

INVESTING IN A CANCER-FREE WORLD 2013

Ohio State Putting Pelotonia Dollars to Work



The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER



AS PELOTONIA ROLLS ON, so do our hopes and chances of one day living in a cancer-free world.

We all should be encouraged by our implacable resolve to expand this grassroots bicycle tour every year, annually attracting more riders and raising millions of dollars for cancer research at Ohio State's Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James). Pelotonia 12 generated \$16.87 million and boosted the four-year total for this popular event to more than \$42 million. Projections suggest that the Pelotonia 13 tally will exceed last year's and boost the five-year total ever higher.

Pelotonia 13 consisted of 248 pelotons (riding groups) that collectively contained a record 6,723 riders from 41 states and nine countries. It also drew 3,451 virtual riders and 2,445 volunteers. And thanks to the event's generous sponsors, every cent raised by riders, virtual riders and donors goes directly to cancer research at the OSUCCC – James. This is especially important at a time when government grants for cancer research are difficult to obtain. Without extraordinary efforts such as Pelotonia, innovative ideas for cancer research, not to mention the ambitions of many young scientists, would languish.

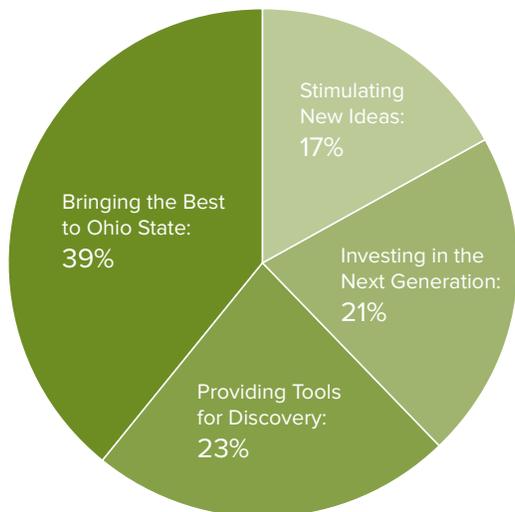
This report will briefly summarize (on the facing page) how Pelotonia funds have been spent over the event's first four years (2009-12). It will then look more closely at our Pelotonia Fellowship Program, our Idea Grants allocations of the past year for teams of faculty scientists, and our most recent equipment purchases and space development. It will also profile two renowned senior scientists who have been recruited to Ohio State's cancer program with support from Pelotonia dollars.

On behalf of the OSUCCC – James family, I once again thank all Pelotonia riders, virtual riders, donors, volunteers, organizers and sponsors for helping advance our shared vision of a cancer-free world. And I look forward to seeing all of you, and still others, 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

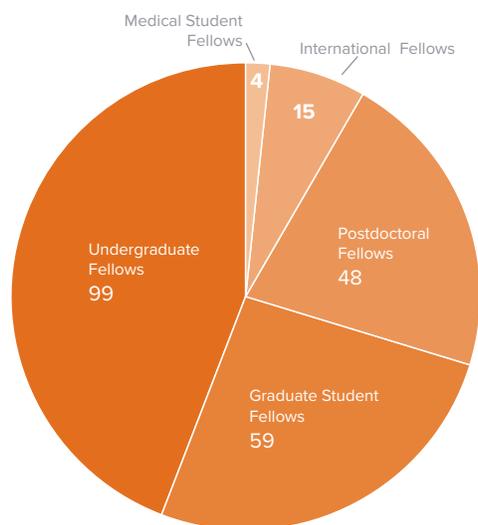
Four-Year Pelotonia Financial Summary

Allocations of Funding From Pelotonia 09, 10, 11, 12



Pelotonia, the annual grassroots bicycle tour established in 2009 to raise money for cancer research at the OSUCCC – James, generated more than \$42 million in its first four years through rider pledges and donations. Thanks to the generous underwriters of the event, every dollar raised by our riders 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 \$7 million in cancer research funding for Ohio State students at all levels of scholarship – undergraduate, graduate, medical school and postdoctoral fellow.

Bringing All Knowledge to Bear in the Fight Against Cancer.

