

TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

PELTONIA SPECIAL EDITION 2017



The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

NCI

Comprehensive
Cancer Center

A Cancer Center Designated by the
National Cancer Institute

THE DIRECTOR'S PERSPECTIVE


MICHAEL A. CALIGIURI, MD

DIRECTOR, THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER
 CEO, JAMES CANCER HOSPITAL AND SOLOVE RESEARCH INSTITUTE
 PRESIDENT, AMERICAN ASSOCIATION FOR CANCER RESEARCH
 JOHN L. MARAKAS NATIONWIDE INSURANCE ENTERPRISE FOUNDATION CHAIR IN CANCER RESEARCH

Imagine your frustration if a bright idea popped into your head—an idea that could help many of people—but you had no means of pursuing it. Instead, it could only flit erratically in your mind like a moth around a porch light, benefiting no one.

Brilliant scientists and students who have innovative ideas that might benefit people with cancer can relate to this scenario. They may have creative insights into how cancer happens, but following up on it would be costly, and federal research funding for cancer has been flat for years. It's become difficult for these innovators—particularly students and junior faculty investigators—to obtain the resources they need to launch their promising projects. Their ambitions are stifled; global progress against this disease is hindered.

Fortunately, thanks to a generous and caring community, we have Pelotonia, our local, annual grassroots bicycle tour, to help fill some of this funding gap. Pelotonia has raised millions of dollars to support cancer research at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James).

Since Pelotonia's first cycling tour in 2009, riders, virtual riders and donors

in this internationally known event have raised more than \$130 million, every cent of which goes directly to cancer research at Ohio State. This is possible thanks to our generous funding partners, who underwrite Pelotonia's administrative costs.

A large share of the money raised by the event nurtures the next generation of cancer researchers through fellowships awarded to Ohio State students in all disciplines and levels of scholarship, providing them an opportunity to do cancer research in the labs of faculty mentors. Pelotonia revenue also supports "Idea Grants" that enable teams of faculty scientists to undertake innovative proof-of-concept projects. Idea Grant recipients can then publish their findings and use them to apply for larger grants to conduct more definitive studies.

I extend my sincerest gratitude to everyone who plays a part in Pelotonia: riders, donors, volunteers, planners, coordinators, communicators, funding partners, roadside well-wishers—the list goes on. Pelotonia helps fuel our shared pursuit of a cancer-free world. The road ahead may be long, but through your combined efforts and support, it grows shorter every year.

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

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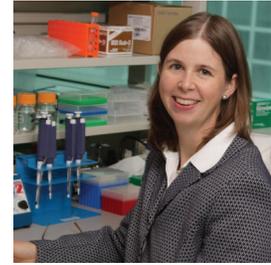
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The jersey of a Pelotonia 2016 rider poignantly underscores the vital need for cancer research



Download Frontiers at <http://cancer.osu.edu/Frontiers>.

FINANCIAL REVIEW

Pelotonia 8-Year Total Exceeds \$130 Million

Riders, virtual riders and donors in Pelotonia 16, the eighth installment of an annual grassroots bicycle tour that generates money for cancer research at Ohio State, raised a record \$24,104,432 and boosted the eight-year total for this event to \$130,159,438.

The 2016 Pelotonia total exceeded the 2015 tally by more than \$2.5 million. Thanks to Pelotonia’s major sponsors—including L Brands Foundation, Huntington, and Peggy and Richard Santulli—every cent raised by riders, virtual riders and donors goes directly to cancer

research at the OSUCCC – James. Pelotonia staff presented a check for the Pelotonia 16 total to OSUCCC Director and James CEO Michael A. Caligiuri, MD, at a Nov. 9, 2016, ceremony at Express Live! in the Arena District of downtown Columbus.

Overall, donors from all 50 states and more than 60 countries contributed to the funds raised by the 275 pelotons (riding groups) that participated in Pelotonia 16. The event unfolded Aug. 6-7 on six bike routes between Columbus and Gambier, Ohio, home to Kenyon College. The

event drew 7,749 riders and 2,790 volunteers who collectively represented 40 states and eight countries.

“To make progress in cancer research and, therefore, in treatment at the bedside, we must have a way to fund big, bold and new ideas for which government grants would be difficult to obtain, and we must do it now,” Caligiuri says. “We are thankful for all riders, virtual riders, volunteers, donors and corporate partners for their support and commitment to our shared vision of a cancer-free world.”

Key Pelotonia Sponsors

Major Funding Partners
 Huntington
 L Brands Foundation
 Peggy and Richard Santulli

Supporting Funding Partners
 AEP
 Nationwide

Notable Funding Partners
 Cardinal Health
 Harold C. Schott Foundation
 Scotts Miracle-Gro
 Kenyon College

