New Pelotonia Institute for Immuno-Oncology Amplifies Promise of Immunotherapy

The James

The Ohio State University
COMPREHENSIVE CANCER CENTER
Despite tremendous advances in cancer research and therapy over the past several decades, cancer in its many forms remains a daunting global problem.

In 2018, more than 1.7 million cases were diagnosed in the United States, and over 600,000 people in this country died of the disease. Worldwide there were an estimated 18 million cancer cases in 2018. Nearly 40 percent of men and women will be diagnosed with cancer at some point in their lives.

For Ohio State’s Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James), the problem is particularly challenging because our primary patient “catchment area”—the entire state of Ohio—has a comparatively high cancer incidence rate and some of the nation’s worst mortality rankings for lung, breast, colorectal and prostate cancers.

However, we believe our cancer program is making a positive difference as evidenced by our continuous growth in patient caseload, grant-funded research and recruitment of top medical scientists, as well as our consistently high patient-satisfaction ratings and a number of planned initiatives that will elevate the program to even greater heights in the next few years.

Some of these achievements are reflected in stories within this issue of Frontiers, which includes information about such initiatives as a Proton Therapy Center and a Pelotonia Institute for Immuno-Oncology (PIIO), along with a roundup of the many research grants and awards we have received for patient care, safety and satisfaction.

Our widening reputation for excellence has made the OSUCCC – James a destination site for cancer care; in fiscal 2019 we drew patients from all 88 Ohio counties, 50 U.S. states and 92 countries. Much work lies ahead, but we remain steadfast in pursuing our vision of a cancer-free world.
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A pseudo-colored scanning electron micrograph shows an oral squamous cancer cell (white) being attacked by two cytotoxic T cells (red), part of a natural immune response.
Source: The website of the National Cancer Institute (https://www.cancer.gov)
This image is part of the NCI Cancer Close Up 2016 collection.

Read Frontiers online or download an issue at cancer.osu.edu/Frontiers.
Raphael Pollock, MD, PhD was admittedly surprised when he was asked in late 2017 to replace the departing Michael A. Caligiuri, MD, as director of The Ohio State University Comprehensive Cancer Center (OSUCCC).

Ohio State’s cancer program had enjoyed many years of growth and rising acclaim, and Pollock realized that the next director would be challenged to guide it to even greater prominence.

Two years later, he’s not only glad he accepted the position but also believes that, thanks to continuous help from many talented professionals, the cancer program remains “on a positive trajectory and headed in the right direction” for pursuing its vision of a cancer-free world.

Those were words that both Pollock and William Farrar, MD, CEO of the James Cancer Hospital and Solove Research Institute, used when delivering a “State of the Cancer Program” address for the OSUCCC – James in which they listed several recent accomplishments and reviewed some exciting research and clinical initiatives that have been launched or are being planned.

Their positive presentation reflected Pollock’s shift from initial surprise to calm confidence as OSUCCC director.

“In candor, I was not looking for this position,” says Pollock, a surgical oncologist and sarcoma specialist who joined the medical faculty at Ohio State in 2013 after 31 years at MD Anderson Cancer Center in Houston. “I felt fulfilled in my roles here as director of the Division of Surgical Oncology, surgeon-in-chief for the Ohio State Wexner Medical Center, maintaining a research lab that is still active, and mentoring inside and outside the division that I led, in addition to managing my surgical practice.”

Although surprised at first by the job offer, Pollock says he would have accepted it “just on behalf of the described need for stability and continuity within the role,” but he became even more interested after discussing its possibilities with Ohio State President Michael Drake, MD, Executive Vice President and Provost Bruce McPherson, and Wexner Medical Center Board Chairman Les Wexner.

“The opportunity to have an even greater impact on the cancer program, medical center and university was very intriguing,” Pollock explains, noting that he also had personal motivations for wanting to serve more deeply. He has three children who are students at Ohio State, and he is being treated at the OSUCCC – James for chronic lymphocytic leukemia (CLL), a story he has widely shared since his January 2017 diagnosis.
As part of Pollock’s treatment, he is on a clinical trial involving the drug ibrutinib and its role in treating CLL. He points out that OSUCCC–James researchers have played a lead role in the drug’s development and clinical application, “and there too I have a strong sense of gratitude for the depth and breadth of our cancer program. So I was pleased and honored to accept the position as director.”

One of the first matters he directed his attention toward was the application process for the next five-year renewal of the program’s National Cancer Institute (NCI) designation as a comprehensive cancer center. The voluminous application was submitted in January 2020.

“I’m fortunate to be surrounded by people who were not only interested in helping with this task but who had participated in the effort before, including some who were here in 2015 when, under my predecessor’s leadership, we received a perfect score,” Pollock says. “Our application contains detailed updates of our five research programs (Cancer Control, Leukemia Research, Cancer Biology, Molecular Carcinogenesis and Chemoprevention, and Translational Therapeutics).”

Pollock also points to several new initiatives either under way or being planned. Among the first to take shape will be a Proton Therapy Center that will be contained in a multi-story West Campus Outpatient Facility to be completed in 2022. The Proton Therapy Center, a collaboration with Nationwide Children’s Hospital (NCH), will provide state-of-the-art radiation oncology treatment for adults and children (see related story, page 31).

Also under development is the Pelotonia Institute for Immuno-Oncology (PIIO) led by recently recruited Zihai Li, MD, PhD, who serves as founding director of the PIIO and will help the cancer program build on its already strong endeavors in immunotherapy, which is considered to be the next frontier in cancer treatment (see related story, page 16).

“I’ve been fortunate in my own professional lifetime to have witnessed a number of incredible breakthroughs, such as germ cell tumors going from uniformly lethal to being cured in a majority of patients ...”
“We already have formidable strengths in cell-based immune therapies, and these are promulgated as a joint program at our main-campus medical center and at NCH,” Pollock says. “Immune checkpoint inhibitor therapy is another area in which we have international visibility. Under Dr. Li’s guidance, we’ll expand our immunotherapy presence by recruiting 30 to 35 faculty over the next five years to develop platforms for collaborative immune discovery and cutting-edge clinical trials.”

Still another area of innovation, Pollock says, is a program in cancer engineering, which is being developed with Ohio State’s College of Engineering.

“We can identify clinical situations in cancer for which engineering solutions might be relevant,” he explains. “For instance, Ohio State has one of the best electron microscopy (EM) units in the world, so the opportunity to develop programs in ultrastructure (cryo-EM) is one example of a program that would fall under the broad rubric of cancer engineering.”

Other areas of potential engineering application, he says, include a nano delivery system for topical application of drugs (bio-mechanics), liquid biopsy, molecular imaging, tissue-engineered tumor models, and personalized drug delivery.

Pollock says planning also has begun for two additional endeavors within the OSUCCC – James: a cancer prevention center and a center for oncogeriatrics.

“These are more theoretical at this point, but we are identifying faculty who might be interested in working in these two areas, both of which we’ll pursue with more vigor in 2020 and beyond,” he explains.

A prevention center, he adds, “would build on our strengths in cancer-prevention activities,” including the cancer program’s national leadership roles in examining cancer disparities and improving cancer screening among underserved populations, as well as its strong smoking-cessation efforts as manifested in a federally funded Center of Excellence in Regulatory Tobacco Science.

And developing a program in oncogeriatrics, Pollock states, would be “very useful to many of our patients, particularly people like myself who are in the later decades of life.”

“We know that the elderly process therapies differently than younger individuals, yet we don’t know much about how this...
happens,” he says. “If you look at the age distribution of cancers, they tend to disproportionately affect older people, which points to the possibility that epigenetics and epigenetic-targeted therapies for the elderly may be important as an additional focus of oncogeriatrics.

“Looking at the underlying genetics of how people process responses to drugs and at how chemoresistance develops is another aspect of this process. Do we need different dosing to accomplish the same therapeutic objectives as a function of a patient’s age? Understanding this would have tremendous implications for treatment and survival.”

Considering initiatives such as these and others, both at Ohio State and elsewhere, Pollock is optimistic about the future of collaborative cancer research and the expanding role that the OSUCCC – James will play in treating and curing this disease in its many forms.

“I’ve been fortunate in my own professional lifetime to have witnessed a number of incredible breakthroughs, such as germ cell tumors going from uniformly lethal to being cured in a majority of patients, remarkable improvements in treating patients with gastrointestinal-stromal tumors (GIST), and the evolving use of targeted therapy drugs such as ibrutinib, rather than highly toxic chemotherapies, to treat CLL patients with promising results and fewer side effects,” he says.

“These are the types of changes we live for in oncology, and while none of them represent silver bullets that imply 100% cure of a given disease, the progress has been very definite across the board,” Pollock adds. “If you look at American Cancer Society five-year survival rates from 1950 compared to 2010, for example, they have increased two and a half-fold for all comers, all stages, all cancers—an improvement that’s ultimately based on research.

