2019 IMPACT: LEADING THE CHARGE

BRILLIANT FUTURE
THE CAMPAIGN FOR UCI
Thanks to you, June 8, 2019 was a banner day in the charge against cancer. You numbered more than 3,000 strong. Collectively, you rode, ran and walked thousands of miles for the UCI Anti-Cancer Challenge — all moving in one direction: to raise awareness and funds for breakthrough cancer research.

Determined to stop at nothing, you generated an event-record $635,000 for basic laboratory and clinical research at the UCI Chao Family Comprehensive Cancer Center. Generous community-minded sponsors offset event costs so that every dollar you raised went to life-saving cancer research at Orange County’s only National Cancer Institute-designated Comprehensive Cancer Center.

When all was said and done, your contributions funded 15 promising projects, each one described in this report.

Where the end of cancer begins
The Chao Family Comprehensive Cancer Center, home to the research you funded, is one of only 51 NCI comprehensive cancer centers in the nation.

We are recognized as a national leader in moving research discoveries, treatments and information from research laboratories to benefit cancer patients and their families, healthcare professionals and others in locally and beyond.

Your participation in the third annual Anti-Cancer Challenge advanced the cancer center’s research mission by helping to:

- 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.

- Advance the discoveries of UCI scientists, including innovative diagnostic devices, novel drugs and biobehavioral interventions through translational research aimed at finding clinical applications.

- Support shared infrastructure and sustain promising research not funded by grants, including the vital work of cancer center researchers who field Anti-Cancer Challenge teams.
WITH YOUR HELP, THERE IS HOPE

Every dollar you contributed to the 2019 UCI Anti-Cancer Challenge helped to fund more grants — and more opportunities to change what it means to be diagnosed with cancer. A grant gives an investigator much-needed time and resources to validate an innovative study concept or maintain momentum on a high-impact clinical trial, often while they pursue larger awards from external sources. In fact, several recipients from the inaugural Anti-Cancer Challenge successfully leveraged their grants to obtain an additional $7 million from other sources, funding progress on their work that might not otherwise have been possible.

Thanks to you, proceeds from the 2019 Anti-Cancer Challenge funded 15 proposals. You have supported a total of 43 exceptional projects since the inaugural event in 2017. Each investigation represents an opportunity to yield important insights that could improve the quality of life for people living with cancer — maybe someone you know — and, perhaps, ultimately lead to the defeat of cancer.
**TRACK 1: PILOT PROJECT AWARDS**

Track 1 awards are for basic and translational pilot project proposals, with an endpoint of a competitive, peer-reviewed extramural grant application. With these awards, researchers seek to understand how cancer cells differ from normal cells and answer the questions of how cancer cells develop, grow and spread. As promising molecules, gene targets or biomarkers are discovered, the goal is to move them from the laboratory bench into clinical studies — Anti-Cancer Challenge track 2 projects — for further testing as potential therapies for cancer treatment.

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**BASIC & TRANSLATIONAL RESEARCH**

Cancer Center researchers collaborate to perform basic cancer research to understand how cancer cells differ from normal cells and to provide answers on how cancer cells develop, grow and spread.

Through this work, promising molecules, gene targets or biomarkers are discovered, which then move to translational research for further testing of potential drugs for cancer treatment.

Target cells or tissues are first tested in vitro (meaning “in glass”) and then in vivo (“in living organisms”) to collect information about the drug works.

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**CLINICAL RESEARCH**

Promising drugs are filed with the Food and Drug Administration before entering a clinical trial to be tested on cancer patients.

Before a clinical trial can begin at UCI, it is rigorously reviewed at several levels including:

- Multidisciplinary teams of doctors, surgeons, and scientists, called Disease-Oriented Teams (DOTs), ensure trials are of high scientific quality and importance.

- Institutional Review Board assures the safety and welfare of participants are protected.
Melanoma Screening and Staging with a Fiber-optic Device

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Melanoma is one of the most difficult skin diseases to diagnose and it progresses quickly. A compact and inexpensive fiber-optic device, equipped with a flexible probe that allows examination of difficult-to-access regions of the skin, could help to reduce misdiagnosis of melanoma, the most aggressive and deadliest form of skin cancer. Once developed and tested, the proposed device would bring high-end optical screening methods to the patient to increase diagnosis accuracy, reduce time-to-result and cost, and help to avoid unnecessary surgery.

