

INVESTING IN A CANCER-FREE WORLD 2014

Putting Pelotonia Dollars to Work



The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER



IT'S GREAT TO KNOW THAT, AFTER SIX YEARS, PELOTONIA IS STILL ON A ROLL.

2014 yielded yet another ridership record for this annual grassroots bicycle tour that raises millions of dollars for cancer research at Ohio State.

The Pelotonia 14 tour consisted of 276 registered pelotons (riding groups) that collectively contained 7,270 riders from 41 states and five countries. It also benefited from more than 3,600 virtual riders and 2,617 volunteers.

In its first five years (2009-13), Pelotonia raised more than \$61 million. On Nov. 13, we learned that Pelotonia 14 generated \$21,049,621, bringing the overall six-year total to more than \$82.34 million – demonstrating once again the community's resolve to take a serious stand against a disease that touches almost everyone.

And thanks to the event's generous sponsors, every cent raised by riders, virtual riders and donors will go directly to groundbreaking research that translates to innovative patient care at Ohio State's Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James).

Without fundraising efforts such as Pelotonia – which has become the nation's largest single-event cycling fundraiser based on ridership – many innovative ideas for cancer research would go nowhere and the field would languish, since government grants are increasingly difficult to obtain.

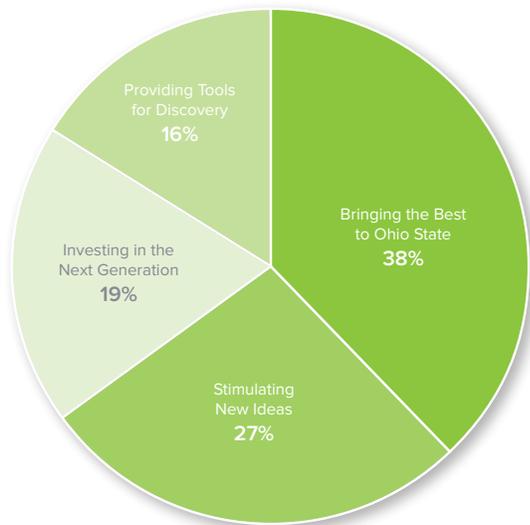
This investment report will briefly summarize (on the facing page) how Pelotonia funds have been distributed over the event's first five years. Then it will offer looks at our Pelotonia Fellowship Program for student researchers, our Idea Grant allocations of the past year to teams of faculty scientists, our most recent equipment purchase with Pelotonia support, published findings from selected Pelotonia-supported studies, and a few of the brilliant scientists whom Pelotonia dollars have helped us recruit to the OSUCCC – James.

We should all be proud of what we are accomplishing together. On behalf of faculty and staff at the OSUCCC – James, I thank everyone associated with Pelotonia for helping us move closer to realizing our shared vision of a cancer-free world. Here's hoping I'll see you all again on next year's ride.

Michael A. Caligiuri, MD
Director, The Ohio State University Comprehensive Cancer Center
CEO, James Cancer Hospital and Solove Research Institute
John L. Marakas Nationwide Insurance Enterprise Foundation Chair in
Cancer Research

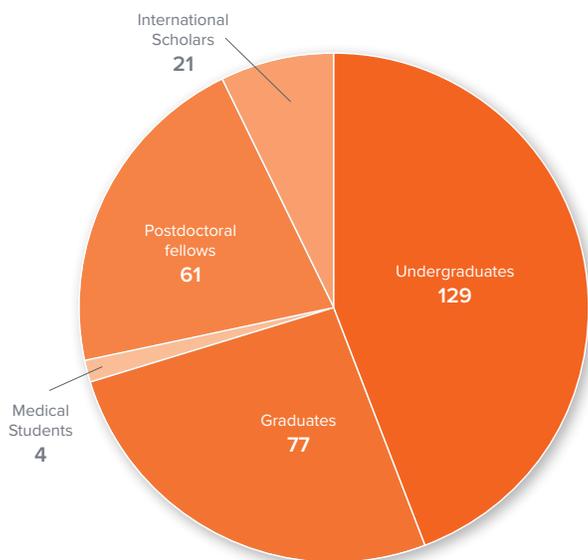
Five-Year Pelotonia Financial Summary

Allocations of Funding From Pelotonia 2009-2013



Pelotonia, the annual grassroots bicycle tour established in 2009 to raise money for cancer research at the OSUCCC – James, generated more than \$61 million in its first five years through rider pledges and donations. Thanks to the generous underwriters of the event, every dollar raised by riders, virtual riders and donors since Pelotonia began has been used to advance cancer research, as shown in the chart to the left.

Fellowship Grants Awarded



Investing in the Next Generation: Pelotonia Fellowship Program

To date, the Pelotonia Fellowship Program has awarded more than \$9 million in cancer research funding for Ohio State students in multiple disciplines and at all levels of scholarship – undergraduate, graduate, medical and postdoctoral fellow – for their work in the labs of faculty mentors.

