

## 2017 Funded Research Projects

### SITEMAN CANCER CENTER

#### The Role of Interferon Gamma Signaling in the Clonal Evolution of Pre-Leukemic Stem Cells

Goal: To understand how mutant stem cells react to specific signals from the bone to become leukemic cells, and to identify methods to eliminate the mutant cells before they can cause cancer.

**Principal Investigator:** Grant Challen, PhD

#### IFN $\gamma$ R and IL6R Signaling Pathways as Therapeutic Targets to Prevent GvHD While Preserving GvL

Goal: To determine how two proteins (IFN $\gamma$ R and IL6R) cause graft-versus-host disease (GvHD) after a bone marrow transplantation in leukemia patients, and to test whether drugs that inactivate these two proteins can prevent GvHD without interfering with the killing of leukemia cells.

**Principal Investigator:** Jaebok Choi, PhD

#### The Impact of Macrophage Origin on the Pathogenesis of Pancreatic Cancer

Goal: To gain an understanding of how to target a subset of immune cells that are responsible for creating a scar-like "armor" thought to protect pancreatic cancer cells and ultimately improve outcomes for pancreatic cancer patients.

**Principal Investigator:** David DeNardo, PhD

#### Development of an Immunocompetent Autochthonous Model of Glioblastoma

Goal: To develop a better understanding of how the immune system recognizes brain tumors and to find a way to study immune response to recurrent tumors.

**Principal Investigator:** Gavin Dunn, MD, PhD

#### Discovering the Role of Phosphorylation in the Pleckstrin Homology Domain

Goal: To uncover an important basic phenomenon that occurs within normal cell biology and gain a better understanding of the role it plays in the development of cancer cells.

**Principal Investigator:** Kristen Naegle, PhD

#### Defining the Role of Long Non-Coding RNAs in Lymphoma Pathogenesis

Goal: To better understand and provide critical insight into the role that a newly discovered class of RNA molecules have in the development of Non-Hodgkin Lymphoma.

**Principal Investigator:** Jacqueline Payton, MD, PhD

#### The Role of the Histone Demethylase KDM6A in Acute Leukemia

Goal: We will characterize how the inactivation of the gene KDM6A can cause specific changes that drive acute myeloid leukemia.

**Principal Investigator:** Lukas Wartman, MD

#### Treatment of Metastatic Prostate Cancer with Radioactive PARP Inhibitors

Goal: To determine how a modified FDA-approved agent that targets prostate cancer cells goes about killing the prostate cancer cells and optimize the amount of drug that is needed to cure mice with prostate tumors.

**Principal Investigators:** Buck Rogers, PhD and Dong Zhou, PhD

#### Role of Interferon Regulatory Factor 4 in Human T Cell Leukemia Virus-Associated Adult T Cell Leukemia Lymphoma

Goal: To understand the role of IRF4 in adult T-cell leukemia lymphoma which will have applications in deciphering its role in other cancers, including multiple myeloma and lymphoma, and developing novel treatment approaches.

**Principal Investigator:** Lee Ratner, MD, PhD

#### Memory-Plasticity Crosstalk in Cancer Cells

Goal: This project will investigate whether invasive breast cancer cells remember their primary tumor environment even after they escape to healthy tissue.

**Principal Investigator:** Amit Pathak, PhD

#### Development of a Superior Mobilizing Regimen for Hematopoietic Stem Cell Transplantation

Goal: The long-term goal of this proposal is to develop a new method to harvest healthy blood stem cells from the bone marrow of donors to use as transplants for patients with leukemia. In addition to mobilizing healthy stem cells from donors, this new method may also be useful in getting leukemia cells out of the bone marrow and into the blood where they will be more sensitive to killing by chemotherapy drugs (chemosensitization).

**Principal Investigator:** Michael Rettig, PhD

#### Posttranscriptional control of breast tumor growth and metastasis

Goal: One major problem about cancer, including breast cancer, is that cancer cells grow uncontrollably. Our goals are to find out the reasons that cause the unstoppable growth of cancer cells, with a focus on the role of a new protein named MCPIP1.

