



2017 INVESTING IN A
CANCER-FREE WORLD

Putting Pelotonia Dollars to Work



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COMPREHENSIVE CANCER CENTER

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With Pelotonia 17 receding into the past, it's time to celebrate yet another successful installment of this annual grassroots event that raises millions of dollars for cancer research at Ohio State.

Projections suggest that Pelotonia 17, which was held Aug. 4-6 on assorted routes between the Columbus area and Gambier, Ohio, may yield another record yearly fundraising amount, boosting the nine-year total to well above the \$130 million Pelotonia raised in its first eight years. At the last published report back in September, Pelotonia 17 riders, virtual riders and donors had raised \$17,329,134—a figure that would keep rising until fundraising officially ended Oct. 6.

That amount had pushed the running nine-year total to \$147.48 million and climbing. At the Nov. 16 check-celebration event, we'll learn the final Pelotonia 17 tally and a new overall total.

Whatever those are, the key thing to remember is that every dollar raised by riders, virtual riders and donors goes to cancer research at the OSUCCC – James thanks to Pelotonia's major sponsors, including L Brands, Huntington, and Peggy and Richard Santulli.

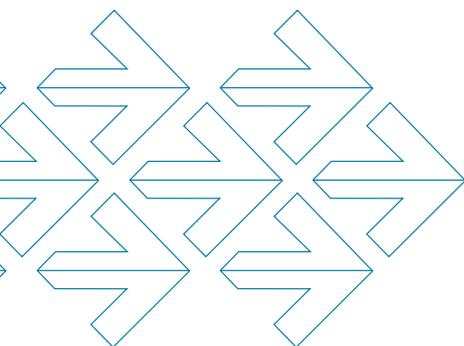
The Pelotonia 17 tour involved 8,022 riders ranging in age from teens to octogenarians. Riders represented more than 40 American states and 10 countries, and they collectively participated in 282 pelotons (riding groups). Overall, Pelotonia 17 donors hail from all 50 states and 66 countries. This year's event also benefited from the invaluable services of more than 3,000 volunteers.

A sobriquet for Pelotonia 17 was "greatest team ever," and I believe that together we have earned it. I can't express my gratitude enough to everyone who played a role, large or small, in this incredible endeavor that is growing exponentially with each passing year.

This investment report summarizes how Pelotonia funds have been distributed over the event's first eight years (money from Pelotonia 17 has not yet been allocated). It also shows how the money you raise benefits such key areas as: our Intramural Research Program for teams of faculty scientists; our Fellowship Program for students doing cancer research with faculty mentors; the purchase of new equipment for cancer research; support for our newly recruited scientists; some large-scale strategic investments; and our statewide initiatives to improve cancer prevention and care around Ohio.

Everyone should be proud of the incalculable good wrought by Pelotonia. We can all expect the momentum to continue as we prepare for the 10th anniversary of this event in 2018. Please continue to ride, to donate and to volunteer, and please encourage others to do the same as we keep pursuing our vision of a cancer-free world.

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



Pelotonia 17 Riders May Push 9-Year Fundraising Total Past \$150 Million



On stage at the Pelotonia 17 opening ceremony, former U.S. Vice President Joe Biden (second from right) and his wife, Dr. Jill Biden, receive a Pelotonia 17 jersey from OSUCCC Director and James CEO Michael A. Caligiuri, MD (right), and Pelotonia President and CEO Doug Ulman (left). The Bidens were among the evening's guest speakers.

Likely no one who attended the Aug. 4 opening ceremony for Pelotonia 17 came away uninspired.

The evening air simmered with a sense of striving toward a lofty goal that was perpetuated by the words of several speakers on hand for the ninth installment of this annual grassroots bicycle tour that, to date, has raised more than \$147 million for cancer research at Ohio State.

Among them was former U.S. Vice President Joe Biden, who quoted an admonition from his mother: "As long as you're alive, you have an obligation to strive..."

The former VP's wife, **Jill Biden**, who has a doctorate in education, told the thousands of riders, virtual riders and volunteers in the audience that their passion, drive and fieriness make Pelotonia "more than an event; it's a movement" by "an army of warriors facing a daunting foe."

Cancer survivor **Ethan Zohn**, a former professional soccer player who in 2002 won the hit reality TV show "Survivor Africa," and who later directed his winnings toward charitable work and community involvement,

noted that, despite individual differences, all humans are "survivors for a very short time in this world...It doesn't matter how you leave the world, but what you do every day to make it better."

OSUCCC Director and James CEO **Michael A. Caligiuri, MD**, punctuated that thought with a simple exclamation: "Wow! Look at what we're doing!"



Ohio State University President Michael Drake, MD (right), and Kenyon College President Sean Decatur (left) pause with cancer survivor Ethan Zohn, a former professional soccer player who in 2002 won the hit reality TV show "Survivor Africa." All three men spoke at the Pelotonia 17 opening ceremony.

(continued on page 4)



Pelotonia riders saw many expressions of gratitude as they pedaled along the roadways.

(continued from page 3)



Signs like these helped Pelotonia riders, volunteers and donors keep their shared vision in mind.

At this writing, Pelotonia 17 riders, virtual riders and donors had raised \$17,329,134, a total that kept climbing until fundraising for this year’s event officially ended on Oct. 6. At last report, the Pelotonia 17 tally had pushed the overall nine-year fundraising figure to more than \$147.48 million, every dollar of which goes to cancer research at the OSUCCC – James thanks to Pelotonia’s major sponsors, including L Brands, Huntington, and Peggy and Richard Santulli.

Total funds raised by Pelotonia 17 **will be announced Nov. 16** at an event at Express Live in downtown Columbus, where a nine-year fundraising total also will be revealed.

“All of the progress that arises from Pelotonia is fueled by your riding, your fundraising, your volunteering and your devotion to Pelotonia’s single goal of ending cancer,” Caligiuri said. “Thank you all so very much.”

Pelotonia President and CEO Doug Ulman said this year’s tour drew 8,022 riders ranging in age from teens to octogenarians. Riders represented more than 40 American states and 10 countries. The riders collectively participated in 282 pelotons (riding groups). And donors to Pelotonia 17 hail from all 50 states and 66 countries.

Ulman also lauded the critical roles played by the many virtual riders and the more than 3,000 volunteers for Pelotonia 17.

“Building the ‘greatest team ever’ takes a lot of hard work,” he said, giving a nod to a slogan for this year’s tour. “This is only possible because of all of you.”

Joe Biden—who along with his wife last summer launched a national venture called the Biden Cancer Initiative to make further progress in cancer prevention, detection, treatment and care while reducing disparities in cancer outcomes—said the Pelotonia spirit provides encouragement to millions who have been or will be touched by cancer.

“When you’re diagnosed with cancer, the fear of God comes to you,” he said. “You need hope, and not just hope in the abstract, but real hope! What you’ve done with Pelotonia over the past nine years—funding science and treatments—is giving people real hope.”

