could thus have a major impact on patient outcomes. We hypothesize that patient-derived
2018	Waks, Adrienne Gropper, MD	Dana-Farber Cancer Institute	Following many important advances in treating HER2-positive breast cancer over the past two decades, a large majority of patients with non-metastatic HER2-positive tumors are cured with today's treatments. For this majority of patients who do well in the long-term, we must begin to identify ways to cure HER2-positive breast cancer with less toxic treatments. Modern treatment regimens for stage II and III non-metastatic HER2-positive breast cancer consist of multiple chemotherapy agents plus HER2-directed therapy with trastuzumab (Herceptin, H) and sometimes pertuzumab (Perjeta, P). Scaling back the number of chemotherapy agents used may allow patients to maintain better quality of life while on treatment, as well as decrease the chance of rare but serious chemotherapy complications. As a Terri Brodeur fellow, Dr. Waks plans to conduct a clinical trial investigating a new treatment approach in stage II and III

2019	Garrido-Castro, Ana, MD	Dana-Farber Cancer Institute	Choosing the best treatments for metastatic breast cancer depends increasingly on molecular features, such as tumor subtype. Patients with hormone receptor-positive/HER2-negative breast cancer are typically treated initially with hormonal therapies, and then subsequently with chemotherapy once hormonal therapy loses its effectiveness. Loss of hormone receptor expression has been described as a mechanism of resistance to hormonal therapy. When this occurs, tumors become hormone receptor-negative and HER2-negative, i.e., triple-negative. It is unknown whether cancers that start out hormone receptor-positive and then become triple-negative (called “subtype switch”) are different than those that remain triple-negative throughout a patient’s disease course. Since treatments depend so heavily on tumor subtype, answering this question could have an immediate impact on patient care. Metastatic triple-negative breast cancer (mTNBC) remains a clinically unmet need, with a highly aggressive clinical course and shorter average survival compared to patients with other subtypes of metastatic breast cancer. Patients whose tumors are initially hormone receptor-positive/HER2-negative and then lose hormone receptor expression (i.e., become triple-negative) are typically eligible for clinical trials and standard-of-care therapies focused on mTNBC. However, comparison of tumor biology and clinical outcomes in patients whose tumors are always triple-negative and those that “switch subtype” has not been studied in detail. Preliminary results from tumor DNA analysis presented by Dr. Garrido-Castro at the 2018 San Antonio Breast Cancer Symposium suggest that primary hormone receptor-positive tumors in patients who later developed mTNBC have similar mutation and gene copy number alterations as primary triple-negative tumors. In addition, hormone receptor-positive breast cancers are generally considered˙cold˙ tumors, characterized by decreased immune cell infiltration and low responsiveness to

2019	Daniels, Veerle, PhD	Dana-Farber Cancer Institute	Despite recent advances in treatment options, breast cancer remains the second leading cause of cancer-related deaths in women. Triple negative breast cancer (TNBC) is a subgroup of breast cancer that is characterized by the absence of the estrogen receptor, the progesterone receptor and HER2-amplification. Because of the lack of these markers, there are at present -unlike for other subgroups of breast cancer- no targeted therapies available for TNBC. Therefore, TNBC is currently treated with conventional chemotherapy in addition to radiotherapy and surgery. Despite the often-good initial response to chemotherapy, therapy resistance is frequent in TNBC, making it one of the most severe subtypes of breast cancer. To improve the perspectives of TNBC patients, there is need for better and more targeted treatments. To address this need, Dr. Daniels aims to identify metabolic pathways that can be targeted in combination with conventional chemotherapy to increase the sensitivity of TNBC to these agents. Dr. Daniels focusses on metabolism, because the metabolic requirements of cancer cells are different than those of normal cells. Therefore, by targeting metabolism cancer cells can be weakened specifically, without affecting normal cells. To determine which metabolic features to target in cancer cells, Dr. Daniels is using a technique called “BH3-profiling”. BH3-profiling was developed by the Letai laboratory to measure the proximity of the cells to dying. This novel
2019	Hu, Jing, PhD	Memorial Sloan Kettering Cancer Center	Metastasis is a major clinical hurdle in breast cancer treatment, with poor prognosis (5-year survival around 26.5%). Despite surgical resection of the primary tumor and systemic therapy to suppress residual disease, distant metastatic relapse may still occur within a few months to years, implying the existence of latent metastatic cells that may last for decades in the distant organs without being detected in clinic. They eventually generate overt metastasis, which is highly resistant to current therapies. Therefore, the predominant concern in the clinic is about how to prevent or treat metastatic relapse by cancer cells that had already disseminated in the distant organs at the time of diagnosis. We recently identified that NK cells suppress outgrowth of disseminated breast cancer cells. However, emergence of immune evasive clones eventually triggers aggressive outbreak. The mechanisms underlying immune evasion of metastatic outbreak are largely unknown. We discovered that breast cancer cells contain cytosolic double-stranded DNA (dsDNA), likely as a result of genomic instability. The stimulator of interferon genes (STING) pathway, triggered by cytosolic dsDNAs, is critical for initiating immune defense against pathogens. Preliminary data suggests that cancer intrinsic STING signal is reduced in immune-evasive

