Propelling Bold Ideas to Transform Cancer Care

Private philanthropic support of novel ideas and early career scientists plays a vital role in accelerating scientific advances, cultivating the next generation of leading cancer researchers, and saving lives. This year, the Catalyst Awards, funded by gifts from friends of Siteman, provided ten grants to support the launch of promising early-stage projects across Siteman's seven research programs. The selected projects embody exceptional potential to drive transformative changes in cancer care, all aimed at improving the lives of patients.

Questions? Contact the Siteman Advancement Office at 314-935-4725 or friendsofsiteman@wustl.edu.

Breast Cancer

**Project Title:** Using intermittent fasting to alter tumor metabolomics and improve breast cancer outcomes

**Objective:** Determine how intermittent fasting in conjunction with radiation therapy affects breast cancer tumor metabolic pathways.

**Description:** Intermittent fasting has potential to decrease tumor growth and enhance treatment effects in patients. Our mouse studies show that alternate-day fasting slows breast cancer growth and enhances radiation therapy. This project aims to determine which tumor metabolic pathways are altered with intermittent fasting in conjunction with radiation therapy. By figuring this out, we can consider drug treatments that could mimic fasting, thus amplifying the effects of fasting or helping patients who cannot fast.

**Project Title:** Breast cancer brain metastases to the cerebellum

**Objective:** Use mouse models and patient samples to characterize the microscopic environment of brain tumors in HER2+ breast cancer brain metastasis.

**Description:** When breast cancer spreads to the brain, particularly to the cerebellum, it represents an emergency for patients. In this project, novel mouse models of breast cancer brain metastasis to the cerebellum have been created using tissue transplantation. Using a molecular genetic technique, researchers will use the mouse models and patient samples to characterize the microscopic environment of the brain at the invading edge of the tumor.
Hematopoietic Development and Malignancy

Project Title: Epitope-edited allogeneic CD2 CART-T (UCART2edit) for T-All
Objective: Use CRISPR to mask healthy immune cells so that they are not killed by therapeutic CAR-T cells in leukemia patients.
Description: CAR-T therapy is a treatment option for patients with an aggressive cancer called T cell acute lymphoblastic leukemia (T-ALL). CAR-T cell therapy engineers healthy T cells that attack T-ALL cancer cells. However, CAR-T cells can attack each other or healthy immune cells, which leads to poor CAR-T function and immunodeficiency. This project aims to use CRISPR to mask CAR-T cells and healthy immune cells so that they are not recognized and killed by CAR-T cells.

Onologic Imaging

Project Title: CD163 targeted PET tracer imaging tumor associated macrophages in cancer
Objective: Develop a novel imaging agent to non-invasively uncover the inflammatory cells that hinder success in head and neck squamous cell cancer patient treatment.
Description: Head and neck squamous cell carcinoma (HNSCC) is a major cause of cancer mortality worldwide. Special types of inflammatory cells called tumor associated macrophages (TAMs) suppress response to standard chemotherapy and radiation in HNSCC patients, hindering success. This project proposes to develop a novel imaging agent to detect TAMs using radioactive tags and scanners to determine how TAMs change as HNSCC tumors develop and following treatment of the tumors. This knowledge can significantly improve current treatment and lead to development of novel therapies to remedy this problem.

Project Title: Precision proton therapy with molecular guidance and positron emission dose verification
Objective: Use positron emission tomography (PET) imaging to measure the dose of radiation that cancer patients receive from proton therapy.
Description: Proton therapy delivers radiation more precisely and effectively to cancer cells than conventional x-rays because the energetic protons are stopped and absorbed completely at the target sites. However, it is a challenge to measure the actual radiation dose delivered to a patient non-invasively due to the lack of appropriate sensors.
Positron emission tomography (PET) is an imaging technology that uses radio-labeled molecules to detect molecular targets associated with many diseases. Interestingly, positron-emitting radionuclides are produced inside a patient’s body where the proton beams deposit most of their energy. This project aims to pair a compact PET imager developed at the Washington University School of Medicine with proton therapy at the treatment room to measure radiation dose delivered to patients. This will improve our understanding of biological responses to proton therapy and make this powerful treatment technique more effective.