“So as long as the United States and other nations retain our societal interest in cancer research, I’m very confident we will continue to make strides toward a cancer-free world. That may not come about in my lifetime, but I believe it will happen eventually.”
Ohio State-Developed Drug Receives FDA Approval for Treatment of CLL & SCL

On Nov. 21, the U.S. Food and Drug Administration (FDA) approved the use of the drug acalabrutinib for first-line therapy in chronic lymphocytic leukemia (CLL) and small cell lymphoma (SCL).

This is the first full approval of the targeted drug therapy, which was developed and tested at the OSUCCC – James in collaboration with pharmaceutical partner Acerta Pharma. Marketed as Calquence®, acalabrutinib is a second-generation Bruton tyrosine kinase (BTK) inhibitor, a newer class of drugs shown to improve the survival of patients with mantle cell lymphoma in addition to CLL and SCL.

The drug works by permanently binding BTK, which is part of a chain of proteins that relays growth signals from the surface of the cancer cell to genes in the cell nucleus, enabling cancer cells to survive and grow. By blocking BTK, the drug halts the flow of these growth signals, and the cancer cells die.

Unlike the first generation BTK inhibitor (ibrutinib, marketed as IMBRUVICA®), preclinical and clinical data shows that acalabrutinib more selectively blocks the BTK pathway without disrupting other key molecular pathways important for preserving platelet and immune function, thereby preventing/minimizing certain side effects associated with cancer treatment.

The foundational basic-science research, initial phase I clinical trial and numerous sequential phase II and phase III clinical trials that led to this new FDA approval of acalabrutinib were performed by researchers at the OSUCCC – James led by John C. Byrd, MD.

This research included collaborative clinical trials with Ohio State's College of Veterinary Medicine and the Comparative and Translational Oncology Program, a research collaboration that integrates nearly 40 scientific investigators from Ohio State's colleges of Medicine, Pharmacy, Nursing and Veterinary Medicine, along with researchers from Nationwide Children's Hospital, to investigate cancers that occur in both humans and animals. William Kisseberth, DVM, PhD, a professor in the College of Veterinary Medicine, directed the studies of acalabrutinib in dogs with lymphoma.

“Acalabrutinib is a potent and selective oral BTK inhibitor that has proven to be very effective for our patients affected by CLL and other blood cancers,” Byrd says.

Collaborator Jennifer Woyach, MD, of the Leukemia Research Program, presented data at the 61st annual meeting of the American Society of Hematology (ASH) on mechanisms of resistance that cause some patients to stop responding to acalabrutinib.
Researchers say offering this type of advanced genetic testing diagnosis could help guide and expedite treatment decisions for patients who have CRC while simultaneously identifying those who also are likely to have Lynch syndrome (LS), which occurs when a person inherits a mutation in one of the DNA repair genes. Individuals with LS are much more likely to develop CRC, uterine, ovarian, stomach and other cancers than the general population.

For this study, researchers wanted to know if an upfront tumor-sequencing approach using a single test that screens for multiple mutations could replace the current multi-test screening approach commonly used to determine whether a patient has LS. To do this, researchers analyzed tumor samples from 419 CRC patients who participated in the Ohio Colorectal Cancer Prevention Initiative (OCCPI), a statewide research study to screen newly diagnosed CRC patients and their biological relatives for LS. A validation cohort of 46 patients with CRC and known to have LS also was included.

All OCCPI study participants had their tumor samples analyzed using the traditional multi-test genetic testing approach and the single, upfront genomic tumor-sequencing testing approach, in which a single tumor sample was analyzed for multiple mutations simultaneously. Researchers compared results from the two screening methods and found that the upfront tumor-sequencing approach was more sensitive and specific for detecting LS than the old, multiple-test model. Tumor sequencing resulted in a 10% improvement in LS detection rates while also providing important information about treatment options for the patients.

“Testing methods of the past would just point to a suspicion of Lynch syndrome, but they could not confirm the diagnosis without multiple additional tests, which slows down the diagnostic process and adds costs,” says Heather Hampel, MS, LGC, corresponding author of the study and principal investigator of the OCCPI.

“This new approach points to the exact mutation patients were born with and does so through a single test,” she adds.

“The mutation will need to be confirmed using a blood test, but this requires a single mutation test, which is less expensive than multi-gene panel testing.”

Published in the journal JAMA Oncology
New Drug Harnesses Immune System to Stop Triple-Negative Breast Cancer

Scientists have identified a viable drug therapy target for treating triple-negative breast cancer (TNBC), according to data published by researchers at the OSUCCC – James.

Zhiwei Hu, MD, PhD, of the Translational Therapeutics Program at the OSUCCC – James, and colleagues reported the first evidence that a molecule called tissue factor (TF) is highly expressed in TNBC—both on the surface of TNBC cancer cells and throughout most of the tumor mass. The molecule is also expressed in the inner layer of tumor blood vessels, which supply oxygen and nutrients to cancer cells and help them spread to distant organs.

Additionally, the researchers have shown that an injectable, second-generation TF-targeting therapeutic molecule can target TNBC cells in laboratory and preclinical animal models. The drug works by triggering the immune system to destroy cancer cells and to stop tumor growth.

The normal function of TF is to initiate blood clotting. The engineered second-generation molecule, known as L-ICON, works by targeting TF expressed specifically on the interior surface of TNBC cells, cutting off blood supply to the tumor vessels.

“Understanding how we can harness the immune system to selectively target TF to stop growth of cancer presents many opportunities,” says Hu, senior author of the study. “What is exciting about this study is that our data shows this second-generation drug is effective for treating TNBC, either with or without BRCA1 and BRCA2 mutations, and is more effective at penetrating and targeting the tumor microenvironment than the first-generation drug.”

Hu was involved in developing the first-generation drug, ICON, while at Yale University. Both drugs have two components: a targeting domain recognizing TF on the surface of the malignant cells paired with a natural antibody domain that activates an attack by the immune system against cancer cells that bind the engineered molecule.

The immune system then attacks tumor blood vessels, and the cancerous tissue dies from lack of blood supply. The first-generation agent is being tested in clinical trials for patients with ocular melanoma and macular degeneration. The team plans to translate the second-generation L-ICON molecule into an early-phase clinical trial for patients with TNBC.

Published in the journal Cancer Immunology Research.
Bile Duct Cancer

Researchers Learn How Resistance Develops in a Lethal Bile Duct Cancer With Novel FGFR Inhibitor

Research at the OSUCCC – James has identified gene mutations that cause resistance to promising new drugs in patients with a rare, lethal form of bile duct cancer.

The disease, called cholangiocarcinoma, has few treatment options and a five-year survival rate of less than 2% for patients with advanced disease. A new group of drugs called FGFR inhibitors offers a promising new treatment for the disease, but tumors can develop resistance to the agents, rendering them ineffective.

In this study, OSUCCC – James researchers describe secondary gene mutations—those that arise during treatment and were not present in the original primary tumor—that caused resistance to an FGFR inhibitor that had initially helped the patient. They also showed that the acquired mutations occurred in subgroups of tumor cells that arose within the metastatic tumors.

“Our results demonstrate the emergence of drug-resistance mutations in subgroups of tumor cells from a patient with cholangiocarcinoma,” says Melanie Krook, PhD, senior postdoctoral researcher at the OSUCCC – James and first author of the paper.

About 20% of patients with this bile duct cancer have mutations in FGFR genes. The mutated genes contribute to tumor development. FGFR inhibitors are designed to block the effects of the mutated genes.

“Ten FGFR inhibitors are in development, and it’s critically important for us to understand how cancer cells develop resistance to them,” says Sameek Roychowdhury, MD, PhD, associate professor in the Division of Medical Oncology at Ohio State and senior author of the study. Roychowdhury also is in the Translational Therapeutics Program at the OSUCCC – James.

This research was conducted through a Body Donation for Cancer Research study at the OSUCCC – James that allows patients to donate their organs and tissue for cancer research after death. Those interested in learning more about supporting this study can contact Jamesline@osumc.edu.

“Studying how drug resistance develops is challenging, since it is hard to study every tumor in a person’s body. We were able to make this discovery because the patient had consented to an organ donation and research autopsy, which can yield unprecedented insights into how cancer evolves and changes during the course of the disease. We are so grateful to our patients and hope to honor their support through research that can help others,” Roychowdhury adds.

