Congratulations to the 2016 TBBCF Research Grant Recipients

After reviewing dozens of grant proposals, our TBBCF Scientific Advisory Committee has awarded fellowships to the following top 2016 researchers.

Cold Spring Harbor Laboratory

Jean Albrengues, PhD

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 tumor cells *in situ*, he will use microscopy in lungs of living mice and determine how these parameters changes when the disseminated, dormant tumor cells are induced to reawaken. Using pharmacological and genetic approaches, he will identify and target specific signals between inflammatory and cancer cells during experimental manipulation of dormancy. Together, these approaches will allow him to determine how communications between tumor cells and inflammatory microenvironment contribute to the reawakening and therapy resistance of the dormant cells. This analysis will likely reveal new strategies for treatment of dormant disease.

Dr. Albrengues received his PhD from the University of Nice Sophia-Antipolis in France under the supervision of Dr. Cedric Gaggioli at the Institute for Research on Cancer and Aging, Nice (IRCAN). Using sophisticated three dimensional assays and *in vivo* models, he demonstrated, during his doctoral studies, the role of the cytokine LIF and the JAK1/STAT3 signaling pathway during the activation and the epigenetic maintenance of activated pro-invasive fibroblasts. Dr. Albrengues is currently a postdoctoral fellow at Cold Spring Harbor Laboratory in the team of Dr. Mikala Egeblad.

Mass General Hospital Cancer Center

Mihriban Karaayvaz, PhD

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 properties of the major breast cell populations in BRCA1/2 carriers compared to controls in order to determine the cause of abnormal function within these cell populations.

Our preliminary data have revealed novel mechanisms of luminal progenitor (LP) cell regulation that may suggest a practical way to reverse cancer-associated LP deregulation and thereby decrease breast cancer risk. These studies are likely to have near-term impact, identifying new targets for breast cancer prevention for future clinical trials.

Dr. Karaayvaz obtained her PhD from Stony Brook University, where she studied the role of microRNAs in cancer and discovered a novel microRNA targeting BCL2 and increasing the cytotoxic effect of 5-fluorouracil. Dr. Karaayvaz has a longstanding interest in breast cancer biology and prevention, and is currently a postdoctoral fellow at the Mass General Cancer Center/Harvard Medical School in the laboratory of Dr. Leif W. Ellisen.

Dana-Farber Cancer Institute

Daniel Stover, MD

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 available datasets to investigate immune cell signatures in thousands of breast tumors. In parallel, he will work to understand immune cell subsets in breast cancer biopsies of patients on clinical trials of chemotherapy and immune-directed therapies. Ultimately, his goal is to develop biologically rational, immune-based biomarkers to guide therapy, including chemotherapy and immune-directed therapies.

Dr. Stover is a *cum laude* graduate of Princeton University and received his MD from Vanderbilt University where he was named to AOA Honor Medical Society. Dr. Stover was a resident in internal medicine at Vanderbilt University Medical Center and was selected to serve as the Hugh J. Morgan Chief Resident in Medicine. He completed his fellowship in medical oncology at the Dana-Farber Cancer Institute/Massachusetts General Hospital/Harvard Cancer Center program. Dr. Daniel Stover is currently an Instructor in Medicine at Dana-Farber Cancer Institute and postdoctoral research fellow in the lab of Joan Brugge, PhD at Harvard Medical School.

Memorial Sloan Kettering Cancer Center

Eneda Toska, PhD

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 crosstalk.

As a Terri Brodeur research fellow, Dr. Toska will explore these newly identified mechanisms of resistance and examine their role on patient biopsies pre-and-on treatment to PI3K inhibitors. With this in mind, she aims to expose new therapeutic targets that could potentially increase treatment success.

Dr. Toska obtained her PhD at University at Buffalo, where she worked under the supervision of Dr. Stefan Roberts. During her doctoral studies, Dr. Toska investigated the mechanisms by which Wilms' tumor 1 (WT1) regulates transcription and its role in both development and cancer. For her postdoctoral training, she joined Dr. José Baselga's laboratory, a world leader in breast cancer research, to study the molecular mechanisms that regulate ER function and contribute to resistance to PI3K inhibitors in patients with ER-positive breast cancers.