**Principal Investigator:** Jianguo Liu, MD, PhD

#### Mechanisms of Gastrointestinal Adenocarcinoma Tumorigenesis

Goal: To identify the genes that may start cancers in the stomach, intestines, liver and pancreas to find drugs targeting those genes to stop cancer before it starts.

**Principal Investigator:** Jason Mills, MD, PhD

# PEDAL THE CAUSE

## 2017 Funded Research Projects

### SITEMAN CANCER CENTER (CONT.)

#### Post-XRT Effects in Brain Parenchyma Promote Dramatic Changes in Glioma Phenotype

Goal: To develop a greater understanding of the factors that affect the growth of recurrent glioblastoma and, ultimately, develop novel therapies to treat this incurable tumor.

**Principal Investigator:** Joel Garbow, PhD; Keith Rich, MD; and, Christina Tsien, MD

#### Characterization and Tumorigenic Action of Osteolineage Cells in the Breast Cancer Microenvironment

Goal: To define the phenotype of “bone-like” stromal cells and how they affect tumor growth and metastasis which may ultimately assist doctors in determining cancer severity and devise new anti-cancer treatments.

**Principal Investigator:** Roberta Faccio, PhD and Roberto Civitelli, MD

### ST. LOUIS CHILDREN'S HOSPITAL

#### Image-guided Drug Delivery for Improved Treatment of Diffuse Intrinsic Pontine Glioma

Goal: Diffuse intrinsic pontine glioma (DIPG) is the single greatest cause of brain tumor-related deaths in children. The location and diffuse nature of the disease prohibit surgical interventions; radiation therapy has proven inadequate for cure; and conventional chemotherapy is ineffective because drug delivery is limited by the intact blood-brain barrier. This project proposes to develop an innovative strategy for the improved treatment of DIPG using focused ultrasound delivery of dissolvable, chemotherapy-loaded copper nanoclusters.

**Principal Investigator:** Hong Chen, Yongjian Liu

#### Memory-like Natural Killer Cell Immunotherapy for Pediatric and Young Adult Leukemia Patients

Goal: This project utilizes these cytokine-induced, memory-like natural killer cells as a personalized cellular immunotherapy strategy for relapsed pediatric/young adult Acute myeloid leukemia patients.

**Principal Investigator:** Jeffrey Bednarski, Todd Fehniger, Rizwan Romee

#### A Pilot Study of a Personalized Vaccine Approach in Patients With Recurrent Pediatric Brain Tumors

Goal: This project proposes the first-ever clinical trial to treat pediatric patients with relapsed or recurrent brain tumors with a personalized vaccine, referred to as a peptide vaccine, developed by targeting genetic abnormalities in each individual tumor.

**Principal Investigator:** Karen Gauvain, Gavin Dunn

#### Clinical Development of CRISPR/Cas9 Gene Edited CAR-T for Treatment of T Cell Malignancies

Goal: T cell leukemias and lymphomas represent a class of devastating cancers with high rates of relapse and mortality in both children and adults for which there are currently no effective or targeted therapies. Despite advances in Chimeric Antigen Receptor (CAR)-T cell immunotherapy for B cell malignancies, several challenges have limited development of CAR-T against T cell malignancies. This is primarily due to the shared expression of antigens on normal T cells and malignant cells. We used gene editing to develop an ‘off-the-shelf’ CAR-T product against T cell acute lymphoblastic leukemia (T-ALL) that does not have the risk of CAR-T cells attacking each other or non-cancer cells in the patient. This proposal is aimed at further optimizing CAR-T to treat T cell malignancies as studied using pre-clinical models. Additionally, we will develop therapeutic strategies to overcome life-threatening cytokine release syndrome (CRS), the major limitation of adoptive T cell immunotherapies in general.

**Principal Investigator:** John Dispersion, Robert Fulton, Shalini Shenoy

It takes world-class research to create a world without cancer. Thank you for supporting Pedal the Cause and helping to fund the best and brightest ideas in cancer research.

A full description of Pedal the Cause-funded research projects are available on our website: [pedalthecause.org](http://pedalthecause.org).



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