Multiple colleges at Ohio State, listed below, as well as Nationwide Children’s Hospital and Cincinnati Children’s Hospital Medical Center, have received Pelotonia funding for cancer research:

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

Pelotonia Fellowship Program Overview

The Pelotonia Fellowship Program trains promising and accomplished undergraduate, graduate, medical and postdoctoral students from any discipline at Ohio State who have the potential to become independent cancer researchers.

The Fellowship Program started in 2010 and to date has awarded 225 student fellowships through an annual allocation of \$2 million in Pelotonia revenue for this program. Scholarship recipients so far include 99 undergraduates, 59 graduates, four medical students, 48 postdoctoral fellows and 15 international scholars.

Most recently, from October 2012-October 2013, the program awarded 58 fellowships to students at all levels of scholarship for conducting cancer research in the labs of faculty mentors. Recipients included 25 undergrads, 15 grad students, one medical student, 11 postdoctoral fellows and six international scholars.

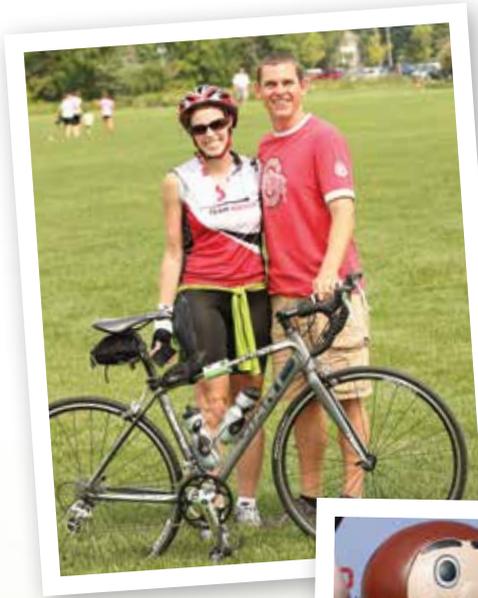
“Annually, we strive to fund 25 undergraduates, 16 graduates, two medical students and 12 postdoctoral fellows, but all funding decisions are based on the quality of the applications, not a firm number of awards,”

says Program Director Gustavo Leone, PhD, noting that the Fellowship Program “is truly multidisciplinary. Projects have been funded from eight colleges and 43 departments at Ohio State, and from applicants at Cincinnati Children’s Hospital.”

The awards are made by a Pelotonia Fellowship Committee that oversees the program and includes some of Ohio State’s most distinguished basic, translational and clinical researchers from many disciplines.