Published in the journal Molecular Case Studies

SAMEEK ROYCHOWDHURY, MD, PHD
Associate Professor, Division of Medical Oncology

“Ten FGFR inhibitors are in development, and it’s critically important for us to understand how cancer cells develop resistance to them.”
ACUTE MYELOID LEUKEMIA

Gene Mutation Combinations Predict AML Outcomes in Older Patients

A study led by researchers at the OSUCCC – James identified combinations of gene mutations that predict whether an older person with acute myeloid leukemia (AML) might achieve complete remission when treated with standard chemotherapy.

The researchers analyzed the AML cells of 423 patients age 60 and older for mutations in 80 cancer- or leukemia-associated genes, then used that information to classify patients into groups that had a good, poor or intermediate outcome after treatment with standard chemotherapy.

The study highlighted the extremely poor outcome of AML patients aged 60 and older with current treatments. However, the authors found mutation combinations that associated with patient survival, some of which were different than those known to be associated with outcome in younger AML patients.

“This study is important because the majority of research in AML is done in patients under age 60, even though the majority of AML patients are of older age,” says study leader Clara D. Bloomfield, MD, a Distinguished University Professor at Ohio State who also serves as cancer scholar and senior adviser to the OSUCCC – James. Bloomfield notes that the findings might refine the classification of older AML patients who are to be treated with chemotherapy.

“We found that the number and types of chromosome changes and gene mutations are different in older AML patients compared with younger patients, along with the significance of some of those abnormalities,” Bloomfield says. “So it’s important that we evaluate older AML patients separately from younger patients.”

First author and OSUCCC – James researcher Ann-Kathrin Eisfeld, MD, a member of Ohio State’s Internal Medicine/Physician-Scientist Training Program, says the favorable complete response rate of the good-risk group did not lead to better overall survival.

Of patients in the good-risk group, 82% experienced relapse, as did patients in the intermediate-risk group. “And those groups did only slightly better than the poor-risk group, where 93% of patients relapsed,” Eisfeld says. “This tells us that, once patients are in remission, they probably require additional or different treatment than chemotherapy alone to extend remission or potentially cure those patients.

“Our findings suggest that older AML patients should be tested for additional gene mutations before receiving standard chemotherapy,” Eisfeld adds.

Published in the journal Leukemia
College of Pharmacy and OSUCCC – James Collaborate to Support Cancer Drug Discovery

The Ohio State University College of Pharmacy (COP) and the OSUCCC – James have initiated a 10-year partnership to expand drug discovery and development in cancer and cancer-related diseases.

Through this agreement, the OSUCCC – James will invest approximately $15 million for renovations of more than 19,300 square feet of the COP Division of Medicinal Chemistry and Pharmacognosy space.

In addition, the OSUCCC – James will allocate $3 million toward a Small Molecule Screening Facility, a shared resource for which Blake Peterson, PhD, chair of the Division of Medicinal Chemistry and Pharmacognosy, will serve as director. The OSUCCC Medicinal Chemistry Shared Resource will also be relocated to the COP, allowing for synergies in the discovery and development of cancer therapeutics.

In recognition of the OSUCCC – James contributions to space renovations and research, the partners will share intellectual property revenue from current and future COP cancer-related drugs, devices and other technologies developed by researchers occupying the renovated space. The COP and the OSUCCC – James also will share the costs of acquiring patents and associated legal fees.

“The College of Pharmacy has had a partnership with the OSUCCC since the cancer center’s inception,” says Henry Mann, PharmD, dean of the COP. “This investment reinforces the groundbreaking work that we are doing to retain world-renowned researchers who are exploring new frontiers in drug discovery and development, pharmaceutical sciences and translational clinical research.”

This most recent agreement builds on a series of joint hires between the OSUCCC – James and the COP that are focused on cancer drug discovery. In 2015, Sharyn Baker, PhD, was recruited as chair of the college’s Division of Pharmaceutics and Pharmaceutical Chemistry and as the OSUCCC’s Gertrude Parker Heer Chair in Cancer Research. Baker also is the OSUCCC associate director for shared resources. Alex Sparreboom, PhD, was recruited at the same time as a professor in the COP and holds the OSUCCC’s Lucius A. Wing Chair of Cancer Research and Therapy.

Peterson, the most recent COP and OSUCCC joint faculty recruit, became chair of the Division of Medicinal Chemistry and Pharmacognosy in August.
Known as PRT543 while in testing, this targeted treatment molecule is among the first in an emerging class of drugs called PRMT5 inhibitors.

Protein arginine methyltransferases (PRMTs) are a family of enzymes that regulate a variety of cellular functions. When dysregulated, PRMTs are associated with several aggressive human cancers, including diffuse large B-cell and mantle cell lymphoma, pancreatic cancer and glioblastoma.

Research published by the OSUCCC – James and other institutions suggests that PRMT5, a member of this family, is a potential oncoprotein involved in transforming a normal cell into a cancer cell and could be an important target for new treatment strategies.

The OSUCCC – James is one of four cancer centers participating in this first-in-human trial, which will enroll 100 patients across the United States. Patients age 18 or older with metastatic or advanced solid tumors, advanced diffuse large B-cell lymphoma, advanced mantle cell lymphoma, relapsed myelodysplastic syndrome or relapsed myelofibrosis may qualify.

Led by Robert Baiocchi, MD, PhD, the OSUCCC – James research team was the first to discover PRMT5 as a cancer driver and the first to develop and report a series of novel molecules to selectively inhibit it. The team has been evaluating PRMT5 inhibitors for the therapeutic treatment of various cancers, as well as benign blood and autoimmune diseases. The targeted molecule currently in testing (PRT543) was developed by Prelude Therapeutics, which is sponsoring the trial.

With support from the Drug Development Institute, a translational accelerator embedded within the OSUCCC – James, this entire portfolio of molecules was licensed to Prelude in 2016. The company is developing drugs that inhibit a specific enzyme (PRMT5) for cancer and other unmet medical needs. Prelude provides financial support for preclinical and clinical research conducted at the OSUCCC – James.

“PRMT5 is a compelling therapeutic target because it acts like a hub that coordinates diverse molecular activities for cancer cells,” Baiocchi says. “PRT543 selectively targets PRMT5. If proven effective in clinical testing, this could radically improve how we treat certain aggressive, recurrent cancers.”
Pilot Study Shows Even Short-Term ‘Vaping’ Causes Inflammation in Non-Smokers

E-cigarette (e-cig) use is rising at concerning levels among both smokers and non-smokers, and new research data suggests that even short-term e-cig use can cause cellular inflammation in never-smoker adults.

Researchers at the OSUCCC – James in October reported the first evidence of biological changes correlated with e-cig use in never-smokers.

Using bronchoscopy to test for inflammation and smoking-related effects, researchers reported a measurable increase in inflammation after four weeks of e-cig use (without nicotine or flavors). Although the magnitude of change was small compared with a control group, the pilot data suggests that even short-term use can cause inflammatory changes at a cellular level. Inflammation from smoking is an important driver of lung cancer and other respiratory disease development.

Peter Shields, MD, senior author of the study and deputy director of the OSUCCC, says any level of cellular inflammation correlated with e-cig use is concerning because the biological and health effects of e-cig constituents such as propylene glycol and vegetable glycerine—while “generally regarded as safe” by the U.S. Food and Drug Administration (FDA) when used in foods and cosmetics—are unknown when heated and inhaled with e-cigs. Researchers noted that, even in this small study, there were observable effects.

“The implication of this study is that longer-term use, increased daily use and the addition of flavors and nicotine may promote additional inflammation,” says Shields. “The general perception among the public is that e-cigs are ‘safer’ than cigarettes. The reality is the industry is changing so fast, and with minimal regulation, that usage is outpacing the rate of our scientific understanding.

“It’s becoming a public health crisis we should all take very seriously from a general pulmonary health, cancer risk and addiction perspective,” he adds. “E-cigs may be safer than smoking, but that is not the same as safe. We need to know how unsafe they are.”

Amid recent reports of lung disease and deaths associated with vaping, scientists believe the effects of vaping nicotine and marijuana oils make this research critical.

Published in the journal Cancer Prevention Research
The Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC – James is just getting started, but founding director Zihai Li, MD, PhD, is excited about its potential contributions to a burgeoning discipline that may hold the keys to controlling cancer.

Li’s confidence in the promise of the PIIO hinges on his belief that immunotherapy, with much refinement, could become another standard treatment modality for cancer along with the more traditional modalities of surgery, systemic therapies (e.g., chemotherapy and hormonal therapy), precision or targeted therapies, and radiation therapy.

Whereas those are innovations of modern medical science, Li says, immunotherapy derives from an ancient gift of nature: the human immune system—perhaps lending ultimate importance to this modality, which is widely considered to be the next frontier of cancer prevention and treatment.

“For however many years human beings have been walking on the planet,” he explains, “our immune system has been with us; without it we wouldn’t survive as a species.”