Pelotonia 16 Notable Numbers

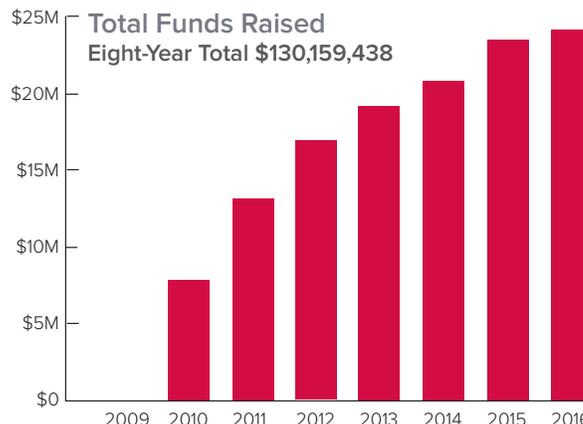
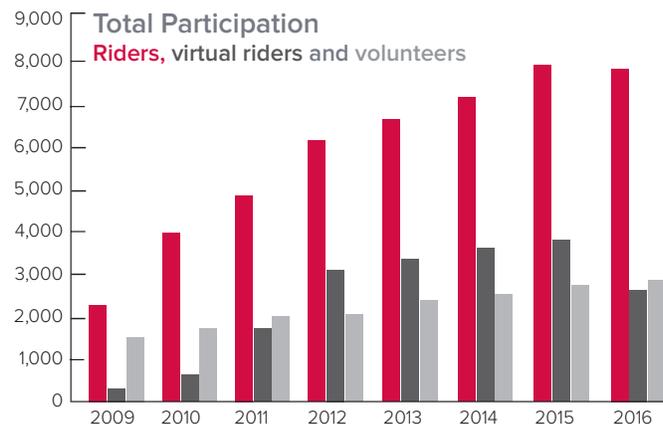
7,749 riders from 40 states, eight countries
2,616 virtual riders
2,790 volunteers
275 registered pelotons (riding groups)

Team Buckeye, Ohio State’s Official Superpeloton

1,358 Team Buckeye members
80 individual pelotons
383 virtual riders
207 volunteers

Team Buckeye Fundraising Total

\$2,938,716



7-Year Pelotonia Financial Summary

Pelotonia supports projects that address many aspects of cancer, including diagnosis, treatment, psychosocial issues, prevention, accelerated drug development, and initiatives to change the landscape of cancer care. Specifically, Pelotonia dollars support four major areas:

- The Fellowship Program—enables Ohio State students in any discipline or level of scholarship to conduct cancer research with faculty mentors;
- The Intramural Research Program—funds Idea Grants, clinical trials and other initiatives;
- New Recruit Research Support—helps junior and senior investigators recruited to Ohio State continue their research upon arrival;
- Instruments of Discovery—purchases state-of-the-art equipment needed for cutting-edge research.

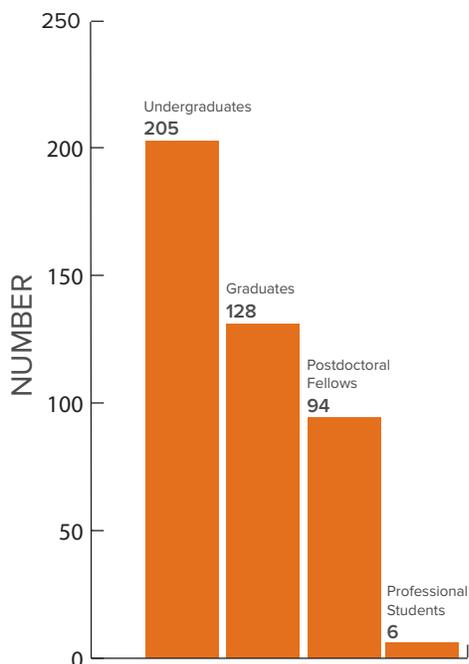
Bringing Knowledge to Bear in the Fight Against Cancer

Pelotonia research funding has been allocated to investigators in 11 Ohio State colleges, as well as at Nationwide Children's Hospital in Columbus and at Cincinnati Children's Hospital Medical Center.

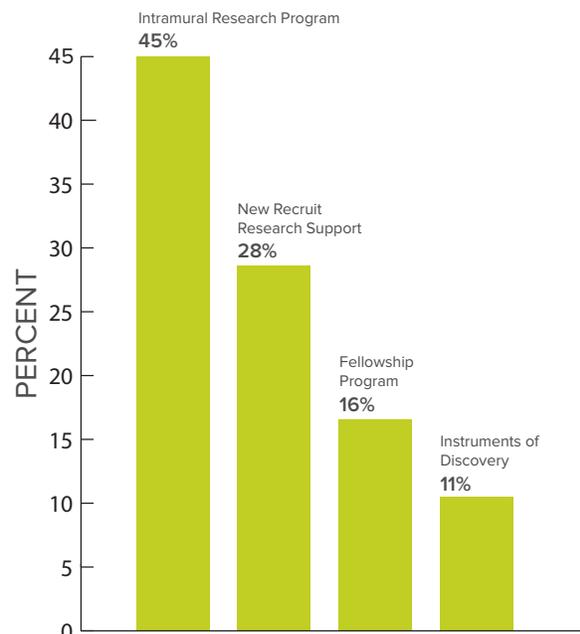
Those colleges are:

- 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

Fellowship Grants Awarded (2009-16)



Allocation of Pelotonia Funds (2009-15)



Research Highlights

Statewide Studies Supported by Pelotonia Will Have Wide Impact



The OSUCCC – James has invested \$4 million in Pelotonia funds to launch a second and a third statewide initiative—one taking aim at lung cancer, the No. 1 cancer killer among men and women in the United States, and the other targeting endometrial (uterine) cancer, one of the few cancers rising with incidence and death rates in this county.

The first statewide effort was the Ohio Colorectal Cancer Prevention Initiative (OCCPI), which was designed to reduce deaths from colorectal cancer across the state.