Bringing All Knowledge to Bear in the Fight Against Cancer

Pelotonia research funding has been allocated to investigators in multiple colleges at Ohio State, as well as at Nationwide Children’s Hospital in Columbus and Cincinnati Children’s Hospital Medical Center:

- College of Public Health
- College of Medicine
- College of Law
- College of Nursing
- College of Pharmacy
- College of Food, Agricultural and Environmental Sciences
- College of Engineering
- College of Veterinary Medicine
- College of Education and Human Ecology
- College of Dentistry
- College of Arts and Sciences
- Nationwide Children’s Hospital
- Cincinnati Children’s Hospital Medical Center

Pelotonia Fellowship Program Overview

Students from any discipline and level of scholarship at Ohio State who have the potential to become independent cancer researchers can receive funded training in the labs of faculty mentors through the Pelotonia Fellowship Program.

Since the program began in 2010, it has received \$9 million in Pelotonia funds to support the award of 292 student fellowship grants to 129 undergraduates, 77 graduates, four medical students, 61 postdoctoral fellows and 21 international scholars.

Most recently, from October 2013-October 2014, the program awarded 65 fellowships to students, including 36 undergraduates, 18 graduates and 11 postdoctoral fellows.

A 43-member Pelotonia Fellowship Committee containing some of Ohio State's most distinguished cancer researchers reviews all fellowship applications and issues the awards. The committee is chaired by Fellowship Program Director **Gustavo Leone, PhD**, associate director for basic research at Ohio State's Comprehensive Cancer Center – James Cancer

Hospital and Solove Research Institute (OSUCCC – James). **Janice Kiecolt-Glaser, PhD**, a Distinguished University Professor in the Department of Psychiatry and Behavioral Health, and a member of the Cancer Control Program at the OSUCCC – James, is co-chair.

Leone says fellowship award decisions are based on quality of applications rather than on a set number to be issued each year. "The program is truly multidisciplinary," he adds. "We have awarded fellowships to students working with mentors in 10 colleges and 48 departments at Ohio State, and from applicants at Nationwide Children's Hospital and Cincinnati Children's Hospital."

The Fellowship Program website (<http://go.osu.edu/pelotoniafellowships>) includes photos of all funded fellows, titles of their projects, their mentor(s), a brief lay summary and a one-paragraph lay abstract describing their work. It also lists members of the Fellowship Committee. In addition, several videos have been produced of the fellows explaining their projects and telling what their funding means to them. These videos can be accessed from the funded fellows' Web page.





Post-Fellowship Highlights

After completing their cancer research, past Pelotonia Fellows have continued to achieve and make a difference. Their pursuits include:

- Medical degrees at Ohio State University
- Educational opportunities in other health-related areas at Ohio State, including graduate programs and postdoctoral fellows in the Comprehensive Cancer Center and the departments of Pathology, Molecular Genetics, Molecular and Cellular Biochemistry, Nutrition, Internal Medicine (divisions of Hematology and Medical Oncology), and Molecular Virology, Immunology and Medical Genetics, as well as in the College of Pharmacy.
- Advanced studies in the health sciences at Ohio State, Harvard, Stanford, Johns Hopkins, Kentucky, Case Western Reserve, Toledo, Michigan, Duke, Baylor, Ohio University, Pittsburgh, Northwestern, Texas, UCLA, MD Anderson Cancer Center, the National Cancer Institute (NCI) at the National Institutes of Health, and the Government of India Institute of Life Sciences, to name a few.
- Professional employment at Nationwide Children's Hospital, Cincinnati Children's Hospital Medical Center, Tufts University, University of California Helen Diller Family Comprehensive Cancer Center, Genentech, Medical University of South Carolina, University of Delaware, Ferris State University, University of Prince Edward Island (Canada), Birla Institute of Technology and Science (India), and Manchester Royal Infirmary Hospital (United Kingdom).



What's the Big Idea?

Pelotonia Grants Help Researchers Answer That Question

Twenty teams of faculty scientists received fiscal 2014 Pelotonia-funded “Idea Grants” that will enable them to develop innovative cancer research studies for which they may later seek large external grants. These “Idea Grants” – each worth \$100,000 over two years – are especially important at a time when government funding is hard to obtain for the early pursuit of promising studies. The grants were awarded by a scientific committee of internal and external reviewers. Chaired by the OSUCCC associate directors, the committee considered the scientific merit of applications submitted by the research teams. Here are the fiscal 2014 “Idea Grants”:

DELIVERING AN AML DRUG IN NANO-SIZED ‘FAT BUBBLES’

(Principal investigators [PIs]: Robert Lee, PhD, and Andrienne Dorrance, PhD)

The drug bortezomib has potential to help patients with acute myeloid leukemia (AML), but the drug is only weakly effective in its current form. Researchers will develop a delivery system by packing the drug into nano-sized bubbles of fat and attaching them to a homing device that seeks out leukemia cells. Study data will determine whether this approach is suitable for testing in humans.