2019	Spring, Laura, MD	Massachusetts General Hospital	Localized breast cancer patients with higher risk disease are often treated with chemotherapy in the neoadjuvant (before surgery) setting. However, it is difficult to predict how breast cancer will respond to treatment given in the neoadjuvant setting and we currently lack any specific blood tests to help answer this question. As a Terri Brodeur grant recipient, I plan to study a method to detect genetic material (DNA) known as circulating tumor DNA (ctDNA) that is released into the blood from some breast cancer tumor cells. One of the main goals of the study is to determine what percentage of breast cancer patients who are receiving treatment before surgery will have ctDNA detectable, as this may represent a group of patients at higher risk for recurrence. For patients with ctDNA present, we will compare the amount before treatment starts and after the first round of treatment. We believe that those with decreasing ctDNA levels will respond to treatment better with improved outcomes at the time of surgery,
2020	Guerriero, Jennifer L., PhD	Dana-Farber Cancer Institute – Harvard Medical School	Modulating the immune system as an anti-cancer strategy has shown great promise in some types of cancer, however there has been limited responses in breast cancer. While the main focus of immunotherapy has been on the adaptive immune system, namely T cells, harnessing innate immune cells such as tumor associated macrophages (TAMs) offers a novel strategy to induce breast tumor regression. Breast tumors are highly infiltrated with suppressive TAMs and clinically, a high number of TAMs in breast tumors correlate with a worse overall prognosis and increased metastasis. Therefore, the proposed research focuses on understanding how TAMs contribute to the suppressive tumor microenvironment. A major goal of the project funded through the Terri Brodeur Breast Cancer Foundation is to reveal novel signaling pathways in TAMs that can be targeted therapeutically. The unique and novel clinical focus of harnessing macrophages has the potential to have a considerable impact in the treatment of breast cancer. Dr. Guerriero received her bachelor's degree in Biochemistry from
2020	Kabraji, Sheheryar K. BM BCh	Dana-Farber Cancer Institute – Harvard Medical School	While effective HER2-targeting drugs have greatly improved outcomes for patients with HER2-positive (HER2+) breast cancer, relapse and recurrence still occur. When HER2+ breast cancer returns after treatment, it is because some cancer cells survive killing, and are known as minimal residual disease (MRD). To study the biology of MRD we have developed a mouse model of HER2+ breast cancer (t-HER2) where we can turn on and turn off tumor formation at will. This model also has an intact immune system, making it ideal to study tumor-immune interactions. When we turn off tumors, we model the scenario in patients where tumors shrink with effective therapy. However, like in some patients, tumors recur spontaneously in our model. Using the t-HER2 model we found that MRD is comprised of rare 'sleeping', or quiescent, cancer cells surrounded by signs of a