8-Year Pelotonia Financial Summary

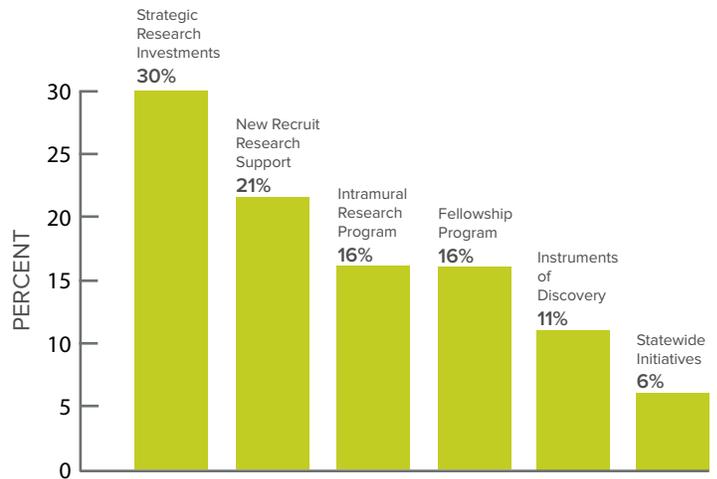
Pelotonia, the annual grassroots bicycle tour that started in 2009 as a means of raising money for cancer research at the OSUCCC – James, generated more than \$130 million in its first eight years through rider pledges and donations. Thanks to the event’s major funding partners, every dollar raised by riders, virtual riders and donors from 2009-16 has been directed toward advancing cancer research, as shown in the bar graph at right.

Pelotonia dollars support six major areas:

- **Intramural Research Program** – funds Idea Grants, clinical trials and other initiatives proposed by teams of faculty researchers who need to gather early data for promising projects that may lead to larger external grants later;
- **Fellowship Program** – enables Ohio State students in any discipline or level of scholarship to conduct cancer research with faculty mentors;
- **New Recruit Research Support** – helps newly recruited junior and senior investigators continue their research upon arrival at Ohio State;
- **Instruments of Discovery** – purchases state-of-the-art equipment needed for cutting-edge cancer research;
- **Statewide Initiatives** – takes aim at specific cancer types by working with community hospitals throughout Ohio to promote prevention, early detection and better outcomes;
- **Strategic Research Investments** – supports such initiatives as a Drug Development Institute, Digital Pathology and a Total Care Care® protocol at the OSUCCC – James.



Allocation of Pelotonia Funds (2009-16)



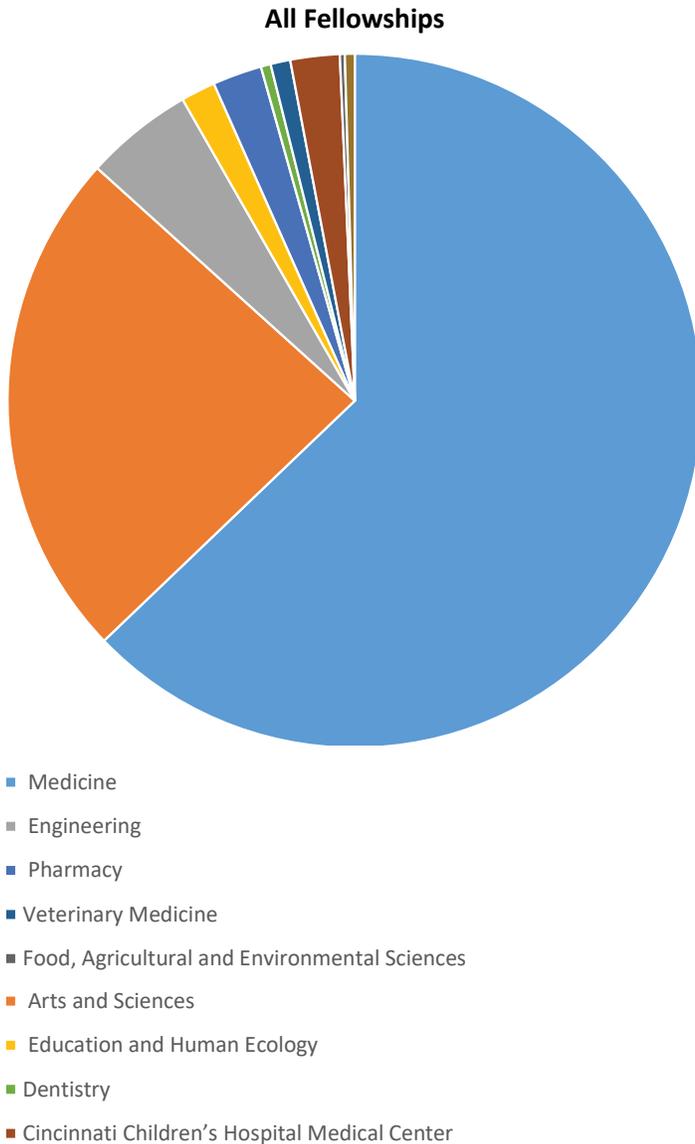
Bringing Knowledge to Bear in the Fight Against Cancer

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 at Cincinnati Children’s Hospital Medical Center:

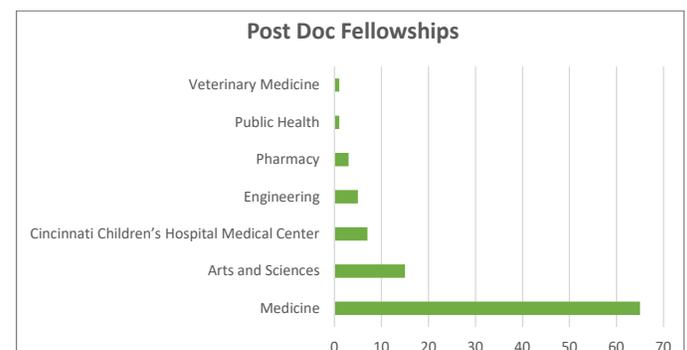
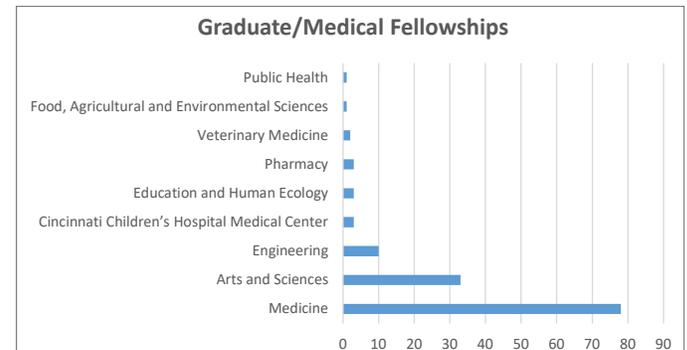
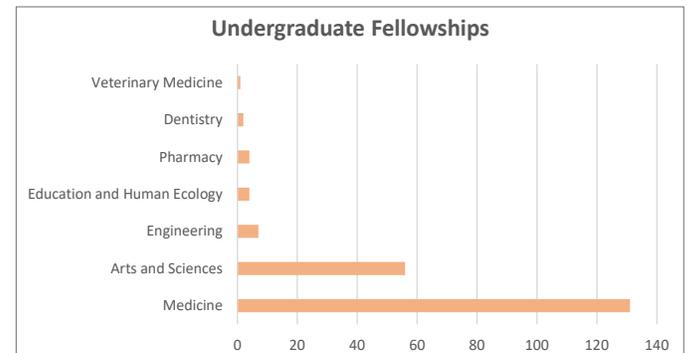
- College of Medicine
- College of Public Health
- College of Nursing
- College of Dentistry
- College of Pharmacy
- College of Veterinary Medicine
- College of Food, Agricultural and Environmental Sciences
- College of Law
- College of Education and Human Ecology
- College of Engineering
- College of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

