TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

SPRING 2024

Flipping Big Tobacco's Script to Improve Public Health

Ohio State's Center for Tobacco Research awarded major grant to put science behind tobacco regulation

The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Researchers gain NCI grant to study novel, Ohio State-developed CAR T-cell therapy for patients with B-cell cancers

A five-year, $3.04 million grant from the National Cancer Institute (NCI) will help researchers at the OSUCCC – James study the effectiveness of a cellular therapy they have developed to more effectively treat patients with relapsed or refractory (treatment-resistant) B-cell malignancies.

Principal investigators for the grant are **Sumithira Vasu, MD**, **Lapo Alinari, MD, PhD**, and **Marcos de Lima, MD**, all of the Division of Hematology at Ohio State and members of the Leukemia and Hematologic Malignancies Program at the OSUCCC – James. Dr. de Lima also directs the Blood and Marrow Transplant (BMT) and Cellular Therapy programs at the OSUCCC – James.

The scientists will conduct a first-in-human phase I clinical trial (already underway) of a trispecific form of chimeric antigen receptor (CAR) T-cell therapy that targets three proteins instead of just one in patients with relapsed/refractory B-cell non-Hodgkin lymphoma, B-cell acute lymphoblastic leukemia, B-cell prolymphocytic leukemia or chronic lymphocytic leukemia.

In their project abstract, they state that CAR T-cell therapy – which involves removing a patient's T cells, modifying them in a laboratory to strengthen their ability to kill cancer cells, and returning them to the patient – has revolutionized cellular immunotherapy for patients with B-cell malignancies. But despite high rates of complete remissions, many patients relapse after CAR T-cell infusion – often within the first year – and thereafter have limited treatment options, "highlighting the need for novel CAR T-cell products."

The researchers add that CAR T-cell therapy typically targets a protein called CD19 that plays a large role in B-cell malignancies; however, scientists at other institutions have developed a CAR T-cell therapy that simultaneously and effectively targets the CD19, CD20 and CD22 proteins in preclinical animal models of lymphoma.

The OSUCCC – James scientists have validated these findings and propose "to address the limitations of commercial CD19 CAR Ts" through a clinical trial that will test the efficacy of a CAR T-cell therapy they have manufactured in **Ohio State's Cell Therapy Lab** to also target the CD19, CD20 and CD22 proteins.

"This is the first investigator-initiated trial at Ohio State in which the cell therapy was manufactured at the OSUCCC – James and has received NIH funding," Dr. Vasu says.

The trial will determine the feasibility and safety of their trispecific therapy and will establish a recommended dose for a projected phase II study. It also will identify key mechanisms of efficacy and resistance to trispecific CAR Ts, shedding light on how these therapies work and sometimes fail.

"By targeting three proteins at the same time (CD19, CD20 and CD22) in patients with B-cell malignancies," the scientists write, "our goal is to improve on the results of single-antigen CAR T-cell therapies."

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SPRING 2024

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The James

The Ohio State University
Comprehensive Cancer Center

Flipping Big Tobacco's Script to Improve Public Health

Ohio State's Center for Tobacco Research receives a major grant to put science behind tobacco regulation

Scientists within the **Center for Tobacco Research (CTR)** at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James) have no doubt about the urgency of their work.

Nor do the U.S. Food and Drug Administration (FDA) or the National Cancer Institute (NCI), which have awarded the CTR a $20 million **Tobacco Center of Regulatory Science (TCORS)** grant to conduct research that will gather scientific evidence needed to inform the FDA's regulation of tobacco products.

Ohio State was one of seven centers across the United States recently selected to receive a TCORS grant, an award based on a rigorous review of recipients' scientific technical skills and the relevance of their proposed projects to the FDA's priorities. Since 2013, the FDA and NIH have funded 29 centers to conduct tobacco regulation science research in epidemiology, economics, toxicology and marketing.

Ohio State's TCORS grant is the latest and largest of several grants that the CTR has received over the past few months as it expands its efforts to assist the FDA by putting science behind regulation – studies designed ultimately to improve people's health and potentially save lives.

"Tobacco use is tied to lung disease, cancer and heart disease, some of the leading causes of death in the United States and around the world," says CTR Director **Ted Wagener, PhD**, who also co-leads the Cancer Control Program at the OSUCCC – James. "Our multidisciplinary center is enabling us to not only better understand and intervene in tobacco use and its effects on negative health outcomes, but to extend our study results to the community for the benefit of all."