Historically, Li says, humans have viewed the immune system primarily as a natural means of fighting infection, but over the past several decades medical scientists have increasingly explored the concept of exploiting its potential against cancer. And recent advances, he adds, have brought immuno-oncology to the forefront of cancer research.

“Immunoncology as a discipline started seriously in the 1950s when people were becoming convinced about the power of vaccines to deal with infectious diseases,” Li says. “So the question was, can cancer be dealt with similarly?”

With the development of genetically similar animals (in-bred rodents) for vaccine experimentation, he says, scientists learned that they could induce immunity against cancer.

“That was interesting, and it conceptually began giving people confidence in the possibility of immunotherapeutic care
for cancer, but many were still skeptical,” Li says.

In succeeding decades, he continues, other forms of cancer treatment that could be considered immunotherapy arose, such as bone marrow transplantation and cytokine therapy.

“But it wasn’t until the early 1990s—so recently—that we were finally able to isolate human T cells that recognized tumors,” Li says. “This was a breakthrough in our understanding that the immune system could indeed recognize cancer.”

Additional developments followed, such as the discovery of co-stimulation signals that can activate the immune system, and the identification of co-inhibitory signals, or so-called immune checkpoints like the programmed cell death protein 1 (PD-1) that can serve as a brake to the immune response against cancer in the tumor microenvironment.

“Now we had three immunity signals: tumor recognition, co-stimulation, and co-inhibitory signals that constrain the immune system,” Li says. “Then people started to experiment: What would happen if we removed this inhibitory signal, this checkpoint? We did, and suddenly the immune system started to attack the tumor. Those discoveries and many others have led us to where we are today.”

And where we are today, he says, is at the threshold of the next frontier in cancer research: immuno-oncology, to which he has devoted his career.

“We finally realize that what keeps patients alive for a long time, meaning cure, is not about how good are surgery, chemo or radiation therapy, but how good is our immune system,” Li says. “Those other modalities are very important and help manage cancer, but it’s really the immune system that ultimately takes care of everything. It comes down to your own body’s defense. Without the immune system, we couldn’t talk about cure.”

Hence the importance of the PIIO, which is committed to studying the immune system and optimizing its potential.

Li, a renowned medical oncologist and immunologist with primary research interests in the mechanisms of immune regulation in cancer, says being recruited to Ohio State from the Medical University of South Carolina (MUSC) last April to establish and direct the institute “is a dream come true. You are doing something that’s so important, something you’ve been working on for many years, something you can keep contributing to. It’s hard to describe how excited I am.”

The PIIO—a comprehensive bench-to-bedside research initiative focused on harnessing the human immune system to fight cancer at all levels, from prevention to treatment and survivorship—was launched last summer through a pledge of $102,265,000 from Pelotonia, an annual grassroots cycling event that raises money for cancer research at the OSUCCC – James. The largest portion of the pledge, $65 million, will directly fund the PIIO. The OSUCCC – James is also supporting it with a $35 million commitment to expand and sustain research infrastructure.

Plans call for hiring 30-35 scientists over the next five years to help drive forward the PIIO’s mission of advancing our understanding of the immune system’s role in fighting cancer.
years to support the PIIO. Li says the number of new recruits is already approaching 10, “and I’m negotiating with others, hoping to convince them to join us soon.”

PIIO investigators will work in five centers being established within the institute: Immunogenomics, Synthetic Immunology, Systems Immunology, Translational Immunology, and Cancer Microbiome. Their studies, along with work by OSUCCC – James scientists who had been conducting immunotherapy research before Li’s arrival, will contribute to what Li and others consider to be the main types of immunotherapy:

- Monoclonal antibodies (drugs that attach to cell targets and create an immune response that destroys cancer cells);
- Cytokine therapy (increases a patient’s cytokines, or the protein molecules that help the immune system bolster its defense against cancer);
- Adoptive cell transfer (removing T cells from a tumor or blood, reproducing or altering them in a lab and returning them to stimulate the immune system);
- CAR T-cell therapy (a type of adoptive cell transfer that involves genetically improving a patient’s white blood cells with protein “receptors” that recognize and eliminate abnormal cells);
- Vaccines (biological preparations that protect the body from cancer recurrence or help the immune system destroy antigens within abnormal cells);
- Drug therapy (administering agents that block mechanisms that enable cancer cells to hide from the immune system).

Li believes cancer patients and their families, not to mention the medical community, should share his excitement for immunotherapy.

“In the past five years we have seen extraordinary results of immunotherapy for several deadly cancer types, including lung cancer, melanoma, leukemia and others,” he says. “For patients with stage IV lung cancer, median survival three years ago was four to six months. Now, with immunotherapy, some 20% of patients can live for five years. That’s an incredible number, even though it’s still small and not nearly enough.”

But even with the recent advances in immuno-oncology and the addition of substantial resources devoted to advancing it further, Li and colleagues realize there are “still many remaining critical unanswered questions” regarding this modality.

“The most important one is how to improve efficacy,” he says. “Why do only 10-20% of patients benefit from current immunotherapies overall? That implies that there are other mechanisms of immune escape or evasion that we need to learn about.”

As an example of a current immunotherapy with limited efficacy he cited PD-1, a checkpoint protein on T cells, which are immune cells that help the body recognize abnormal cells and disease. PD-1 normally acts as an “off switch” that keeps
T cells from attacking other cells. PD-1 inhibitors are monoclonal antibodies that are used in oncology to selectively block this protein and boost immune response to attack cancer cells. But some cancer patients do not respond to PD-1 therapy because their fighter T cells (known as CD8 T cells) are unable to invade the tumor microenvironment.

In a recent study published in the *Journal of Clinical Investigation*, **Yiping Yang, MD, PhD**, who directs the Division of Hematology at Ohio State and is a researcher in both the PIIO and the OSUCCC – James, identified cellular mechanisms that limit the ability of CD8 T cells to infiltrate the tumor microenvironment. By blocking that cellular pathway (called hedgehog signaling), the researchers reversed the process and promoted CD8 T cell infiltration in preclinical models of liver and lung cancer.

“At this point we often give immunotherapy for patients with metastatic disease almost as a last resort,” Li explains. “Could it be more effective if we give it for early-stage cancer? Can we incorporate it into standard practice in a smarter way?”

“Right now the usual order of treatment is surgery followed by chemo, radiation and then immunotherapy,” he says. “How can we make immunotherapy a front-line modality? Can we sequence patient care in a way that’s guided by science? And could we one day generate immune strategy to prevent cancer from developing in the first place? Cancer vaccines are currently used to prevent recurrence, but I think eventually we can develop them to help prevent initial carcinogenesis.

“Sometimes things that seemed impossible yesterday are possible now. But the only way to answer our questions and continue advancing this discipline is through research and clinical trials. That’s the mission of the PIIO.”
Partial Breast Irradiation Effective, Convenient Treatment Option for Low-Risk Breast Cancer

Data from a national clinical trial demonstrates that partial breast irradiation produces similar long-term survival rates and risk for recurrence compared with whole breast irradiation for many women with low-risk, early-stage breast cancer.

In a large group of women with stage 0, 1 or 2 breast cancer. More than 4,200 patients were enrolled in the study as part of an NRG Oncology cooperative group clinical trial.

Study results showed that, while partial breast irradiation does not produce equivalent cancer control for all breast cancer patients with stage 0, 1 and 2 disease, it should still be considered as an alternative for women with DCIS (ductal carcinoma in situ) and early-stage breast cancers deemed “low risk” based on other tumor characteristics.

Among the entire study population, women who received partial breast irradiation experienced a 4.6% recurrence rate. Those who underwent whole breast irradiation experienced a 3.9% rate of recurrence. Toxicity from treatment was similar, as well as the risk for secondary cancers.

However, researchers also looked at how this played out in sub-segments of the population and found that rates of recurrence were nearly identical for women with DCIS, regardless of whether they received whole or partial breast irradiation. This was also true for women with breast cancer classified as low risk based on American Society for Radiation Oncology (ASTRO) clinical guidelines.

Researchers showed that, in this sub-segment of breast cancer patients, the likelihood of recurrence 10 years post-treatment was very low overall and almost identical between women who received whole breast irradiation (2.3%) and partial breast irradiation (2.7%).

Julia White, MD, co-principal investigator of the national trial and head of breast radiation oncology at the OSUCCC – James, says this is very important because it reduces the burden of care for women who can still achieve cancer control with fewer treatments over a shorter period.

“A significant portion of the breast cancer patient population nationally—about 25,000 to 30,000 women—would qualify for partial breast irradiation. This is tremendously important because it allows us to give women the right amount of treatment for their disease and potentially allows better access to effective breast conservation for those who live far from a radiation facility,” says White, who also is a professor in the Department of Radiation Oncology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James.