Novel Inhibitors of Phosphoinositide 3-Kinase (PI3K) That Target Scaffold Protein-mediated Interactions

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A potent, cancer-causing gene known as PIK3CA, is one of the most frequently mutated genes in human cancer. The strategy of this basic science investigation is to interfere with the cellular location of the cancer-causing PIK3CA molecules, rather than inhibit the activity of all PIK3CA molecules in the cell. In this way, it may be possible to maintain efficacy, while limiting toxicity. Another goal is to develop new drug leads for targeting PIK3CA in this novel fashion.
Factors Associated with Helicobacter Pylori Screening and Treatment among High-Risk Asians in Orange County: Mixed-Methods Research to Examine Stomach Cancer Disparity

INVESTIGATOR

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Asians have unusually high incidence and mortality of stomach cancer, and helicobacter pylori (H. pylori) infection is known to be one of the strongest risk factors for stomach cancer. This study examines factors associated with H. pylori screening and treatment in the high-risk Asian population in Orange County. Findings from the study will be used to design a randomized, controlled study to increase H.pylori screening and treatment and, ultimately, reduce the burden of stomach cancer in the high-risk Asian population.

Clock-dependent Inflammatory and Metabolic Alterations in Colorectal Cancer

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The internal biological clock controls sleep/wake cycles, feeding and metabolism. Disruption of the clock has been reported in several cancer types, including colon cancer. The precise process of clock disruption in colon cancer remains undefined. This research explores how the disruption can promote colon cancer by changing the cues that direct cancer-initiating cells. The goal is to identify new directions to pursue in the search for effective colon cancer prevention strategies that may involve alleviating disruption of circadian rhythms.
The Burgeoning Cannabis Industry and Availability of Cheap Tobacco in Orange County

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Smoking is linked to about 80 percent of lung cancer deaths. This project seeks to assess whether the availability and marketing of tobacco products such as cigarillos, blunt wraps and cigar wraps, which are popular among cannabis users, increased as a result of the legalized sales of cannabis for recreational use. The first aim is to assess whether Orange County tobacco retailers, who did not sell these tobacco products in 2016, began to carry them when nearby dispensaries started selling cannabis for recreational use. The second aim is to collect cannabis-themed marketing data from the same tobacco retailers. If the tobacco retailers near cannabis dispensaries now market cigarillos and blunt/cigar wraps with cannabis references, then findings from this project could inform authorities in Orange County about the need for advocating for tobacco regulations such as a minimum pack size for cigarillos.

Restoring p53 Activity in Human Cancer

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P53 is the most frequently mutated protein in human cancers. Each year, in the US alone, about 600,000 new cancer patients are diagnosed with tumors carrying p53 cancer mutants, which are particularly aggressive and hard to treat. High percentages of ovarian cancers, triple negative breast cancers, pancreatic cancers and lung cancers depend on p53 hotspot mutations. Thus, p53 cancer mutations present an exceptionally attractive therapeutic target. This project seeks to advance approaches to pharmaceutical reactivation of the body’s own anti-tumor mechanism, the tumor suppressor protein p53. Pharmaceutical reactivation of mutant p53 in cancer could be truly transformative.
Dissecting MAP4K Kinases in Cancer Development and Therapy

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Cancer cells are prone to survive when exposed to extremely stressful conditions including nutrient deprivation, hypoxia, oxidative stress and chemotherapy. Cancer cells are able to take advantage of a physiological process known as autophagy to get around these stresses and fulfill the high metabolic and energetic demands of cell proliferation. Targeting autophagy in advanced cancers shows promising anti-cancer effects; therefore, elucidating the regulation of autophagy can lead to the development of novel therapeutic strategies for cancers. In this pilot project, we dissect a novel metabolic stress signaling that is centered on MAP4K2 and perform a translational study by taking the MAP4K2-autophagy signaling as a target in cancer therapy.

