SITEMAN CANCER CENTER

2024 Catalyst Awards

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

Nusayba Bagegni, MD
Associate Professor
Department of Medicine
Division of Oncology

Project Title: NeoTAILOR: A phase II biomarker-directed approach to guide neoadjuvant therapy for patients with stage II/III ER-positive, HER2-negative breast cancer

Summary: Use biomarkers to better tailor pre-surgical therapy for patients with stage II/III HR positive, HER2 negative breast cancer.

Description: Hormone-receptor positive (HR+) breast cancer is treated with hormone- blocking endocrine therapy (ET). In patients with stage 2-3 breast cancer, treatments may be given prior to surgery to help shrink the tumor. Some patients will have excellent response to ET, but others may also require chemotherapy. Doctors use standard tools to decide which patients need chemotherapy, yet these tools remain inadequate, particularly in Black women who are underrepresented in clinical trials. Testing tumor cell growth response (called Ki67) after only a few weeks of ET identifies ET-resistant breast cancer with a higher risk for recurrence. Additionally, studies show that certain breast cancer subtypes may respond better to ET than others, and Black women tend to have higher incidence of ET-resistant subtypes. This trial will utilize a novel approach by combining breast cancer subtype plus Ki67 response to ET to personalize treatment, with a focus on enrolling Black patients, to improve treatment selection and outcomes.

Priyanka Verma, PhD
Assistant Professor
Department of Medicine
Division of Oncology

Project Title: Define cancer cell intrinsic vulnerabilities to improve PARP inhibitor response in BRCA-mutant breast cancers.

Summary: Use cell models to investigate how to make PARPi treatment more effective & less toxic for breast cancer patients with BRCA mutation.

Description: BRCA-mutant breast cancers are highly aggressive and difficult to treat. Poly (ADP-ribose) polymerase inhibitor treatment (PARPi) is promising, but treatment resistance and side effects hold this therapy back. Depletion of an enzyme, Amplified in Liver Cancer 1 (ALC1), can make cancer cells more susceptible to PARPi while keeping normal cells safe. We will use ALC1-deficient BRCA-mutant breast cancer cells to define cancer cell features that enhance the impact of PARPi and lower PARPi dosage to reduce side effects, and map genomic regions that are impacted by PARPi-based therapies. This information will help improve and predict outcomes of PARPi therapy for patients with BRCA-mutations who have limited therapeutic options.

Hematopoietic Development & Malignancy Program

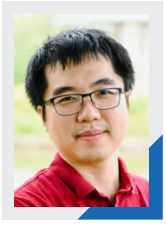
Sena Kim, PhD
Instructor
Department of Medicine
Division of Oncology

Project Title: IUpregulation of AMPK by targeting VLDLR reduces GvHD while maintaining GvL

Objective: Use unique circular RNA protein markers to develop better cancer vaccines.

Description: Bone marrow transplantation (BMT) is an effective treatment for patients with blood cancers, utilizing health donor cells to fight the diseases. However, these donor cells contain specialized immune cells (T cells) that can also attack and damage healthy organs in the patient's body, which is known as graft-versus-host disease (GvHD). Therefore, it is difficult to distinguish between the beneficial effects of the T cells that fight the cancer and detrimental effects that cause GvHD, both of which are mediated by the same T cells. Consequently, global immune suppressive drugs that are commonly used against GvHD can also reduce the ability of the donor T cells to fight cancer, leading to cancer recurrence. Despite numerous strategies attempted for this challenge over the past five decades, none of the prevention strategies against GvHD have been effective in preventing cancer recurrence. We have identified a novel gene candidate that has the potential to overcome this challenge and found that deleting the gene, Vldlr, in donor T cells selectively suppresses T cells' GvHD-causing function while preserving their ability to fight cancer. In this proposal, we will investigate the potential of pharmacologic targeting of this gene, which could selectively eliminate GvHD without compromising the T cells' anti-tumor effects in preclinical models of BMT. Additionally, we will investigate the cellular mechanisms by which targeting the gene separates GvHD from anti-tumor effects. If successful, our studies may have a practice-changing impact on the fields of BMT.

