SAA - BALTIMORE

2020 GRANT AMOUNT: $415,000

GRANT RECIPIENT: Dung Le, MD

PROJECT: Multi-agent low dose chemotherapy with or without dostarlimab and niraparib in untreated oligometastatic pancreatic ductal adenocarcinoma

Project Details: We hypothesize that a low dose chemotherapy protocol in combination with anti-programmed death-1 (PD-1) and PARP inhibition will be active in patients with newly-diagnosed, oligometastatic pancreatic cancer and lead to a high resection rate and long term disease control. The successful execution of this protocol could support the development of a new therapeutic combination, provide preliminary data for the use of resection of oligometastatic disease in the modern chemotherapy era, and will provide valuable biologic insights into the effects of chemotherapy with and without immunotherapy in the tumor microenvironment niche of both primary and metastatic disease.

GRANT RECIPIENT: Brian H. Ladle, MD, PhD

SIDNEY KIMMEL COMP. CANCER CENTER

PROJECT: Generating Systemic Anti-tumor Immunity via MRI-guided Cryotherapy and Intratumoral STING agonist injection in Canine Osteosarcoma (OSA)

Project Details: Our proposal will determine the impact of MRI-guided cryoablation of canine OSA tumors, CT-guided intratumoral STING agonist injection, and the combination therapy which will couple the immune activating capabilities of both modalities. Rigorous immune analysis and clinical outcome measures will direct the next steps toward a human clinical trial. The specific aims of the proposal are:

1. We hypothesize that the combination of cryotherapy with intratumoral STING agonist injection will generate a potent anti- tumor immune response. We will compare the immune response in resected tumors following treatment in dogs treated with cryotherapy alone, STING agonist alone, and with both modalities. We will assess the immune response with cytokine assays, immunohistochemistry (IHC) detecting immune infiltrates, and functional T cell immunoassays.
2. To determine whether MRI-guided cryoablation combined with image-guided intratumoral STING agonist administration prevents metastatic disease progression and prolongs survival compared with standard-of-care treatment for OSA.

SWIM ACROSS AMERICA
MAKING WAVES TO FIGHT CANCER

JOHNS HOPKINS MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

GRANT RECIPIENT: Rajarsi Mandal, MD

PROJECT: Genomic and Epigenomic landscape of the TME as mediators of the variable response to anti-PD-1 immunotherapy via their interplay with antigen-reactive tumor-infiltrating lymphocytes (TILs).

Project Details: The genomic and epigenomic landscape of the TME are critical mediators of the variable response to anti-PD-1 immunotherapy via their interplay with antigen-reactive tumor-infiltrating lymphocytes (TILs). A major barrier to understanding variable resistance mechanisms is a lack adequate translational experimental models to investigate patterns of immunotherapeutic resistance in human tumors. Furthermore, analysis of human tumors without functional experimental validation calls into question the biological meaningfulness or utility of widely performed human sample analysis. Therefore, we will utilize a novel clinically-mirrored patient-derived organoid (PDO) approach to provide an experimental functional model in addition to human sample analysis to interrogate our study questions and provide a robust platform for discovery. Importantly, this is an entirely novel approach to mirror tumor samples analysis from immunotherapy clinical trials to experimentally tested autologous patient-derived organoids.

GRANT RECIPIENT: Cara Rabik, MD, PhD

PROJECT: Relapsed B-ALL (B-cell acute lymphoblastic leukemia) and response rates of standard chemotherapy versus blinatumomab after reinduction.

Project Details: Tumor antigen-directed immunotherapies have shown striking efficacy in highly chemotherapy-resistant relapsed and refractory B-ALL. Blinatumomab was recently FDA-approved for relapsed and refractory B-ALL, though not all patients respond to blinatumomab, and it is not known why many patients fail to respond, as CD19 density on ALL cells, absolute lymphocyte count, and T-cell subsets are noninformative. With the availability of the COG protocol AALL1331 patient samples, we have the ability to perform state-of-the-art immunoassays in a large sample size to address the immunologic basis of response and resistance to blinatumomab. The objectives of this proposal are to discover the mechanisms that determine the observed heterogeneity of clinical responses to blinatumomab in relapsed B-ALL. There are currently no established biomarkers to predict this response. We plan to use this knowledge to improve the efficacy of blinatumomab via rational patient selection and combination treatment strategies – including, but not limited to, the combination of blinatumomab with other immunotherapies, including PD-1/PDL-1 inhibitors (nivolumab, pembrolizumab), alternative therapies. Currently, patients are randomized to these immunotherapies with no testing performed prior to giving blinatumomab to assess for response or nonresponse. This work will develop an immunophenotype that we hope will be able to predict patients who will benefit from blinatumomab therapy and which patients would likely benefit from alternative therapies.

SWIM ACROSS AMERICA
MAKING WAVES TO FIGHT CANCER

JOHNS HOPKINS MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

GRANT RECIPIENT: Kellie N. Smith, PhD

PROJECT: Expression profiling of neoantigen-specific T cells in resectable NSCLC

Project Details: It is urgently important that we develop methods to enumerate the expression profile of neoantigen-specific T cells to better understand endogenous tumor-immune interactions and inform future immunotherapeutic treatment decisions. We propose to link MANAFEST with single cell RNA sequencing of TIL to enable acquisition of the full transcriptomic profile of neoantigen-specific T cells in patients with resectable disease. This will be the first immunogenomic method that enables comprehensive evaluation of T cell phenotype and function. The data generated will be incorporated into a relational database and machine learning approaches to associate immunogenomic findings with clinical and demographic parameters. Our findings will provide a detailed atlas of the immune system and will deepen our understanding of the immune response to cancer.

GRANT RECIPIENT: Franck Housseau, PhD

PROJECT: A pre-clinical model of metabolic and immune checkpoint inhibitor combination for the treatment of DNA Mismatch Repair Profiicient Colorectal Cancer

Project Details: The detection of a preexisting anti-tumor immune response in irMMRP CRC may 11ọt be sufficient to predict a clinical response to checkpoint inhibitors (IDO1/PD-L inhibitors) and we propose that the detection of IL17 cells in the TiMEmay preclude responses to iinmunotherapy. Combination of checkpoint inliibitors with drugs targeting the ILI 7 signaling could improve the impact of immunotherapy on MMRP CRC.

SWIM ACROSS AMERICA HAS SUPPORTED SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER SINCE 2009