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

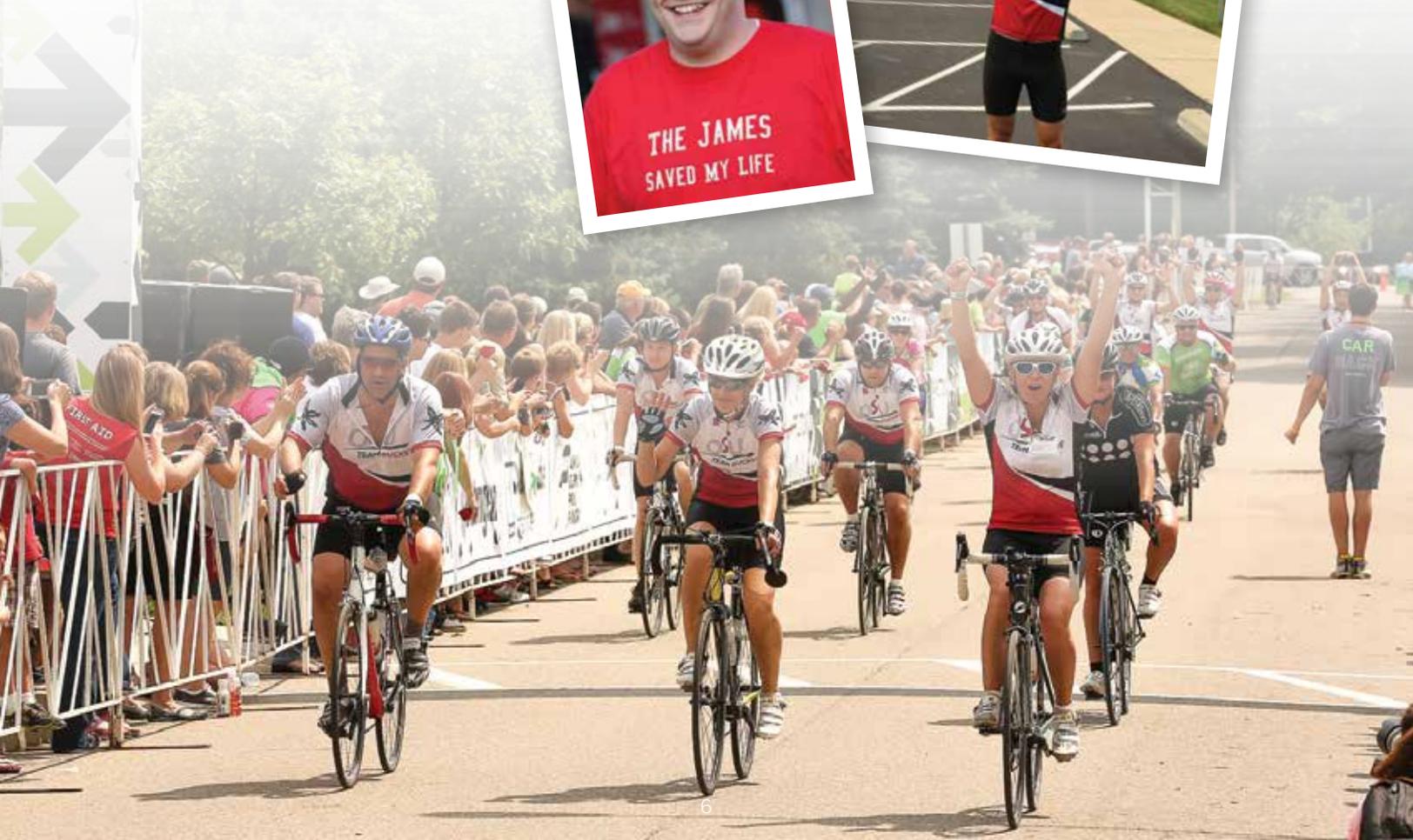




Post-Fellowship Highlights

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

- Medical degrees at Ohio State's College of Medicine (COM).
- 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 Pharmacy, Pathology, Molecular Genetics, Molecular and Cellular Biochemistry, Internal Medicine (divisions of Hematology and Medical Oncology), and Molecular Virology, Immunology and Medical Genetics.
- Advanced studies in the health sciences at Ohio State, Harvard, Stanford, Johns Hopkins, Kentucky, Case Western Reserve, Michigan, Northwestern, Texas, UCLA 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, Boston University, University of California Helen Diller Family Comprehensive Cancer Center, University of Prince Edward Island (Canada), and Birla Institute of Technology and Science (India).



Idea Grants Support Innovative Thinking in Cancer Research

Pelotonia dollars boosted team science at the OSUCCC – James in 2013 by supporting nine idea grants and one protocol-specific research (PSR) grant. The grants were awarded to teams of faculty researchers who are pursuing early work in basic, clinical/translational or population science that could lead to larger grants from external sources. These grants are especially important because government funding is difficult to obtain for the early pursuit of innovative ideas. The grants were awarded by a scientific review committee of external and internal reviewers that was chaired by the OSUCCC associate directors. The committee considered the scientific merit of competitive applications submitted by the research teams.

CD200R SIGNALING IN MELANOMA PROGRESSION AND IMMUNOTHERAPY

Xue-feng Bai, MD, PhD; Lai-Chu Wu, PhD

This team's studies have shown that melanoma cell expression of CD200, a cell-surface glycoprotein, can inhibit melanoma tumor formation and spread. This inhibition appears to be mediated by CD200 receptor (CR200R)-positive myeloid cells. Information generated by this study will help the investigators understand the role of CD200R signaling in causing melanoma and in immunotherapy for this disease, which is the deadliest form of skin cancer.

CS-1-TARGETED NK VS. T-CELL CHIMERIC ANTIGEN RECEPTOR THERAPY WITH OR WITHOUT ELOTUZUMAB

Jianhua Yu, PhD; Craig Hofmeister, MD

Researchers hypothesize that targeting CS-1, an antigen that is highly expressed on multiple myeloma (MM) cells, by a specific type of the body's immune cells, either alone or in combination with other immune cells or a drug called elotuzumab, is a promising therapeutic strategy for patients with MM, a currently incurable cancer of white blood cells called plasma cells. This team will test its hypothesis in both *in vitro* studies and *in vivo* model systems to lay the foundation for a phase I clinical trial for patients with relapsed MM using each patient's own immune cells.