Investing in the Next Generation

Allocations of Funding for Pelotonia 09-16



Since it began in 2010, the Pelotonia Fellowship Program has awarded more than \$13 million for 436 peer-reviewed cancer research projects by students working in the labs of faculty mentors. The students are in multiple disciplines and all levels of scholarship: undergraduate, graduate, postdoctoral and medical. To date, fellowships have been awarded to 205 undergraduates, 128 graduates, 97 postdoctoral fellows and six medical students. Their mentors represent multiple departments in several colleges at Ohio State, Nationwide Children's Hospital and Cincinnati Children's Hospital Medical Center (see charts).



From Ideas to Impact

Discoveries & Initiatives Supported by Pelotonia



Pelotonia funds support far-reaching initiatives and groundbreaking preliminary studies at the OSUCCC – James. These studies produce data and publications that can lead to grants for larger studies. In this way, Pelotonia helps to advance cancer treatment and improve patient care. Here are three examples of that work.

Predicting a Skin-Cancer's Spread

About 700,000 cases of cutaneous squamous cell carcinoma (cSCC), a form of skin cancer, are diagnosed annually in the United States. Most of the time, the disease is curable. But in about 15 percent of cases, the cancer metastasizes (spreads) to other areas of the body, causing up to 8,800 deaths per year.

Doctors have no way to predict the patients in whom the disease might spread, and there are no U.S. Food and Drug Administration (FDA)-approved targeted therapies for treating metastatic cSCC.

In 2011, **Amanda Ewart Toland, PhD**, associate professor in the Department of Cancer Biology and Genetics, received a Pelotonia Idea Grant for a study designed to identify genomic changes that cause squamous cell skin cancer to metastasize. The findings could contribute to the development of therapies for treating these aggressive tumors.





Her research led to two papers published in scientific journals. In one, Toland and collaborators compared levels of molecules called microRNAs that were present in metastatic cSCC tumor cells relative to cSCC cells from the initial tumor. The researchers identified several microRNAs that were present at significantly higher levels in the metastatic cSCC cells. “These microRNAs may be useful as biomarkers for identifying tumors that might metastasize or as potential therapeutic targets,” Toland says.

In the second study, Toland and colleagues used gene sequencing to identify gene mutations found in metastatic cSCC cells compared with cSCC cells from the primary tumor. This study found two genes in particular that were mutated much more often in metastatic cSCC cells.

Toland hopes to confirm the microRNA findings in a larger study and to determine the biological role of the mutated cSCC genes. She believes her findings eventually will contribute to improving the treatment of metastatic cSCC.

Preparing for Resistance

A 2014 Pelotonia Idea Grant helped **Sameek Roychowdhury, MD, PhD**, learn how lung, bladder, breast and other cancers could develop resistance to a new class of targeted drugs called fibroblast growth factor receptor (FGFR) inhibitors. His team is involved in three clinical trials for FGFR inhibitors, including a trial led by OSUCCC – James investigators.

“Understanding how drug resistance develops can help in the design of new agents or strategies to overcome resistance,” Roychowdhury says.

Roychowdhury and collaborators used a laboratory model to show how cancer can evade these agents. “Our findings also provide insights into how clinical trials for these therapies could be further developed to overcome the problem of drug resistance,” he adds.

Examining other molecules in the FGFR pathway, the researchers found that a regulatory protein called Akt remained highly active, even when FGFR is blocked by an FGFR inhibitor. Akt is a key regulator of cell biology, and it is directly involved in cell proliferation, cell survival and cell growth.

They also found that using a second targeted drug to block Akt, along with an FGFR inhibitor, could significantly slow cell proliferation, cell migration and cell invasion in lung cancer and bladder cancer cells.

“FGFR inhibitors are new therapies being developed in clinical trials for patients whose cancer cells have genetic alterations in this family of genes,” Roychowdhury says. “We believe our findings will help improve this therapy for lung, bladder and other cancers.”

Developing a Blood Test to Detect Lung Cancer Early

Lung cancer is a leading cause of cancer death worldwide. It is expected to kill nearly 156,000 Americans this year. This disease causes so many deaths in part because it is difficult to detect early and is generally diagnosed at a late stage, when a cure is difficult.

In 2013, **L. James Lee, PhD**, professor of Chemical and Biomolecular Engineering, and a team of OSUCCC – James researchers were awarded a Pelotonia Idea Grant to support preliminary studies on a high-tech way of using a blood sample to detect lung cancer early.

Their innovative project tested the feasibility of using a low-cost technology called a tethered lipoplex nanoparticle (TLN) biochip for detecting signs of lung cancer in the bloodstream. TLN essentially consists of molecular probes encapsulated in nanoparticle complexes tethered to a biochip that sits on a glass microscope slide.

The tethered nanoparticle complex captures submicroscopic vesicles called exosomes and detects certain molecular RNA targets. The tiny vesicles are given off by cancer cells and are found in a patient’s blood. They contain molecules called messenger RNA and microRNA that can be a signal for lung cancer.

“Initial testing of the tethered lipoplex nanoparticle biochip for detecting lung cancer has been promising,” Lee says. “If this new method proves reliable and practical, it may also be applicable to other cancers and to viral infections.”

The findings from the Idea Grant study led to three published papers and a federal grant.



Training the Next Generation

*Pelotonia Fellowships Support & Encourage
Future Cancer Researchers*



Promising and accomplished undergraduate, graduate, medical and postdoctoral students who want to conduct cancer research with faculty mentors are getting their chance through the Pelotonia Fellowship Program.

Since it started in 2010, the Fellowship Program has allocated more than \$13 million to award fellowships to 436 students, including 205 undergraduates, 128 graduates, 97 postdoctoral researchers and six medical students.

