



The James

Ohio State is a Comprehensive Cancer Center designated by the National Cancer Institute

PELTONIA SPECIAL EDITION

# frontiers

TURNING CANCER DISCOVERIES INTO TREATMENTS



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OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER—JAMES CANCER HOSPITAL AND SOLOVE RESEARCH INSTITUTE



A Comprehensive Cancer Center Designated by the National Cancer Institute

# UPFRONT

The Director's Perspective

## A New Funding Cycle

In its first two years, Pelotonia raised more than \$12 million for cancer research at Ohio State, and last year, it raised more than \$13 million, bringing the three-year total to a remarkable \$25.5 million. The stories chronicled here show how we invested the dollars raised from Pelotonia 09 and Pelotonia 10. As we invest the dollars from Pelotonia 11, we'll continue to build remarkable stories of discovery, expertise and resources – all brought to bear against this devastating disease.

In 2009, to cope with the prolonged decline in federal support for cancer research, we established our annual Pelotonia cycling tour to raise money for cancer research at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

The event generated \$12.3 million in its first two years. Thanks to generous underwriters, every dollar raised goes to cancer research at Ohio State. This special issue of *Frontiers* presents how we've applied these funds in three major areas: Discovery and Innovation, Bringing the Best to Ohio State, and Expanding Research Capabilities.

We've invested \$4.7 million in "Discovery and Innovation." These funds stimulate and train outstanding

Ohio State undergraduate, graduate and medical students, and postdoctoral investigators for future cancer research (see page 6). Pelotonia also funds team studies by OSUCCC – James investigators, using a rigorous peer-review approval process in which the reviewers select studies that could move us more quickly toward a cancer-free world (see page 8). Pelotonia also supports two clinical trials, one investigating a breast-cancer vaccine developed at Ohio State, the other a promising therapy for chronic lymphocytic leukemia (see page 14).

Pelotonia is critical for bringing the best minds to our center. We invested \$5.4 million into the "Best to Ohio State" fund, which supports start-up research projects, staff and supplies needed to establish 16 new cancer investigators at



**MICHAEL A. CALIGIURI, MD**  
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CHIEF EXECUTIVE  
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FOUNDATION CHAIR IN  
CANCER RESEARCH

Ohio State (see page 19). These learned faculty will stimulate our already great team to be even greater.

Finally, we've invested \$2.6 million of Pelotonia funds in "Expanding Research Capabilities" to help outfit new laboratories and purchase high-tech equipment (see page 17). A solid research infrastructure is essential for turning ideas into discoveries. These instruments are available to all OSUCCC – James investigators.

Pelotonia 11 raised more than \$13.1 million, and we're now investing those dollars into Ohio State cancer research. I look forward to sharing that story with you next year. Pelotonia 12 is Aug. 10-12. Thousands of riders will take to the roads, pedaling on multiple routes between Ohio State and Kenyon College in Gambier, Ohio. Please join us!

### THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER – ARTHUR G. JAMES CANCER HOSPITAL AND RICHARD J. SOLOVE RESEARCH INSTITUTE

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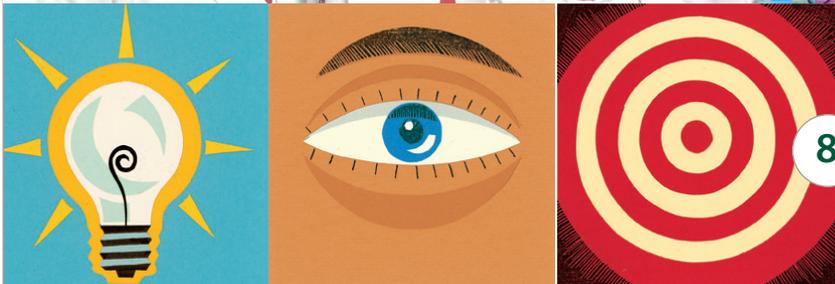
# frontiers

PELTONIA | A SPECIAL FRONTIERS REPORT 2012



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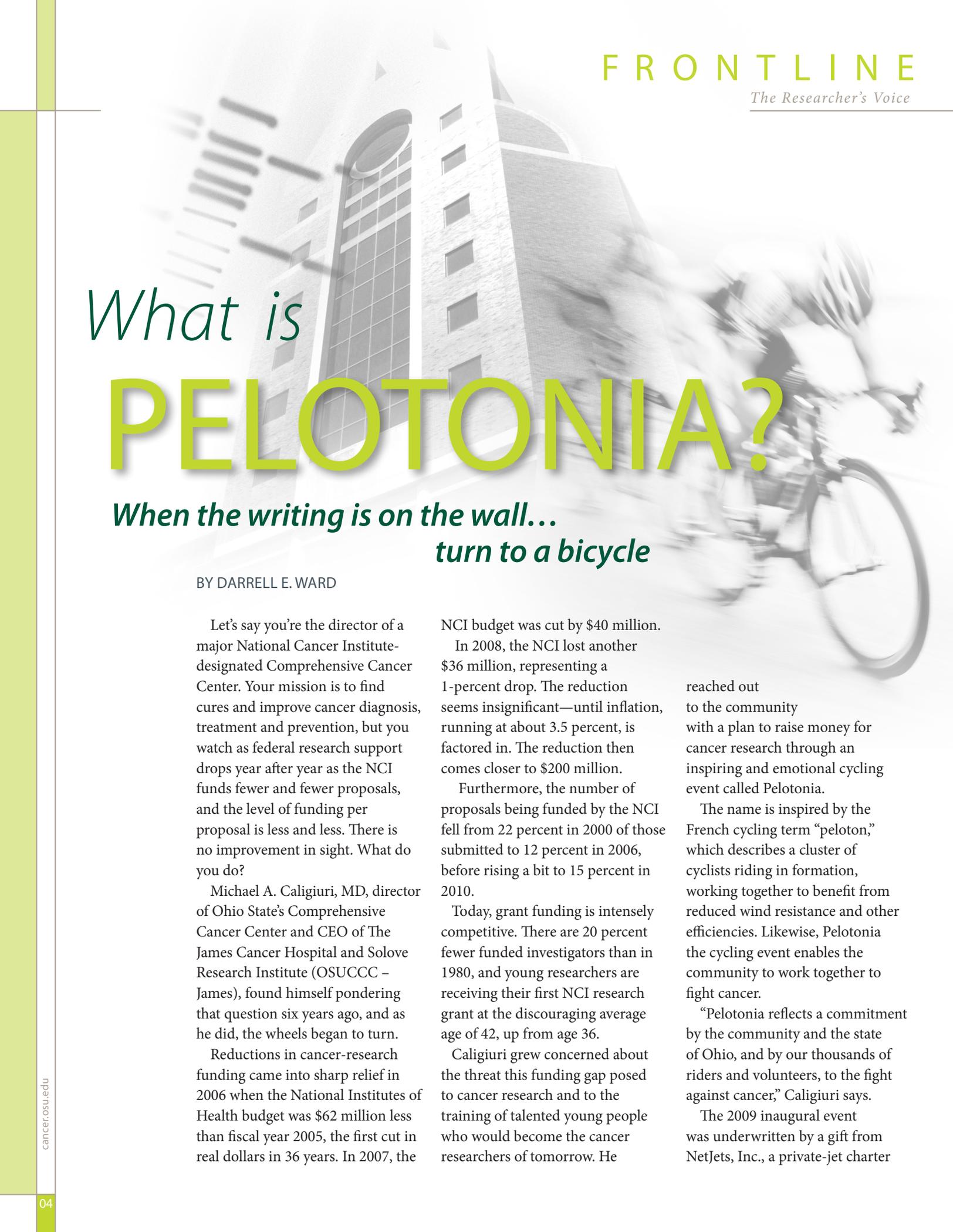
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**ON THE COVER:**  
PELTONIA FELLOWSHIP RECIPIENTS  
(FROM LEFT) DANIEL KISS, PHD,  
JONATHAN LEE AND SALENE WU  
(SEE PAGE 6).