Idea Grants Support Innovative Thinking in Cancer Research continued on page 8



TETHERED CATIONIC LIPOPLEX NANOPARTICLE (TCLN) ASSAY FOR EARLY LUNG AND LIVER CANCER DETECTION AND SURVEILLANCE VIA EXTRACELLULAR RNAs IN EXOSOMES AND CIRCULATING TUMOR CELLS

L. James Lee, PhD; Patrick Nana-Sinkam, MD; Kalpana Ghoshal, PhD; Michael Paulaitis, PhD; Carl Schmidt, MD

This team has developed a low-cost “Tethered Cationic Lipoplex Nanoparticle (TCLN)” biochip that may provide a patient-friendly early detection and surveillance assay for lung and liver cancer by detecting circulating tumor cells or extracellular RNAs in patient blood samples. The team will evaluate the feasibility of this technique in animal-model and patient samples, then use the data to submit two grant proposals to the NCI in two years and a third proposal in the future.

STAT3 AS A MEDIATOR OF IMMUNE SUPPRESSION IN THE PANCREATIC CANCER STROMA

Gregory Lesinski, PhD, MPH; Michael Ostrowski, PhD

A hallmark of pancreatic cancer is a network of pancreatic stellate cells (PSCs) that arise from chronic inflammation and surround each tumor to help it grow while suppressing the immune system. This team seeks to understand how PSCs influence immune suppression in pancreatic cancer so they can prioritize cellular targets and manipulate them to enhance immunotherapy. They believe a gene called *STAT3* in PSCs plays a key role in immune suppression, a hypothesis they will test by developing a mouse model of pancreatic cancer so they can study how *STAT3* promotes PSC survival and use these data for a future NCI grant application.

NOVEL SMALL MOLECULE INHIBITOR OF PHD3 EFFECTS ON HUMAN BREAST CANCER METASTASIS AND MIGRATION ON NANOSCALE VARIABLE MODULUS DEVICES

Tim Eubank, PhD; John Lannutti, PhD

In search of better treatments for triple-negative breast cancer (TNBC) – an aggressive and often fatal form of the disease that accounts for about 15 percent of all breast cancers – this team has discovered a pathway activated by a small molecule inhibitor of an enzyme called prolyl hydroxylase 3 (PHD3), which is thought to play a part in TNBC tumor metastasis (spread). The team will study the ability of their PHD3 inhibitor to reduce the metastatic potential of TNBC cells in an animal model. This study will use nanoscaled tools originating within the Nanoscale Science and Engineering Center at Ohio State.

INSULIN RECEPTOR SPLICING IN RESPONSE TO HYPOXIA AND DRUG RESISTANCE: A PILOT STUDY

Dawn Chandler, PhD; Peter Houghton, PhD

Solid tumors are characterized by hypoxia (oxygen deficiency), and the ability of the tumor cells to adapt to hypoxia is essential for tumor progression. This study seeks to understand the mechanisms and consequences of insulin receptor (*IN-R*) gene splicing, or natural chemical alteration of DNA, in response to hypoxia – testing the hypothesis that splicing factors are modulated in response to hypoxia and are thus involved in the alternative splicing of the *IN-R* gene that contributes to tumor formation. The team has developed a splicing method that mimics cells that have undergone hypoxia. They will use this to study regulatory mechanisms for this process in hopes of finding targets for therapeutic intervention.



PRMT5 DYSREGULATION AS A DRIVER EVENT IN RICHTER'S TRANSFORMATION

Rosa Lapalombella, PhD; Robert Baiocchi, MD, PhD

Richter's transformation (RS) is a complication of chronic lymphocytic leukemia (CLL) in which the leukemia changes into a rapidly proliferating and aggressive form of lymphoma with a poor prognosis despite the use of standard lymphoma therapy. The cause(s) of this transformation is not well understood. This team hypothesizes that dysregulation of a protein called PRMT5, which is variably expressed in CLL and overexpressed (overly active) in RS, is a driver event in CLL transformation to lymphoma. Using gene- and RNA-sequencing methods, they hope to shed light on how PRMT5 dysregulation causes the transformation. This information may lead to new therapeutic approaches to RS.