SOCIAL ISOLATION'S ROLE IN BREAST CANCER DEVELOPMENT AND PROGRESSION

(PIs: Courtney DeVries, PhD; Maryam Lustberg, MD; Cynthia Timmers, PhD)

Studies show that women with breast cancer who are socially isolated have worse outcomes. This team will examine whether loneliness and isolation alter cancer-related gene activity in breast tissue. This information could reveal new diagnostic, therapeutic and prognostic tools for breast cancer prevention and treatment.

MENTAL HEALTH, STRESS AND THE RESPONSE TO CANCER TREATMENT

(PIs: Amy Johnson, PhD, and Barbara Andersen, PhD)

This project will assess stress, depression and quality of life in patients with chronic lymphocytic leukemia who are treated with ibrutinib, a drug that has been studied extensively in clinical trials at the OSUCCC – James. Examining the relationship between cancer growth factors and psychological function may help doctors make treatment decisions by identifying patients at risk for poor outcomes.



Thank You
for helping to create a
cancer-free world

The James
The Ohio State University
Comprehensive Cancer Center

BIOMARKER-BASED 2-DRUG THERAPY FOR ACUTE MYELOID LEUKEMIA

(PI: Alison Walker, MD)

Overall survival is low for pediatric and adult patients with acute myeloid leukemia (AML) on standard chemotherapy, but this phase I clinical trial will test a two-drug approach that could significantly increase remission in AML patients. The drugs involved are AR-42, which was developed at Ohio State, and decitabine. This strategy may help more AML patients achieve complete remission (see related story, page 14).

STUDYING HEALTH DISPARITIES IN 100,000 UNDERSERVED IN AMERICA

(PIs: Electra Paskett, PhD, MSPH; Peter Shields, MD; Mira Katz, PhD; Paul Reiter, PhD; Eric Seiber, PhD; Mike Pennell, PhD)

A Pelotonia Idea Grant will support a project that aims to establish a cohort of 100,000 underserved people from four U.S. populations – African-American, Appalachian, Asian and Hispanic – to better understand the causes of cancer disparities in the United States. The grant will help with recruiting study participants and with forming a coordinating center to collect and analyze data and biospecimens from the OSUCCC – James network of collaborating recruitment sites.

TARGETING ONCOGENES FOR NEW LIVER CANCER DRUGS

(PI: Kalpana Ghoshal, PhD)

Developing drugs that can penetrate the liver and target cancerous cells has been challenging. Researchers in this study will conduct preclinical tests to determine the effectiveness of new drugs that target two oncogenes and a tumor-suppressing microRNA called miR-122 that is critical for normal liver function. Study results could lead to a phase I clinical trial for liver cancer patients.

UNDERSTANDING MOLECULAR CROSSTALK DRIVING AGGRESSIVE BREAST CANCER

(PI: Ramesh Ganju, PhD)

Having a better understanding of molecular pathways that contribute to cancer could help scientists identify points in the pathways to intervene and curb cancer development. This project will further characterize the role of proteins in two targeted pathways to shed light on breast cancer growth, blood vessel formation and tumor spread.

BRAIN INFLAMMATION, DEPRESSION AND ANXIETY IN BREAST CANCER PATIENTS

(PIs: Courtney DeVries, PhD, and Maryam Lustberg, MD)

Inflammatory changes in the brain could be a primary cause of depression and anxiety commonly experienced by breast cancer survivors, particularly when undergoing chemotherapy. This team will study whether reducing brain inflammation using a well-tolerated drug called minocycline reduces depression and anxiety during chemotherapy.

DIGITAL IMAGE ANALYSIS, TARGETED THERAPIES FOR GLIOBLASTOMA

(PIs: Metin Gurcan, PhD; Jose Otero, MD, PhD; Brad Elder, MD; Vinay Puduvalli, MD; Jessica Winter, PhD)

Despite aggressive treatment, patients with glioblastoma, the most common and deadly of primary brain tumors, live an average of only 15 months. This team is developing advanced image analysis techniques to help guide decisions in patient treatment before and after brain surgery. This technology could guide personalized treatment based on the molecular characteristics of each tumor via unbiased quantitation of signal transduction cascades in tumor cells.

TACKLING TREATMENT-RESISTANT PROSTATE CANCER

(PIs: Qianben Wang, PhD; Steven Clinton, MD, PhD)

When prostate cancer returns after surgery and initial androgen-deprivation therapy, it often no longer responds to drug treatment. For this study, OSUCCC – James researchers will identify genes that castration-resistant prostate tumors need to grow and that could be new targets for prostate cancer drugs. The findings may lead to new treatments for prostate tumors that currently have no effective therapy.

PREPARING FOR RESISTANCE

(PI: Sameek Roychowdhury, MD, PhD)

OSUCCC – James researchers have designed a phase II clinical trial to test a drug called ponatinib that inhibits certain genes that drive cancer. Anticipating that cancer cells may develop resistance to ponatinib in this trial, this team will collect biopsy samples from each participant's tumor before and after treatment, then sequence 20,000 genes in each sample and look for gene changes that could lead to drug resistance.