Developing the Next-Generation Antibody Drug Conjugates

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Antibody-drug conjugates (ADCs) leverage the high specificity of an antibody to act as a molecular global positioning system combined with the potent anti-cancer activity of an attached cytotoxic drug. Highly effective in the clinic against several cancers, ADCs are valued for their favorable safety profiles in comparison to traditional chemotherapy. However, conventional methods for synthesizing ADCs result in random attachments of drug to antibody, reducing the ADCs’ medicinal properties. This project explores a new chemical reaction to more selectively and effectively install drugs on antibody surfaces. The project also aims to create a new class of multi-functional ADCs carrying several small molecules to tumors for simultaneous imaging and treatment, an approach sometimes termed theranostics.
**TRACK 2: EARLY-PHASE CLINICAL TRIAL AWARDS**

Track 2 awards are for early-phase clinical research projects that serve to determine whether new treatments do what they are expected to do, assess their safety and potential side effects, or evaluate whether they work. The goal is to move these projects into interventional, investigator-initiated treatment trials.

**PHASES OF CLINICAL TRIALS**

**PRECLINICAL PHASE**
- Phase 0 studies are exploratory studies that often use only a few small doses of a new drug in a few patients.
  - Tested in a small group of volunteers: less than 15
  - Find out if the drugs do what they are expected to do
  - How the drugs are absorbed or acts in the body

**PHASE 1**
- Phase 1 trials find the best dose of a new treatment with the fewest side effects.
  - Tested in a small group of volunteers: 15 to 20
  - Designed to decide how a new treatment should be given
  - To see how the new treatment affects the human body and fights cancer
  - Can take several months to complete

**PHASE 2**
- Phase 2 trials continue evaluating safety.
  - Tested in larger groups of volunteers: 25 to 100
  - Designed to determine if a drug or treatment has an effect on a certain cancer
  - Can take about two years to complete

**PHASE 3**
- Phase 3 trials compare a new drug or treatment to standard-of-care.
  - Tested in a much larger group of volunteers: 100s to several 1000
  - Trials assess the side effects of each drug or treatment and evaluate which works better
  - Patients are randomly assigned to receive either the new treatment or the best existing treatment
  - Volunteers are followed for several years

**PHASE 4**
- Phase 4 trials, the final phase, asks new questions about standard treatments.
  - Begins after a drug or treatment is approved by the FDA and made available to the public
  - Trials evaluate the long-term benefits, side effects and how well the drug works when used more widely
  - Data collected on the drug or treatment’s risks, benefits and optimal uses

**Phase 1-3: 10-15 years**
This project combines standard liver-directed therapy using TACE (transarterial chemoembolization) with a novel combination of dual-immunotherapy drugs (nivolumab and ipilimumab), plus a small molecule inhibitor (cabozantinib). This disrupts vital survival pathways in liver cancer cells and their surrounding stroma (non-cancerous cells that actively support the growth of cancer cells by providing nutrition and suppressing the body’s immune system).

This study represents a powerful multipronged approach to attacking liver cancer from multiple angles, with the goal being to minimize resistance and thus maximize tumor shrinkage and long-term survival. The results could establish a new liver cancer treatment option with unprecedented efficacy.

Cancers of the liver are relatively rare in the U.S. Nonetheless, due to their deadly nature, they are among the top five causes of cancer-related deaths in the U.S. When liver tumors grow to more than one to two inches, or when there are more than three tumors in the liver, surgery or transplant is no longer possible. At this point, the goal of treatment is to prolong survival.

Historically, local liver-directed treatment was the only available standard offering some tumor control. Most cancers recurred in less than a year.

Advanced liver cancer has a survival of about 10 to 12 months, despite all the new drug developments. Improving patient survival means identifying effective treatment at an earlier stage, before the cancer recurs and spreads beyond the liver.
A Randomized Clinical Trial to Assess the Impact of a Remotely Administered Mediterranean Diet Intervention on Symptom Burden and Inflammatory Cytokines in Myeloproliferative Neoplasm

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Myeloproliferative neoplasm (MPN) is an incurable blood cancer, with severe symptoms that are driven by inflammation. A Mediterranean diet reduces inflammation in other diseases, but hasn’t been studied in blood cancers. This is a large, internet-based study to test whether a Mediterranean diet reduces symptoms and inflammation in MPN patients.