Dr. Wagener says this work is even more pressing as new tobacco products – electronic cigarettes (e-cigs) and oral nicotine products – are continually being developed and marketed with little regulatory oversight or scientific knowledge of possible harm to consumers.

Consolidating efforts

Recognizing the need for collaborative, evidence-based tobacco research, the OSUCCC – James created the CTR in 2020 to consolidate the university's tobacco research programs under the direction of Dr. Wagener, a licensed psychologist who specializes in health psychology/behavioral medicine. The CTR involves experts from many disciplines, including psychology, epidemiology, biostatistics, environmental health, health communications, chemistry, biochemistry, cancer biology and law.

Dr. Wagener is a veteran researcher who focuses his studies on tobacco regulatory sciences, including the evaluation of behavioral, pharmacological and toxicological effects of cigarette and non-cigarette tobacco products such as e-cigs and hookah. In addition, he develops and tests motivational, enhancement-based smoking cessation and secondhand smoke-reduction interventions for children of parents who smoke.

His current research examines how youth, young adults and adults use e-cigs; how e-liquids affect the way nicotine is delivered to the brain and other organs; and whether there are ways to reduce e-cigs' abuse potential for youth but still have them be effective in helping adults stop smoking. He's particularly concerned about regulators and public health officials striking the right balance in regulating e-cigs.

"The FDA must decide how to balance its goals of protecting young people and offering harm-reduction options to adults who smoke," Dr. Wagener says.

A researcher weighting vape product.

These research efforts will be enhanced by the new TCORS grant, which is co-led by Dr. Wagener and **Peter Shields, MD**, an emeritus professor in the College of Medicine and College of Public Health at Ohio State who is an internationally known physician-scientist and expert in cancer prevention. Dr. Shields is renowned for his work in breast cancer risk, lung cancer, and tobacco use and disease.

The TCORS grant is organized around the theme of "Flipping the Script" on the tobacco industry's nicotine playbook as a means of improving public health.

"For years, the tobacco industry has manipulated nicotine in tobacco products to sustain dependence among existing users and increase their appeal and addictiveness for young people and non-users," Dr. Wagener says. "We believe we can reverse-engineer their strategies and make products unappealing to young people and non-users but still have less harmful products that are satisfying for adult smokers and smokeless tobacco users to switch to."

Ted Wagener, PhD, with Jean Nshimiyimana, clinical research coordinator, measuring puff data.

TCORS grant strategy

The grant is divided into four projects, each led by members of the OSUCCC – James Cancer Control Program:

- **Informing e-cig nicotine regulations to promote public health** (led by **Ahmad El Hellani, PhD**, and Dr. Wagener) – This project examines how manipulating the dimensions of nicotine affects the extent to which smokers and e-cig users like these products, how often they use them and how harmful these products are. It will also determine ways to regulate nicotine that makes e-cigs unattractive to young people and non-users while still giving adult smokers a less harmful and satisfying alternative.
- **Informing oral nicotine pouch regulations to promote public health** (Led by **Brittany Keller-Hamilton, PhD, MPH**, and **Marielle Brinkman, BS**) – This project examines how dimensions of nicotine affect the appeal, addictiveness and use of oral nicotine pouches. It also is examining how these factors influence product switching (e.g., from smokeless tobacco or combustible cigarettes to pouches) and how the use of these products impacts the microbiome of pouch users vs. cigarette and smokeless tobacco users.
- **Nicotine product claims on appeal, perceptions and usage behaviors** (Led by **Darren Mays, PhD, MPH**) – This project examines how features of oral nicotine pouch packaging affect the appeal, use and perceptions of pouches among young people, and whether those features create preferences compared to e-cigs, cigarettes and smokeless tobacco. The goal is to determine how product packages should be regulated so they appeal to adult tobacco users but have minimal appeal to young people.
- **Naturalistic assessment of e-cig and oral nicotine pouch use among adolescents and young adults** (Led by **Amy Ferketich, PhD**, and **Megan Roberts, PhD**) – This two-year prospective observational study of 2,000 youths and young adults across the United States seeks to identify marketing exposures and product design characteristics that drive continued use, product escalation and nicotine dependence, paying particular attention to the impact on populations historically targeted by the tobacco industry.