“The goal of our statewide initiative program is to take state-of-the-art science and translate it into communities across Ohio to elevate cancer patient care, prevention and education, and to reduce healthcare costs,” says

OSUCCC Director and James CEO Michael A. Caligiuri, MD.

Beating Lung Cancer – in Ohio (BLC-IO)

Supported by \$3 million in Pelotonia funds, this initiative—led by Peter Shields, MD, David Carbone, MD, PhD, and Mary Ellen Wewers, RN, PhD, MPH—will draw upon an existing network of more than 50 partner hospitals from communities across Ohio. The network was established as part of the OCCPI.

Patient recruitment began last March and will continue for three years. 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 4, 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 possible 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-approved targeted therapies or drugs in clinical trial testing.

“Lung cancer is most often diagnosed in a metastatic (stage 4) state, so getting patients on the right treatment, the first time, is critical.”

– David Carbone, MD, PhD

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 to kick the habit long-term,” 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, working 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 says.

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 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 for endometrial, colon, stomach and ovarian cancer.

Tumor samples from study participants also undergo molecular profiling to guide and personalize treatment according to each patient’s tumor characteristics. Patients identified with LS and their at-risk family members will be educated on the importance of genetic testing and of cancer-prevention strategies based on their increased risk for 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 to develop new therapies,” says Cohn, director of the Division of Gynecologic Oncology at Ohio State.

Over 61,000 women are diagnosed with endometrial cancer annually in the United States, and up to 5 percent of them have inherited LS. The lifetime risk for endometrial cancer in a woman with LS is 50 percent, 10 times higher than

for a woman without LS. Women with LS have a similar risk for colorectal cancer.

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. OPTEC also will help LS patients and their at-risk family members understand the importance of genetic testing and cancer-prevention strategies based on their increased risk for LS-associated cancers.

“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.”

To help increase compliance with follow-up care for cancer prevention, researchers also are creating a registry to track endometrial cancer patients from the OPTEC study, and colon cancer patients identified through the earlier OCCPI, along with affected family members. **■**

Training the Next Generation

Pelotonia Fellowships Support & Encourage Future Cancer Researchers

The Pelotonia Fellowship Program annually allots \$2 million to help promising Ohio State students in any discipline or level of scholarship who want to conduct cancer research in the labs of OSUCCC – James faculty mentors.

Since the program started in 2010, it has awarded more than \$13 million in fellowships for 433 cancer research projects undertaken by students, including 205 undergraduates, 128 graduates, 94 postdoctoral fellows and six professional 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 peer-reviewed and issued by a committee of faculty cancer researchers chaired by Joanna Groden, PhD, of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, and co-chaired by Janice Kiecolt-Glaser, PhD, of the OSUCCC – James Cancer Control Program. Here's a look at three recent Pelotonia fellowship recipients and their research.

Khara Walker



An exercise-science major who plans to attend medical school after graduating in August, Khara Walker has spent a year evaluating immunogenetics and long-term survival of patients with ocular (eye) melanoma in the lab of

Mohamed Abdel-Rahmen, MD, PhD.

“The immune system is critical to combatting many cancers, but little is known about the details of the (body’s immune) response and why some patients live longer than others,” Walker writes in her project summary, adding that her team would try to determine key genes involved in immune responses by natural killer (NK) cells—immune cells that play an important role in controlling ocular melanoma.

Walker and colleagues have looked at differences in immune responses in the original tumor and in secondary tumors throughout the body, correlating the responses with patient prognosis, time between recurrences and patient survival rates. “This information can provide a foundation for developing strategies to boost immune responses (that can) improve one’s chances of surviving cancer,” she writes.

Walker, who was a track athlete at Ohio State, faced two devastating setbacks in 2014: the death of her mother, who succumbed to cervical cancer, and a track injury that dashed her plans of running professionally after college to raise money for medical school. But in Walker’s words, she both “stepped back” from her depression to realize that cancer has affected not only her but others, and “stepped up” by earning a 2016 Pelotonia Fellowship Award that has enabled her to do something positive against cancer.

Busily preparing for Medical College Admission Tests, Khara will be a virtual rider in Pelotonia 17 instead of an actual rider as she was last year, but

she knows her contribution will still be significant, because “every dollar raised, every mile pedaled, and every fellow who is funded” has an impact on this disease.

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 to study liposarcoma

with mentors Denis Guttridge, PhD, and Raphael Pollock, MD, PhD.

“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 writes in his project summary. His work focuses on sarcomas—rare cancers that arise from bone, muscle and fat.

His Pelotonia-supported research 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 recently 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, an Illinois native with a bachelor’s degree in psychology from Northwestern University, says his Pelotonia fellowship not only enabled him to work with sarcoma cells in the lab, but also helped him realize that he wants to be an academic physician-scientist in medical oncology. “I want to devote my career to thinking deeply and creatively about the biology of sarcomas and pinpoint vulnerabilities that lead to treatments that will save lives.”

He plans to ride the full 180 miles in Pelotonia 17 as co-captain of the BSR-Spin Doctors peloton, a part of Team Buckeye. “Riding in Pelotonia means bringing more hope to patients and their loved ones,” he says. “It means remembering those we have lost and fighting for those who need help.”

Emily Theisen, PhD



When Emily Theisen, 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 became mentors to Theisen at Utah and “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 calls “a laser focus on Ewing sarcoma.”