What is

# PELOTONIA?

*When the writing is on the wall...  
turn to a bicycle*

BY DARRELL E. WARD

Let's say you're the director of a major National Cancer Institute-designated Comprehensive Cancer Center. Your mission is to find cures and improve cancer diagnosis, treatment and prevention, but you watch as federal research support drops year after year as the NCI funds fewer and fewer proposals, and the level of funding per proposal is less and less. There is no improvement in sight. What do you do?

Michael A. Caligiuri, MD, director of Ohio State's Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute (OSUCCC – James), found himself pondering that question six years ago, and as he did, the wheels began to turn.

Reductions in cancer-research funding came into sharp relief in 2006 when the National Institutes of Health budget was \$62 million less than fiscal year 2005, the first cut in real dollars in 36 years. In 2007, the

NCI budget was cut by \$40 million.

In 2008, the NCI lost another \$36 million, representing a 1-percent drop. The reduction seems insignificant—until inflation, running at about 3.5 percent, is factored in. The reduction then comes closer to \$200 million.

Furthermore, the number of proposals being funded by the NCI fell from 22 percent in 2000 of those submitted to 12 percent in 2006, before rising a bit to 15 percent in 2010.

Today, grant funding is intensely competitive. There are 20 percent fewer funded investigators than in 1980, and young researchers are receiving their first NCI research grant at the discouraging average age of 42, up from age 36.

Caligiuri grew concerned about the threat this funding gap posed to cancer research and to the training of talented young people who would become the cancer researchers of tomorrow. He

reached out to the community with a plan to raise money for cancer research through an inspiring and emotional cycling event called Pelotonia.

The name is inspired by the French cycling term “peloton,” which describes a cluster of cyclists riding in formation, working together to benefit from reduced wind resistance and other efficiencies. Likewise, Pelotonia the cycling event enables the community to work together to fight cancer.

“Pelotonia reflects a commitment by the community and the state of Ohio, and by our thousands of riders and volunteers, to the fight against cancer,” Caligiuri says.

The 2009 inaugural event was underwritten by a gift from NetJets, Inc., a private-jet charter

*"Pelotonia funds are making a difference, not just for our time but for all time."*

company based in Columbus. The gift established Pelotonia as a nonprofit organization headed by CEO Tom Lennox, formerly head of communications at Abercrombie & Fitch, and it enabled 100 percent of all donations raised by cyclists to support cancer research at the OSUCCC – James. Subsequent Pelotonias have been supported by gifts from Huntington, Limited Brands Foundation, Peggy and Richard Santulli, American Electric Power Foundation, Nationwide Insurance, Cardinal Health and Chemical Abstracts Service. Thanks to these generous gifts, all funds raised by riders and individual donors are dedicated to cancer research at the OSUCCC – James.

Cyclists in the first three Pelotonias could choose from routes of varying distances between Ohio State in Columbus and Ohio University in Athens, Ohio. Pelotonia 12 will offer six routes of various distances between Columbus and Gambier, Ohio, home to Kenyon College.

Pelotonia was inspired in part by the Pan-Massachusetts Challenge, the largest single athletic fundraising event in the United States. Established in 1980, the Pan Mass Challenge is an endurance cycling event that benefits the Dana Farber Cancer Institute. In 2008, the event raised approximately \$33 million. Pan Mass founder and executive director Billy Starr collaborated with Pelotonia's leadership to organize the Ohio event.

Pelotonia's 2009 inaugural event attracted 2,265 cyclists from 31 states and Canada. They ranged

in age from 11 to 77 and **raised more than \$4.5 million** for cancer research at the OSUCCC – James. More than 1,000 volunteers assisted the riders along the way.

The following year, Pelotonia 10 attracted 4,047 riders and **raised \$7.8 million**. Enthusiastic support continued last year as well, when 4,986 riders from 38 states and four countries, along with 1,700 volunteers, participated in Pelotonia 11, which **raised a record \$13,108,639** for cancer research at the OSUCCC – James, a 68-percent increase over the 2010 total. The three-year fundraising total is approximately \$25.5 million.

Funds raised by Pelotonia riders and donors support cancer research at the OSUCCC – James in diverse, forward-looking ways:

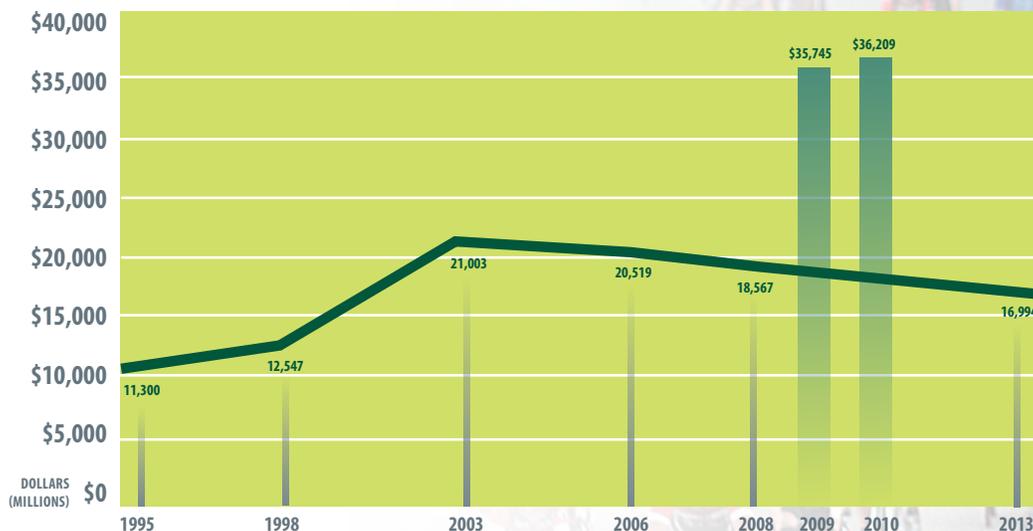
- Pelotonia Fellowship Grants attract young minds to careers

in cancer research by supporting undergraduates, graduate students, medical students and postdoctoral investigators (see page 6).

- Pelotonia Idea Grants invest in outstanding, original ideas by teams of OSUCCC – James investigators (see page 8.)
- Other Pelotonia funds are used to recruit talented cancer researchers to Ohio State, to retain those already here and to purchase sophisticated equipment that helps more than 280 scientists at the OSUCCC – James conduct research.