“Partial breast irradiation can also be delivered in five consecutive days versus whole breast, which can involve four to six consecutive weeks of multi-day treatment,” White adds. “There is no denying that the five-day treatment is less costly and less disruptive to life.”

At the OSUCCC – James, breast radiation is also delivered in the face-down (prone) position to reduce radiation exposure in the chest wall, which has been linked to increased risk of heart and lung disease post-cancer treatment.

Data from this NRG Oncology study was presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.
FROM THE LABORATORY TO THE CLINIC

A Phase I/II Study of AZD9291 (Osimertinib) and CB-839 Hydrochloride HCl in Patients With EGFR-Mutant Non-Small Cell Lung Cancer

SUMMARY: This interventional study, which is open to patient accrual at Ohio State, will examine the side effects and best dose of the glutaminase inhibitor CB-839 hydrochloride (HCl), and will also see how well this agent works when given together with osimertinib in treating patients with stage IV non-small cell lung cancer (NSCLC) and a mutation in the EGFR gene. Treatment with the glutaminase inhibitor CB-839 HCl and osimertinib may stop the growth of tumor cells by interfering with the enzymes used by cancer cells for growth.

STUDY DESIGN: Patients receive glutaminase inhibitor CB-839 hydrochloride orally twice daily and osimertinib once daily (starting cycle 1 day 16 of phase I). Cycles repeat every 28 days in the absence of disease progression or unacceptable toxicity. After completion of study treatment, patients are followed up at 30 days. The estimated study completion date is June 1, 2021.

PRIMARY OBJECTIVES:
I. To assess the safety and tolerability of this drug combination and recommend a phase II dose for patients with metastatic EGFR-activating mutation-positive NSCLC;
II. To determine the efficacy of this combination in patients who have developed progressive disease on front-line EGFR inhibitor therapy.

SECONDARY OBJECTIVES:
I. To determine toxicity profile of the combination of AZD9291 and CB-839 HCl (telaglenastat) in patients with metastatic EGFR-activating mutation-positive NSCLC. (Phase I)
II. To assess the pharmacokinetics of CB-839 HCl (telaglenastat) and AZD9291 in patients with metastatic EGFR-activating mutation positive. (Phase I)
III. To determine progression-free survival of AZD9291 and CB-839 HCl (telaglenastat) in patients with EGFR mutation-positive, T790M mutation-negative NSCLC who have developed progressive disease (PD) on front-line EGFR inhibitor therapy. (Phase II)
IV. To determine the overall survival (OS) of AZD9291 and CB-839 HCl (telaglenastat) in patients with EGFR mutation-positive, T790M mutation-negative NSCLC who have developed PD on front-line EGFR inhibitor therapy. (Phase II).

STUDY LEADER: Principal investigator for this clinical trial is Dwight Owen, MD, assistant professor in the Division of Medical Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James. Questions and trial referrals should be directed to katie.dicostanzo@osumc.edu.

AT A GLANCE

Trial No.: OSU-19016
gov identifier: NCT03831932
PI: Dwight Owen, MD
Phone: (614) 685-2039
Email: dwight.owen@osumc.edu

Eligibility: Men and women 18 years of age or older; ability to swallow pills; life expectancy greater than three months; histologically confirmed stage IV NSCLC, with advanced or metastatic disease; activating mutation present in the EGFR gene (L858R or exon 19 deletion, alone or in combination with other EGFR mutations) as per local assessment of a tissue biopsy specimen obtained since the time of disease progression on prior therapy; must have had progressive disease on prior EGFR inhibitor therapy (gefitinib, erlotinib, afatinib or osimertinib); no limit to lines of prior tyrosine kinase inhibitor (TKI) therapy; (other eligibility requirements and exclusion criteria may be viewed at OSU-19016).
The National Institutes of Health (NIH) awarded a $25 million Clinical and Translational Science Award to Rebecca Jackson, MD, a member of the Cancer Control Program at the OSUCCC – James and director of Ohio State's Center for Clinical and Translational Science (CCTS). The grant will further the CCTS mission of translating discoveries into therapies to improve human health. This is the CCTS’ third five-year cycle of funding since 2008 from the NIH’s National Center for Advancing Translational Sciences. The CCTS is a collaboration of Ohio State’s College of Medicine, other colleges at Ohio State, and Nationwide Children's Hospital.

The National Cancer Institute (NCI) awarded a $12.7 million, five-year Program Progress Grant to OSUCCC Deputy Director Peter Shields, MD, and Dorothy Hatsumaki, PhD, of the University of Minnesota, to help researchers conduct comprehensive, systematic and integrated projects on the relative toxicity, addictiveness and appeal of unventilated vs. ventilated filter cigarettes. Shields also is principal investigator for a two-year, $1.36 million NCI grant to study the potential lung toxicity for inhaling electronic cigarette (e-cigs) aerosols relative to smoking.

A major public health initiative to prevent cervical cancer in at-risk Appalachian families in four states is underway with support from an $11 million Program Progress Grant from the NCI to the OSUCCC – James. The institution is collaborating with 10 health systems throughout Appalachian Ohio, Kentucky, Virginia and West Virginia to conduct this study in connection with the University of Kentucky, University of Virginia and West Virginia University. Led by Electra Paskett, PhD, MSPH, associate director for population sciences and co-leader of the Cancer Control Program at the OSUCCC – James, the initiative will focus on reducing cervical cancer incidence in at-risk communities by targeting the major causes of this disease: tobacco smoking, human papillomavirus (HPV) infection and lack of cervical cancer screening.

The NCI awarded a $10.2 million Cancer Moonshot grant to researchers at Nationwide Children’s Hospital (NCH) in support of multiple ongoing projects led by the Pediatric Ohio-New York Cancer (Peds-ONC) Immunotherapy Center, which includes collaborators at The Ohio State University, the New York College of Medicine and the University of Minnesota. The multi-year grant will fund an immunotherapy project led by Timothy Cripe, MD, PhD, and Elaine Mardis, PhD, along with a viral oncology project led by Kevin Cassady, MD, and a natural killer (NK) cell efficacy project led by Dean Lee, MD, PhD (all shown above from left). Cripe, Mardis and Cassady are in the Translational Therapeutics Program at the OSUCCC – James, and Lee is in the Leukemia Research Program.

OSUCCC – James researchers led by Purnima Kumar, DDS, PhD, landed a five-year, $3.12 million grant from the National Institute of Dental and Craniofacial Research to conduct the first comprehensive examination of the body’s biological responses to electronic nicotine delivery systems (ENDS), also known as e-cigs. The researchers will use the oral cavity as a model system for their study, since it is the first area of the body affected by ENDS and the most accessible for examination. Kumar is a professor in the College of Dentistry and member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.

A $2.2 million, five-year grant from the NCI will help researchers led by Bhuvaneswari Ramaswamy, MD, address cancer disparity by defining the molecular link between breastfeeding and triple-negative breast cancer (TNBC). Ramaswamy, associate professor in the Division of Medical Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, and colleagues state in their project abstract that African-American women with breast cancer face higher mortality rates due to a greater incidence
of aggressive TNBC. The scientists say population studies have linked reduced rates of breastfeeding among black women to this higher TNBC, but the mechanism for this circumstance is unknown.

The NCI awarded a five-year grant of nearly $2.83 million to help a research team at the OSUCCC – James conduct a clinical trial that will assess a potential new treatment for patients with glioblastoma, a lethal primary brain tumor with limited treatment options. The team is led by co-principal investigators Vinay Puduvalli, MBBS (left), professor in the Department of Neurological Surgery at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, and Deepa Sampath, PhD (right), assistant professor in the Division of Hematology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James.

The NCI awarded Matthew Ringel, MD, professor and director of the Division of Endocrinology, Diabetes and Metabolism at Ohio State, a $1.89 million R01 grant to study the role of p21-activated kinases in thyroid cancer development and progression. This work by Ringel and colleagues will define the function of these proteins in thyroid cancer and determine whether the PAK pathway is a viable therapeutic target for certain patients with this disease. The project is part of an $11.3 million Specialized Program of Research Excellence (SPORE) grant awarded by the NCI in 2013 for a six-year thyroid cancer project involving researchers at the OSUCCC – James and MD Anderson Cancer Center. Ringel, who also co-leads the Cancer Biology Program at the OSUCCC – James, is national PI for the SPORE grant.

Carolyn Presley, MD, MPH (left), and Colleen Spees, PhD, MEd, RDN (right), received a three-year, $2.3 million research grant funded by Bristol-Myers Squibb Foundation to conduct a randomized clinical trial evaluating the impact of nutritional counseling and medically tailored meals for patients with lung cancer. The study will take place at the OSUCCC – James, Tufts Medical Center, Fox Chase Cancer Center and MD Anderson Cancer Center. Spees, an associate professor in the Division of Medical Dietsetics & Health Sciences at Ohio State, is the study principal investigator. Presley, an assistant professor in the Division of Medical Oncology at Ohio State, is site PI. Both are also members of the OSUCCC – James.