In addition to these awards, the program has provided international research experiences for 21 Ohio State undergraduate students in India and Brazil, and it has brought 14 students from India and Brazil to contribute to cancer research in Ohio State labs.

The fellowships are awarded by a committee that oversees the program and includes some of Ohio State's most distinguished basic, translational and clinical researchers from many disciplines. The committee is

chaired by Pelotonia Program Director Joanna Groden, PhD, of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, and is co-chaired by Janice Kiecolt-Glaser, PhD, of the OSUCCC – James Cancer Control Program.

“Research grants from external sources are very difficult to obtain, especially for students,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD, “so it’s important for us to support the next generation of promising young cancer researchers so we can continue working toward our goal of ending this disease.”

The Fellowship Program website (cancer.osu.edu/pelotoniaresearch) includes the names of all funded fellows and their project titles. It also includes photos of the most recent fellowship recipients.

Here’s a look at three Pelotonia recipients, their projects and continued progress.

Jackson Killian



In science, learning from studies that go awry can be as rewarding as learning from successful projects.

Jackson Killian, a fifth-year undergraduate majoring in Physics and Computer & Information Science, found that out while conducting cancer research as a Pelotonia fellowship recipient.

Working with faculty co-advisers Ralf Bundschuh, PhD, and Pearly Yan, PhD, Killian tried to develop a computational technique that would give researchers a key to access older, lower-quality cancer tissue samples that are largely unusable in modern studies, which use techniques requiring high-quality samples.

“We studied and characterized many effects that make using lower quality samples challenging, but ultimately the effects we corrected for did not open the door to as many samples as we had hoped,” Killian says.

Although disappointed that his hypothesis did not pan out, he thinks of the setback as part of his learning experience. He also agrees with a widely held view among scientists that interpreting unexpected outcomes and trying to understand what happened is part of the challenge—and fun—of research.

“In fact, my favorite moment from working on my fellowship centered on an instance like this,” Killian recalls. While looking for an effect that he was sure would be expressed in low-quality tissue samples, he found the effect to be “perplexingly invisible. So I dug through literature for days to interpret this outcome and tweaked my analysis. With my new analysis, this effect exploded off the page. I will never forget how gratifying that feeling of discovery was.”

The New Jersey native also completed a secondary project with Bundschuh and Yan in which they developed a Web-based tool called FuSpot that enables researchers to build pictures of gene fusions from the DNA of cancer tissue samples. (Fusions occur when sections of DNA break from their original positions and merge into new DNA strands that can create or exacerbate cancers.)

“FuSpot will aid in the detection and validation of new cancerous fusions, and in the future it could even assist with diagnoses,” Killian says. He lectured on FuSpot at the 2017 Pelotonia Fellowship Symposium on Oct. 24 in Ohio State’s Biomedical Research Tower.

Killian, who considers Bundschuh and Yan to be “invaluable mentors,” says his career goal is “to conduct research that applies computational techniques from computer science to challenging problems affecting social good.”

He is grateful for the opportunity “to have trained at one of the nation’s top research hospitals” and to “give back to this amazing community through my future research.”

He also rode 50 miles in Pelotonia 16 as a member of Team Buckeye on behalf of his grandmother, Ethel, who lived with his family for two years before passing away after a battle with ovarian cancer.

“She was the voice of my childhood that made me own the belief that I could conquer any challenge,” Killian says. “I rode for her.”

Peter Yu



Peter Yu, an MD candidate in the class of 2018, devoted two years to full-time cancer research between his third and fourth years of medical school at Ohio State. That experience included a 2016-17 Pelotonia fellowship he received to study liposarcoma with faculty mentors Denis Guttridge, PhD, Raphael Pollock, MD, PhD, and Hans Iwenofu, MD.

“I started a small project in cancer research during my first two years of medical school, but it wasn’t until I started clinical rotations and was learning how to take care of patients with cancer that I realized I needed to return to the lab to advance cancer research,” Yu wrote in his project summary. His work focuses on sarcomas—rare cancers that arise from bone, muscle and fat.

His Pelotonia-supported research, which he completed earlier this year, involved liposarcoma, the second most common type of sarcoma. “A microRNA is a small molecule that can affect hundreds of genes at once. Our laboratory team found that a microRNA that stops muscle cancer might also stop liposarcoma,” Yu says. “Understanding how this microRNA works in liposarcoma could lead us to more effective treatments.”

Yu, who is still conducting cancer research with Guttridge and Pollock as his co-mentors, lectured about his Pelotonia-funded work at the annual Pelotonia Fellowship Symposium held Oct. 24 in Ohio State’s Biomedical Research Tower. His presentation focused on dedifferentiated liposarcoma and how his team found the loss of a microRNA called miR-133a in this disease.

"I explained the experiments we conducted to understand how miR-133a functions in this disease," Yu says, adding that his team discovered "that miR-133a affects the metabolism of dedifferentiated liposarcoma. My presentation was from my Pelotonia fellowship study, and I have continued to work on this project."

In fact, he will keep studying cancer throughout his medical school experience. "I am completing an Advanced Competency in Research during my fourth year, which gives me lots of time to commit to full-time cancer research," Yu says, noting that he also received an Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship to support his studies.

Yu, an Illinois native with a bachelor's degree in psychology from Northwestern University, completed the full 180-mile ride in Pelotonia 17 as co-captain of the BSR-Spin Doctors Peloton (riding group). After he earns his MD, he plans to become an academic medical oncologist with laboratory and clinical responsibilities.

"I am applying to several internal medicine physician scientist training programs," he says. "The research experience and training provided by my Pelotonia fellowship were instrumental in helping me realize my passions and career goals."



Emily Theisen, PhD



When Emily Theisen, PhD, a postdoctoral scientist in the lab of Stephen Lessnick, MD, PhD, at Nationwide Children's Hospital (NCH), set out to earn her PhD in pharmaceutical sciences at the University of Utah College of Pharmacy, she didn't plan to devote her research to childhood cancer.

"I just wanted to design better drugs. I think (the discipline of) pediatric cancer found me, not the other way around," Theisen says, explaining that her PhD project involved compounds that "serendipitously worked in two pediatric cancers: Ewing sarcoma and T-cell acute lymphocytic leukemia. We still don't fully understand how these compounds work, and it strikes me that there's so much we don't know that could help kids with cancer."

Two pediatric physicians who mentored Theisen at Utah "showed me how important research is in pediatric cancer. My hope is to stay in academia and run my own research program."

At NCH, Theisen is part of a team that has what she describes as "a laser focus on Ewing sarcoma." She explains that this disease is caused by a single mutant protein called EWS/FLI that is found only in Ewing sarcoma cells, and she notes that all attempts to target it with drugs have failed. Theisen is working to figure out how the normal machinery in the cell gets hijacked by EWS/FLI in order to design better therapies.