A PLANT COMPONENT THAT MIGHT HELP IMMUNE CELLS CONTROL CANCER

(PI: Jianhua Yu, PhD)

Can a substance from edible plants boost the cancer-cell killing activity of a type of immune cell? This study will investigate the ability of a substance called phyllanthusin C (PL-C) to stimulate the activity of natural killer (NK) cells. The researchers hope to show that PL-C in the diet will help NK cells control acute myeloid leukemia and other cancers.

PROBING A NEW TARGET IN TRIPLE-NEGATIVE BREAST CANCER

(PIs: Robert Brueggemeier, PhD; Harold Fisk, PhD; Chenglong Li, PhD; Pui-Kai Li, PhD; Yasuro Sugimoto, PhD)

Triple-negative breast cancer (TNBC) is an aggressive disease defined by the absence of estrogen, progesterone and HER2 receptors. Without these molecules to target, the usual breast cancer drugs are ineffective for treating TNBC. This team will design and develop drugs that inhibit a molecule called Mps1/TTK as a promising treatment for TNBC and other aggressive breast cancers.

A NEW APPROACH TO CERVICAL-CANCER PREVENTION

(PIs: Paul Reiter, PhD, MPH; Mira Katz, PhD, MPH)

Several types of human papillomavirus (HPV) cause cervical cancer, but the disease is largely preventable through regular screening. This team will develop a pilot program for HPV self-testing among women in Appalachia who have undergone little if any cervical cancer screening. Results will identify the best strategy for improving cervical cancer screening among this population.

PERSONALIZING MULTIPLE MYELOMA TREATMENT

(PI: Mitch Phelps, PhD; Ming Poi, PharmD, PhD; Craig Hofmeister, MD)

A treatment using stem cell transplantation plus high doses of a drug called melphalan often prolongs the lives of patients with multiple myeloma (MM) and stops disease progression, but patients have variable side effects and response. This team is developing a procedure to personalize dosing of melphalan to improve its effectiveness in killing MM cells while minimizing the drug's harsh side effects.

A WEARABLE GUIDANCE SYSTEM FOR BETTER CANCER SURGERY

(PIs: Ronald Xu, PhD; Michael Tweedle, PhD; Alper Yilmaz, PhD)

Tools that could help surgeons determine where a tumor ends and healthy tissue begins, and that could help detect hidden cancer cells, could greatly reduce cancer recurrence rates and improve long-term outcomes of patients after cancer surgery. This project will help develop and test a guidance system worn during surgery to identify surgical margins and guide the removal of tumors.

INCREASING INSIGHT INTO CHEMOTHERAPY SIDE EFFECTS

(PI: Kristen Carpenter, PhD)

Pelotonia funds will support a clinical trial to learn if there is a correlation between chemotherapy treatment and side effects that include fatigue, nausea, vomiting, sensory neuropathy, pain, depression and insomnia. It will investigate whether individual differences in psychological/behavioral variables, such as patient optimism and coping, might influence these side effects. Findings could provide insight into which patients might be most vulnerable to debilitating chemotherapy side effects and strategies that might alleviate them best.

REVERSING DRUG RESISTANCE IN OVARIAN CANCER

(PIs: Jeffrey Parvin, MD, PhD, and David Cohn, MD)

These investigators have found that a protein called histone deacetylase 10 (HDAC10) is part of a DNA repair system that may allow some ovarian cancer cells to survive chemotherapy used to treat the disease. They will examine whether drugs called HDAC inhibitors will knock out the HDAC10-powered DNA repair system and knock out a pathway that makes ovarian cancers become drug resistant.

ARRESTING A GENE THAT MIGHT DRIVE ESOPHAGEAL CANCER

(PIs: Zui Pan, PhD; Tong Chen, MD, PhD)

This team hypothesizes that the hyperactive *Orai1* gene causes abnormal changes in calcium levels in cells and contributes to esophageal cancer progression. They also believe that inhibiting the over-activity of this gene could help control the disease. They will conduct experiments to reveal more about the role of *Orai1* in esophageal cancer, the sixth-leading cause of cancer death worldwide.

TARGETING TWO GENES MIGHT IMPROVE MELANOMA TREATMENT

(PIs: William Carson III, MD; Albert de la Chapelle, MD, PhD; Ann-Kathrin Eisfeld, MD)

About 40 percent of all patients with melanoma, the deadliest form of skin cancer, have a mutation in a gene called *BRAF*. This team will investigate *BRAF*-mutated melanoma and the role of a gene called *microRNA-3151*. Their project will explore the mechanism of *microRNA-3151* and evaluate whether *BRAF*-inhibiting drugs might more effectively treat melanoma when combined with drugs that inhibit *miR-3151*.

Providing Tools for Discovery

The OSUCCC – James has contributed Pelotonia dollars to an Ohio State and state of Ohio investment in a significant upgrade and expansion of nuclear magnetic resonance (NMR) capabilities on Ohio State’s main campus.