“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. “The Pelotonia fellowship was the game changer for me. It’s 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.”

Last year she and her mother, a former tour cyclist, rode 25 miles in Pelotonia 16. In Pelotonia 17, Theisen will ride the full 180 miles with the Nationwide Children’s Hospital Peloton, and her mother will be a virtual rider. Noting that her mother “raised us to embrace challenges in life, always emphasizing running and biking uphill for fun,” Theisen looks forward to the road ahead. 

RESEARCHER PROFILE: Yael Vodovotz, PhD

Researcher Rides in Memory and in Gratitude



Yael Vodovotz, PhD, an OSUCCC – James researcher, has ridden in Pelotonia every year since the event began in 2009, except for last year when she had to participate as a virtual rider.

Vodovotz will be riding in Pelotonia 17 also, and this year's event will be particularly poignant for her. "My dad succumbed to lung cancer in May, after a courageous three-and-a-half year fight," she says.

"It's been a difficult time for my family. But it's also been inspirational. I heard amazing stories from the researchers, caregivers and physicians who were involved in my dad's care. Their love and dedication to him was more than I could ever have predicted.

"It is for my dad AND for all those wonderful people that I ride this year, and I'm doing it with added enthusiasm to raise funds for cancer research," says

Vodovotz, a physical chemist and food scientist in the Department of Food Science and Technology.

Earlier in her career, Vodovotz worked for NASA, formulating foods for the mission to Mars. There, she began developing a soy bread high in bioactive substances, a project she completed when she moved to Ohio State and joined the

OSUCCC – James. This soy bread and an offshoot soy-almond bread were used in a clinical trial for the prevention of prostate cancer.

More recently, she and a group of multidisciplinary colleagues at Ohio State's Crops to Clinic program developed a black raspberry confection, which will be handed out at the James Cancer Hospital and Solove Research Institute tent during the opening ceremony of this year's Pelotonia.

"We have studied these confections extensively in our lab for their bioactivity and health-promoting properties, and they've undergone several human clinical trials with promising results," she says.

In 2015, Vodovotz teamed with chef Drew Patterson, who runs the Bloch Café on the 14th floor of The James, to sell the dark-chocolate-wrapped black raspberry confection, first at that restaurant, then at other Ohio State locations.

"The confection is made locally in Columbus, with profits supporting further functional food research at The Ohio State University," Vodovotz says.

Sales were good, so Vodovotz and Patterson formed a company called Foods For Purpose, and they will soon begin selling the confection outside of Ohio State. Part of the profits from the sales will continue to support research into the development of health-promoting foods high in bioactive compounds.

"This project would not have gotten off the ground without support from Pelotonia," Vodovotz adds.

"Pelotonia is an amazing event," she says. "It sometimes takes quite a bit to raise the donations, but it's for a good cause. And it all comes together that weekend.

"Most importantly, I'm doing this for my dad and to support cancer research. I hope that future patients won't go through what he went through, particularly those with lung cancer.

"I also want to extend thanks to all the researchers doing the work, and to the physicians and nurses who treated him so well," says Vodovotz, whose father was treated at a cancer center in Florida. "They are great people." ■

Going Bold

Pelotonia Idea Grants Encourage Innovative Approaches to Difficult Questions

Twice a year, OSUCCC – James researchers compete for Pelotonia Idea Grants, which provide two years of funding to teams of OSUCCC – James scientists who propose novel ways to approach difficult problems.

The grants encourage researchers to submit original ideas and break new ground to hasten the development of safer, more effective cancer diagnosis, detection, treatment and prevention strategies.

The grants provide funding that awardees use for studies to test their hypotheses and produce data needed to obtain larger grants for more definitive research.

Since the program's inception, funding has been awarded to 108 research teams. The collaborating OSUCCC – James researchers come from several Ohio State colleges and departments and

three academic institutions, including Nationwide Children's Hospital.

Here are four examples of the Pelotonia Idea Grants awarded in 2016.

Understanding Potential Protective Effect of Female Hormones in Melanoma



Craig Burd, PhD,
assistant
professor of
Molecular
Genetics

Melanoma typically arises from moles that have cells with mutations in genes called BRAF and NRAS that promote cancer. Usually, these cells do not become cancerous, but when they do, the progression to

cancer is thought to be triggered by exposure to ultraviolet (UV) radiation, such as the UV in sunlight, which causes additional damage to the cells.

Research shows that malignant melanoma occurs more often in men than in women, and that it is more often fatal in men. Why this happens is poorly understood, but growing evidence suggests that the hormone estrogen helps protect women against the disease.

The researchers in this Idea Grant study want to learn at the molecular level how estrogen protects against melanoma. Their work focuses on a protein called estrogen receptor beta (ERβ), a molecule present in normal melanocytes that has several functions, including regulating genes involved in the repair of damaged DNA. The levels of ERβ



IDEA GRANTS

drop in melanoma cells as the cancer develops.

This study will help the investigators learn what ERb does in normal melanocytes and how it contributes to preventing melanoma, and it will identify targets for future drugs to prevent the disease.

Helping Oropharynx Cancer Survivors Breathe and Swallow Safely



Loni Arrese, PhD, assistant professor of Otolaryngology and of Speech and Hearing

The incidence of head and neck cancer has increased 225 percent during the last two decades. The increase is largely due to the growing incidence of a type of throat cancer caused by HPV (human papillomavirus) infection. Called oropharyngeal cancer, it occurs mainly in middle-aged people who have no significant

history of tobacco or alcohol use.