"Pelotonia funds are making a difference, not just for our time but for all time," Caligiuri says. To learn more, download the Pelotonia Funding Achievements and Investment Report at [http://cancer.osu.edu/pdfs/pelotonia/Pelotonia\\_investment\\_2011.pdf](http://cancer.osu.edu/pdfs/pelotonia/Pelotonia_investment_2011.pdf). 

## NIH APPROPRIATION IN CONSTANT DOLLARS



Overall appropriations since 1995 for the National Institutes of Health adjusted for inflation illustrates the drop in federal medical-research support beginning in 2003. Funding for the NCI closely follows that of the NIH. 2009/2010 includes supplemental appropriations (ARRA). (Data provided by the Federation of American Societies for Experimental Biology Office of Public Affairs.)

# PELTONIA Fellowships Fund Young Cancer Researchers

BY BOB HECKER

On the eve of Pelotonia 11, Michael A. Caligiuri, MD, stood before nearly 5,000 bicyclists and thanked them for escorting student researchers toward scientific stardom.

“We have many bright young minds here who, in today’s economy, had no chance of receiving external funding for their cancer research ideas,” said Caligiuri, director of Ohio State’s Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute (OSUCCC – James).

This funding problem could discourage the next generation of great scientists from pursuing new cancer cures, he said. “But since all of you have stepped up, we have taken some of the money you have raised through this grassroots event and started a Pelotonia Fellowship Program that provides students with money to pursue their ideas.”

Caligiuri then invited the 60-some fellowship recipients in the audience to stand for applause. “This is the generation that’s going to bring home the cancer cures and prevention strategies.”

To date, the Pelotonia Fellowship Program has awarded 116 grants to 56 Ohio State undergraduates, 32 graduate students and two medical students, as well as 26 postdoctoral fellows from around the world. The awards go to selected students in any discipline who want to pursue a cancer research project under the guidance of an Ohio State faculty mentor.

In all, the Pelotonia bicycle tour has raised approximately \$25.5 million from thousands of participating cyclists and virtual riders backed by pledges, and from individual donors. Thanks to a handful of underwriters, all the money raised by riders and donors goes to cancer research at the OSUCCC – James. **About \$2 million per year in Pelotonia funds** is committed to the fellowship program.

A 17-member faculty committee chaired by Gustavo Leone, PhD, a professor in the Department of Molecular Virology, Immunology and Medical Genetics, and associate director for basic research at the OSUCCC – James, awards the fellowships. The committee bases the awards on each applicant’s strengths and research potential, the mentor’s qualifications and training record, and the potential impact of the project.

“The students who receive fellowships are really inspiring,” says Program Director Jeff Mason. “It’s incredible how much they can contribute at such an early age.”

Here’s a look at three Pelotonia fellowship recipients – an undergraduate, a graduate student and a postdoctoral fellow – from among the many whose work is making a difference.

## JONATHAN LEE

A senior in molecular genetics, Jonathan Lee is seeing firsthand how even the study of insects can contribute to cancer research.



JONATHAN LEE

Working in the lab of Maki Asano, MD, PhD, of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, Lee is conducting a genomewide screening of *Drosophila melanogaster*, a species of fruit fly used by biologists as a model organism, to identify factors needed for a cell-cycle process called endoreduplication. This process occurs naturally in many cells, and it can help cancer cells escape programmed cell death, or apoptosis, enabling them to survive and proliferate.

“Our lab has found that a component of the prereplicative complex, called ORC1, is indispensable for endoreduplication,” Lee says. He is now working to identify other endoreduplication factors.

“We have screened 1,200 genes of the *Drosophila* genome, and we have several candidates that we will test further,” he says. “The findings could open new options for therapy, such as drugs targeting mitotic replication and endoreduplication in cancer cells.”

Lee says working in the Asano lab has taught him the importance of unity. “There needs to be a purpose that fuels the lab and its work. The person in charge of the project needs a unified sense of what it entails to address issues that may arise.”



SALENE WU

### SALENE WU

When Salene Wu, a graduate student in Psychology, was a therapist on a clinical trial testing a treatment for depression among cancer survivors, she noticed they had worries that she didn't see among her other patients.

"I wondered if these worries – mostly about their health and how it affected their loved ones – might be related to other aspects of their survivorship experience, like physical health and quality of life," Wu says.

This question, together with her long-standing interest in connections between the mind and body, led her to investigate possible links between psychological factors such as anxiety and the immune system's ability to fight cancer.

Working with Barbara Andersen, PhD, a professor of Psychology and member of the Cancer Control Program at the OSUCCC – James, Wu has asked women with advanced recurrent cancer to complete questionnaires about mood, worries and health, and to give a blood sample that will be analyzed for biomarkers of inflammation.

"We will soon analyze data for 56 women. This is my second-favorite part of the study, after hearing



DANIEL KISS

survivors' stories," Wu says, adding that she will finish her analysis this spring and defend the project as her dissertation in June.

After earning her degree, she hopes to continue with both cancer survivorship research and working in patient care. "Being a researcher would allow me to deliver the most effective treatments possible, while being a clinician would help keep me grounded and inspired," she says.

Wu felt honored to receive a Pelotonia fellowship. "I have been only a virtual rider in Pelotonia, but that's a great option. Someone who doesn't do well on a bike, like me, or is no longer in Ohio can still contribute. Grassroots efforts like this are crucial for medical research."

### DANIEL KISS, PHD

Intriguing research in the lab of Daniel Schoenberg, PhD, director of the Center for RNA Biology and a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, first attracted Daniel Kiss, PhD, to Ohio State as a postdoctoral fellow.

"The Schoenberg and other labs showed that a population of uncapped messenger RNAs (mRNAs) could be recapped in

the cytoplasm of a cell," says Kiss, who was pursuing his PhD at Case Western Reserve University when he learned of Schoenberg's work. "This offered a mechanism by which mRNAs stored in processing bodies (P-bodies) could exit the P-bodies and re-enter the actively translating pool of mRNAs."

Kiss says mechanisms governing the storage of silenced mRNAs in P-bodies and their escape from silencing remain mostly unknown but are important to cancer research because the protein products of both silenced and released mRNAs can alter cancer-cell behavior.

He is working to understand mRNA cycling and storage mechanisms, focusing on mRNAs cycling back to an active state. "This may identify mRNAs that promote malignancy, making this mRNA regulatory process a potential therapeutic target."

His Pelotonia fellowship enables him to study the relationship of P-bodies to the reactivation of mRNAs silenced by microRNA. Using a population of uncapped mRNAs identified by his colleagues as a starting point, he is employing bioinformatics to predict the positions of mRNA recapping and will then test those predictions in the lab.

Kiss views his Pelotonia fellowship both as recognition for his hard work as a graduate student and a challenge to work even harder now.

He rode a 43-mile Pelotonia route last year and is gearing up for a 100-mile Pelotonia ride this year. "I plan to ride every year I'm in Columbus, even after my fellowship has run its full duration." 

# When Insight



Meets

*Pelotonia funds help bright ideas become breakthroughs*

# Imagination

BY DARRELL E. WARD

“Brilliant ideas can lead to extraordinary breakthroughs, but without data to back them up, they have little chance of being funded or of the breakthroughs ever seeing the light of day,” says Michael A. Caligiuri, MD, director of Ohio State’s Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute.

The Pelotonia Idea Grant program gives life to such high-risk, high-reward research by teams of OSUCCC – James investigators.