GENE DISCOVERY USING A DROSOPHILA TUMOR MODEL

Amanda Simcox, PhD; Victor Jin, PhD

Because the *RAS* gene signaling pathway is implicated in multiple cancers, an intense effort is under way to study *RAS* regulators and effectors. This team has developed a conditional *RAS*-driven tumor cell model in fruit flies that they will use to discover genes in the *RAS* pathway and also to investigate tumor cell dormancy, which is important because, in this state, the cells evade cancer therapies that target proliferating cells. These dormant cells need to be killed too, because they can later cause cancer recurrence.

THE ROLE OF THE EPSTEIN-BARR VIRUS IN NK-CELL LYMPHOMA

Aharon Freud, MD, PhD; Robert Baiocchi, MD, PhD; Pierluigi Porcu, MD

Extranodal natural killer (NK) cell lymphoma, nasal type (ENKL) is an aggressive disease that stems from the Epstein-Barr virus (EBV) infecting and transforming NK immune cells. Very little is known about how this rare form of invasive cancer develops, and even less is known about the mechanisms of drug resistance that limit the effectiveness of chemotherapy for patients with ENKL. Based on hypotheses stemming from their earlier work, this team will develop laboratory models to study mechanisms of EBV-induced NK cell transformation and to characterize the body's immune response to ENKL for therapeutic purposes.

PSR Grant

TANGERINE TOMATO PHYTOCHEMICAL BIOAVAILABILITY AND METABOLISM IN MEN WITH PROSTATE CANCER

Steven Schwartz, PhD

This study will determine whether the tangerine-type tomato should be the principal tomato used in the university's ongoing tomato-soy juice project targeted toward prostate cancer. The tangerine tomato is a unique cultivar bred at Ohio State that accumulates a natural substance called lycopene in a form that is more bioavailable than that in red tomatoes. Pelotonia funding will support a clinical trial in which men with prostate cancer who are about to undergo prostate removal will be assigned to a low-lycopene diet or consume two servings of either tangerine tomato juice or red tomato juice for four weeks before surgery. Data on the absorption and biodistribution of lycopene will affect study design for an NIH grant renewal application in 2014.

Providing Tools for Discovery

Pelotonia funds have helped bring new laboratories on line in Ohio State's Biomedical Research Tower and have supported the purchase of scientific instrumentation. Technology purchased in the past year includes:

- REES Enterprise Environmental Monitoring System
- Sciclone NGS (Next Generation Sequencing) Workstation
- Diagenode IPStar Compact for epigenetic applications

This instrumentation and other Pelotonia-funded equipment is accessible to and will benefit the research of more than 200 cancer investigators at the OSUCCC -- James in the coming year.

The environmental monitoring system warns against equipment failure caused by faulty equipment, building issues (electrical outages, overheating, etc.), or other factors. Most users rely on the system to monitor freezers, refrigerators (reagents primarily) and incubators -- all of vital importance in preserving research samples and other materials.

Researchers have used the Diagenode IPStar Compact to generate useful data. They have enriched methylated DNA from more than 250 samples and turned it into low-input sequencing libraries using a loaner robot called IntegenX Apollo 324.

The PerkinElmer Sciclone NGS Workstation provides an automated solution for high-throughput sequencing sample preparation. It is a complete benchtop solution for library prep sequence capture and normalization. OSUCCC -- James researchers are working to optimize the different library generation protocols. So far, they have generated RNA-seq libraries and TruSeq Exome libraries.



From Ideas to Impact

Pelotonia's impact is perhaps most obvious in discoveries made and initiatives launched by teams of researchers who have received support from Pelotonia revenue over the past four years. Some examples:



Tsonwin Hai, PhD



Denis Guttridge, PhD

With a Pelotonia Idea Grant as partial support, a team of OSUCCC – James researchers has linked a stress gene called *ATF3* in immune cells to breast cancer metastasis, a process of spreading cancer cells from a tumor to other parts of the body. Metastasis is the major cause of death in cancer patients. The researchers say their study suggests that *ATF3* may be the crucial link between stress and cancer. Previous studies have shown that stress is a risk factor for cancer. This research suggests that cancer cells, by acting as stress signals, coax immune cells that have been recruited to a tumor to express *ATF3*. Though it's unclear how, *ATF3* promotes the immune cells to act erratically and give cancer an escape route from the tumor site to other areas of the body. "If your body does not help cancer cells, they cannot spread as far," says **Tsonwin Hai, PhD**, senior author of the study, which

was published in the *Journal of Clinical Investigation*. "So the rest of the cells in the body help cancer cells move to distant sites. And one of the unifying themes is stress." Hai says this stress gene could one day function as a drug target to combat cancer metastasis.