Mechanisms of Cancer Biology



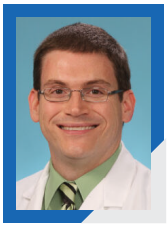
Chun-Kan Chen, PhD
Assistant Professor
Department of
Cell Biology & Physiology

Project Title: Identification of CircRNA-Derived Neoantigens to Enhance Cancer Immunotherapy

Objective: Use unique circular RNA protein markers to develop better cancer vaccines.

Description: Vaccines targeting unique cancer markers have shown great promise. The challenge lies in identifying suitable cancer markers, as many cancers exhibit few mutations, making these markers scarce. Circular RNA molecules produce novel protein markers that differ from typical ones. These proteins serve as ideal targets for vaccines because some are uniquely expressed in cancer cells, but not in healthy cells. This project aims to: (i) assess the effectiveness of vaccines targeting circular RNA proteins in cancer cells, and (ii) explore their potential in mouse tumor models. This strategy would revolutionize cancer vaccine development, allowing for more precise and effective therapies.

Oncologic Imaging Program



Joseph Ippolito, MD, PhD
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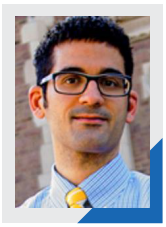
Department of Radiology
Principal Investigator

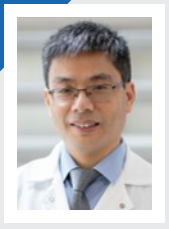


Gary Patti, PhD
Professor
Department of Chemistry
Co-PI

Project Title: Imaging the cancer folate cycle with deuterium metabolic imaging.

Objective: Use a new type of non-invasive MRI imaging to see if a tumor will respond to anti-folate chemotherapy.

Description: The folate cycle is a source of energy and building blocks that cancer needs to survive. The cycle targeted by chemotherapeutics called anti-folates. These medications may not work due to treatment resistance. Clinicians have no way of knowing if a tumor will be resistant. Non-invasive imaging would be ideal for predicting this. This project will develop a new MRI-based technology, deuterium metabolic imaging (DMI), to visualize the folate cycle noninvasively. DMI shows real-time consumption and metabolism of nutrients in the tumor, showing if chemotherapy is going to work. We will test our technology in mouse models of lung cancer. If successful, this will be translatable to humans.



Hanwen Zhang, PhD
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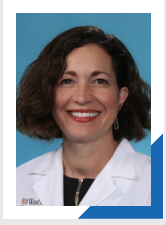
Department of Radiology
Principal Investigator



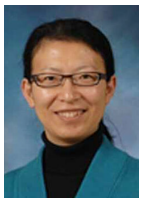
Katherine Weilbaecher, MD
Professor
Department of Medicine
Division of Oncology
Co-PI

Project Title: Ablation of breastbone metastasis with in vivo alpha emitter generator 212Pb/212Bi via RGD-targeted to αvβ3 integrin.

Objective: Use a novel radiotherapy agent to specifically target and destroy metastatic breast cancer that has spread to bone.

Description: Seventy percent of metastatic breast cancers spread to the skeleton, causing fractures, spinal cord compression, and bone pain. Managing this spread proves challenging because bone shields cancer cells from treatment. Certain cancer cell receptors (called integrin αvβ3) become more abundant when they are activated as new blood vessels form at sites where the cancer has spread. This receptor can be targeted by its affinity molecule called RGD peptide to detect, monitor and treat bone metastasis lesions. RGD peptide will be used to deliver a new type of radiotherapy agent, called in vivo alpha emitter generator, 212Pb/212Bi to target and destroy breast cancer bone lesions that are otherwise untreatable.

Prevention and Control



Esther Lu, PhD
Associate Professor
Department of Surgery
Division of Public Health Sciences

Project Title: Investigate the effect of churn rate on optimal open-cohort longitudinal cluster randomized trials

Objective: Examine current NIH trial design & drop-out rate in order to propose more efficient & accurate clinical trials.

Description: Cluster randomized trials (CRTs) are important in scientific research when we want to see how well a health intervention works in real-world settings. Instead of randomly assigning individual people to different treatments, CRTs randomly assign each cluster, like medical center or clinic, to one of treatments, and all individuals within a cluster receive the same treatment assignment. This helps reduce severe bias of the treatment effect due to contamination. Individuals in a longitudinal CRT are often measured at multiple time points but may contribute a different number of measurements. This study will propose optimal designs to help researchers get the most efficient design under a given budget for such a longitudinal CRT. The proportion of Individuals in one period who do not appear in the other period will be examined using two ongoing NIH-funded PA-CRTs (PRECISE & MOTIVATE).