Vicki Wysocki, PhD, an Ohio Eminent Scholar in the Department of Chemistry and Biochemistry in Ohio State’s College of Arts and Sciences, says several state-of-the-art instruments for measurements in both solution and solids were purchased and outfitted with a broad range of capabilities, including high-field superconducting magnets, cryogenically cooled measurement probes to optimize sensitivity, and sample robots for high-throughput applications.

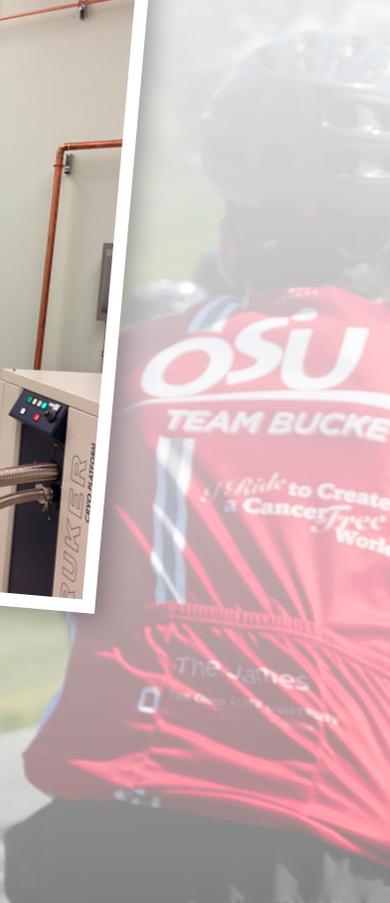
“These capabilities are invaluable to cancer researchers at OSU as they will allow them to show the characterization at atomic detail of the structure and conformational dynamics of onco-proteins, their binding to small drugs and potential drug candidates, and the signature of changes in metabolic profiles in cancer during disease and treatment,” adds **Rafael Bruschweiler, PhD**, an Ohio Research Scholar with joint appointments in the Department of Chemistry and Biochemistry and in the College of Medicine at Ohio State.

Many of the new instruments are housed in Ohio State’s Campus Chemical Instrument Center (CCIC), which was founded in 1981 as a unit of the OSU Office of Research to provide research facilities for the entire campus in three areas: nuclear magnetic resonance, mass spectrometry and proteomics, and macromolecular X-ray crystallography.

“The CCIC is an interdisciplinary unit, servicing faculty from the colleges of Arts and Sciences; Education and Human Ecology; Engineering; Food, Agricultural and Environmental Sciences; Medicine; Optometry; Pharmacy; Veterinary Medicine; and Ohio State’s Comprehensive Cancer Center, to name a few,” Wysocki says.

She notes that the CCIC also is a hub for the Ohio NMR and Ohio MS Consortiums, providing researchers in colleges and universities throughout Ohio with access to all of the center’s facilities with on-campus user fees.

“In NMR, the existing 600 and 800 MHz instruments in the Riffe Building have recently been upgraded with new consoles, and a 700 MHz instrument has been installed in the same location as part of the overall upgrade,” Wysocki says, adding that installation of an 850 MHz instrument has begun in the new Chemical and Biomedical Engineering and Chemistry building, a second location of CCIC NMR. “That instrument will be joined by several other new instruments in the coming months.”



From Ideas to Impact

Pelotonia's impact is perhaps most obvious in discoveries made and published in scientific journals by teams of researchers who have received Pelotonia support over the past few years. Some examples:



Craig Hofmeister, MD, MPH

Form of Immune Therapy Might Be Effective for Multiple Myeloma

A study by researchers at the OSUCCC – James provided evidence that genetically modifying immune cells may effectively treat multiple myeloma, a disease that will account for an estimated 24,000 new cases and 11,100 deaths in 2014. The researchers, supported by a Pelotonia Idea Grant, modified a type of human immune cell called T cells to target a molecule called CS1, which is found on more than 95 percent of myeloma cells, and to kill those cells. They grew the modified cells in the lab to increase their numbers and injected them into an animal model, where they again killed human myeloma cells. The findings were published in

the journal *Clinical Cancer Research*.

“Despite current drugs and use of bone marrow transplantation, multiple myeloma is still incurable, and almost all patients eventually relapse,” says co-principal investigator **Craig Hofmeister, MD, MPH**. “This study presents a novel strategy for treating multiple myeloma, and we hope to bring it to patients as part of a phase I clinical trial as soon as possible.” Principal Investigator **Jianhua Yu, PhD**, says the study “shows that we can modify T cells to target CS1, and that these cells efficiently destroy human multiple myeloma cells.” Yu notes that these therapeutic T cells have the potential to replicate in the body and therefore might suppress tumor growth and prevent relapse for a prolonged period.