Researchers at the OSUCCC – James have discovered a mechanism responsible for the loss of a critical tumor-suppressor gene called *A20* in rhabdomyosarcoma and other soft-tissue sarcomas – rare cancers that strike mainly children and often respond poorly to treatment. Knowledge of the mechanism could guide the development of more effective therapies for these malignancies. The researchers found that *A20* is silenced not by mutation, as in many other cancers, but because a second molecule is lost – a small molecule called microRNA-29. They also found that microRNA-29 normally

From Ideas to Impact continued on page 12





Mumtaz Yaseen Balkhi, PhD



Clara D. Bloomfield, MD

protects *A20* from destruction. When microRNA-29 is absent, *A20* is degraded. Loss of *A20*, in turn, leads to a rise in levels of a protein called NF- κ B and to tumor progression. The findings were published in the journal *Science Signaling*. “We know that NF- κ B is a tumor promoter, but we don’t know why it is upregulated in many cancers,” says principal investigator **Denis Guttridge, PhD**. “Our study indicates that it involves a regulatory circuit between NF- κ B, microRNA-29 and the *A20* tumor-suppressor gene. It also identifies NF- κ B as a therapeutic target in sarcoma, and *A20* and microRNA-29 as potential biomarkers for sarcoma.” First author **Mumtaz Yaseen Balkhi, PhD**, a former Pelotonia fellowship recipient, says the findings move research a step closer toward developing microRNA-29 therapy against NF- κ B activation in cancers.

A study supported in part by Pelotonia dollars identified microRNA-155 as a new independent prognostic marker and treatment target in patients with acute myeloid leukemia that has normal-looking chromosomes under the microscope (called cytogenetically normal acute

myeloid leukemia, or CN-AML). The study found that when microRNA-155 is present at abnormally high levels in CN-AML cells, patients are less likely to have a complete remission, and they experience a shorter disease-free period and shorter overall survival. Published in the *Journal of Clinical Oncology*, the findings suggest that miR-155 plays a pivotal role in CN-AML development and could be a valuable target for an emerging class of drugs designed to inhibit microRNAs. The researchers say miR-155 would be relatively easy to measure at the time of diagnosis. They believe it will prove to be a good marker for stratifying patients according to recurrence risk and a good target for emerging compounds designed to inhibit microRNAs. Senior author **Clara D. Bloomfield, MD**, notes that, overall, “Our findings indicate that miR-155 expression is a strong and independent prognostic marker in CN-AML, and they provide clinical validation of data from preclinical models that support a crucial role of miR-155 in leukemia.”





Heather Hampel

Pelotonia dollars have helped the OSUCCC – James launch a statewide initiative to screen newly diagnosed colorectal cancer (CRC) patients and their biological relatives for Lynch syndrome (LS), a major cause of inherited colorectal, ovarian and uterine cancer. This effort, called the Ohio Colorectal Cancer Prevention Initiative (OCCPI), reveals others who may be at risk of developing these cancers so they can take precautionary measures. The initiative is led by **Heather Hampel**, a certified genetic counselor at Ohio State. Hampel says about 3 percent of CRC cases result from LS, which is characterized by inherited mutations in certain genes. Each CRC patient found to have LS has, on average, an additional three relatives with LS.