The American Cancer Society (ACS) awarded a $1.7 million, five-year grant to Jennifer Kue, PhD (left), assistant professor in The Ohio State University College of Nursing, to fund the “Intergenerational Refugee and Immigrant Cancer Screening Project,” for which Kue is principal investigator (PI). Kue also is in the Cancer Control Program at the OSUCCC – James. The study aims to increase awareness of and screening for breast and cervical cancer among intergenerational Southeast Asian immigrant women. A co-PI for the project is Maryam Lustberg, MD, MPH (right), associate professor in the Division of Medical Oncology at Ohio State and member of the Cancer Control Program at the OSUCCC – James.

A five-year, $5.7 million, multi-institutional grant from the NCI will help investigators at the OSUCCC – James and the University of Kentucky collaborate to increase screening and follow-up care for colorectal cancer in central Appalachia, a medically underserved region. The grant, part of the NCI Cancer Moonshot initiative to boost cancer research nationwide, will support a multi-site project.
called Accelerating Colorectal Cancer Screening Through Implementation Science (ACCSIS) in Appalachia. Principal investigators are Mark Dignan, PhD, MPH, a professor at the University of Kentucky, and Electra Paskett, PhD, MSPH, associate director for population sciences and co-leader of the Cancer Control Program at the OSUCCC – James.

The NCI awarded a five-year, $1.78 million grant to Zobeida Cruz-Monserrate, PhD, assistant professor in the Division of Gastroenterology, Hepatology and Nutrition at Ohio State, to help her and colleagues study the role of the lipocalin 2 (LCN2) protein in pancreatic cancer. Cruz-Monserrate, a member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James, says their project will provide insights into blocking LCN2 and its associated pathways to help better treat or prevent pancreatic ductal adenocarcinoma.

Ann Scheck McAlearney, ScD, MS, professor and vice chair for research in the Department of Family Medicine, received a $1.89 million grant from the Agency for Healthcare Research and Quality for a study titled “Searching for Management Approaches to Reduce Healthcare-Associated Infections (HAI) Transmission (SMART).” McAlearney, who is in the Cancer Control Program at the OSUCCC – James, and colleagues will develop a management practice SMART toolkit for use by hospitals and health systems nationwide.

Susheela Tridandapani, PhD (left), professor in the Division of Hematology, and Jon Butchar, PhD (right), assistant professor in the Division of Hematology, lead a team that received a $1.75 million grant from the NCI for a study titled “Myeloid Cell-Derived Granzyme B as an Inducible Enhancer of Cancer Immunotherapy.” Tridandapani and Butchar are in the Leukemia Research Program at the OSUCCC – James.

The U.S. Department of Defense awarded a three-year, $1.17 million grant to help OSUCCC – James researchers develop a cell-surface molecule called RAGE (receptor for advanced glycation end products) as a biomarker and therapeutic target for triple-negative breast cancer (TNBC). Principal investigator is Ramesh Ganju, PhD (left), professor in the Department of Pathology at Ohio State and member of the Cancer Biology Program at the OSUCCC – James. Ganju and co-investigators Bhuvaneswari Ramaswamy, MD (right), of the Translational Therapeutics Program at the OSUCCC – James, and Dinesh Aahirwar, PhD, assistant professor in the Department of Pathology, have shown that RAGE is expressed in a panel of aggressive breast cancer cell lines, TNBC and metastatic patient samples.

The OSUCCC – James will address a priority of both the NCI and Ohio State by using a five-year, $1.03 million NCI grant to establish a postdoctoral training program for cancer prevention and control. The T-32 grant, awarded to principal investigator (PI) and project leader Peter Shields, MD (left), deputy director of the OSUCCC, and co-PI Christopher Weghorst, PhD (right), professor in the College of Public Health, will support transdisciplinary training that will prepare postdoctoral fellows to be independent researchers.

The National Institute of Neurological Disorders and Stroke awarded a $2 million, five-year grant to help Ohio State researchers study glioblastoma (GBM), an incurable brain cancer. Primary investigators are Deliang Guo, PhD (left), associate professor in the Department of Radiation Oncology, and Radiation Oncology Department Professor and Chair Arnab Chakravarti, MD (right). Researchers hope to reveal the role lipid droplets play in GBM, its method of molecular regulation and its therapeutic potential.
William Farrar, MD, was named CEO of The James after serving as interim CEO for nearly two years. Farrar has had a long and successful history as a surgical oncologist, serving on The James medical staff since the hospital opened in 1990. The late Arthur G. James, MD, for whom the hospital is named, mentored and later worked alongside Farrar, who has held a number of leadership positions. He also directs the Stefanie Spielman Comprehensive Breast Center at the OSUCCC – James.

Clara D. Bloomfield, MD, a Distinguished University Professor at Ohio State who serves as cancer scholar and senior adviser to the OSUCCC – James, received a European LeukemiaNet Merit Award for her contributions to international integration of leukemia research, particularly in acute myeloid leukemia. A globally known medical scientist, Bloomfield has earned many accolades since she came to Ohio State in 1997.

The American College of Nuclear Medicine (ACNM) re-elected Michael Knopp, MD, PhD (left), and Chadwick Wright, MD, PhD (right), to its board of directors. The ACNM is dedicated to enhancing the practice of nuclear medicine through the study, education and improvement of clinical practice. Knopp is a professor, Distinguished University Scholar and Novartis Chair of Imaging Research in the Department of Radiology at Ohio State. Wright is an assistant professor in the Department of Radiology. Knopp also is in the Translational Therapeutics Program at the OSUCCC – James.

The NCI appointed Lynne Abruzzo, MD, PhD, professor in the Department of Pathology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James, to its Board of Scientific Counselors – Clinical Sciences and Epidemiology. Abruzzo focuses her research on low-grade B-cell leukemia and lymphoma, including chronic lymphocytic leukemia.

A study by Naduparambil Jacob, PhD, associate professor in the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was one of 10 proposals selected by NASA to support astronaut health and performance on longer missions to the moon and Mars. Jacob aims to study predictive biomarkers for space radiation-induced cancer and cardiovascular injury risk assessment.

Floor Backes, MD, associate professor in the Division of Gynecologic Oncology at Ohio State and member of the Cancer Control Program at the OSUCCC – James, has assumed the national role of co-chair for the NRG Oncology Developmental Therapeutics Committee. NRG Oncology is a non-profit research organization formed to conduct national and international oncologic clinical research and to disseminate study results for informing clinical decision making and healthcare policy. Backes also was named local lead investigator for the Gynecologic Oncology Group (GOG) Foundation Inc.

The Ovarian Cancer Research Fund Alliance (OCRFA) presented the Liz Tilberis Research Prize for Outstanding Early Career Investigators to Selvendiran Karuppayyah, PhD, associate professor in the Department of Obstetrics and Gynecology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James. OCRFA bestows this distinction annually on one individual who has impacted the field of ovarian cancer research.

The American College of Gastroenterology presented Darrell Gray II, MD, MPH, assistant professor in the Division of Gastroenterology, Hepatology and Nutrition at Ohio State, a Service Award for Colorectal Cancer Outreach, Prevention and Year-Round Excellence for Best Community Service Delivery and Comprehensive Community Education Initiative. Gray is in the Cancer Control Program at the OSUCCC – James.
Larry Copeland, MD, professor in the Department of Obstetrics and Gynecology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, is president of the Gynecologic Oncology Group (GOG) Foundation Inc. after previously serving as vice president. The GOG Foundation is an independent, international, non-profit organization that promotes the quality and integrity of clinical and basic scientific research in gynecologic malignancies.

Nilendu Gupta, PhD, associate professor in the Department of Radiation Oncology at Ohio State, was elected as a Fellow of the American Association of Physicists in Medicine (AAPM). The category of Fellow honors AAPM members who have distinguished themselves by contributions in research, education or leadership in the medical physics community. For the past decade Gupta has been the chief medical physicist in the Department of Radiation Oncology.

David Cohn, MD, chief medical officer at the OSUCCC – James, was elected president of the Society of Gynecologic Oncology (SGO) for the 2020-21 term year. Cohn’s four-year commitment began in March 2018 when he became president-elect II for one year. He is now serving as president-elect I, after which he will serve as president (2020-21) and past president (2021-22).

Ritu Salani, MD, MBA, professor in the Department of Obstetrics and Gynecology at Ohio State and member of the Cancer Control Program at the OSUCCC – James, was elected to a three-year term as co-chair of the Cervical Task Force established by the NCI’s Gynecologic Cancers Steering Committee. Her term extends through May 31, 2021. Salani also serves as chair of the International Gynecologic Cancer Society’s (IGCS) Education Committee, and as chair of the Compliance Committee for the Society of Gynecologic Oncology (SGO).