Jianhua Yu, PhD

From Ideas to Impact continued on page 12





Clara D. Bloomfield, MD



Albert de la Chapelle, MD, PhD



Ann-Kathrin Eisfeld, MD

AML Score That Combines Genetic and Epigenetic Changes May Help Guide Therapy

Currently, doctors use chromosome markers and gene mutations to determine the best treatment for patients with acute myeloid leukemia (AML). But a study at the OSUCCC – James suggests that a score based on seven mutated genes and the epigenetic changes that the researchers discovered were present might help guide treatment by identifying novel subsets of patients. The findings, published in the *Journal of Clinical Oncology*, come from a study supported in part by funds from the Pelotonia Fellowship Program. Overall, the findings suggest that patients with a low score – indicating that one or none of the seven genes is overexpressed (too active) in AML cells – had the best outcomes, and that patients with high scores – that is, with six or seven genes highly expressed – had the poorest outcomes. “To date, disease classification and prognostication for AML patients have been based largely on chromosomal and genetic markers,” says principal investigator **Clara D. Bloomfield, MD**, a Distinguished University Professor at Ohio State and senior adviser to the OSUCCC – James. “Epigenetic changes that affect gene expression have not been considered. Here, we show that epigenetic changes in previously recognized and prognostically important mutated genes can identify novel patient subgroups, which might better help guide therapy.” Guido Marcucci, MD, also of the OSUCCC – James, was first author for the study.

Cancer Gene *NRAS* Produces 5 Variants, Study Finds

A gene called *NRAS* that was discovered 30 years ago and is now known to play a fundamental role in cancer development produces five gene variants (called isoforms) rather than just the original form, a study at the OSUCCC – James showed. The study, supported by funds from the Pelotonia Fellowship Program and published in *Proceedings of the National Academy of Sciences of the USA*, identified four previously unknown variants that the *NRAS* gene produces. The finding might help improve drugs for cancers in which aberrant activation of *NRAS* plays a crucial role. “We believe the existence of these isoforms may be one reason why *NRAS* inhibitors have so far been unsuccessful,” says corresponding author **Albert de la Chapelle, MD, PhD**, a Distinguished University Professor at Ohio State. Co-senior author **Clara D. Bloomfield, MD**, also a Distinguished University Professor at Ohio State, notes that one of the newly discovered isoforms might play a greater role in the development of some cancers than the known protein itself. “The discovery of these isoforms might open a new chapter in the study of *NRAS*,” says first author **Ann-Kathrin Eisfeld, MD**, a postdoctoral fellow in the laboratories of de la Chapelle and of Bloomfield. “Knowing that they exist may lead to the development of drugs that decrease or increase the expression of one of them and provide more effective treatment for selected cancer patients.”



Pelotonia Funds Support Development of Anticancer Agents by OSU Researchers



Timothy Wright



Bence Boelcskevy, PhD

In 2011, the OSUCCC – James collaborated with the colleges of Medicine, Pharmacy and Business in organizing The Ohio State University Drug Development Institute (DDI) to guide the development of promising anticancer drugs produced by OSUCCC – James researchers.

Timothy Wright, a former executive of several pharmaceutical companies, directs the institute in conjunction with **Bence Boelcskevy, PhD**, also a former pharmaceutical executive. They are fast-tracking promising compounds through the testing needed for use in clinical trials.

“The DDI is focused on solving important unmet needs in cancer and other diseases,” Wright says. “Our portfolio consists of novel mechanisms to address these unmet needs.” Currently, the institute is facilitating 15 projects involving seven novel anticancer agents within five areas of study that are supported by Pelotonia dollars:

PRMT5 Inhibitor

PRMT5, an enzyme that plays a vital role in cancer-cell growth, is highly expressed in lymphoma, acute leukemia and other hematologic malignancies, and in solid tumors, including head and neck, lung, melanoma and brain. OSUCCC – James researchers have developed a first-in-class PRMT5 inhibitor that they believe will stop tumor growth. The inhibitor is in preclinical testing. The DDI is also facilitating a parallel project with this inhibitor in multiple sclerosis, so the institute’s influence is expanding beyond oncology.

STAT3 Inhibitor

Tumor growth can be promoted or suppressed by signaling pathways in cancer cells, including STAT3. The tumor-suppressor role of STAT3 has been reported in human glioblastoma (brain cancer). Recent studies have shown that STAT3 also has an inhibiting role in colon cancer, depending on tumor stage. OSUCCC – James researchers are collaborating with Nationwide Children’s Hospital to define the STAT3 effects in sarcoma, and they are initiating a multi-pronged research program to study the effects of this inhibitor in melanoma, lung, pancreatic, breast and prostate cancer.

RAS Inhibitors

The National Cancer Institute (NCI) defines RAS as a family of genes that make proteins involved in cell signaling pathways, cell growth and cell death; members of the RAS family include KRAS, HRAS and NRAS. The NCI says these genes may cause cancer when they are mutated, but agents that block mutated RAS genes or their proteins may inhibit cancer growth. OSUCCC – James researchers have developed antibody-like agents that can inhibit KRAS, a protein implicated in 30 percent of all cancers.

Epstein-Barr Virus Vaccine

Epstein-Barr virus (EBV) is a common infection that causes mononucleosis. It is also associated with Hodgkin’s lymphoma, Burkitt’s lymphoma and other cancers; with conditions associated with HIV infection; and with autoimmune diseases. If EBV is in a blood stem cell or a donated solid organ, it can cause post-transplant lymphoproliferative disease (PTLD). This often-fatal complication can follow a stem-cell or organ transplant. Researchers at the OSUCCC – James are developing an EBV vaccine to prevent PTLD and help other EBV-related conditions.