“Pelotonia Idea Grants provide seed funding for ideas that can lead to critical preliminary data, new collaborations, and ultimately discovery – which can in turn lead to breakthroughs in science, prevention and treatments, and to larger grants,” Caligiuri says.

Applications for **Idea Grants, which provide \$100,000 over two years**, are judged using a peer-review process that considers a study’s potential for discovery, publication, clinical trials,

patients and leverage for subsequent funding from the National Cancer Institute. Applicants also must provide a “commitment to ridership” to ensure that they will participate in Pelotonia to help raise money for cancer research at the OSUCCC – James.

The first Pelotonia Idea Grants, 10 in all, were awarded in 2010 using a portion of the \$4.5 million raised during the inaugural Pelotonia cycling tour the previous year. Two examples of the innovative ideas funded by Pelotonia Idea Grants are provided below; the remaining eight projects are listed in the sidebar.

## IMAGING PRECANCEROUS PANCREATIC LESIONS

Pancreatic cancer is nearly universally fatal, and effective ways to detect it early and prevent the disease are needed. Recent research has identified precancerous abnormalities in the pancreatic duct that might help identify people at risk, but current imaging methods are unable to detect these abnormalities.

A team of OSUCCC – James researchers is working to solve the problem by adapting an experimental imaging technology called Optical Coherence Tomography (OCT), which might detect these precancerous lesions.

Mark Bloomston, MD, a surgeon specializing in gastrointestinal oncology and a member of the OSUCCC – James Molecular Biology and Cancer Genetics Program; Wendy Frankel, MD, a pathologist and member of the cancer center’s Innate Immunity Program; and Lanchun Lu, PhD, assistant professor of Radiation Oncology at the OSUCCC – James, make up the Ohio State team. They are collaborating with Zhilin Hu, PhD, a researcher in Biomedical Engineering at Washington University, who developed the technology.

OCT can image the lining of the pancreatic duct at the cellular level. The device uses a fiber-sized probe that can be inserted non-invasively into the pancreatic duct to provide 3-D images. This reveals abnormal cells that would not be detectable using current imaging technology.

The researchers will use OCT in the operating room to image the duct after the pancreas has been removed from patients with suspected precancerous lesions. They will confirm the findings with histological examinations.

“We expect to detect occult cancers in six to eight of the 30 to 40 patients we estimate will have this surgery at Ohio State over the

*continued on page 10*

## A CHANCE TO HELP OTHERS

Pelotonia means many things to many people. For cancer researcher and Pelotonia-rider **Anjali Mishra, PhD**, it's a chance to help others.

"The first time that I signed up for Pelotonia, I did not fully understand the commitment and dedication needed to raise funds for cancer research," Mishra says. "But the first opening ceremony changed my perception of this grassroots event, which brings together people from all walks of life for one goal: to beat cancer. It was fantastic, exciting."

Mishra has ridden all three Pelotonia events, which have taken her along the back roads of central Ohio. What she hadn't anticipated, however, were the benefits of raising the funds each rider pledges to donate.

"We organized a number of fundraising events, and for me, a foreigner, each one offered an opportunity to interact with local people. Last year, in addition to bake sales, we painted a barn that belonged to the grandparents of a colleague. The money we raised from that went straight toward my fundraising goal."

The first year, Mishra rode the 43-mile route, which she rode again the second year because of an injury. "My biggest Pelotonia challenge was

overcoming a fear of biking on hills," she says.

"Last year there were some 4,000 bikers,

and I rode 102 miles, which was pretty good...and those hills were really very, very cool! I plan to ride 180 miles this year in Pelotonia 12, for sure," she says.

Mishra is a researcher in the laboratory of Michael A. Caligiuri, MD, director of Ohio State's Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute. She is working to discover new models for the study of highly aggressive leukemias and lymphomas.

"We're trying to identify novel molecular pathways that we can exploit as targets to develop new therapies for these incurable diseases," she says.

Mishra earned her PhD at Hannover Medical School in Germany. She worked in a pediatric clinic where she saw many small children with very aggressive leukemia.

"There was no cure for those kids," she says. "We could prolong their life for a time, but their quality of life was not what it should have been. Those were the patients that affected me most, and



**ANJALI MISHRA, PhD**

**“. . . the first opening ceremony changed my perception of this grassroots event, which brings together people from all walks of life for one goal: to beat cancer. It was fantastic, exciting.”**

when I think about cancer, and when I'm riding in Pelotonia, those kids pop in front of my eyes. That is who I think about."

Those children come to mind, too, when she watches cancer-research funding fall. "As a researcher, I know that our funding is much lower now, which means we cannot do the large experiments that we need to do. We had to do something about it, and this is what's really great about Pelotonia: It brings people together from all walks of life to raise money for cancer research. This is why I'm a proud supporter of Pelotonia and The James, because they are leading a charge against cancer.

"Pelotonia is a fantastic cause," Mishra says. "A hundred percent of the money raised goes to cancer research. The money stays here in Ohio, but the research that the money supports will be available to people suffering from cancer on any continent. That is the great thing about it. This research will go around the globe."

two years of the project,” Bloomston says.

If the OCT proves reliable, Bloomston and his colleagues will undertake a larger project to image prior to surgery the pancreas of patients at high risk for pancreatic cancer.

The OCT device also is designed to deliver radiation therapy, potentially enabling the treatment of precancerous lesions without the need for radical surgery.

“Such an advance could revolutionize the early detection and prevention of pancreatic cancer,” Bloomston says.

#### DEVELOPING A RATIONAL THERAPY FOR NEUROFIBROMATOSIS

Neurofibromatosis type 1 (NF1)

is an inherited, autosomal-dominant disorder that causes nerve tissue to produce tumors, which sometimes become malignant. The condition affects Schwann cells, melanocytes and endoneural fibroblasts. Tumors can develop throughout the body and cause problems by compressing peripheral and spinal nerves, and by affecting bones and other tissues. Affected melanocytes cause skin discolorations called café au lait spots.

The molecular cause of NF1 is poorly understood. Research by Jianqiang Wu, MD, a researcher with the OSUCCC – James Experimental Therapeutics Program, and James Fuchs, PhD, assistant professor of Medicinal Chemistry and Pharmacognosy in Ohio State’s College of Pharmacy, has shown

that the gene called *STAT3* is constitutively activated in Schwann cells.

The investigators hypothesize that *STAT3* activation in Schwann cells and their precursors contributes to NF1 development, and that *STAT3* activity is stimulated by epidermal growth factor receptor, interleukin-6 or both.

The study has several key components:

- Investigate whether targeted deletion of *STAT3* in Schwann cells or their precursors will decrease or eliminate neurofibroma formation in an NF1 mouse model. Related to this, they will determine the mechanism(s) of *STAT3* in nerve disruption and NF formation.
- Test the effect of a novel *STAT3* inhibitor, a curcumin analog

## PELTONIA MEANINGFUL ON MANY LEVELS FOR CLINICIAN RIDER

One evening just before Christmas in 1999, **Donald Mack, MD**, then a family-practice doctor in the small town of Spencerville, Ohio, discovered a lump on his testicle. It was still there next morning, so he had it examined. “I was fortunate; I found the tumor early, while it was still confined to the gland,” Mack says.