Oropharynx cancers that test positive for HPV are often treated with chemotherapy and radiation. These treatments damage muscles and structures in the throat, causing swallowing problems, which also may impair the person's ability to protect the airway during swallowing. That, in turn, can result in lower quality of life, use of a feeding tube, hospitalizations for aspiration pneumonia and a shorter life span.

This Idea Grant study will evaluate the use of a targeted exercise program called expiratory muscle strength training (EMST) in these patients. EMST currently is used in people with certain degenerative muscular diseases to improve swallowing function. Researchers will measure the clinical effects of traditional swallow intervention studies versus traditional swallowing interventions plus EMST on swallowing and respiratory function.

The findings could lead to improved targeted swallowing

and respiratory-strength exercise programs, and help these cancer survivors maintain better health and a higher quality of life.

Gaining Insight Into Why Low-Risk Breast Cancer Patients Choose Double Mastectomy



Clara Lee, MD, associate professor of Plastic Surgery and of Health Services

Management and Policy

A growing number of women with early-stage breast cancer are choosing to have both breasts removed. Generally, double mastectomies are recommended only for women at high risk of cancer in the opposite breast. That is, those with a strong family history of breast cancer or who have a mutation in the *BRCA1* or *BRCA2* genes.

However, the procedure is most often performed in women who do not have a *BRCA* mutation



or a family history of breast cancer and who do not need the procedure for medical reasons.

Potential harms of a double mastectomy include a higher risk of complications, longer surgery and recovery times, and greater short-term costs. Women who have complications from breast reconstruction are at risk for poorer body image or poorer sexual outcomes.

This study will evaluate how women with early-stage breast cancer make treatment decisions and how communication with their physicians affects their decision-making. The study is developing a novel mobile application that patients can use to easily record their conversations with providers. The study also examines women's knowledge, preference and expectations about future well-being.

Information from this study will be used to obtain funding for a larger, multicenter study. Ultimately, the research should help physicians communicate with women with breast cancer about the risks, benefits and need for double mastectomy.

Evaluating 'Research Autopsies' for Understanding Advanced Cancers



Sameek Roychowdhury, MD, PhD, professor of Medicine, Division of Medical Oncology

Scientists now know that the cancer cells in a patient's tumor have many differences in the genes that they carry. This phenomenon is called tumor heterogeneity.

These genetic differences can help some tumor cells survive during treatment. They might, for example, make the cells less sensitive to the person's chemotherapy or targeted therapy. Those few surviving cancer cells might later cause the cancer to recur.

This study, funded by an Idea Grant obtained by Sameek Roychowdhury, MD, PhD, and led by physician-scientist and

medical-oncologist trainee Hui-Zi Chen, MD, PhD (who has also received a Pelotonia postdoctoral fellowship), is designed to gain a better understanding of tumor heterogeneity and how it leads to drug resistance and cancer recurrence in advanced cancer. The researchers, who will have received informed consent for the procedure, will perform rapid research autopsies soon after patients die of their cancer. The autopsy involves taking samples of cancer cells from organs affected by the disease.

The team will study these cancer cells for genetic differences to better understand how some of them acquired drug resistance. They will then use this knowledge to advance the discovery of new cancer drugs.

In addition, the study will evaluate a form of biopsy called liquid biopsy. This type of biopsy examines DNA from tumor cells that is isolated from blood plasma or urine. The researchers will determine whether circulating tumor DNA can be used to monitor how well a patient's targeted therapy or chemotherapy is working. **F**



RIDER PROFILE: Tim Pawlik, MD, MPH, PhD

Surgical Oncologist Rides for His Patients



Tim Pawlik, MD, MPH, PhD, is excited about his impending 50-mile ride in Pelotonia 17 despite having almost no time to prepare for it.

After all, the surgical oncologist and liver cancer expert

did survive last year's Pelotonia ride of the same distance, which took place only a couple of weeks after he arrived at The Ohio State University College of Medicine to become professor and chair of the Department of Surgery.

"We showed up in Columbus just before the event, I got a bike, took one 10-mile ride in preparation, and a week later my wife Megan and I rode 50 miles," recalls Pawlik. A Massachusetts native, he was recruited to Ohio State from Johns Hopkins Hospital, where he was chief of the Division of Surgical Oncology and director of the Johns Hopkins Liver Tumor Center. "I've never been a cyclist, and I really didn't train for it at all except for that 10-mile ride.

"And Megan and I loved it," he adds. "It was incredibly inspiring to be out there among all of those people, to ride through the towns, to hear the high school bands, and to see so many people along the road. Many held up pictures of family members and loved ones who have had cancer and have benefited from the fundraising that has occurred through Pelotonia to help the OSUCCC – James conduct research and identify treatments.

"It was truly motivating—and I needed every ounce of motivation I could get, because I barely made it to the finish," he laughs.

His Pelotonia 17 training regimen is as spare as last year's.

"I hope to go out one time, maybe one 10-mile ride. My schedule is really busy, and most of my time away from work is spent with my family and going to our kids' sporting events," he explains. He and Megan have four children: Katie, 15; Molly, 13; Emma, 10; and Michael, 7. This year, instead of his wife, his daughter Katie will ride with him as members of the SUPER Friends peloton (riding group), which is part of the Team Buckeye superpeloton.