Fenretinide Oral Patch (a Pharma Industry Partnership)

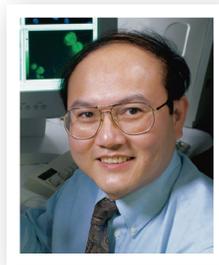
About 300,000 Americans annually develop precancerous lesions in the mouth that can progress to oral cancer, and nearly 36,000 people in the United States develop oral cancer yearly. These lesions are removed surgically, but they tend to recur. A team of OSUCCC – James researchers has developed a patch that adheres to the lesions and releases a promising anticancer drug called fenretinide to treat them. The patch could provide an alternative to surgery and reduce the incidence of oral cancer. With help from the DDI, Ohio State and a pharmaceutical firm called Venture Therapeutics have signed a co-development agreement and formed a company, Serona Therapeutics, that is incorporated to fully develop the fenretinide oral patch. Preclinical work is complete. An Institutional New Drug (IND) filing with the NCI and the start of clinical trials are projected for 2015.



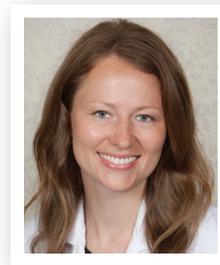
Balveen Kaur, PhD



Alison Walker, MD



Ching-Shih Chen, PhD



Erin Macrae, MD



Maryam Lustberg, MD

Generating New Hope Through Pelotonia-Funded Research

Pelotonia funds support cancer drug development projects at Ohio State. Here's a brief look at a basic-science study of a targeted agent that may improve cancer-killing virus therapy, and two clinical trials on novel drug combinations – one for patients with acute myeloid leukemia and the other for patients with triple-negative breast cancer.

Low Dose of Targeted Agent Could Improve Cancer-Killing Virus Therapy

Giving low doses of a particular targeted agent with a cancer-killing virus might improve the effectiveness of the virus in treating cancer. Viruses that are designed to kill cancer cells – called oncolytic viruses – have shown promise in clinical trials for the treatment of brain cancer and other solid tumors. This cell and animal study, led by principal investigator **Balveen Kaur, PhD**, and published in the journal *Clinical Cancer Research*, suggested that combining low doses of the drug bortezomib with a particular oncolytic virus might significantly improve the ability of the virus to kill cancer cells during oncolytic virus therapy.

Testing a 2-Drug Combination Against AML

Adult and pediatric patients with acute myeloid leukemia (AML) have a poor prognosis overall, but **Alison Walker, MD**, leads a phase I clinical trial for a two-drug combination that could significantly improve AML remission rates. Her team observed that patients with higher levels of a substance called miR-29b in their blood respond better to the chemotherapy drug decitabine than those with lower levels. Patients in this trial first receive a drug called AR-42, developed at

Ohio State by a team led by **Ching-Shih Chen, PhD**, to raise their miR-29b levels, followed by decitabine therapy. Researchers want to see whether this combination will help more patients achieve complete remission.

Targeting Triple-Negative Breast Cancer

OSUCCC – James researchers are investigating novel combinations of targeted agents for patients with triple-negative breast cancer (TNBC), an aggressive malignancy with a high rate of recurrence and poor prognosis. **Erin Macrae, MD**, is principal investigator for a phase II clinical trial in which patients with TNBC initially receive a drug called trametinib, followed by trametinib in combination with a drug called GSK2141795. The investigators hypothesize that these agents may stop the growth of tumor cells by blocking enzymes needed for the cells to grow. “By blocking these cancer-promoting pathways simultaneously, you have the potential to stop a cancer’s ability to become resistant to treatment,” says sub-investigator **Maryam Lustberg, MD**. Macrae notes that TNBC tumors fail to respond to targeted regimens currently available. “Our study explores a regimen that we hope will help these patients,” she says.

Bringing the Best to Ohio State

Pelotonia funds have been committed to recruiting or retaining some of the brightest minds in cancer research to Ohio State. Among those recruited with the help of Pelotonia dollars in 2014 are:



ROMAN SKORACKI, MD, FRCSC, FACS, professor in the College of Medicine, Department of Plastic Surgery, where he directs the department's Oncology Section. Skoracki came to Ohio State from The University of Texas MD Anderson Cancer Center in Houston. His areas of clinical expertise include lymphedema surgery, reconstructive microsurgery of the head, neck and breast, sarcoma reconstruction, abdominal wall reconstruction and other areas of reconstructive surgery – all focused on improving patient outcomes physically and psychologically. He also has a strong research interest and collaborates with scientists in various disciplines related to the care of cancer patients. Accompanying Skoracki as a new member of Ohio State's faculty (though not supported by Pelotonia dollars) is his former MD Anderson colleague **David Cabiling, MD**. An assistant professor in the College of Medicine, Department of Plastic Surgery, Cabiling has clinical expertise in microvascular reconstructive surgery and oncology reconstruction. His research interests include outcomes in breast cancer reconstruction and microvascular treatments for lymphedema.