His treatment involved surgery and radiation therapy. “I’d go for what I called my ‘tanning treatment,’” he says. “It sometimes left me a little tired, but it wasn’t nearly what most people with cancer experience.”

In 2010, Mack relocated his practice in Spencerville and came to work for The Ohio State University. When he interviewed for the position that April, he learned about Pelotonia. “I immediately wanted to do it,” he says.

Though it had been awhile since he’d been on a bike, he enjoyed bicycling. Before starting medical school he’d ridden across the United States with a group of cyclists. Yes, he was now 50 years old, but he wanted to tackle the August ride in recognition of the 10th anniversary of his cancer diagnosis. That it was an Ohio State and James Cancer Hospital event gave it added meaning.

He’d left the month of June free, prior to starting his new job at Ohio State in July, and now he could use it for training. “I became very familiar with



**DONALD MACK**

the Olentangy bike trail,” he says. Once he started work, he rode evenings and weekends.

When Pelotonia weekend arrived, he completed the two-day, 180-mile route, the longest of the rides.

## THE EIGHT REMAINING 2010 PELTONIA IDEA GRANTS

Here are the titles of the remaining 2010 Pelotonia Idea Grants. Information about the projects is available at [cancer.osu.edu/pelotonia](http://cancer.osu.edu/pelotonia).

- “Microenvironmental influences on AKT1-regulated transcriptome in tumorigenesis”
- “E-health program to reduce obesity in Appalachia”
- “CBL and EGFR in triple-negative breast cancers”
- “Genomic analysis of primary tumor lesions as an approach to early chemoprevention”
- “NF- $\kappa$ B inhibition cancer therapy”
- “Chemopreventive effects of strawberries on the modulation of the cigarette-smoke-altered transcriptome in human oral mucosa”
- “Understanding resistance mechanisms to MEK inhibitors in BRAF-activated juvenile pilocytic astrocytomas”
- “PD-1 blockade enhances natural killer cell cytotoxicity against multiple myeloma: Determining molecular mechanisms and *in vivo* efficacy”

developed by OSUCCC – James investigators in Ohio State’s College of Pharmacy, on tumor development in the NF1 mouse model.

- Define the upstream pathways that activate *STAT3* during NF1 development and determine the role played by interleukin-6 in regulating *STAT3* activity.

“Our long-term goal is to identify the *STAT3* pathways involved in neurofibroma formation and to learn if blocking specific pathways could be a potential treatment strategy,” Wu says. Based on their preliminary data, Wu and Fuchs have already received a grant from the U.S. Department of Defense to pursue this research further. 

Mack has had many encounters with cancer. As a teenager, his maternal grandmother developed breast cancer. Later, as a physician, he provided end-of-life care for his paternal grandmother, who died of a brain tumor. He knows first-hand the anxiety experienced by cancer survivors who come to him for care. “With every test you wonder: What if they find something? What will it mean? What will I do?”

Mack rode Pelotonia again in 2011. A family friend had been diagnosed and treated for breast cancer, and on the day of the ride, a woman close to his family was in The James undergoing treatment for acute myeloid leukemia; her brother had been treated there earlier for pharyngeal cancer.

As Mack prepared that morning to ride, the woman’s son and husband were there to see him off. “For them to come was really touching,” he says. As he rode, he had all these people—friends, family and patients—in mind.

“I’m a slower rider but pretty determined,” Mack says. He wore the Pelotonia shirt that identified him as a survivor, and some riders slowed to talk along the way.

“Other survivors had a much more difficult experience than I did,” he says. “One was a young man in his mid-20s, my son’s age, who was treated for a childhood cancer and still had memories of it. Another had a fairly advanced renal cancer, and he’d had all sorts of treatments, but boy could he pedal. He left me in his dust as he rode

off down the way.”

As he rides, Mack says, “I’m working to prove to myself that I can overcome the physical challenge.” That was especially true in 2011. During a training ride in May, his bike slipped out from under him on wet pavement, leaving him with a cracked helmet, a concussion and a fractured pelvis. He healed well, and his orthopedist said he could ride Pelotonia, “but I’d have to work for it,” he says.

He again completed the 180-mile course.

“I think Pelotonia is a significant event for the riders, most of whom are riding for someone with cancer, and that is multiplied by the good will that comes from raising money to fight cancer and support cancer research at Ohio State’s cancer center and The James Cancer Hospital,” he says.

Cancer research is vital, he adds. “In 25 years, I’ve seen so many changes in how we treat cancer. We are making strides every day.”

In addition, he says, “Pelotonia raises awareness and draws support for families that are battling cancer or have lost a loved one or for someone recently diagnosed.

“I still remember going back to practice in my small hometown in the ‘80s; they still had polio dinners. Polio was gone, but there were still many polio survivors, and the community still raised money for those kinds of charities. Those events drew communities together, they drew people to think about these demons that are out there, and anything that does that is good.”

# SYMPOSIUM SHOWCASES STUDENT RESEARCHERS

BY BOB HECKER

In a room filled with young scholarly minds, Ohio State cancer researcher Gustavo Leone, PhD, made a pertinent point.

**GUSTAVO LEONE, PhD,**  
associate director for  
basic research



“Some of the best ideas in cancer research come from students,” he said, “because they often think outside the box.”

Leone, associate director for basic research at Ohio State’s Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James), chairs an internal scientific committee that awards fellowships to Ohio State students at all levels – undergrads, graduates, medical students and postdoctoral fellows – who apply to conduct cancer-related research in the labs of faculty mentors at the OSUCCC

– James, and across the entire Ohio State University campus.

The fellowships are funded by revenue from the annual grassroots Pelotonia bicycle tour that raises millions of dollars for cancer research at the OSUCCC – James. The first three Pelotonias, held in 2009, ’10 and ’11 between Columbus and Athens, Ohio, collectively raised approximately \$25.5 million. The fourth annual tour is set for Aug. 10-12 between Columbus and Gambier, Ohio, home to Kenyon College. Speaking at the inaugural Pelotonia Fellowship Reception on May 31, 2011, Leone addressed an audience of student recipients, their faculty mentors and several Pelotonia riders and donors who were interested in learning how some of the money they helped raise is being used.

The reception was designed “to connect Pelotonia riders and donors to the students who actually do the cancer research so you can learn what’s going on,” Leone said at the reception. Profiles of all fellowship recipients and their projects were available in booklets given to guests.

“I encourage you to leaf through them, and if you see something that interests you, try to find that person and talk to him or her about their research,” Leone said.

The first Pelotonia Fellowship Symposium took place the following day with research presentations by fellowship recipients and lectures by guest speakers John Petrini, PhD, and Ross Levine, MD, from Memorial Sloan-Kettering Cancer Center, and Judith Campisi, PhD, from the University of California. The second annual Pelotonia Fellowship Symposium is scheduled for May 30

## FELLOWSHIP PRESENTERS AT THE 2011 SYMPOSIUM

- **Jonathan Lee**  
a Molecular Genetics major (faculty mentor Maki Asano, MD, PhD);
- **Kevin Kauffman**  
a Chemical Engineering major (faculty mentor Kristy Ainsle, PhD);
- **Dustin Gable**  
a Biomedical Sciences major (faculty mentor Amanda Toland, PhD);

## GRADUATE-STUDENT FELLOWS

- **April Gocha**  
Integrated Biomedical Science Graduate Program  
(faculty mentor Joanna Groden, PhD);
- **Hsiao-Chiang Chuang**  
Pharmacy Graduate Program  
(faculty mentor Ching-Shih Chen, PhD);
- **Nripersh Dhungel**  
Molecular Genetics Graduate Program  
(faculty mentor Anita Hopper, PhD);

## POSTDOCTORAL FELLOWS

- **Enrico Caserta, PhD**  
(faculty mentor Gustavo Leone, PhD);
- **Parvathi Ranganathan, PhD**  
(faculty mentor Ramiro Garzon, MD);
- **Jiang Li, PhD**  
(faculty mentor Dongping Zhong, PhD).