### Prevention and Control

**Project Title:** Leading with the community: Building equitable and sustainable pediatric cancer rehabilitation programs

**Objective:** Interview pediatric cancer patients and families to uncover reasons why rehabilitation services are often not utilized, and use this information to improve access to these critical resources.

**Description:** Children with cancer often experience challenges due to treatment such as difficulty with walking, thinking skills, communication, and mental health. Oncologists can recommend rehabilitation services to help children adapt to these challenges, but this does not occur often. This research project seeks to interview cancer patients and families to understand why this gap exists, and share this information with families, oncologists, and rehabilitation teams to improve access to these critical resources.

**Project Title:** Youth-elder participatory action research for cancer health equity among St. Louis Asian communities

**Objective:** Develop a cohort of Asian American research scholars who will map and identify needs and barriers related to cancer prevention and control in the Asian American community.

**Description:** Cancer is the leading cause of death in Asian Americans. Asian Americans also often face major barriers to accessing cancer screening and care, including language accessibility, lack of insurance, and provider discrimination. In this project, a multi-generational cohort of Asian community research scholars will generate maps of existing community health resources and interview community members to identify barriers related to cancer prevention and control. These efforts will empower Asian community members, strengthen community trust, and develop culturally accessible cancer interventions.

### Solid Tumor Therapeutics

**George Souroullas, PhD**  
Assistant Professor  
Department of Medicine  
Division of Oncology
**Project Title:** Investigate the role of autophagy on the tumor immune response of Ezh2-mutant melanoma  

**Objective:** Investigate epigenetic regulator mechanisms to improve immunotherapy response in melanoma patients.  

**Description:** While immunotherapy has improved survival rates in melanoma patients, many patients experience side effects or lack of response to this treatment. There are a group of genes that, when turned on or off, can have an effect on how the immune system recognizes and destroys melanoma cells. These genes, called epigenetic regulators, affect the cell’s ability to degrade and recycle factors that regulate the immune system’s ability to recognize cancer cells. This project will investigate this process to improve immunotherapy approaches.

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**Tumor Immunology**

**Naresha Saligrama, PhD**  
Assistant Professor  
Department of Neurology

**Project Title:** Assessment of local and systemic immune responses to T-VEC therapy  

**Objective:** Investigate why some melanoma patients respond better to T-VEC intratumoral immunotherapy than others to improve immunotherapy response.  

**Description:** While immunotherapies like immune checkpoint inhibitors (ICIs) show efficacy against melanoma, there are gaps in success due to adverse effects and limitations in types of tumors that respond to ICIs. One reason ICIs may not work is because of insufficient immune stimulation in the tumor, which may be remedied by injecting immune-stimulatory agents like talimogene laherparepvec (T-VEC) directly into tumors. This project aims to understand why some patients respond well to T-VEC therapy, while others do not. Doing so could allow us to increase efficacy of local, tumor-directed therapies in combination with systemic therapies and broaden the type of tumors that respond to ICIs.

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**Jeffrey Ward, MD, PhD**  
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**Project Title:** Assessment of tissue-specific t-cell dysfunction programs in lung tumors and lymph node metastases  

**Objective:** Use a mouse model and single-cell RNA sequencing to investigate the characteristics of exhausted T-cells in lung tumors and lymph node metastases to guide the development of better immunotherapies for non-small cell lung cancer patients.  

**Description:** While programmed cell death 1 (PD-1) inhibitors can help non-small cell lung cancer (NSCLC) patients by unleashing tumor-specific T-cells to destroy cancer, only a minority of patients respond to this therapy and the effects are short-lived. T-cells can become exhausted over time, which reduces their killing potential but avoids damaging healthy tissues. PD-1 inhibitors can rescue the function of some T-cells, but not terminally exhausted ones. There is not much known about the T-cells that could respond to PD-1 inhibitors in NSCLC tumors. This study will use a mouse model of NSCLC and single-cell RNA sequencing to understand the characteristics of exhausted T-cells in tumors and metastatic lymph nodes in order to clarify and identify the cell types that respond to immunotherapies.

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