Beryne Odeny, MD, PhD, MPH
Assistant Professor
Department of Surgery
Division of Public Health Sciences

Project Title: Lung Cancer Screening and Atherosclerotic Cardiovascular Disease Risk Prevention in Missouri: A Pre-Implementation Mixed Methods Study

Objective: Patients undergoing lung cancer screening (LCS) face a very high risk of developing heart disease and dying. However, not all individuals undergoing LCS receive necessary preventive care to reduce the risk of heart disease. Our aims are to investigate the extent to which LCS patients receive screening & drugs to prevent heart disease & mortality.

Description: Lung cancer and heart diseases share common risk factors such as smoking, advanced age, and obesity. Within the population accessing LCS, healthcare providers have an opportunity to proactively screen for and detect heart disease early. Among other uses, statins drugs are used to prevent heart disease in individuals at high risk. Our study seeks to evaluate the proportion of LCS patients who undergo screening for heart disease and receive statin treatment if eligible. Moreover, we aim to investigate why certain LCS patients may not be prescribed statins for heart disease prevention. We will investigate how demographic factors like race, education, income, and geographic location impact access to preventive care and heart disease screening. Additionally, we will explore barriers to heart disease screening and statin treatment among LCS patients and potential interventions to overcome these barriers in order to improve health outcomes.

Solid Tumor

Tanner Johanns, MD, PhD
Assistant Professor
Department of Medicine
Division of Oncology

Project Title: Impact of 7HP349 in combination with neoantigen vaccination.

Objective: Use a novel compound called 7HP349 to make cancer vaccines more effective in priming the immune system to attack cancer cells.

Description: Neoantigen vaccines are personalized treatments for cancer that train the immune system to recognize and attack cancer cells by targeting unique

mutations or changes in the cancer cells that are not found in healthy cells. These vaccines could be made more effective by combining them with other substances. A compound called 7HP349 could boost the immune response to neoantigen vaccines by improving how certain immune cells interact with each other. If successful in mouse brain cancer models, 7HP349 could be used in future studies for patients with brain tumors and other cancers like melanoma, lung, breast, and pancreatic.

Tumor Immunology

Melissa Mavers, MD, PhD
Assistant Professor
Department of Pediatrics
Division of Hematology and Oncology

Project Title: Protein validation of transcriptionally distinct human iNKT cells to inform cellular therapy development

Objective: Investigate how to safely & efficiently use a type of healthy donor cells better than CAR-T cells to deliver CAR cancer therapy more effectively.

Description: Chimeric antigen receptor T (CAR-T) cell therapy can cure certain cancers, but this treatment has problems. CAR-T cells are engineered from a patient's own cells, but CAR-T cells sometimes cannot be created due to chemotherapy or rapidly progressing cancer. CAR-T cells made from someone else's cells can injure patients. A special cell type, called invariant natural killer T (iNKT) cells, can be used to safely make CAR therapy (CAR-iNKT cells) from a healthy donor's cells without injuring patients. There are different subsets of iNKT cells: some good, some bad. We will determine how we can remove the cells that are bad for making CAR-iNKT cells. This will make CAR therapies more effective.

Anjali Rohatgi, MD, PhD
Assistant Professor
Department of Medicine
Division of Oncology

Project Title: A Pilot Investigation of Immune Infiltration of Non-Small Cell Lung Cancer Biopsy and Resection Specimens pre and post Neoadjuvant Chemotherapy and Immunotherapy.
Objective: Analyze data from lung tumor tissue samples to determine if types of immune cells present in the samples can predict which patients will most benefit from different therapy types in non-small cell lung cancer.

Description: Non-small cell lung cancer is an aggressive disease with high risk of recurrence and metastasis after surgery. Chemotherapy and immunotherapy prior to surgery (neoadjuvant therapy) reduces these risks for some patients. Oncologists cannot predict who will benefit from chemotherapy and immunotherapy prior to surgery, versus those who should proceed directly to surgery. We will use tissue samples from the lung cancer tumor bank to investigate whether the types of immune cells present in the tumor can predict who will benefit the most from neoadjuvant therapy. This will help identify which therapies are best based on the features of each patient's cancer.