UCI Anti-Cancer Challenge

2018 IMPACT REPORT

#WEAREANTICANCER

YOUR SUPPORT OF THE UCI ANTI-CANCER CHALLENGE IS PLANTING THE SEEDS FROM WHICH UCI RESEARCH WILL GROW TO IMPROVE CANCER THERAPIES!

As Orange County's only National Cancer Institute-designated cancer center, the UC Irvine Chao Family Comprehensive Cancer Center has a special mission — to conduct research into the causes, prevention, diagnosis and treatment of cancer to improve the outcomes for cancer patients in Orange County and alleviate the burden of cancer on our residents. Cancer centers that lack a research mission can follow treatment guidelines, but they cannot lead in advancing the standards of care.

Every penny of the funds raised by Anti-Cancer Challenge participants is directed towards advancing innovative basic, translational and clinical cancer research that will lead to the next breakthroughs in cancer treatment.

Proceeds from our second annual event, held in May 2018, have been directed to support three objectives:

1. Fund pilot projects that help investigators generate crucial preliminary data for high impact research necessary to secure larger grants from the National Institutes of Health and other external agencies.

2. Advance the discoveries of UCI scientists, including innovative diagnostic devices, novel drugs and biobehavioral interventions through the translational pipeline towards clinical application.

3. Support for research programs and shared infrastructure, including shared resources.

CANCER RESEARCH GRANT AWARDEES

With the funds raised by enthusiastic Anti-Cancer Challenge participants in 2018, UCI awarded 16 cancer research grants enabling nationally renowned physician-scientists at the UC Irvine Chao Family Comprehensive Cancer Center to explore new ways to fight cancer.

TRACK 1
PILOT PROJECT AWARDS

Development and Testing of a Mobile Application for Young Adults with Cancer

Investigator
Michael Hoyt, Ph.D.
Department of Population Health & Disease Prevention

Young adulthood is a critical developmental phase in which young adults are negotiating greater independence and autonomy in social, professional and physical domains. Cancer diagnosis, especially one that threatens sexuality and reproductive health, can be distressing and may contributes to a reduction in quality of life. Managing the demands of cancer treatment and re-entry to post-cancer life can be difficult for some. While a proliferation of smartphone-based mobile applications developed in the past decade deliver evidence-based advice for health management, no such intervention exists to assist young adult cancer survivors in re-negotiating life goals and managing cancer-related emotions. Smartphone-based interventions offer an opportunity to overcome obstacles to accessing in-person supportive care, as well as peer support and socially-shared expression that can be linguistically and culturally tailored as needed to provide skills to improve quality of life and better cancer adjustment. In a collaboration between UCI and the Children's Hospital of Orange County (CHOC), this study will develop and pilot a mobile device application specifically tailored to the supportive needs of young adult cancer survivors with the goal of improving patient-centered outcomes

A Mechanistic Study of Age-Dependent Gender Difference in Melanoma Risk

Investigator
Feng Liu-Smith, Ph.D.
Department of Epidemiology

The incidence of melanoma continues to increase despite extensive public advocacy for decreasing exposure to harmful ultraviolet (UV) radiation from sunlight. A better understanding of melanoma risks and new prevention methods are therefore needed. Our long-term goal is to develop effective melanoma prevention strategies based on a comprehensive understanding of UV and non-UV melanoma risk factors, and to establish a melanoma center with integrated epidemiological and molecular databases for prevention, treatment and research. In this study, we propose to examine a two-sided mechanism of melanoma development based on better understanding age- and gender-specific melanoma risks at both the population and basic science levels. If our hypothesis and model are proven correct, we should be able to change the current paradigm of melanoma prevention and add new elements based on hormone levels and gender-based genetic variants.

UHRF1 as a Therapeutic Target for Osteosarcoma

Investigator
Claudia Benevente, PhD
Department of Pharmaceutical Sciences

Metastasis remains the most significant complication of osteosarcoma, a childhood cancer of the bone. Among the patients who develop metastasis, less than 1 in 5 survive. Thus, there is a pressing clinical need to determine how these tumors metastasize in order to develop new therapeutic strategies. We identified UHRF1 as a protein highly expressed in osteosarcoma and which appears to be critical for osteosarcoma growth and metastasis. This project will further our understanding of UHRF1 in tumor formation and metastasis and will evaluate its potential as therapeutic target for anti-cancer treatment. Given that UHRF1 is highly expressed in multiple cancers, this research proposal has the potential to impact human health beyond osteosarcoma.