The board of directors for the International Thyroid Oncology Group (ITOG) elected Manisha Shah, MD, professor in the Division of Medical Oncology, to a three-year term as chair of the ITOG. Her term began in 2018. Shah is in the Translational Therapeutics Program at the OSUCCC – James.

Barbara Andersen, PhD, a Distinguished University Professor in the Department of Psychology at Ohio State and member of the Cancer Control Program at the OSUCCC – James, co-authored an expert commentary and accompanying podcast for the American Society of Clinical Oncology (ASCO) on recognizing, assessing, referring and monitoring cancer patients with symptoms of moderate to severe anxiety or depression. Her co-author was Marlena Ryba, PhD, assistant professor of psychology at Coastal Carolina University. Their commentary appeared in ASCO Daily News.

Patrick Green, PhD, professor and associate dean for research and graduate studies in The Ohio State University College of Veterinary Medicine, was named associate director for basic sciences at the OSUCCC – James. He facilitates basic science throughout the cancer program and works with the other associate directors to foster translational research initiatives. Green is in the Leukemia Research Program and also directs Ohio State’s Center for Retrovirus Research.

Janice Kiecolt-Glaser, PhD, director of the Ohio State University Institute for Behavioral Medicine Research and a member of the Cancer Control Program at the OSUCCC – James, received the 2018 American Psychological Association Award for Distinguished Scientific Contributions. Kiecolt-Glaser is a Distinguished University Professor in the departments of Psychology and Psychiatry at Ohio State. Her citation appeared in the journal American Psychologist.
John Grecula, MD, professor in the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was elected as president-elect of the International Society of Intraoperative Radiation Therapy (ISIORT). This organization provides a platform for scientists and clinicians from around the world to present new research, developments and clinical data. Grecula also is an elected board member of ISIORT.

Ann-Kathrin Eisfeld, MD (left), hematology/oncology fellow in the Physician Scientist Training Program at Ohio State, and Meixiao Long, MD, PhD (right), assistant professor in the Division of Hematology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James, both received a 2019 American Society of Hematology (ASH) Scholar Award in the Basic/Translational Junior Faculty category. Eisfeld’s award will help her continue her research as a “Young Investigator,” receiving senior support from Elaine Mardis, PhD, Clara D. Bloomfield, MD, and Albert de la Chapelle, MD, PhD. Under the direction of John C. Byrd, MD, Long and colleagues are studying the immune modulatory effects of small molecule kinase inhibitors and their potential for immunotherapy. ALSO, Eisfeld was honored as one of 15 NextGen Stars for 2019 at the American Association for Cancer Research (AACR) Annual Meeting. The NextGen Stars program represents one of the highest honors for young investigators at the AACR.

Jonathan Song, PhD, assistant professor in the College of Engineering at Ohio State and member of the Cancer Biology Program at the OSUCCC – James, received a $187,772 grant from The Mark Foundation® for Cancer Research to support his development of a preclinical disease model to precisely interrogate how brain metastases obtain vasculature through the co-option of pre-existing blood vessels. Song leads an interdisciplinary lab at Ohio State that applies microtechnology, principles from tissue engineering, and quantitative engineering analysis for studying dynamics of tumor and vascular biology.

Ricardo Carrau, MD, professor in the Department of Otolaryngology – Head and Neck Surgery at Ohio State, has been elected president of the board of directors of the North American Skull Base Society, a professional medical society that facilitates communication worldwide between individuals pursuing clinical and research excellence in skull-base surgery. Carrau is an otolaryngologist – head and neck surgeon at the OSUCCC – James who has many clinical and research interests.

Carolyn Presley, MD, assistant professor in the Division of Medical Oncology at Ohio State and member of the Cancer Control Program at the OSUCCC – James, received the 2019 Health in Aging Foundation New Investigator Award from the American Geriatrics Society. This national award recognizes individuals who are committed to a career in aging research. Presley is a thoracic and geriatric oncologist specializing in the treatment of older adults with advanced lung cancer.

The Society of University Surgeons (SUS) recently bestowed its Mid-Career Award on Clara Lee, MD, MPP, associate professor in the Department of Plastic and Reconstructive Surgery at Ohio State and a member of the Cancer Control Program at the OSUCCC – James. Given to one person annually, this prestigious award supports Lee’s research on the implementation of breast reconstruction decision support in diverse practice settings.

The National Minority Quality Forum recognized Lanla Conteh, MD, MPH, assistant professor in the Division of Gastroenterology, Hepatology and Nutrition at Ohio State, as a 2019 40 Under 40 Leader in Minority Health. Representing the next generation of thought leaders in reducing health disparities, only 40 outstanding individuals are selected nationally each year for this honor. Conditions that Conteh treats as a physician include hepatitis, cirrhosis and liver cancer.
The American Board of Neurological Surgery (ABNS) elected Russell Lonser, MD, professor and chair of the Department of Neurological Surgery at Ohio State, as an ABNS director. The ABNS consists of 15 directors and officers elected from among practicing neurosurgeons certified by the board. Directors are elected to a single six-year term. As a neurosurgeon, Lonser provides treatment for several cancers.

Julia White, MD, professor in the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was co-principal investigator for a national clinical trial that the American Society for Radiation Oncology (ASTRO) highlighted as a top-rated study at its annual meeting in Chicago. At the Plenary Session, White presented an abstract titled “Cosmetic Outcome From Post-Lumpectomy Whole Breast Irradiation (WBI) versus Partial Breast Irradiation (PBI) on the NRG Oncology/NSABP B39-RTOG 0413 Phase III Clinical Trial.”

Elaine Mardis, PhD, professor in the Department of Pediatrics at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was elected to the National Academy of Medicine (NAM), an organization that recognizes individuals who have demonstrated outstanding professional achievement and commitment to service. Election to the NAM is considered one of the highest honors in the fields of health and medicine.

Allan Tsung, MD, professor and director of the Division of Surgical Oncology at Ohio State, was elected as president-elect of the Society of Asian Academic Surgeons (SAAS). The SAAS was founded to focus on the personal and professional development of Asian academic surgeons. Tsung also is in the Translational Therapeutics Program at the OSUCCC – James.

Ann-Kathrin Eisfeld, MD, a hematology/oncology fellow in the Physician Scientist Training Program at Ohio State, was selected to receive an American Society of Hematology (ASH) Abstract Achievement Award for her abstract titled “The 2017 European Leukemianet Genetic Risk Classification Performs Poorly in Older Patients With Acute Myeloid Leukemia (AML) and Should be Refined to Identify Patients Requiring Additional or Alternative Treatment.” The abstract was featured at the 61st ASH Annual Meeting in Orlando, Fla.

Joel Mayerson, MD, professor in the Department of Orthopaedics at Ohio State and medical director of Perioperative Services and the Sarcoma Service Line at The James, was inducted to a one-year term as president of the Musculoskeletal Tumor Society (MSTS) at the 2019 MSTS annual meeting in Portland, Ore. The MSTS is the premier source of research, education and advocacy for patients with musculoskeletal cancers and is the largest professional specialty society in musculoskeletal oncology in North America. Mayerson also directs the Division of Musculoskeletal Oncology at Ohio State.

Claire Verschraegen, MD, professor and director of the Division of Medical Oncology at Ohio State, and associate director for translational research at the OSUCCC – James, was named 2019 Woman Oncologist of the Year at the first-ever Leadership Empowerment and Development (LEAD) 2020 Conference: Enriching Experiences for Women in Hematology and Oncology held in October 2019 in Santa Monica, Calif. More than 100 women from across the nation attended the conference, which addressed challenges women face in the hematology/oncology field and identified strategies for women to advance into leadership roles.
The Ohio State University was among seven recipients of an “80% BY 2018 NATIONAL ACHIEVEMENT AWARD” from the National Colorectal Cancer Roundtable. The award recognizes individuals and organizations who dedicate time, talent and expertise to advancing initiatives to reach the national goal of regularly screening 80 percent of adults age 50 or over for colorectal cancer. Ohio State’s Provider and Community Engagement (PACE) Program for Health Equity in Colorectal Cancer Prevention promotes screening in central Ohio and beyond. The program is led by Darrell Gray II, MD, MPH, of the OSUCCC – James.

The Sickle Cell Program at the OSUCCC – James in 2018 received the nation’s first DISEASE-SPECIFIC CARE CERTIFICATION IN SICKLE CELL DISEASE from The Joint Commission following a two-day on-site survey that yielded no findings. The Joint Commission disease-specific certification initiative involves evaluation of clinical programs across the continuum of care for compliance with standardized requirements and expectations for ensuring quality care and patient safety.