## 2012 FELLOWSHIP SYMPOSIUM SET FOR MAY 30

(see sidebar).

To date, the Pelotonia Fellowship Program has awarded 116 grants to 56 undergrads, 32 graduate students, two medical students and 26 postdoctoral fellows. Awards may go to students in any discipline who want to pursue a project relating to cancer research under the guidance of a faculty mentor, said Program Director Jeff Mason.

During the fellowship reception, OSUCCC Director and James CEO Michael A. Caligiuri, MD, emphasized not only the importance of the fellowship research but also the need to continue generating funds to support it through future Pelotonias.

He noted other ways that Pelotonia dollars are applied to cancer research. For example, they fund “Idea Grants” that are awarded to teams of scientists at the OSUCCC – James who want to pursue new high-risk studies that could lead to breakthroughs and to future external funding.

The money also supports clinical trials, recruitment and retention of top cancer scientists, and purchase of sophisticated equipment needed by the community of OSUCCC – James researchers to further their projects.

“We continuously want to recruit the best and brightest minds in cancer research to our program, and this takes millions of dollars because they often bring their entire lab team and lots of expensive equipment,” Caligiuri explained.

“We want all of you here today to mix and mingle, get turned on to the science, ride more and raise more,” he told reception guests. “The dollars drive the discoveries, and the discoveries drive cancer care and uncover the cures.” 

The cancer research of several 2010-11 undergrads, graduate students and postdoctoral fellows whose work is supported by Pelotonia funds will be featured at the 2012 Pelotonia Fellowship Symposium from 8:30 a.m.-4:30 p.m. on Wednesday, May 30, in Room 115 of Ohio State’s Biomedical Research Tower, 460 W. 12th Ave., Columbus.

The symposium also will feature presentations by three nationally known cancer researchers:



**Charles Sherr, MD, PhD**, chair of Tumor Cell Biology at St. Jude Children’s Research Hospital. Sherr is also an investigator at the Howard Hughes Medical Institute, co-director of the Molecular Oncology Program and Herrick Foundation Chair;



**Martine Roussel, PhD**, co-director of the Cancer Center Signal Transduction Program at St. Jude Children’s Research Hospital, where she holds the Endowed Chair in Molecular Oncogenesis. Roussel is also a professor in the Department of Molecular Sciences at The University of Tennessee, Memphis;



**David Fisher, MD, PhD**, chief of the Department of Dermatology at Massachusetts General Hospital. Fisher is also the Edward Wigglesworth Professor of Dermatology at Harvard Medical School.

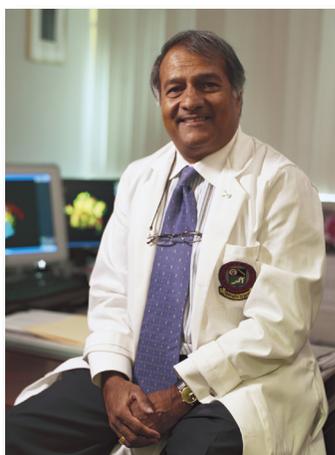
Visit [www.cancer.osu.edu/FellowshipSymposium](http://www.cancer.osu.edu/FellowshipSymposium) to RSVP and for more information, or contact Sarah Schmidt at [sarah.schmidt@osumc.edu](mailto:sarah.schmidt@osumc.edu) or (614) 293-5521.

# Where the Rubber Meets the Road

BY DARRELL E. WARD

“Pelotonia funds are extremely important for this trial,” Kaumaya says.

“They pay for needed pharmacy services, tests for patients and the purchase of vaccine adjuvants, and they help support correlative studies.”



**PRAVIN KAUMAYA, PhD,**  
*professor and director of the Vaccine Research Division in the Department of Obstetrics and Gynecology*

Clinical trials culminate years of laboratory and preclinical research. They determine whether promising experimental agents will benefit people and prevent, treat or perhaps even cure a form of cancer.

Pelotonia funds support two clinical trials at the OSUCCC – James: an early-phase study of a novel anticancer vaccine to prevent several types of solid tumors, and a safety and efficacy trial of a promising agent for treating chronic lymphocytic leukemia (CLL).

## A NOVEL ANTICANCER VACCINE

**Pravin Kaumaya, PhD,** professor and director of the Vaccine Research Division in the Department of Obstetrics and Gynecology, led development of this experimental vaccine, which targets two cell-surface receptors that help sustain many types of cancer.

The vaccine targets two specific regions of the human epidermal growth factor receptor 2 (HER-2), a molecule that occurs at abnormally high levels in up to 30 percent of breast cancers. In addition, the vaccine targets

HER-1 (also called epidermal growth factor receptor, or EGFR), a molecule overexpressed in many other solid tumors, including ovarian, renal, colon, lung and gastrointestinal cancers.

The phase I trial will 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. The study also includes an innovative efficacy arm that was approved by the U.S. Food and Drug Administration. The trial (ClinicalTrials.gov identifier NCT01376505) was open to accrual in August 2011 and has completed cohort 1 (six patients, dose level 1). The second cohort opened March 1, 2012.

Kaumaya led development of the protocol for the trial and serves as the trial’s overall chair. Clinical principal investigator for the trial is Tanios Bekaii-Saab, MD, assistant professor of Medicine and of Pharmacology, and medical director of Gastrointestinal Oncology. Co-principal investigator is William Carson III, MD, professor of Surgery and associate director for

clinical research at the OSUCCC – James.

“Pelotonia funds are extremely important for this trial,” Kaumaya says. “They pay for needed pharmacy services, tests for patients and the purchase of vaccine adjuvants, and they help support correlative studies.”

#### A PROMISING TARGETED AGENT FOR TREATMENT OF CLL

Chronic lymphocytic leukemia (CLL) is the most common leukemia diagnosed in the United States, with an annual incidence of about 15,000 and mortality of about 4,400. The treatment of CLL has greatly improved over the last three decades, but relapse is inevitable so new therapies are needed.

This safety and efficacy trial, which is led by **John C. Byrd, MD**, director of Hematology and professor of Medicine, of Medicinal Chemistry and of Veterinary Biosciences, evaluates a promising agent called ibrutinib (formerly PCI-32765) in combination with a monoclonal antibody called ofatumumab.

Ibrutinib is the first drug designed to target Bruton’s tyrosine kinase, a protein that is essential for CLL-cell survival and proliferation. Earlier trials evaluating ibrutinib as a single

agent at the OSUCCC – James and elsewhere have shown promising results.

