Patients with triple negative breast cancer (TNBC) have few effective treatment options as they derive no benefit from molecularly targeted treatments such as endocrine therapy or trastuzumab, because they lack the appropriate targets for these drugs. Therefore, patients with TNBC generally receive neoadjuvant chemotherapy. While a fraction of patients will achieve pathologic complete response (pCR), the vast majority will have residual disease (RD) and have a worse overall survival (OS) compared to patients who have RD in non-TNBC. Recently, poly (ADP-ribose) polymerase (PARP) inhibitor therapy has emerged as a promising strategy to treat BRCA-mutated TNBC, and there are at least 5 PARP inhibitors that are in clinical trials. While objective responses for PARP inhibitors are promising, remissions have not been durable. Here we target the urgent need to overcome chemotherapy and PARP inhibitor resistance and tumor recurrence in TNBC.

Immunotherapy targeting suppressive T cells has been explored as a possible treatment option for TNBC, however there has been only modest benefit, as these tumors establish a strongly immunosuppressive tumor microenvironment. Interestingly, we show that TNBC is highly infiltrated with other immune cells such as tumor-associated macrophages (TAMs), which are associated with metastasis and poor survival. Indeed, we have found that nearly all TNBC tumors are highly infiltrated by macrophages, but not T cells. We provide evidence that modulating tumor macrophages through two opposing strategies: (1) activating anti-tumor macrophages, or (2) inhibiting pro-tumor macrophages decreases primary and metastatic tumor burden and increases CD8+ T cells within the tumor, and enhances chemotherapy, targeted therapy and immunotherapy. The molecular biology of BRCA-mutations may make these tumors more vulnerable to macrophage targeting therapy and will be discussed.

Biography
Dr. Jennifer Guerriero is an Instructor in Medicine at Harvard Medical School and is the Director of the Breast Immunology Laboratory at Dana-Farber Cancer Institute. She received her PhD in Molecular and Cellular Biology and Immunology and Pathology from Stony Brook University. Dr. Guerriero’s research focuses on harnessing myeloid cells to overcome resistance to chemo- and immuno-therapy.