The OCCPI includes around 40 hospitals from throughout Ohio that have implemented the LS screening program. The partner hospitals advise patients and their physicians of the results, offer genetic counseling and make cancer surveillance recommendations to patients and family members found to have LS. “If you find people with LS before they get cancer, you have the potential to really save lives,” says Hampel, explaining that these patients can have colonoscopies earlier and more frequently so precancerous polyps can be detected and removed, or so cancer can be detected early when it is more treatable. Hospitals participating in the OCCPI include:

Cleveland Clinic Foundation, James Cancer Hospital and Solove Research Institute, Riverside Methodist Hospital (Columbus), The Christ Hospital (Cincinnati), Mount Carmel East (Columbus), Summa Akron City/St. Thomas Hospital (Akron), Aultman Hospital (Canton), Kettering Medical Center (Dayton), Miami Valley Hospital (Dayton), Bethesda North Hospital-TriHealth (Cincinnati), ProMedica Toledo Hospital, Hillcrest Hospital (Mayfield Heights), Mount Carmel West (Columbus), St. Rita’s Medical Center (Lima), Good Samaritan Hospital-TriHealth (Cincinnati), MetroHealth System (Cleveland), Genesis Healthcare System (Zanesville), ProMedica Flower Hospital (Sylvania), Fairview Hospital (Cleveland), Good Samaritan Hospital (Dayton), Akron General Medical Center, Mercy Medical

Center (Canton), Springfield Regional Medical Center, Blanchard Valley Regional Health Center (Findlay), Upper Valley Medical Center (Troy), Atrium Medical Center (Middletown), Adena Health System (Chillicothe), Robinson Memorial Hospital (Ravenna), Mount Carmel St. Ann’s (Westerville), Southern Ohio Medical Center (Portsmouth), Grant Medical Center (Columbus), Marietta Memorial Hospital, Summa Barberton Hospital, Doctors Hospital West (Columbus), Licking Memorial Hospital (Newark), Knox Community Hospital (Mount Vernon), Grady Memorial Hospital (Delaware), Summa Western Reserve (Cuyahoga Falls), Wayne Hospital (Greenville), ProMedica St. Luke’s Hospital (Maumee).



Generating New Hope Through Pelotonia-Funded Research

Pelotonia funds support cancer drug development projects at Ohio State, including an early-phase clinical trial on the safety of an anticancer vaccine designed to prevent the recurrence of several types of solid tumors, a phase II clinical trial of an experimental drug for patients with certain forms of leukemia, and basic-science studies that discovered how tamoxifen-resistant breast cancer cells grow and proliferate.



Kami Maddocks, MD

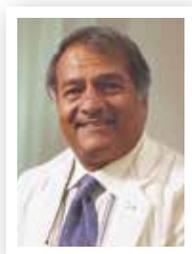
The phase II clinical trial will determine the effectiveness of a promising drug called ibrutinib as a targeted agent for patients with chronic lymphocytic leukemia (CLL)/small lymphocytic leukemia (SLL) who have not responded to or who have relapsed after standard treatment. The trial will help to identify if ibrutinib works in patients with high-risk disease as well as it works in patients with better-risk disease. It will also help to identify why some patients don't respond for long to the drug.

Principal investigator **Kami Maddocks, MD**, says ibrutinib inhibits a certain protein that is believed to help blood cancer cells live and grow. "By inhibiting or 'blocking' the activity of this protein," Maddocks says, "it is possible that ibrutinib may kill the cancer cells or stop them from growing". The trial, which opened in April 2012, accrued its original target of 68 patients – many of whom have no other treatment options – and was then amended to enroll another 78 patients, which provided them access to ibrutinib during a period when the drug would not otherwise be available.

This phase II clinical trial, open only at Ohio State, is part of a larger body of research at this university and other institutions that is showing ibrutinib to have strong potential as a safe, effective, targeted treatment for patients with CLL or mantle cell lymphoma (MCL), currently incurable cancers. Studies within this body of work have already had a global impact by leading to recent FDA approval of ibrutinib for the treatment of patients with relapsed MCL. Researchers hope this agent may also soon be approved for treating CLL in certain patients.