JAMES ROCCO, MD, PHD, who in January 2015 will join Ohio State's faculty as a professor in the College of Medicine, Department of Otolaryngology – Head and Neck Cancer Surgery. Rocco, an otolaryngologist who specializes in head and neck cancer surgery, will direct the department's Division of Head and Neck Oncology. He was recruited from the Massachusetts Eye and Ear Infirmary and Massachusetts General Hospital, where he was director of head and neck cancer research and held the Daniel Miller Chair in Otolaryngology and Laryngology at Harvard Medical School. As a researcher, he has translated basic science investigations on mechanisms of cell death after therapy into clinical practice by identifying novel biomarkers that predict survival in patients with head and neck cancer.



MICHELLE NAUGHTON, PHD, MPH, a professor in the College of Medicine, Department of Internal Medicine, Division of Cancer Prevention and Control. Naughton, who also is a member of the Cancer Control Program at the OSUCCC – James, came to Ohio State from the Wake Forest School of Medicine. Her research focuses on the impact of cancer and its treatments on the health-related quality of life and daily functioning of patients and long-term survivors.



TAKESHI KURITA, PHD, associate professor in the College of Medicine, Department of Molecular and Cellular Biochemistry. Kurita, who also is a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, came to Ohio State from Northwestern University. His lab team primarily uses genetically engineered mouse models to investigate molecular mechanisms of development and carcinogenesis of the reproductive organs. They also utilize the xenograft model of human tissue to study the etiology of human diseases, including uterine leiomyoma and endometrial (uterine) cancer.

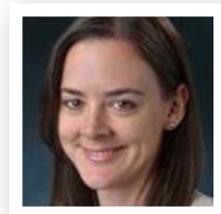


JAMES S. BLACHLY, MD, assistant professor in the College of Medicine, Department of Internal Medicine, Division of Hematology. Blachly, who also is a member of the Leukemia Research Program at the OSUCCC – James, completed a three-year fellowship in hematology and medical oncology at Ohio State before joining the faculty in 2014. His clinical specialty is mature B cell leukemia and lymphoma. His research primarily explores genomic and transcriptomic correlates in experimental therapeutics/clinical trials. This encompasses three areas of specialization: computational biology, genomics and lymphoid malignancy.

Bringing the Best to Ohio State (cont.)



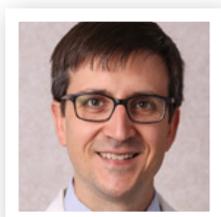
JONATHAN SONG, PHD, assistant professor in the College of Engineering, Department of Mechanical and Aerospace Engineering. Song, who also is a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, was recruited to Ohio State after completing a postdoctoral fellowship at Massachusetts General Hospital and Harvard Medical School. His research interests include: microscale technology for biology and medicine; biomechanical determinants of new blood vessel growth and remodeling; microengineering of the tumor microenvironment; mechanobiology of tumor invasion and metastasis; and development of microphysiological systems for screening of therapeutics for oncology.



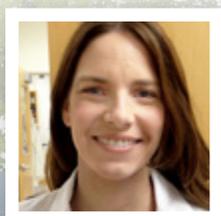
JENNIFER LEIGHT, PHD, assistant professor in the College of Engineering, Department of Biomedical Engineering. Leight, who also is a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, was recruited from the Howard Hughes Medical Institute at the University of Colorado. Her lab team uses cutting-edge biomaterials techniques to precisely vary the spatial and temporal presentation of 3D extracellular cues and to develop sensors for measuring activity of members of the matrix metalloproteinase (MMP) family. Using these materials, they study regulation of MMP activity, cancer cell function and response to treatment.



RAJU RAVAL, MD, DPHIL, assistant professor in the College of Medicine, Department of Radiation Oncology. Raval, a Rhodes Scholar, was recruited to Ohio State after completing his residency at Johns Hopkins Hospital. He treats central nervous system and genitourinary tumors with radiation therapy. His laboratory interests include translational cancer research combining immunotherapy with radiation and techniques for targeted radiosensitization.



LAWRENCE SHIRLEY, MD, assistant professor in the College of Medicine, Department of Surgery, Division of Surgical Oncology. Shirley was recruited to Ohio State's faculty after completing a fellowship here in 2014. His clinical interests include thyroid, parathyroid and adrenal diseases, particularly malignancies. His research focuses on developing therapeutics for advanced thyroid cancers.



ANNE STROHECKER, PHD, assistant professor in the College of Medicine, Department of Molecular Virology, Immunology and Molecular Genetics, and in the Division of Surgical Oncology. Strohecker was recruited to Ohio State from The Cancer Institute of New Jersey, Rutgers University, following postdoctoral training. Her research focuses on how autophagy, a program that controls protein and organelle homeostasis, impacts tumorigenesis with an ultimate goal of identifying mechanisms to modulate the pathway as a therapeutic modality for cancer.

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TOGETHER WE ARE UNSTOPPABLE