"Our group wants to bring insights gained from a deep understanding of basic disease biology to a place where they make a difference for patients," she says. "My Pelotonia fellowship (which extends through April 30, 2018) was the game changer for me. It allowed me to hire the first member of my team, a research technician. I can't emphasize enough how much this support has impacted my decision to devote my career to pediatric cancer."

Theisen and her mother, a former tour cyclist, rode 25 miles in Pelotonia 16. In Pelotonia 17, Theisen rode the full 180 miles with the Nationwide Children's Hospital Peloton; her mother was a virtual rider.

Noting that her mother "raised us to embrace the challenges in life, always emphasizing running and biking uphill for fun," Theisen looks forward to the professional challenges that lie ahead as she continues on a career trek to help end cancer.

Teaming Up Against Cancer

Pelotonia-Funded Grants Support 8 Additional Cancer Research Projects



Eight teams of Ohio State faculty scientists recently received a combined total of \$1.14 million in Pelotonia funding that will help them gather early data for innovative projects so they can apply later for larger grants from external sources to support these efforts.

The eight projects will be funded by the OSUCCC – James' Intramural Research Program (IRP), which receives extensive Pelotonia support. IRP funding can include:

- Idea Grants that support early work in high-risk, high-payoff research for which government grants are difficult to obtain;
- Community Partnership Awards that support investigators who team with a community entity on a cancer-focused study;
- Clinical Trial Awards, which support studies that seek ways to prevent, diagnose and treat cancer while providing participating patients with some of the most advanced treatments available anywhere;

- Bridge Funding Awards, which help researchers with competitive renewal applications for National Cancer Institute (NCI) grants that were not funded on their first submission, or for grants whose initial funding has expired.

This IRP funding, awarded through a competitive peer-review process conducted by internal and external scientists not competing for grants in the current funding year, is critical at a time when government grants are difficult to obtain for the early pursuit of promising studies.

Over the past seven years, 108 OSUCCC – James research teams have received Pelotonia-supported IRP awards totaling \$11.1 million. Each award provides support for two years.

“Scientists working on these creative projects are ‘thinking outside the box’ and need funding support to gain traction for ideas that could lead to breakthroughs,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD. “They likely couldn’t pursue these projects



without funding raised by the thousands of Pelotonia riders, virtual riders and donors.”

Here are summaries of the eight most recently funded projects:

Understanding Cancer Stem Cells in Ovarian Cancer

Investigator: Qi-En Wang, MD, PhD, OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program

Only 45 percent of ovarian cancer patients reach the five-year survival mark, mainly due to high rates of advanced disease and disease recurrence. Researchers believe cancer stem cells are the root of many solid tumors, including ovarian. OSUCCC – James researchers recently discovered a protein (DDB2) that stops the growth of ovarian cancer stem cells. This study further investigates mechanisms by which DDB2 stops cancer stem cell survival. Results may lead to better strategies for preventing ovarian cancer spread and recurrence.

Evaluating New Targets for Glioblastoma Treatment

Investigator: Deliang Guo, PhD, OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program

Glioblastoma (GBM) is the most common type of adult malignant brain tumor. Because most patients live only 12 to 15 months after diagnosis, new molecular targets are needed to improve patient survival. Guo and team recently revealed that a protein called SCAP is essential for activation of SREBP-1, a gene/protein involved in GBM growth. This study will advance knowledge of how cellular metabolism is “reprogrammed” in GBM—information that could help identify new molecular targets for the disease.

Improved Imaging for Bladder Cancer Diagnosis and Staging

Investigators: Cheryl Lee, MD, Chair, Department of Urology, and OSUCCC – James Urologist; and Metin Gurcan, PhD, OSUCCC – James Molecular Biology and Cancer Genetics Program

Accurate staging of bladder cancer can be difficult with the imaging tools currently available, making it hard for urologists to recommend the best treatment for each patient’s disease characteristics. This study will develop pathological image analysis tools to accurately stage and stratify patients by disease risk. This will help urologists make treatment decisions that balance the best chance of long-term cancer control while avoiding over-treatment.



Stimulating the Immune System to Fight Cancer

Investigator: Robert Wesolowski, MD, OSUCCC – James Translational Therapeutics Program

Cancer activates cells that interfere with the immune system's ability to kill cancer. Recent OSUCCC – James research showed that these cells—known as myeloid-derived suppressor cells—can be stopped with the drug ibrutinib. In preclinical studies, researchers also showed that ibrutinib was most effective in combination with a second drug that activates immune-boosting T-cells called immune checkpoint inhibitors. Initial results showed a complete elimination of breast cancer tumors in 50 percent of subjects treated with ibrutinib and immune checkpoint inhibitors. The team will conduct a pilot study to confirm these results in patients with metastatic solid tumors who will receive the immunotherapy with an immune checkpoint inhibitor called nivolumab.

Immunotherapy to Treat Patients With Acute Myeloid Leukemia

Investigator: Sumithra Vasu, MBBS, OSUCCC – James Leukemia Research Program

This grant will provide expanded support for two ongoing clinical trials in acute myeloid leukemia (AML), a cancer that occurs in more than 62,000 people annually and affects the blood-forming cells in the marrow. The trials explore the combination of a more tolerable anti-leukemia drug, decitabine (DAC), given with a new targeted antibody that has been shown in preclinical testing to improve the immune system's natural ability to recognize and eradicate cancer cells. This grant will help conduct studies to launch future studies combining decitabine and cellular therapies.

New Targeted Therapies for Thyroid Cancer

Investigator: Manisha Shah, MD, OSUCCC – James Translational Therapeutics Program, and Cynthia Timmers, PhD, Solid Tumor Translational Science Shared Resource

Thyroid cancer is the ninth most common cancer in the United States, but there is no curative treatment available for patients with subsets of the disease that have spread to other parts of the body. OSUCCC – James researchers have shown that two different targeted therapies, given alone or in combination, are effective for treating a subset of advanced papillary thyroid cancer patients with *BRAF* gene mutations. This grant will fund evaluation of patient tumors and blood to learn how cancer cells become resistant, which will guide research to help improve treatment.

Combining Radiation and Immunotherapy to Treat Brain Tumors

Investigator: Raju Raval, MD, DPhil, OSUCCC – James Translational Therapeutics Program

Glioblastoma is the most common primary adult cancer affecting the central nervous system, and treatment outcomes are very poor. Scientists believe that a variety of mechanisms prevents the immune system from eradicating these tumors. In this project, researchers will test the effectiveness of radiation with immune modulating treatments in a clinical model to identify potential ideal combination therapeutic strategies. This may lead to an optimal approach for translating these findings to human clinical trials.