			Dr Sheheryar Kabraji received his medical degree from Oxford University Medical School and completed internal medicine residency at Massachusetts General Hospital. As a medical oncology fellow in the Dana Farber/Partners Hematology/Oncology Fellowship Program, he undertook post-doctoral research in the laboratory of Sridhar Ramaswamy at the Mass General Cancer Center where he demonstrated that AKTlow quiescent cancer cells can be found in
2020	Perurena, Naiara PhD, PharmD	Brigham and Women's Hospital – Harvard Medical School	Around 15-20% of breast cancers are characterized by the amplification or overexpression of the receptor tyrosine kinase HER2 and are therefore classified as HER2-positive. In these tumors, HER2 drives tumor formation and progression by activating an oncogenic signaling cascade. Fortunately, the development of therapeutic agents that directly target HER2 has substantially improved the clinical outcome of individuals with HER2-positive breast cancer. Nevertheless, resistance to HER2 inhibitors remains a major challenge, especially in the metastatic setting. Currently, there are no cures for metastatic breast cancer. In addition, while many individuals with localized disease initially respond to HER2-directed therapies, a subset of patients with no overt signs of metastasis may still relapse. Therefore, there is an urgent need to 1) understand the mechanisms that underlie resistance to current treatments, 2) identify robust biomarkers of therapeutic resistance, and 3) develop improved, and more importantly, curative therapies. As a Terri Brodeur Fellow, Dr. Perurena aims to define the role of two
2020	Remsik, Jan PhD, PharmD	Memorial Sloan Kettering Cancer Center	Leptomeningeal metastasis (LM), or the spread of tumor cells into the cerebrospinal fluid, is an increasingly common complication of cancer that results in rapid neurologic disability and death. Colonization of leptomeningeal space by cancer cells can take years or even decades after primary cancer diagnosis. The molecular basis of this devastating process remains virtually unknown. In the proposed project, we plan to investigate why some breast cancers become metastatic and lead to LM, how therapy contributes to the dormancy and re-emergence of these cells, and ultimately, which genes are involved in lethal recurrence. Working from our observations from patient samples and unique

2021	Abravanel, Daniel L. MD, PhD	Dana-Farber Cancer Institute – Harvard Medical School	Metastatic breast cancer (MBC) – breast cancer that has spread to other organs – unfortunately remains incurable. In spite of the increasing number of treatments available that can benefit patients with MBC, the disease eventually develops resistance to each therapy. As such, there is a critical need to characterize resistance in patients as insights have the potential for rapid translation to improve quality of life and survival. Most breast cancers express the estrogen receptor (ER). As these depend on estrogen, hormonal therapies are a mainstay of treatment. However, their efficacy is also limited by resistance. In fact, most breast cancer-related deaths result from ER+ MBC that develops resistance to hormonal therapy. One apparent pathway to resistance in ER+ tumors is for the cancer to become ER-negative. This phenomenon of "ER loss" impacts a substantial number of patients, limits treatment options, and is associated with
2021	Malani, Rachna, MD	Memorial Sloan Kettering Cancer Center	A growing problem facing cancer patients today is metastatic disease, especially metastases to the central nervous system (CNS). As things stand today, we have large knowledge gaps in understanding why some breast cancer becomes metastatic to the CNS and how we can effectively identify CNS disease earlier. CNS disease is a serious complication of cancer and a major cause of death and well as disability. Breast cancer is the second most common cancer to spread to the CNS. Over time, this problem has been growing and we see more patients now with CNS disease than ever before. Today, this disease is typically found once patients become symptomatic and we are left to react. Part of this devasting problem, is that our understanding of why this disease occurs is lacking. In turn, this limits our ability to develop more effective treatments. Through this study, we aim to change this. We propose to create a novel approach to
2021	Micalizzi, Douglas MD, PhD	Massachuttes General Hospital Cancer Center	Circulating tumor cells (CTCs) are cells that are derived from a tumor, but are isolated from the blood of cancer patients. Only recently has technological advances permitted the isolation and characterization of these rare cells. CTCs offer a snapshot of the invasive cancer cells that give rise to metastatic lesions and an important model to study cancer and the stages of metastasis. The study of CTCs and the mechanisms of metastasis has the potential to catalyze the development of new treatments for breast cancer that more effectively target CTCs and prevent or suppress the development of metastasis. To investigate breast cancer CTCs and metastasis, I have generated a mouse model of breast cancer metastasis and performed a screen to identify regulators of metastasis. From this screen I identified RPL15, an integral component of the ribosome, to