“This is an exciting agent,” says Byrd, who is a member of the OSUCCC – James Experimental Therapeutics and Innate Immunity programs and holds the D. Warren Brown Designated Chair of Leukemia Research. “It seems to be a highly active oral therapeutic that produces remissions that often last months on end in patients with relapsed and refractory CLL. These responses last for many months in part because patients are willing to remain on the drug since the side effects are very tolerable.”

Amy Johnson, PhD, assistant professor of medicine at the OSUCCC – James, co-led preclinical research on ibrutinib showing that the agent is selective for B lymphocytes.

The trial combining ibrutinib with ofatumumab (OSU-10053, PCYC-1109) is being performed only at Ohio State in people with relapsed or refractory CLL, small lymphocytic lymphoma or prolymphocytic leukemia.

“The commitment of Pelotonia funds to this trial is important,” Byrd says. “Pelotonia dollars will support the patient-care costs associated with the trial.” 



**JOHN C. BYRD, MD**,  
director of Hematology  
and professor of  
Medicine, of Medicinal  
Chemistry and of  
Veterinary Biosciences

“The commitment of Pelotonia funds to this trial is important,” Byrd says. “Pelotonia dollars will support the patient-care costs associated with the trial.”

# Myeloma Survivor Gears Up for His Third Pelotonia Ride

BY BOB HECKER

**Matt Hare, 28**, of New Albany, has felt a strong connection to the annual Pelotonia bicycle tour from its beginning, almost as if lightning struck.

In a sense, it did.

One Friday in August 2009, Hare was a patient at the Cleveland Clinic, where he had been diagnosed with multiple myeloma and amyloidosis. He was undergoing chemotherapy during what would be a seven-week stay.

He and his parents wanted to return to central Ohio but thought there were no doctors there who specialized in his illness, until his aunt showed them an article in the *Columbus Dispatch* featuring Don Benson, MD, PhD, at the OSUCCC – James. Benson’s clinical interests include multiple myeloma. “That’s Matt’s cancer!” his aunt said.

Hare’s father called Benson’s cell phone and left a message. In Columbus, it was the inaugural Pelotonia’s opening-night ceremony. When a huge thunderstorm disrupted the festivities, Benson, who was attending as a rider, dashed to his car for shelter and received the cell-phone message. He immediately returned the call.

“He himself called us – not someone on his staff,” Hare recalls. Benson became his doctor, and Hare continued his chemotherapy at the OSUCCC – James, which was much closer to home. “I believe I have the greatest doctor in the world, and his team has the same determination and kindness he displays. They’ve become such a huge part of my life – I can’t help but feel this has all somehow come together for me.”

Hare’s chemotherapy ended that November, and in January 2010 he had a bone marrow transplant that has kept him in remission. Because multiple myeloma has a high rate of recurrence, he sees Benson for a checkup every three months.

Although he occasionally feels down about the relatively rare and incurable disease that has invaded his formerly healthy and active life, Hare says he no longer lives in fear of cancer and is hopeful for the future, realizing that research is leading to better treatments.

“I feel fine physically, and I’ve decided that, rather than worrying about it all the time, I will focus on the positives,” he says, explaining that he often speaks to groups about his experience and helps raise money for Multiple Myeloma Opportunities for Research and Education (MMORE), a non-profit corporation that supports medical research for this disease.

“I was told that I might never get back to feeling as good as I did before I got sick, but I feel much better now than in the days before my diagnosis,” he says. “It seems like I’ve taken a great turn for the better.”

In August, Hare will ride in his third Pelotonia. Cycling with him will be his parents and his wife Kate, whom he married last September.

“I did 25 miles in 2010 and 43 miles last year,” Hare says. “This year I’ll do a 100-mile route. I started training for it in February; I definitely need to step my game up.”

Something he knows how to do.



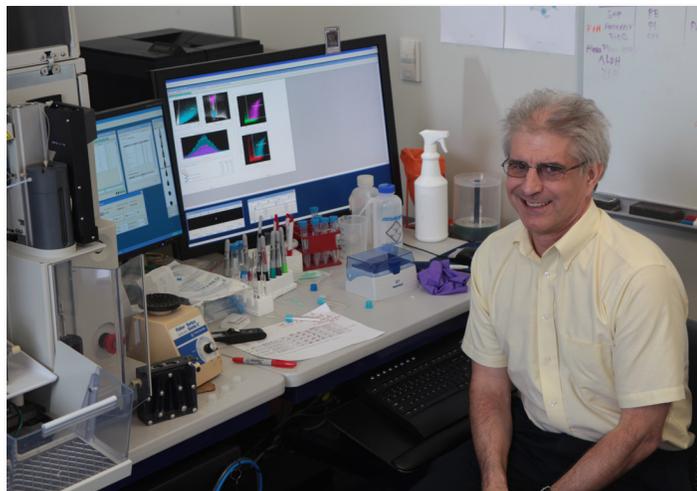
# Providing Tools for Discovery

*Cancer research today requires sophisticated equipment for gene sequencing, cell sorting and characterization, bioimaging, microscopy, data collection and other procedures. Revenue from Pelotonia has helped bring nearly \$2 million worth of advanced technology to the OSUCCC – James in the form of these powerful instruments.*

BY BOB HECKER

- Special BD FacsAria analytical cytometer** – This flow cytometer, the fourth and most sophisticated cytometer now in use by scientists at the OSUCCC – James, uses four lasers, rather than two or three, and multiple detectors for high-speed sorting and advanced analysis of up to 13 cellular parameters. Efficient flow cytometry is fundamental to advanced cancer research, says **Jeffrey Chalmers, PhD**, director of the Analytical Cytometry Shared Resource. “The more we can learn about cells, the more we can understand cancer and how to treat it. This instrument serves scientists studying all forms of cancer – solid tumors and hematologic malignancies – so everyone benefits.”

- Hi-Seq 2000 Sequencing System** – “This instrument lowers the accessibility bar and increases user-friendliness for global genomic and epigenomic analyses in terms of cost, data output quantity and quality, and the flexibility for running trial samples alongside actual samples in a single analysis,” says **Pearlly Yan, PhD**, technical director of the OSUCCC-Illumina Core. Since its launch in 2010, the HiSeq 2000 has undergone major changes,



**JEFFREY CHALMERS, PhD,**  
director of the  
Analytical Cytometry  
Shared Resource



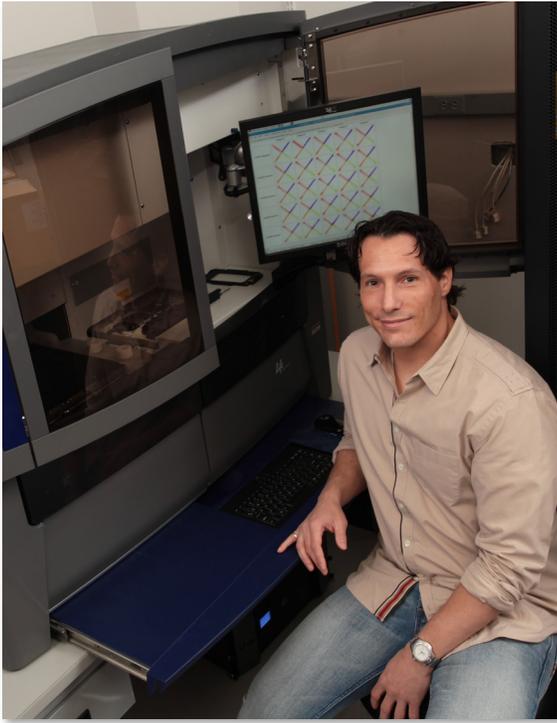
*BD FACSARIA cell sorter*

including larger flow cells and new image analysis software to bring sequencing output to 1.6 billion (200 million reads per lane, eight lanes per flow cell) passed filter reads. “The new sequencing chemistry (version 3) significantly improves coverage uniformity by reducing density-dependent GC bias and by increasing cluster density, thereby resulting in the lowest number of gaps and minimal risk of missing variants in sequencing data,” Yan says.