Understanding Genetic Predisposition to Acute Myeloid Leukemia

Investigators: Clara D. Bloomfield, MD, OSUCCC – James Leukemia Research Program, and Albert de la Chapelle, MD, PhD, OSUCCC – James Molecular Biology and Cancer Genetics Program

Differences in a person's DNA make each person unique. These differences can also make individuals more susceptible to developing diseases like cancer. This study is aimed at discovering genetic differences that exist in the general (non-cancer patient) population that make people more susceptible to acute myeloid leukemia (AML). This information will help scientists better understand inherited risk of the disease to improve overall understanding of biologic causes of leukemia and inform future clinical practice.



Statewide Initiatives

Pelotonia-Funded Initiatives Take Aim at Colorectal, Endometrial and Lung Cancers in Ohio



The OSUCCC – James has invested millions of dollars in Pelotonia funds to support three statewide initiatives that promote early detection and better outcomes in colorectal, endometrial (uterine) and lung cancers in Ohio.

The initiatives take the OSUCCC – James' individualized genetic screenings, education and care on the road through partnerships with a network of some 50 Ohio community hospitals.

“The goal of our statewide initiative program is to take state-of-the-art science and translate it to the communities across Ohio to help elevate cancer patient care, prevention and education, and to reduce healthcare costs while saving lives,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD.

The first initiative, called the Ohio Colorectal Cancer Prevention Initiative (OCCPI), began in 2013 and involved \$4 million in Pelotonia funds. The project set out to screen newly diagnosed colorectal cancer (CRC) patients and their biological relatives for Lynch

syndrome (LS), a cancer-causing condition that occurs when a person inherits a mutation in one of four genes. Individuals with LS are very likely to develop CRC, uterine, ovarian, stomach or other cancers. The screenings identified family members who may be at risk of developing these cancers so they can take precautionary measures.

“People with Lynch syndrome need intensive surveillance, with annual colonoscopies beginning at age 20-25,” says OCCPI principal investigator **Heather Hampel, MS, LGC**, associate director for the Division of Human Genetics at Ohio State. “This increased monitoring can save lives by catching precancerous polyps early, before cancer develops.”

Beating Lung Cancer – in Ohio (BLC-IO)

Supported by \$3 million in Pelotonia funds and other philanthropy, this initiative—led by **Peter Shields, MD, David Carbone, MD, PhD**, and **Mary Ellen Wewers, RN, PhD, MPH**—also will draw upon a network of 50 partner hospitals in communities across Ohio (the same network created by the OCCPI).

A three-year period of patient recruitment began last March. BLC-IO has two aims: to evaluate the effect of advanced gene testing combined with expert advice on lung cancer treatment and patient survival, and to improve smoking-cessation rates among smokers with lung cancer and their family members. Quality of life also will be assessed for all patients.

Project leaders expect more than 2,000 newly diagnosed, stage IV, non-small-cell lung cancer patients to enroll in the BLC-IO trial. Enrollees will receive free testing for more than 300 genes in their cancer specimens. Local treating physicians will receive expert support for interpreting test results and determining treatments.

Published data suggests that up to 64 percent of lung cancer patients have genetic mutations in their tumor cells that can be treated with U.S. Food and Drug Administration (FDA)-approved targeted therapies or drugs in clinical trial testing. “Lung cancer is most often diagnosed in a metastatic (stage IV) state, so getting patients on the right treatment—the first time—is critical,” says Carbone, who directs the Thoracic Oncology Center at the OSUCCC – James.

BLC-IO also will provide smoking-cessation support for up to three years to all participating lung cancer patients and their family members.

“Smoking addiction is a chronic, relapsing disease, and many factors contribute to a person’s success or failure in kicking the habit,” says Shields, deputy director of the OSUCCC – James. “Science has shown that smokers with cancer have more toxicity and shorter survival, and that some drugs work less effectively in these patients.”

Researchers will test different models for smoking-cessation support among lung cancer patients and their families in collaboration with the patients’ primary care physicians. “We believe there is a strong potential to save many years of life, and millions of dollars associated with cancer treatment later, by helping people reduce their risk for lung and other cancers through smoking cessation,” Shields adds.



Ohio Prevention & Treatment of Endometrial Cancer (OPTEC)

Through an allocation of \$1 million in Pelotonia funding, the OSUCCC – James has launched the OPTEC initiative, which will recruit up to 700 women with endometrial (uterine) cancer from at least 25 partner hospitals in communities around Ohio.

The women will be screened for Lynch syndrome (LS) and other inherited genetic mutations that increase the risk of endometrial, colon, stomach and ovarian cancer. Tumor samples from study participants will also undergo molecular profiling to guide and personalize treatment according to each patient’s tumor characteristics.

Patients who are identified with LS and their at-risk family members will be educated about the importance of genetic testing and cancer-prevention strategies based on their higher risk of LS-associated cancers. Patients whose tumors have defective DNA mismatch repair will be considered for novel immunotherapy clinical trials for their endometrial cancer.

OPTEC is led by **David Cohn, MD**, and **Paul Goodfellow, PhD**, with multiple collaborators from the OSUCCC – James and Nationwide Children’s Research Institute.

“Because endometrial cancer incidence and death rates are rising in the United States, we must escalate our efforts to understand this disease and develop new therapies,” says Cohn, who directs the Division of Gynecologic Oncology at Ohio State.

OPTEC will test endometrial cancer patients in Ohio for LS using a novel genetic sequencing technique developed by Goodfellow, a geneticist at the OSUCCC – James, and **Elaine Mardis, PhD**, a geneticist at Nationwide Children’s Research Institute.

“In the past, genetic testing for LS was a multi-step process associated with higher costs and delayed results. We have developed a one-step tumor-sequencing method that allows us to test for inherited genetic mutations rather than relying on sequential screening and testing,” Goodfellow explains. “We will confirm all inherited LS mutations that are identified in patient tumors with a follow-up test that identifies the mutation in white blood cells and is conducted in a clinical genetics laboratory.”

Genomic profiling through OPTEC will also help identify patients most likely to benefit from new medical therapies, including immunotherapy drugs that target the PD-1 (programmed cell death-1) protein. Drugs targeting PD-1 have emerged as promising approaches to treating tumors in patients with LS.

Strategic Research Investments

Pelotonia Dollars Support Long-Lasting Strategic Initiatives



Anil Parwani, MD, PhD, MBA, director of digital pathology, and vice chair and director of the Division of Anatomic Pathology in the Department of Pathology

The OSUCCC – James invests substantial Pelotonia funds in large-scale initiatives designed to have a long-term impact on cancer research and patient care. Here are two of the largest investments of this type that have been supported by Pelotonia to date.

Drug Development Institute – As the foundation for new cancer treatments, promising laboratory discoveries made by OSUCCC – James researchers must enter a “drug development process”—a myriad of synchronized activities that need to be completed before a new drug can be marketed.

Typically, these activities are in the purview of pharmaceutical companies that specialize in taking ideas from the laboratory through product development, manufacturing, review by the U.S. Food and Drug Administration (FDA), and clinical trials involving patients. But thanks to the support of Pelotonia, the Harry T. Mangurian Jr. Foundation and other philanthropic sources, Ohio State has established a Drug Development Institute (DDI) in which a team of experts is dedicated to steering discoveries through the preclinical drug development process.