Molecular Mechanism of APOBEC3B-Mediated Mutation Shower in Ovarian Cancer

Investigators
Rémi Buisson, PhD
Department of Biological Chemistry

In 2018, more than 22,000 women were diagnosed with ovarian cancer in the U.S., and such patients are typically treated with chemotherapy after surgery. However, about half of these patients will develop resistance to the chemotherapy drugs and will ultimately succumb to their disease, motivating the search for alternative treatments. APOBEC3B (A3B) is a major driver of mutations in ovarian cancer that promote cancer progression and drug resistance. By directly attacking DNA and increasing genomic instability, A3B creates a vulnerability that can be exploited to develop new targeted therapies. The goal of this project is to determine how A3B generates mutations in patients with ovarian cancer and to develop novel strategies to specifically target A3B-expressing cancers. Determining the function and regulation of A3B is crucial in resolving the fundamental mechanism through which ovarian cancer cells accumulate mutations, increase genomic instability, and develop resistance to current therapies.

Control of B-cell Survival & Transformation by the eIF4F Translation Initiation Complex

Investigator
David Fruman, PhD
Department of Molecular Biology & Biochemistry

Each year, approximately 20,000 people in the U.S. die from B-cell lymphomas and 100, 000 more cases are diagnosed. Progress in treating these patients has been fueled by basic research on the signaling mechanisms of B cells, a type of immune system cell. The goal of this project is to advance the field of B cell tumor biology through increased mechanistic knowledge of the mRNA translation initiation complex known as eIF4F. The project will address an urgent need to develop new mouse models to define the function of eIF4F components in normal B cells and B-cell tumors, an effort that will have substantial positive impact on development of therapeutic approaches targeting mRNA translation.

Advancing Oro-Pharyngeal Cancer Screening and Diagnosis to Overcome Disparities and Improve Control and Outcomes

Investigators
Petra Wilder-Smith, DDS, PhD
Beckman Laser Institute

Worldwide, 223,000 deaths occur annually from oral and oropharyngeal cancer (OC). Another 650,000 cases are diagnosed. The mean 5-year survival rate in the U.S. for OC it is approximately 50% and has not improved in decades. The goal of this project is to reduce the pain, suffering and deaths associated with oral and oropharyngeal cancer, which is typically detected only after it has spread. Late diagnosis and treatment are the main cause for the limited treatment options and unusually high mortality of OC. As low-resource and underserved populations have the highest rates of OC in the U.S., our very low cost artificial intelligence-enabled smartphone approach for detecting early and managing OC is specifically designed to be used by community workers or other non-specialist individuals in remote, community or even home settings.

Macropinocytosis Drives Anabolism and Drug Resistance in Breast Cancer

Investigator
Aimee Edinger, DVM, PhD
Department of Developmental & Cell Biology

Cancer cells require a steady stream of nutrients to support their unchecked growth. The bloodstream supplies tumor cells with nutrients, but many cancer cells supplement their diet by feeding on the corpses of nearby dead cells using a process called “macropinocytosis.” This pilot project proposal will test whether attacking and disabling these “supply wagons” could be an effective strategy to fight cancer. Preliminary studies suggest that blocking this ghoulish behavior with macropinocytosis inhibitors will shrink tumors by starving cancer cells. Corpse-feeding also makes tumor cells resistant to radiation and chemotherapy; blocking macropinocytosis could make these standard therapies more effective and limit the development of tumor resistance.

Single-cell Transcriptome Analysis of Human Merkel Cell Carcinoma Heterogeneity by Single-cell RNA Sequencing

Investigator
Ling Gao, MD, PhD
Department of Dermatology

Merkel cell carcinoma is a highly malignant skin cancer with no effective treatment, despite recent advances in immunotherapy. We plan to use novel biotechniques such as droplet-based single cell RNA sequencing to elucidate gene expression patterns in this type of tumor at the level of individual cancer cells. This work will help develop insights into distinctive biological differences found in MCC tumors and develop new drugs to treat this devastating cancer.

DNA Methylation Markers for Exposures to BPA and Related Compounds and Breast Cancer Risk

Investigator
Hannah Park, PhD
Department of Epidemiology

Bisphenol A (BPA) and its related compounds, BPF and BPS, are commonly used in plastics and are thought to be potential endocrine disruptors that may play a role in development of breast cancer and other hormone-related cancers. However, the relationship between BPA/BPF/BPS exposure and cancer risk has not been adequately studied. We propose to identify biomarkers that can be used in both previous and future large epidemiologic studies to study the potential link between BPA/BPF/BPS exposure and cancer risk. These markers may improve risk prediction for cancer and other diseases that may have an environmental component.

True Multi-modal Image-guided Intervention System

Investigators
Farouk Nouizi, PhD
Department of Radiology

Tumor vasculature is a critical component of the tumor microenvironment and is essential for tumor growth and metastasis. Both tumor growth and high dose radiation therapy can decrease tumor blood flow and cause hypoxia, which can affect chemotherapy drug delivery and make the tumors less sensitive to radiation. We have built a first-of-its-kind compact multimodality theranostic instrument by incorporating Fluorescence Molecular Imaging (FMI) into a highly focused radiation system (X-ray SmART, Precision X-ray Inc.) for use in preclinical cancer studies in mouse tumor models. In this project, we will test whether FMI can not only guide the radiation therapy but also provide unique molecular information about the tumor microenvironment and the outcome of radiotherapy.