"Katie is quite athletic," says Pawlik, who also holds a Master of Divinity Degree. "She attends Columbus School for Girls and does cross country and track. She's in great shape. I'm going to use her as my inspiration this year."

Despite his lack of biking aplomb, he believes riding in Pelotonia is worth the effort. "It's an amazing event," he says. "I was blown away last year by how well it's organized, its extremely high production quality, the pre-event activities, the ride itself, the friendliness of the people, the professionalism of the organizers, and then the post-ride festivities. I'm looking forward to it."

Another thing that struck him was the number of people wearing jerseys with the words "I ride for..." and the names of family members, friends and loved ones. On his jersey were the words "I ride for my patients."

"That's what it's all about. For me, the fight against cancer is personal," Pawlik says. "I've had a lot of cancer in my family, and like all caregivers at The James, I care deeply about my patients and want to participate in things that help us improve treatment."

A passing visitor wishes him good luck in his ride. He replies, "Thanks, I'll need it."

When the physician is reminded that Katie will be there to inspire him, he grins. "My wife didn't leave me in the dust, but my daughter may!" 



RIDER PROFILE: Aaron Conley

Cancer Survivor Finds Hope in Pelotonia Pedaling



Aaron Conley's devotion to the Pelotonia goal of ending cancer stems from his own journey as a cancer survivor and from the cancer journey of a friend who died last year.

"I am riding in memory of my good friend Max Vokhgelt, who passed away in 2016 from complications with treatment in his second battle with leukemia," Conley writes in his profile for Pelotonia 17. "Max and I connected over being survivors and started a business together. This year I will ride 180 miles in his memory, and in hope of a future without cancer."

His route—the longest available in Pelotonia 17—will take him from Columbus to Gambier and back as captain of the NextGen James Ambassadors peloton, a part of Team Buckeye.

Conley, a director of foundation relations for The Ohio State University Wexner Medical Center, has always loved cycling and credits that sport in part with saving his life.

In 2013 he noticed that he felt weak riding and that his cycling times were slowing. Suspecting that he had a heart problem, Conley had a check-up and learned that he was severely anemic, a condition that was affecting his heart and vision. A subsequent colonoscopy revealed a large bleeding tumor in his colon. On Nov. 1 of that year, at age 27, he was diagnosed with stage III colorectal cancer.

Three days later, Conley had abdominal surgery at another area institution to remove a fist-sized tumor, eight inches of his colon and 32 lymph nodes, five of which were cancerous. "After recovering for a month, I started six months of intensive chemo once every two weeks, connected for 49 hours at a time to a chest port." Conley completed therapy on May 16, 2014.

In August 2014, he rode 100 miles in his first Pelotonia, and he has ridden in it ever since. He notes that he has already been personally impacted by Pelotonia due to receiving free genetics testing through the Ohio Colorectal Cancer Prevention Initiative (OCCPI), a Pelotonia-funded study.

When Pelotonia 17 arrives, more than three years will have passed since he finished chemotherapy. His tests and check-ups have been clear, and his blood counts have been normal. "I'm in remission!" he says, attributing his good fortune in large part "to the support and love of so many family members, friends and co-workers."

Conley began working at Ohio State in December 2015 and is continuing his journey as a cancer survivor at Ohio State's Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James).

In his work at Ohio State, he has primary responsibilities for units of the Wexner Medical Center, including the OSUCCC – James and the Neurological Institute, working with researchers, doctors, faculty and staff to secure foundation funding.

Throughout his journey, he has focused on "staying positive and living in courage, knowing that so many others, including close friends, have faced cancer like mine or worse and stayed strong."

"No one my age, or any age, should have to face this struggle," Conley says. "Pelotonia is a way for me to continue getting back on my bike and helping work toward Pelotonia's one goal of ending cancer. Pelotonia gives me hope." **F**

From Ideas to Impact

Discoveries Made With Pelotonia support

Pelotonia funds help support groundbreaking preliminary studies at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James). These studies produce data and publications that can lead to grants for larger studies. In this way, Pelotonia helps 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 5 percent of cases, the cancer spreads to other areas of the body – it metastasizes – causing up to 8,800 deaths per year.

There is no way for doctors to predict the patients in which the disease might spread, and there

are no FDA-approved targeted therapies for treating metastatic cSCC.



In 2011, **Amanda Toland, PhD, associate professor of Cancer Biology and Genetics,**

was awarded 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. In one, Toland and her 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 a second study, Toland and her colleagues used gene sequencing to identify gene mutations found in metastatic cSCC cells compared with cSCC cells from the primary tumor. That 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 will eventually 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. The team is involved in three different clinical trials for FGFR inhibitors, including a trial led by OSUCCC investigators.

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

Roychowdhury and his 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.

Furthermore, they 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 the 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’s expected to kill nearly 156,000 Americans alone this year. Lung cancer causes so many deaths in part because it is difficult to detect early. Consequently, it is generally diagnosed at a late stage of disease, when a cure is difficult.



In 2013, L. James Lee, PhD, professor of Chemical and Bio-molecular Engineering,

and a team of OSUCCC – James researchers were awarded an Idea Grant to support preliminary studies on a high-tech way to detect lung cancer early using a blood sample.

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 that are tethered to a biochip. The biochip sits on a glass microscope slide.