Pelotonia funds support such project costs as research reagents, cellular assays, chemical manufacturing and specialized analytics. The funds are used to build value into DDI-invested projects.

Led by **Jeff Patrick, PharmD**, the DDI is a biotech-like institute staffed by scientists who have worked in the pharmaceutical industry and have diverse experience in bringing new therapies to market. An external advisory board provides scientific, clinical and strategic guidance. The board consists of pharmaceutical industry executives and expert OSUCCC – James physician-scientists. The DDI has a cancer-focused portfolio and continuously evaluates new projects. To date, it has evaluated more than 100 potential projects for investment and is currently managing seven.

Digital Pathology – An accurate and timely diagnosis is the first step in every cancer patient’s treatment. Pathologists traditionally have placed diseased tissue on glass slides and examined them under a microscope, but slides are difficult for pathologists to share with colleagues and have other problems as well.

In 2017, the FDA approved digital pathology for use in primary cancer diagnosis. Digital pathology takes tissues mounted on glass slides, scans them bit by bit and digitally knits the individual pictures together to make one highly detailed image. This virtual image is paired with associated clinical information to quickly give pathologists an integrated picture of each patient’s unique cancer so optimum therapy can be delivered sooner.

Moreover, this technology enables pathologists to perform tests and other diagnostics that are not possible with glass slides, and the digital images can be shared with experts worldwide. The OSUCCC – James is implementing a digital pathology service led by **Anil Parwani, MD, PhD, MBA**, through which all patient pathology slides are being digitized, along with those of the past seven years.

Pelotonia dollars are contributing to this effort by helping to create a digital archive of past pathology specimens and their associated clinical data for use by researchers. The specimens and information in the archive will be “de-identified” (containing no identifying patient information) and made available to cancer investigators anywhere in the world.

New Hope

Pelotonia Dollars Support Innovative Clinical Trials



Clinical trials evaluate the safety and effectiveness of new treatments and study ways to improve them. In this manner, clinical trials improve cancer care and bring renewed hope to patients. Here's an example of how Pelotonia funds are helping to solve important questions related to a trial at the OSUCCC – James. To learn more about these and other trials, call The James Line at 800-293-5066 or visit www.cancer.osu.edu.

Pelotonia Funding Helps Thyroid Cancer Trial Answer Additional Questions

Besides comparing new therapies with a current standard of treatment, most clinical trials also include studies designed to learn more about the drug or the treatment being evaluated by the trial.

Pelotonia funds can be used to support these additional studies, known as correlative studies. For example, Pelotonia money is supporting a correlative study that is part of a clinical trial for a form of thyroid cancer called

papillary thyroid carcinoma (PTC). About 80 percent of the 57,000 thyroid cancer cases expected in the United States in 2017 will be PTC.

Moreover, some 44 percent of PTC patients have a mutation in a gene called *BRAF*. The mutated genes send signals that cause cells to become cancerous and play a role in the development of thyroid, lung, melanoma and other cancers. But two targeted drugs, dabrafenib and trametinib, that have been approved by the U.S. Food and Drug Administration (FDA) for treating melanoma also show promise for treating cases of PTC that have *BRAF* mutations.

Dabrafenib blocks signals sent out by mutated *BRAF*, and trametinib targets a different gene that scientists believe helps PTC cells develop resistance to dabrafenib.

At the OSUCCC – James, a multicenter clinical trial led by medical oncologist **Manisha Shah, MD**, is testing the effectiveness of the two drugs.



About half of the 53 trial participants were treated with dabrafenib alone; the other half received dabrafenib plus trametinib. (Patients who took dabrafenib alone and whose disease began progressing were able to cross over into the group taking both agents.)

The trial was designed to show if *BRAF*-targeted therapies (one or two drugs) are effective and whether receiving the two drugs together would improve outcomes in PTC patients compared with PTC patients treated with dabrafenib alone. Last June at the annual meeting of the American Society of Clinical Oncology (ASCO), the OSUCCC – James team presented its findings that both dabrafenib alone and dabrafenib plus trametinib were well-tolerated by patients, resulting in a 50- to 54-percent response rate.

“Both therapy approaches resulted in positive outcomes for patients, and that gives us more treatment options,” says Shah, a member of the Translational Therapeutics Program at the OSUCCC – James. “Targeted therapy has the potential to change the standard of care for patients with this aggressive form of thyroid cancer.”

A Kinder, Gentler Biopsy

Shah and collaborators continue to follow patients in this trial to determine whether dabrafenib alone or combined with trametinib is more effective in the long term.

In addition, OSUCCC – James researchers are exploring other questions through the Pelotonia-supported correlative studies associated with this trial.

One of those studies is evaluating a procedure called liquid biopsy. Typically, biopsies for solid tumors such as PTC require needles, sometimes guided by ultrasound, to obtain a small tumor sample. For certain cancers, a biopsy requires a surgical procedure. The tumor sample is then studied by a pathologist, whose findings help determine optimum treatment.

A liquid biopsy involves the use of blood, urine or saliva samples, all of which can contain cell-free DNA. In people with cancer, dying tumor cells shed DNA into their circulatory system. This Pelotonia-supported correlative study is evaluating whether circulating tumor DNA in trial participants can predict how well they are responding to therapy or whether their tumor is progressing.

This study is the first to use this assay prospectively to follow treatment response and early detection of resistance in PTC.

Furthermore, the researchers will sequence the circulating tumor DNA to learn whether resistance mutations are present. This would be the first study of its kind in solid tumors performed at Ohio State. The scientists believe it could open the door for the analysis of other tumor types in which invasive biopsies are unattainable.



Instruments of Discovery

4 Pieces of Equipment Your Pelotonia Dollars Have Purchased

Conducting cutting-edge cancer research is complex and requires sophisticated equipment for ready use by the talented researchers who strive to turn laboratory discoveries into treatments.

That's where Pelotonia dollars make a big impact. Some of the money raised by riders, virtual riders and donors in this annual bicycle tour is allotted to help purchase the latest instruments and technology to assist the more than 330 researchers at the OSUCCC – James. Here's a look at four of the instruments purchased during the past few years with Pelotonia funding support.

Helios Mass Cytometer – Pelotonia assisted in the purchase of this instrument, which paved the way for recruiting **Gregory Behbehani, MD, PhD**, from Stanford University to build a research program in the field of mass cytometry.

“The Helios mass cytometer allows us to look at one cell at a time and use lots of measures to see exactly what type of cell this is, and combine it with measurements of how the cell behaves,” Behbehani says. “When you put these together, you get a complex, rich picture of the cancer, and we can discover how it responds to standard treatment or novel treatment.”