Role of Phosphatase Methylation in One-Carbon Metabolism and Cancer

Investigator
Peter Kaiser, PhD
Department of Biological Chemistry

Numerous studies have shown that most cancer cells and tumors, independent of tissue origin, are highly sensitive to reduced availability of the amino acid methionine. Exploitation of this metabolic Achilles' heel of cancer has been hampered by the lack of molecular understanding of this metabolic dependency of cancer and the lack of biomarkers to monitor efficiency of interventions that lower available methionine. This proposal aims to develop such an understanding and will evaluate potential biomarkers.

TRACK 2
EARLY PHASE CLINICAL TRIALS

A Phase 1 Study of Pitavastatin in Combination with Venetoclax for Chronic Lymphocytic Leukemia (CLL) or Acute Myeloid Leukemia (AML)

Investigator
Elizabeth Brém, MD
Division of Hematology-Oncology
Department of Medicine

Venetoclax is the first FDA-approved medication in a class of drugs called BH3 mimetics. It is a once-a-day oral medication that is approved for 2 kinds of leukemia – chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML). A class of medicines called statins are used commonly to lower cholesterol, and studies in cell culture and in mice demonstrate that statins improve the ability of venetoclax to kill leukemia cells. In this project, we will launch a first-in-human clinical trial to determine what dose of a statin called pitavastatin to use in combination with venetoclax and make sure the combination is safe, as the basis for launching future clinical trials to determine efficacy.

A Phase 1b Study of TAS102 in Combination with Irinotecan in Patients with Advanced Gastric and Gastroesophageal Adenocarcinoma

Investigator
Farshid Dayyani, MD
Division of Hematology-Oncology
Department of Medicine

Cancers of the stomach and lower esophagus are relatively rare in the U.S., but are globally among the top five causes for cancer-related death, and also disproportionately affect the Asian-American and Hispanic residents of Orange County. When the disease has spread to other organs, surgery no longer possible. Thus, the goal of treatment is not cure, but rather to prolong survival. However, current available treatments result in an estimated survival of only about a year after a patient is diagnosed with advanced stomach cancer. The proposed study will combine two chemotherapy drugs, irinotecan and TAS102, in order to determine whether this combination is active in patients with stage 4 stomach cancer after their cancer has become resistant to standard chemotherapy. The results could establish a new effective treatment option for this highly aggressive disease.

Experimental Therapeutics for Primary Pediatric Brain Tumors

Investigator
Ashley Plant, MD
Department of Pediatrics

Pediatric brain tumors are the second most common cancer in children and account for the majority of cancer-related deaths. The outcome for children with malignant brain tumors has changed very little over the past 35 years. Here, we propose to create a translational research platform that allows us to rapidly screen a large number of drug compounds on brain tumor tissue from patients undergoing surgery at Children's Hospital Orange County. We will use cell cultures and animal models to test various novel, targeted therapies on the tumor cells with the goal of moving those drug compounds that are thought to be effective against these tumors into clinical trials for our patients.

Improving Depression Screening in a Multi-ethnic Cancer Population

Investigator
Lari Wenzel, PhD
Department of Public Health

Cancer patients experiencing depression may have worse health outcomes than those who are not experiencing depression. However, screening and referrals for depression in the oncology setting are uneven, and not adequately addressed. The purpose of this pilot project is to assess, via oncology team surveys, the current clinical climate among providers with respect to depression screening and referrals at UCI and UCSF. The results will inform our capacity to develop and test an efficient and novel mechanism to screen for depressive spectrum disorders among cancer patients, thereby ultimately improving cancer-related outcomes.

The Relationship between the Gut Microbiome and the Efficacy of Immune Checkpoint Inhibitors in Patients with Gynecologic Malignancy

Investigator
Krishnansu Tewari, MD
Division of Gynecologic Oncology

Immune checkpoint inhibitors (ICI) are a new type of cancer therapy that enhance the ability of the immune system to recognize and attack cancer cells. Despite the recent widespread usage of ICI therapy, a majority of patients still do not respond to this therapy. One reason for poor response may be differences in the gut microbiome, which is the unique set of bacteria and other microorganisms that colonize our intestines. Studies have shown that the gut microbiome is closely related to overall immune system function and that changes in immune system function can impact the effectiveness of ICI. The goal of this study is to study the gut microbiome in patients with gynecologic cancers being treated with ICI to identify which bacteria may be associated with better responses to therapy.

THANK YOU FOR BEING PART OF THE ANTI-CANCER CHALLENGE.