Goal-directed Intervention for Adolescent Cancer Survivors

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Having cancer can disrupt an adolescent’s ability to identify and accomplish life goals. Evidence consistently shows that adult survivors of childhood cancer have lower educational and occupational achievement than their peers. A previously developed intervention known as Goal-focused Emotion-regulation Therapy (GET) was designed to help young adult cancer survivors pursue goals following cancer treatment. This intervention is being adapted for the adolescent cancer population to improve their emotional, physical, educational and occupational functioning after completing cancer treatment.
Pilot Study for Evaluating the Multiphoton Microscopy Potential for Non-invasive, Early Diagnosis of Melanoma

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This pilot project evaluates the potential of an optical imaging technology for non-invasive diagnosis of melanoma. The instrument used in this study was developed at the UCI Beckman Laser Institute & Medical Clinic. It enables rapid acquisition of images with sub-cellular resolution from unprecedented large volumes of lesions. This study is intended to provide key preliminary data that would strengthen an application for funding a clinical trial to evaluate whether the imaging technology can diagnose melanoma more accurately by detecting it early and also reduce the number of unnecessary biopsies.

Neoadjuvant Combination Therapy with Cabozantinib and Nivolumab in Patients with Muscle-invasive Urothelial Carcinoma of the Bladder Who Are Cisplatin-eligible and Are Candidates for Radical Cystectomy

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Standard-of-care treatment for non-metastatic bladder cancer consists of up-front chemotherapy, followed by surgical removal of the bladder, or cystectomy. Due to multiple possible side effects of chemotherapy, and in an effort to improve treatment effectiveness, multiple studies replacing chemotherapy with alternative treatments are underway. This is a study of the use of cabozantinib and nivolumab in patients with non-metastatic bladder cancer, with treatment administered for 12 weeks prior to cystectomy. The study examines the efficacy and safety of this drug combination, as well as analyze the genetic and molecular characteristics of tumors from participating patients.
Feasibility of a Biobehavioral Intervention to Reduce Adverse Outcomes in Young Adult Hispanic Men with Testicular Cancer

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Many young adult cancer survivors experience adverse outcomes that persist long after completion of primary medical treatment. These outcomes might include psychological distress and poor psychosocial adjustment, impaired ability to navigate and pursue life goals, persistent treatment side effects, elevated risk of secondary malignancies and chronic illness, or biobehavioral burdens such as enhanced inflammation or dysregulated diurnal stress hormones. Hispanic/Latino young men are at heightened risk for such adverse outcomes. Yet few targeted, culturally tailored interventions exist to help this group renegotiate life goals and regulate cancer-related emotions. None focus on reducing the burden of morbidity via biobehavioral mechanisms.

This study explores the feasibility of Goal-focused Emotion Regulation Therapy (GET) to improve depressive symptoms as well as emotion regulation, goal attainment skills, and career confusion in Hispanic/Latino young adult testicular cancer patients. It is designed to assess whether GET is associated with reductions in biological markers of stress and inflammation. And it looks at whether cultural processes (i.e., familism, simpatia, machismo/caballerismo, acculturation/acculturative stress) underlie change.

Pilot Study of the Safety and Feasibility of Immediate Postoperative Chemotherapy in Patients with Metastatic Invasive Colonic Adenocarcinoma

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Many metastatic colon cancer patients choose not to have their tumor removed because they fear the risks of stopping chemotherapy for surgery. This can lead to major complications with the colon tumor; complications that may lead to the same thing they fear the inability to receive chemotherapy. This study explores a protocol that allows the tumor to be safely removed without delaying chemotherapy. It allows for the administration of systemic treatments at the time of tumor resection. The hypothesis is that this will eliminate chemotherapy delays and tumor complications, ultimately leading to improved cancer survival.
Thank you for leading the charge to defeat cancer.