The James Medical Intensive Care Unit (MICU) earned a three-year gold-level BEACON AWARD FOR EXCELLENCE from the American Association of Critical Care Nurses (AACN). Gold is the highest level Beacon Award that can be achieved. The Beacon Award, considered to be a milestone on the path to exceptional patient care and healthy work environments, honors individual units that distinguish themselves by improving every facet of patient care.

The OSUCCC – James in November 2019 earned two national awards for excellence in patient care delivery from Press Ganey, a healthcare performance-improvement organization that works with more than 41,000 healthcare facilities. This is the fourth consecutive year The James has received a PRESS GANEY GUARDIAN OF EXCELLENCE AWARD, which recognizes top-performing healthcare organizations that have achieved the 95th percentile or above for performance in patient experience. In addition, The James received a 2019 PRESS GANEY PINNACLE OF EXCELLENCE AWARD. This honor is given to top-three performing organizations in each award category. The award recognizes providers who have maintained consistently high levels of excellence over three years in patient experience, employee engagement, physician engagement and clinical quality improvement.

The James Cancer Hospital/ Vizient Nurse Residency Program was awarded a three-year ACCREDITATION WITH DISTINCTION by the American Nurses Credentialing Center’s (AAN) Practice Transition Program (PTAP)™. The ANCC PTAP sets the global standard for residency or fellowship programs that transition registered nurses (RNs) and advanced practice registered nurses (APRNs) into new practice settings that meet evidence-based standards for quality and excellence.

Ohio State’s cancer program has received two prestigious re-accreditations following separate site surveys by components of the AMERICAN COLLEGE OF SURGEONS (ACoS). The James Cancer Hospital and Solove Research Institute earned a full three-year re-accreditation from the ACoS Commission on Cancer (ACoS-CoC), and the Stefanie Spielman Comprehensive Breast Center earned a full three-year re-accreditation from the ACoS National Accreditation Program for Breast Centers (ACoS-NAPBC).
Genomics Shared Resource Offers Services to OSUCCC and Nationwide Children’s Hospital Researchers

Working together to expand genomics services across institutions, the OSUCCC – James and Nationwide Children’s Hospital’s Institute for Genomic Medicine (IGM) collaborate in a Genomics Shared Resource (GSR) for cancer researchers.

The GSR enables researchers to use the expertise and state-of-the-art genomics services found at both institutions. Led by scientists from the OSUCCC – James and Nationwide Children’s IGM, this shared resource provides high-throughput genomics technologies along with consultation and assistance in experimental design, troubleshooting, training and development of novel methodologies.

Nationwide Children’s IGM Director Richard Wilson, PhD, who also is a professor in the Department of Pediatrics at Ohio State, serves as director of the GSR, focusing on next-generation sequencing (NGS) and overseeing development of new technologies at both locations. The team at Nationwide Children’s can assist investigators with multiple aspects of NGS, including library preparation, sequence generation and data analysis.

Amanda Toland, PhD, associate professor in the Department of Cancer Biology and Genetics at Ohio State, is co-director of the GSR. She is responsible for the direction and development of all non-NGS services (Sanger sequencing, cell line verification, gene expression profiling, microarrays, QC and Nanostring) and oversees NGS library generation, including single cell libraries, at Ohio State.

Technical directors for the GSR are Pearly Yan, PhD, research assistant professor in the Division of Hematology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James; and Vincent Magrini, PhD, research assistant professor in the Department of Pediatrics at Ohio State and senior director in the IGM.

Faculty leaders at the OSUCCC – James and Nationwide Children’s IGM believe that, through the GSR, the institutions have formed a centralized, comprehensive hub for genomic research in Ohio and beyond. They anticipate that this collaborative service will enhance opportunities for more National Cancer Institute-sponsored research.

For more information about services available through the GSR, call (614) 247-8185 or email amanda.toland@osumc.edu.

For more information about high-throughput sequencing and library generation, call (614) 685-9164 or email pearlly-yan@osumc.edu.

To learn more about services offered through the lab at Nationwide Children’s IGM, call (614) 355-3530 or email vincent.magrini@nationwidechildrens.org or amy.wetzel@nationwidechildrens.org.

NOTE: The Shared Resources and core facilities at the OSUCCC – James are a National Cancer Institute-recognized network of specialized service facilities that enhance an investigator’s ability to conduct cancer research by reaching across medical disciplines and offering: expert leadership and training; clinical, administrative and technical support; and state-of-the-art instrumentation. This issue of Frontiers highlights the Genomics Shared Resource (GSR).
The $100 million center, to occupy 55,000 square feet in a multi-story West Campus Ambulatory Facility being planned at Ohio State, is a collaboration among the Ohio State Wexner Medical Center, the OSUCCC – James and Nationwide Children’s Hospital (NCH), which has committed to up to half of the cost.

Proton therapy is a form of radiation treatment that uses protons instead of X-rays to kill cancer cells. A machine called a cyclotron delivers a high-energy proton beam painlessly through the skin from outside the body.

This therapy, which targets tumor cells and limits damage to healthy surrounding cells, can be used alone or with other therapies to treat several localized cancers, including prostate, brain, head and neck, lung, spine and gastrointestinal cancers in adults, and brain cancer, lymphoma, retinoblastomas and sarcomas in children.

“As central and southern Ohio’s only National Cancer Institute-designated comprehensive cancer center, it’s our duty to bring advanced, evidence-based treatment options like proton therapy to the region to benefit patients who need this subspecialized care,” says William Farrar, MD, CEO of the James Cancer Hospital and Solove Research Institute.

Timothy Cripe, MD, PhD, division chief of Hematology, Oncology and Bone Marrow Transplantation at NCH, and a member of the OSUCCC – James, says having a proton therapy facility in Columbus will enable more central Ohio pediatric patients to receive all of their cancer treatment closer to home.

“As a national leader in pediatric research and quality improvement, we can establish clinical trials that focus on how proton therapy affects specific types of pediatric cancer,” Cripe says. “Because we seek to provide best outcomes for patients, we’ll examine quality improvement best practices for administration and safety.”

The OSUCCC – James and NCH also have reported that a new and highly targeted form of proton therapy known as “FLASH” will be investigated at the center in clinical trial participants with certain newly diagnosed, recurrent or advanced cancers. According to preclinical data, FLASH therapy could reduce what is typically 30 days of treatment into a single treatment delivered in less than one second. FLASH is being studied in preclinical models and is not yet approved by the U.S. Food and Drug Administration.

Medical officials note that children are vulnerable to the long-term side effects of radiation, including growth abnormalities, cognitive impairment, heart damage and such complications as radiation-induced secondary cancers later in life. The American Society of Clinical Oncology reports proton therapy may deliver up to 60% less radiation to healthy surrounding tissue and a higher dose to the tumor.

“It’s important to note that traditional targeted radiation therapy techniques are still highly effective for many solid tumors, but proton therapy is an exciting new option for localized tumors,” says Arnab Chakravarti, MD, chair of the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James.

The new proton therapy center, to be managed by radiation oncology experts at the OSUCCC – James, will be one component of the planned West Campus Ambulatory Facility, which also will include outpatient operating rooms, an endoscopy unit, an urgent care center and a pre-anesthesia center.
Pelotonia Funding Allocations Support Student & Faculty Cancer Research

Recent new allocations of funding from Pelotonia, an annual cycling event that raises millions of dollars for cancer research at Ohio State, will support several projects initiated by teams of OSUCCC – James scientists and by Ohio State students working in the labs of faculty mentors.

The faculty-team projects will be funded by the OSUCCC – James’ Intramural Research Program (IRP), which receives extensive Pelotonia support. IRP funding, which includes Idea Grants and other awards, goes to groups of scientists who competitively propose innovative studies that will generate data to help them compete later for larger grants from the National Cancer Institute and other external sources.

Since 2010, Pelotonia money has enabled the OSUCCC – James to fund 166 faculty-team projects involving more than 300 investigators who have represented 11 colleges at Ohio State, as well as Nationwide Children’s Hospital in Columbus and Cincinnati Children’s Hospital Medical Center. Recently funded projects focus on such topics as immunotherapy for lung cancer, a new targeted therapy for ovarian cancer, pancreatic cancer immune suppression and disease progression, reducing neurologic side effects of colorectal cancer treatment, and exploring genomic targets for cancer prevention, to name some.

The Pelotonia Fellowship Program also started in 2010 and, through an annual allocation of $2 million, has awarded 534 fellowships to Ohio State students in any discipline or level of scholarship who want to conduct cancer research with faculty guidance. Collectively the awards have gone to 244 undergraduates, 158 graduates, 126 postdoctoral fellows and six professional students.