2021	Rosenbluth, Jennifer MD, PhD	Dana-Farber Cancer Institute – Harvard Medical School	Currently one in eight women in the US are predicted to develop breast cancer in their lifetime, but what is unknown is how many of these cancers can be prevented through advances in precision medicine. At this time, prevention strategies focus on radiographic screening for patients above a certain age, or in those at high risk, removal of the breast tissues, a procedure that can lead to physical and mental hardship. Few chemo-preventative compounds are approved and methods for determining which patients would benefit from these agents are lacking. Thus, there is an urgent need for improved cancer prevention strategies for breast cancer. The overall goal of the research being supported by the Terri Brodeur Breast Cancer Foundation is to evaluate novel cell types present in the breast tissues of women at increased risk of breast cancer as potential targets for breast cancer prevention. In particular, we have developed a biobank
2022	Ferraro, Emanula MD	Memorial Sloan Kettering Cancer Center	The prognosis of breast cancer patients is dramatically affected by the seeding of cancer cells in the brain. The impact of brain involvement on quality of life and survival of breast cancer patients is challenging and therapeutic options are currently limited. Although new local treatment approaches in the field of surgery and radiotherapy have improved the local control brain metastases (BM), the responses are often not durable and re-treatment not always feasible. In addition, the short and long terms neurological complications of the treatment contribute to complicate the management of these subset of patients. Unlike other sites of disease spreading, most of chemotherapeutic do not help so much to block the progression in the brain. Indeed, brain is a “sanctuary” for cancer cells, and it is protected from the drugs in the bloodstream. Therefore, BM can be considered the *sword of Damocles* for breast cancer patients and new treatment
2022	Schade, Amy PhD	Brigham and Women's Hospital Harvard University	Triple Negative Breast Cancer (TNBC) is an aggressive subtype of breast cancer which represents approximately 15% of all cases. TNBC tumors frequently recur and metastatic disease is incurable. The standard of care for most TNBCs includes chemotherapy yet many tumors develop resistance. There is an urgent, unmet clinical need for effective therapeutics for advanced and metastatic TNBC. In our preliminary studies, Dr. Schade has identified a promising new therapeutic combination that is effective in a TNBC tumor model. As a Terri Brodeur Fellow, Dr. Schade plans to extensively test this combination in TNBC tumor models, deconstruct the mechanism by which it functions, and identify biomarkers to help select patients that are likely to respond. Importantly, this combination kills

2022	Sribenja, Sirinapa PhD	Roswell Park Alliance Foundation	Breast cancer presents as several clinical subtypes that have different progression trajectories and disparate prognoses. However, there are two primary etiologic subtypes, each associated with a distinct set of risk factors and genetic profiles that essentially correspond to estrogen receptor positive (ER+) and negative (ER-) disease, and the ER status serves as an important marker for treatment options and prognosis in breast cancer patients. Compared with women diagnosed with ER+ breast cancer, those with ER- tumors generally have a poorer prognosis, partly because of their aggressive phenotype and the lack of targeted therapy. In addition, high-grade, ER- breast cancer is more common among American women of African ancestry (AA) than among those of European ancestry (EA). Presently, the underlying causes of this increased risk of ER- breast cancer in AA women are not clear, but the causes are likely multifaceted. In the last few decades, a substantial amount of research has been devoted to the identification of epigenetic and transcriptomic alterations that drive tumorigenesis. These efforts have led to an improved understanding of its mechanisms and advanced methods for targeted therapeutic strategies for cancer and its complications. However, evidence linking RNA modifications to the development, maintenance, and progression of breast cancer is still lacking. By using my expertise in molecular and cellular biology, and by taking advantage of novel, state-of-the-art high-