Orbitrap Fusion™ and Quantiva Mass Spectrometers – These instruments aid in the understanding of cancer cell biology. They detect abnormal proteins shed by tumor cells via urine, blood or saliva—proteins that originate in the tumor or the tumor microenvironment. **Michael Freitas, PhD**, is an analytical chemist who specializes in protein characterization using mass spectrometers. His work depends on the capability of the instruments he uses.

“Sometimes you have very few cells to work with,” Freitas says. “Developments in mass spectrometry are improving the sensitivity of instruments to see less material. They can also look at more proteins in a given time. We get more data and more insight because of Pelotonia.”

The Sciclone NGS (Next Generation Sequencing) Workstation – This robotic device prepares batches of cancer cells for genome sequencing. As opposed to having a technician prepare samples in test tubes with a single pipette, the Sciclone



NGS does the pipetting en masse, preparing up to 96 samples at once to create consistency and free up lab personnel for other work. Genome sequencing is vital to determining how cancer hijacks normal cell functions; this device makes that preparation faster and easier.

REES Enterprise Environmental Monitoring System – This system can be regarded as a quiet workhorse of cancer research—technology that works around the clock and, if all goes well, is rarely heard from by the researchers and lab supervisors who rely on it. It may not analyze cells or diagnose cancer, but it does its part for cancer research by monitoring the freezers that store samples of DNA, plasma and serum, which would be useless if they thawed.

The REES system monitors multiple locations, ensuring ongoing monitoring in all situations. **Heather Hampel, MS, LGC**, director of Biospecimen Services at the OSUCCC – James, and others receive an alert via phone call, text or email if the temperature drops below an acceptable level. This allows them to act quickly to protect the stored samples.

Bringing the Best Research to Ohio State



The OSUCCC – James attracts some of the brightest minds in cancer research, and Pelotonia dollars help them continue their research when they arrive. Recent recruits include these prominent researchers:



Kellie Archer, PhD, is a professor and chair of the Division of Biostatistics in the College of Public Health. She also is a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. Her primary research area has been the development of statistical methods and computational algorithms for analyzing genomic data. She came to Ohio State from Virginia Commonwealth University (VCU), where she directed the VCU Massey Cancer Center Biostatistics Shared Resource.



Allan V. Espinosa, MD, is in the College of Medicine, Department of Internal Medicine, Division of Medical Oncology, where he has clinical and research interests in neuroendocrine malignancies and thyroid cancers. He performed translational research on thyroid cancer as a postdoctoral researcher at the OSUCCC – James, and then transitioned to clinical training in Internal Medicine at Ohio State Wexner Medical Center. After completing a fellowship in Hematology/Oncology at Vanderbilt University, he served the communities of northern Maine, where he was in charge of the Hematology/Oncology clinics at Cary Medical Center, Northern Maine Medical Center and Millinocket Regional Hospital.



Valerie Grignol, MD, is a surgical oncologist in the College of Medicine, Department of Surgery, Division of Surgical Oncology. She joined the Ohio State medical faculty after completing her fellowship training in surgical oncology here. Grignol treats

patients suffering from breast cancer and sarcoma. Her research interests focus on clinical trials and outcomes for sarcoma patients.



Clara Lee, MD, MPP, is in the College of Medicine, Department of Plastic Surgery, and in the College of Public Health, Division of Health Services Management and Policy. She also is in the Cancer Control Program at the OSUCCC – James. As a plastic surgeon, she specializes in microsurgery and cancer reconstruction, including breast, sarcoma and melanoma. Her research focuses on understanding and improving how patients and providers make decisions about cancer surgery. She came to Ohio State from the University of North Carolina at Chapel Hill.



Stephen Lessnick, MD, PhD, is in the College of Medicine and directs the Center for Childhood Cancer and Blood Disorders at Nationwide Children’s Hospital, where he leads a team of pediatric researchers working to better understand childhood cancer and to transform diagnostic and treatment strategies. Lessnick also is in the OSUCCC – James Molecular Biology and Cancer Genetics Program. He came to Ohio State from the University of Utah and Huntsman Cancer Center.



Wayne Miles, PhD, is in the College of Arts and Sciences, Division of Molecular Genetics, and a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. His research focuses on understanding how loss of the *retinoblastoma 1 (RB1)* tumor-suppressor gene changes the transcriptome and proteome of cancer cells. He was recruited to Ohio State from Massachusetts General Hospital Cancer Center and Harvard Medical School.



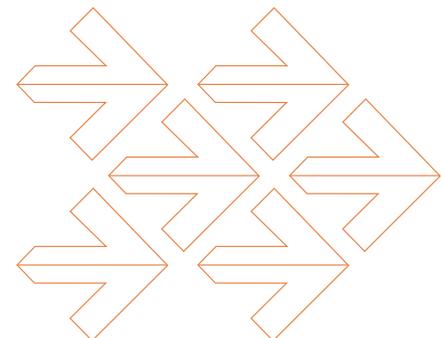
Jeffrey VanDeusen, MD, PhD, is in the College of Medicine, Department of Internal Medicine, Division of Medical Oncology, where he has a clinical and research focus on breast malignancies. He also serves as associate director for community network relations at the OSUCCC – James. Before coming to Ohio State, he was medical director of the Adena Cancer Center in Chillicothe, Ohio. While there, he and his staff designed and launched a free lung cancer screening program. He presented its successful execution at the national Lung Cancer Screening Conference.



Monica Venere, PhD, is in the Department of Radiation Oncology and a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. The overarching goal of her research is to elucidate points of fragility for glioblastoma (brain cancer) using cell and molecular biology as well as animal models, and to exploit these findings to develop new treatment modalities and improve current therapies. She was recruited to Ohio State from the Cleveland Clinic.



Claire Verschraegen, MD, MS, former director of Hematology/Oncology at the University of Vermont, is a professor and director of the Division of Medical Oncology in the College of Medicine’s Department of Internal Medicine. She also is associate director for translational research at the OSUCCC – James. Verschraegen specializes in rare cancers, including mesothelioma, metastatic melanoma, sarcomas and gynecologic malignancies, along with the study of new anticancer drugs and treatments for solid tumors.



LOOKING AHEAD TO PELOTONIA 18

It's not too early to start planning for Pelotonia 18, which will unfold on **Friday-Sunday, Aug. 3-5, 2018**, between the Columbus area and Gambier, Ohio (home to Kenyon College), as the 10th installment of this annual grassroots bicycle tour to raise money for cancer research at Ohio State. Everyone is encouraged to ride, donate or volunteer for this monumental event, which will mark a decade of critical fundraising for life-saving cancer research at the OSUCCC – James. Registration for Pelotonia 18 will open in early 2018. Watch for details on Pelotonia.org.



Ride. Donate. Volunteer.
Pelotonia 18
Friday-Sunday, Aug. 3-5, 2018
Pelotonia.org

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