*continued...*



**JOHN CURFMAN,**  
Research Associate,  
OSUCCC – James



**JEFF PALATINI**  
*technical director of the  
OSUCCC – James  
Microarray Shared  
Resource*

**“The new instruments are an improvement in terms of higher throughput, but more importantly they reduce the cost of next-generation genomics and make it accessible to more researchers.”**

• **The SOLiD™ System** – Pelotonia money has supported the purchase of two new SOLiD 5500xl high-throughput analyzers that represent a significant upgrade to Ohio State’s next-generation gene-sequencing platform. In addition, the system’s older SOLiD 4 instrument has been retained for transition projects and to help manage overflow. “The new instruments are an improvement in terms of higher throughput, but more importantly they reduce the cost of next-generation genomics and make it accessible to more researchers,” says **Jeff Palatini**, technical director of the OSUCCC – James Microarray Shared Resource. “These instruments

are unrivaled in their accuracy, and they have the flexibility and scalability to run different types of experiments at the same time. This means faster time to results, from lab bench to bedside.”



# Bringing the Best to Ohio State

Funds raised by the Pelotonia rides have been committed to continuing to recruit some of the brightest minds in cancer to Ohio State, and keeping them here. Below are some of the new basic, clinical, translational and population scientists who strive every day - in the lab, the hospital and the community - to create a cancer-free world.



**ERIN BERTINO, MD**  
Assistant Professor  
Medical Oncology - Inpatient Care  
Recruited from Ohio State



**RICHARD GOLDBERG, MD**  
Physician-in-Chief, OSUCCC - James  
Medical Oncology - GI  
Recruited from University of North Carolina  
at Chapel Hill



**DELIANG GUO, PhD**  
Assistant Professor  
Radiation Oncology - Tumor-Cell Metabolism  
Recruited from UCLA



**THOMAS LUDWIG, PhD**  
Visiting Associate Professor  
Molecular and Cellular Biochemistry  
Modeling BRCA-1 and BRCA-2 Loss  
Recruited from Ohio State



**MARK LUSTBERG, MD, PhD**  
Assistant Professor  
Infectious Disease  
Recruited from Ohio State



**ERIN OLSON, MD**  
Assistant Professor  
Medical Oncology - Breast Cancer  
Recruited from Dana Farber Cancer Institute  
Harvard Medical School



**FLAVIA PICHIORRI, PhD**  
Assistant Professor  
Division of Hematology - Multiple Myeloma  
Department of Internal Medicine  
Recruited from Ohio State



**PAUL REITER, PhD, MPH**  
Assistant Professor  
Cancer Prevention and Control  
Recruited from University of North Carolina  
at Chapel Hill



**PETER SHIELDS, MD**  
Deputy Director, OSUCCC - James  
Cancer Prevention and Control, and  
Medical Oncology - Biomarkers of Cancer Risk  
Recruited from Lombardi Comprehensive  
Cancer Center, Georgetown University



**COLLEEN SPEES, PhD, MEd**  
Assistant Professor  
Medical Dietetics  
and Health Sciences  
School of Allied Medical Professions  
Recruited from Ohio State



**MENG WELLIVER, MD, PhD**  
Assistant Professor  
Radiation Oncology - Novel Lung  
Cancer Treatments  
Recruited from University of Pennsylvania



**TERENCE WILLIAMS, MD**  
Radiation Oncology - Targeted Therapy  
Recruited from  
University of Michigan



**CHRISTINA WU, MD**  
Assistant Professor - Clinical  
Medical Oncology - High-Risk Colon Cancer  
Recruited from Lombardi Comprehensive  
Cancer Center, Georgetown University



**JIANHUA YU, PhD**  
Assistant Professor  
Hematology-Immuno-Cellular Therapy  
Recruited from Ohio State



**FEN XIA, MD, PhD**  
Associate Professor  
Radiation Oncology - DNA Repair  
Recruited from Vanderbilt University

►► FUNDRAISING

## Registration Open for PELOTONIA 12

Anyone who would like to participate in Pelotonia 12 as a rider, virtual rider or volunteer should visit <http://pelotonia.org/register/> to register for this year's tour, which will unfold Aug. 10-12 on six routes of varying distances between Columbus and Gambier, Ohio (home to Kenyon College).



This webpage provides details and online forms for registering as an adult (16 or older), as a minor (those 14 or 15 may ride the 25- or 50-mile routes), as a virtual rider or as a volunteer. Riders must agree to raise the amount of funds specified for their chosen route. Thanks to generous event underwriters, all money raised by riders, virtual riders and donors will go directly to cancer research at the OSUCCC – James.

Last year's Pelotonia attracted nearly 5,000 riders from 38 states and four nations. It also involved some 1,700 volunteers. The event raised \$13.1 million, bringing the three-year fundraising total for Pelotonia to approximately \$25.5 million. Questions? Contact Karl Koon, director of development/Pelotonia at the OSUCCC – James, at [karl.koon@osumc.edu](mailto:karl.koon@osumc.edu).

## Apply Now for Pelotonia Post-Doc Fellowships

The Pelotonia Fellowship Program at Ohio State provides two-year research fellowships for promising postdoctoral candidates from any discipline—from the traditional sciences to such fields as history, business, engineering and humanities—who want to help cure cancer. These fellowships pay a competitive annual stipend based on National Institutes of Health (NIH) guidelines for postdoctoral fellows.

Applications are scored on:

- Applicant strengths and research potential (emphasis is given to clinical fellows and to applicants who received their doctorate within the past year and will be new to Ohio State, or who have been at the University less than one year, and who have the potential to become independent scientists);
- Mentor/adviser qualifications and training record;
- Innovativeness and impact of the project to cancer research.

Applications are due three times per year. For more information, including eligibility guidelines and an application, visit <http://cancer.osu.edu/go/pelotoniafellowship> or send an email to [Jeffrey.Mason@osumc.edu](mailto:Jeffrey.Mason@osumc.edu).

### IN THE SPRING ISSUE OF **frontiers**...

#### ORTHOPAEDIC ONCOLOGY

Joel Mayerson, MD, specializes in bone and soft-tissue tumors of the arms, legs and pelvis, and metastatic bone disease. With extraordinary surgical skill and sensitivity toward quality of life, he has changed an ankle into a knee and returned a child to the playing field.

#### DRUG DISCOVERY BY COMPUTATION

*In silico* drug design applies computers, databases, and computational and design software to discover and optimize new anticancer agents. OSUCCC – James researchers are using this fascinating combination of technologies to develop novel and first-in-their-class targeted agents.