The tethered nanoparticle complex is designed to capture submicroscopic vesicles called exosomes and detect 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 (mRNA) and microRNA that can serve as 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. **F**

New Hope

Pelotonia Funds Support Cancer Clinical Trials at OSUCCC – James

Clinical trials evaluate the safety and effectiveness of new treatments and study ways to improve those treatments. In this manner, clinical trials improve cancer care and bring renewed hope to patients. Here is an example of how Pelotonia funds are helping to solve important questions related to a trial at the OSUCCC – James.

To learn more about this and other OSUCCC – James trials, call The James Line at 800-293-5066 or visit cancer.osu.edu.

Pelotonia Funding Helps a Thyroid Cancer Trial Answer Additional Questions

In addition to comparing innovative new therapies with the current standard treatment, most clinical trials also include studies that are designed to learn more about the drug or treatment being evaluated by the trial.

Pelotonia funds can be used to help support these additional studies, which are referred to as correlative studies. For example, Pelotonia funds are supporting an interesting 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 this year in the United States will be PTC.

Furthermore, about 44 percent of PTC patients have a mutation in a gene called *BRAF* (pronounced “B raf”). The mutated gene sends signals that cause cells to become cancerous and plays a role in the development of melanoma, lung, thyroid and other cancers.

Two targeted drugs approved by the U.S. Food and Drug Administration for treating melanoma also show promise for treating cases of PTC that have *BRAF* mutations. The two targeted agents are called dabrafenib and trametinib.

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



At the OSUCCC – James, a multi-center trial led by **Manisha Shah, MD**, a medical

oncologist, is testing the effectiveness of the two agents.

About half 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 whether receiving the two drugs together – that is, inhibiting both the mutated gene and the second gene – will improve outcomes in PTC patients compared with PTC patients who are treated with dabrafenib alone.

The OSUCCC – James team presented its initial findings last June at the American Association of Clinical Oncology (ASCO) annual meeting in Chicago. The data showed that both dabrafenib alone and dabrafenib combined with trametinib were well

tolerated by patients, resulting in a 50- to 54-percent response rate.

“This is an entirely new approach to treating a disease that has limited treatment options. There is no clear ‘winner’ between single- and dual-agent targeted therapy yet, but both therapy approaches resulted in positive outcomes for patients, and that gives us more treatment options to help patients with this disease,” says Shah, a member of the OSUCCC – James Translational Therapeutics Program. “Targeted therapy has the potential to change the standard of care for patients affected by this aggressive form of thyroid cancer.”

A Kinder, Gentler Biopsy

Shah and her collaborators will continue to follow patients on this trial to determine whether dabrafenib alone or dabrafenib plus trametinib is more effective in the long term.

In addition, the trial explored other questions through the

Pelotonia-supported correlative studies associated with the trial.

One of those studies is evaluating a procedure called a liquid biopsy. Typically, biopsies for solid tumors such as PTC require the use of needles, sometimes guided by ultrasound, to obtain a small sample of a tumor. For certain cancers, a biopsy requires a surgical procedure.

The tumor sample is then studied by a pathologist, and the information helps determine the patient’s treatment.

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



“This study would be the first to use this assay in a prospective study to follow treatment

response and early detection of resistance in PTC,” says **Cynthia Timmers, PhD**, director of the OSUCCC – James Solid Tumor Translational Science Shared Resource, who leads the liquid-biopsy study.

“Furthermore, we will sequence the circulating tumor DNA to learn if resistance mutations are present,” Timmers adds. “This would be the first study of its kind in solid tumors performed at Ohio State, and it could open the door for the analysis of other tumor types in which invasive biopsies are unattainable.” ■



Drug Development Institute

Where Pelotonia Funds Help Translate OSUCCC – James Discoveries into New Cancer Treatments



The Ohio State University Comprehensive Cancer Center (OSUCCC) is a place where discovery is focused on understanding how cancer works and how we might beat it.

These discoveries are the foundation for new cancer treatments. Promising discoveries then enter the “drug development process,” a myriad of activities that must align and be completed before a new drug can be marketed.

These activities are typically in the purview of pharmaceutical companies, which specialize in taking ideas from the laboratory through product development, manufacturing, review by the U.S. Food and Drug Administration (FDA) and clinical trials.

Thanks to the support of Pelotonia, the Harry T. Mangurian Jr. Foundation and other philanthropic sources, Ohio State has a team at the Drug Development Institute (DDI), which is dedicated to steering new discoveries through the preclinical drug development process.

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



The DDI, led by **Jeff Patrick, PharmD**, is a biotech-like institute staffed by scientists

who have previously 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. It is made up of pharmaceutical industry executives and expert OSUCCC physician-scientists John C. Byrd, MD, and David Carbone, MD, PhD.

The DDI has an innovative, cancer-focused portfolio and continuously evaluates new projects to add to its pipeline. In all, the DDI has evaluated over 100 potential projects for investment, with seven projects currently under management.

A key consideration is whether a project addresses an unmet need of a patient population.

When the DDI invests in a project, it builds a collaborative team that is tailored to the project’s specific needs. This could include a chemist to synthesize molecules to target a specific pathway, or a regulatory consultant to help approach the FDA about starting a clinical trial.

The DDI team develops a project plan that includes timelines and criteria for success. It coordinates and streamlines activities to ensure that projects reach milestones efficiently and on budget. Effective management of these activities is essential for reducing the costs and delays of translating good research ideas into candidates for clinical trials testing.