Generating New Hope Through Pelotonia-Funded Research continued on page 15





Pravin Kaumaya, PhD



Tanios Bekaii-Saab, MD



Jeffrey Fowler, MD



William Carson III, MD



Sarmila Majumder, PhD



Bhuvana Ramaswamy, MD

Generating New Hope Through Pelotonia-Funded Research continued from page 14

The vaccine trial, led by overall chair **Pravin Kaumaya, PhD**, and clinical co-principal investigators **Tanios Bekaii-Saab, MD**, **Jeffrey Fowler, MD**, and **William Carson III, MD**, is in the final stages of accrual. Thirty patients have received the vaccine since the trial opened at The James in July 2011. One component of the vaccine targets a molecule that occurs at abnormally high levels in up to 30 percent of breast cancers. Another component targets a molecule that is overexpressed in many other solid tumors, including ovarian, renal, colon, lung and gastrointestinal cancers. “The goals are to determine the safety and optimal dose of the vaccine, evaluate whether it shows therapeutic benefit by stimulating the immune system to respond to the patient’s tumor, and document any clinical responses that may occur,” Kaumaya says. The investigators report that eight patients receiving the vaccine in group/dose level 1 and level 2 had stable disease, and four patients have received a six-month booster so far. One of those four also had received a 12-month booster and is to receive an 18-month booster in December. In addition, a fifth patient is due for a six-month booster.

Some 30-40 percent of breast cancer patients who are treated with tamoxifen, which works by targeting high

levels of estrogen found in two thirds of cases, become resistant to this drug after about five years. A study led by **Sarmila Majumder, PhD**, and **Bhuvana Ramaswamy, MD**, showed how tamoxifen-resistant breast cancer cells grow and proliferate, and it also suggested that an experimental drug called vismodegib may offer a new targeted therapy in patients for whom tamoxifen therapy has failed. The study, published in the journal *Cancer Research* in 2012, showed that a signaling pathway called hedgehog takes over in promoting breast cancer growth after tamoxifen does its initial work in stopping the disease. This was later found to be true for other endocrine-resistant breast cancer, namely faslodex and aromatase inhibitor-resistant disease. But vismodegib, they learned, blocks the hedgehog pathway and inhibits the growth of tamoxifen-resistant human breast tumors in an animal model. The researchers are designing a clinical trial to use vismodegib in patients who failed endocrine therapy as a first line of treatment. “Pelotonia support has been crucial in helping us understand this potential therapy,” says Ramaswamy, who notes that Pelotonia dollars also are helping them obtain data and translate the findings for a clinical trial involving this therapy in patients with triple-negative breast cancer, which has few treatment options and poor outcomes.

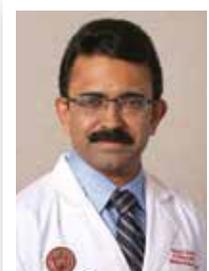


Bringing the Best to Ohio State

Funds raised by Pelotonia have helped recruit and retain some of the brightest minds in cancer research to Ohio State. We highlight just two of the renowned senior researchers who were recruited with Pelotonia support in the past year.



RAPHAEL E. POLLOCK, MD, PHD, is a globally respected cancer surgeon, researcher and educator of physicians-in-training. On Sept. 1, 2013, Pollock became a professor and director of the Division of Surgical Oncology at Ohio State, and he also serves as chief of surgical services of the OSUCCC – James. He came to Ohio State after 31 years at The University of Texas MD Anderson Cancer Center, where he played several leadership roles. Pollock’s clinical practice and laboratory research focus on soft tissue sarcoma, a rare cancer in adults but rather prevalent in children. He is principal investigator of an \$11.5 million National Cancer Institute (NCI) Specialized Programs of Research Excellence (SPORE) grant to support collaborative sarcoma translational research. The grant is one of the largest awards ever to study sarcoma. Pollock’s SPORE research component is now located at the OSUCCC – James.



VINAY PUDUVALLI, MBBS, is a noted authority on developing therapies for patients with brain and spine malignancies using a combined approach of targeted therapies, innovative clinical trial designs and rational combinations of anticancer agents. Puduvalli, who serves as professor and director of the Division of Neuro-Oncology in the Department of Neurological Surgery, was recruited to Ohio State in December 2012 from MD Anderson Cancer Center, where he played several leadership roles. His research focuses on understanding the role of epigenetics in brain tumor and glioma stem cell biology, and on translating these findings to new treatment options. His lab team also works to identify mechanisms of treatment resistance, including resistance to cell death and to signaling pathway inhibitors in brain tumors. In this context, he leads several clinical trials involving epigenetic therapies and novel targeted agents.



For more information about Ohio State’s cancer program, visit cancer.osu.edu. For more information about Pelotonia, visit pelotonia.org.