When a project reaches the point where a biotech or pharma company must continue its development, the DDI works to partner the project with the pharmaceutical industry.

That partnering point may come early or when a project has matured, but the DDI exists to “de-risk” therapeutic candidates so they are more likely to reach the patients who need them.

The DDI plays an important collaborative role at the OSUCCC – James, which conducts such a high volume of outstanding basic research. It is here as a partner to help grow discoveries into new cancer treatments.

Learn more about Ohio State’s Drug Development Institute at cancer.osu.edu/ddi 



INSTRUMENTS OF DISCOVERY

Digital Pathology



Anil Parwani, MD, PhD, director of digital pathology and vice chair and director of Anatomic Pathology

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

In April 2017, the U.S. Food and Drug Administration (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 the person's unique cancer, enabling patients to receive life-saving therapies sooner.

Furthermore, pathologists can perform tests and other

diagnostics that are not possible on traditional glass slides, and share the images electronically with experts worldwide.

The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James) is now implementing a digital pathology service. All new patient pathology slides are being digitized, along with those of the past five years.

In addition, Pelotonia funds are helping to create a digital archive of past pathology specimens, and with their associated clinical data for use by researchers. The specimens and information in the archive will be “de-identified” – that is, no identifying patient information will be included – and then made available to cancer investigators anywhere in the world.

“Thanks to Pelotonia, those specimens will see new life and contribute to the discovery of new

biomarkers and new ways to more accurately diagnose cancer,” says Anil Parwani, MD, PhD, director of digital pathology and vice chair and director of Anatomic Pathology at The Ohio State University College of Medicine Department of Pathology.

“Leveraging this type of de-identified big data for research collaboration is critical as we move forward in an era of predictive precision cancer medicine – finding ways to match the right patient with the right drug at the right time is absolutely critical, and this is taking another step toward that goal,” adds Michael A. Caligiuri, MD, director of the OSUCCC and CEO of The James.

“Cancer pathologic diagnosis is needed at all hours of the day and in every community across the globe,” adds Parwani. “This technology will allow us to take that subspecialized consultation and diagnosis to patients – regardless of where they live.” ■

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 studies when they arrive. Recent recruits include these prominent researchers:



Kellie Archer, PhD, is 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, 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. Although her specialty is surgery, she considers herself a cancer doctor first and foremost.



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 Institute.



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. 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 design and execution at the national Lung Cancer Screening Conference.



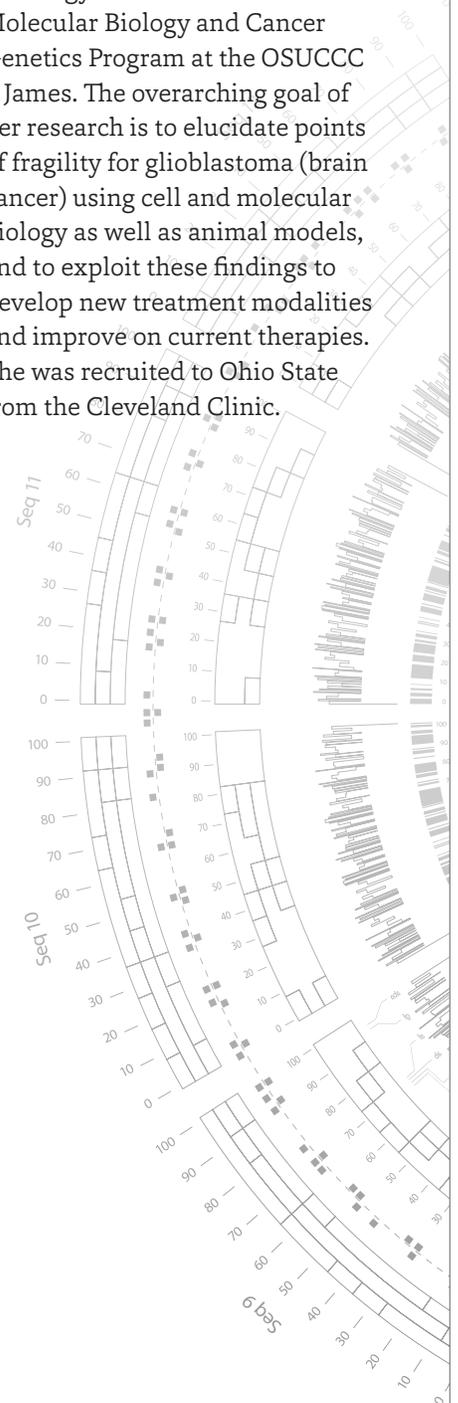
Monica Venere, PhD, is in the Department of Radiation Oncology and a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. The overarching goal of her research is to elucidate points of fragility for glioblastoma (brain cancer) using cell and molecular biology as well as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



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.



Claire Verschraegen, MD, MS, former director of Hematology/Oncology at the University of Vermont, is 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.



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INSIDE THE NEXT FRONTIERS

RAS WORKS

The *RAS* oncogene was discovered more than 30 years ago. Mutations in the *RAS* gene drive more than 30 percent of all cancers, including 95 percent of pancreatic cancers and 45 percent of colorectal cancers. Research has yet to produce an effective way to block the mutant *RAS* proteins. OSUCCC – James researchers are working to solve the problem.