"This grant enables us to conduct critical research to guide the FDA's regulation of nicotine in e-cigs and oral nicotine pouches," Dr. Wagener says. "We argue that, just as the tobacco industry manipulates nicotine in its products to ignite epidemic use, science-based regulation of nicotine has the potential to spur major public health victories."

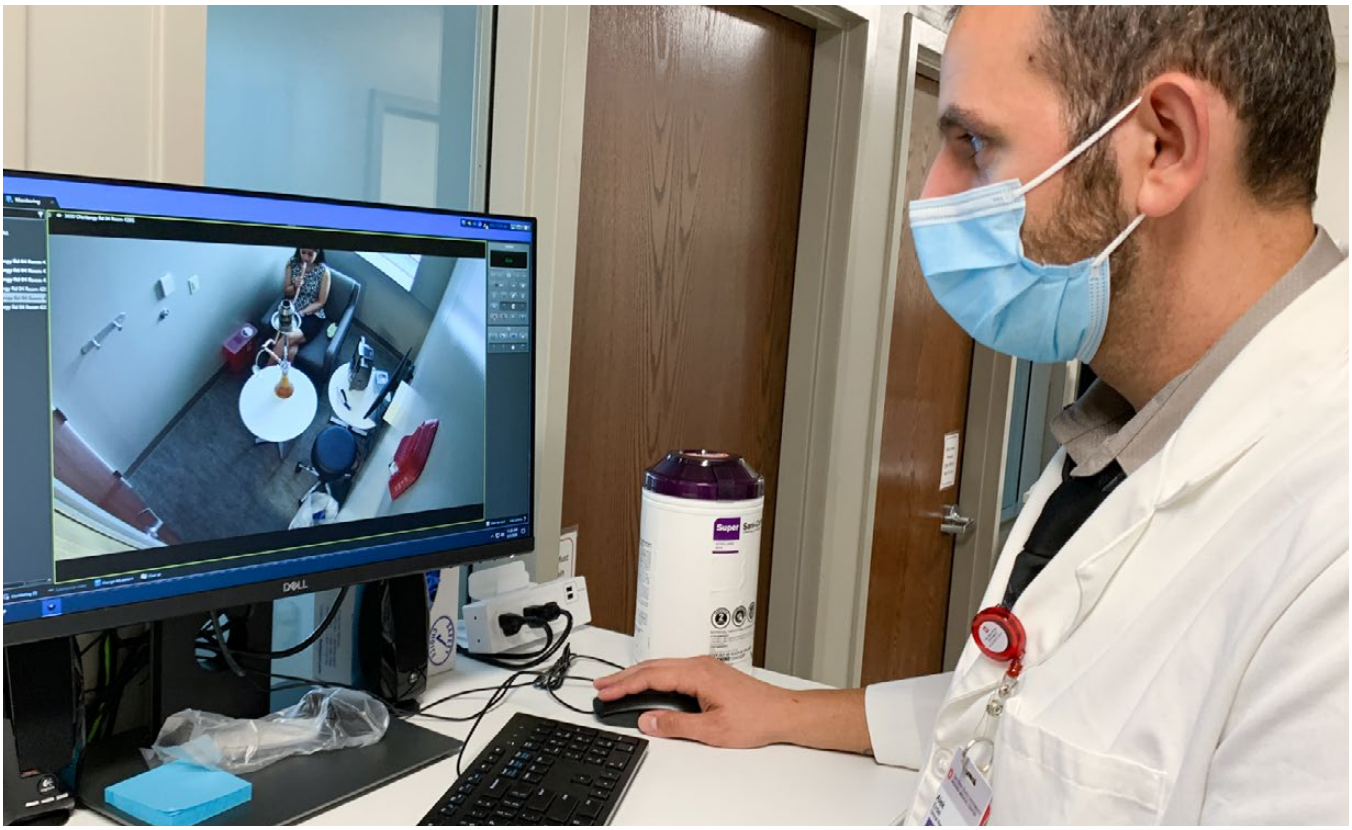
> *"Our ultimate goal is to determine which regulations will lead to reduced youth use of e-cigs and oral nicotine pouches while simultaneously supporting smokers and smokeless tobacco users looking to switch to less harmful alternatives."*
>
> **Ted Wagener, PhD**

Earlier grants

Dr. Wagener points out that the CTR within the past few months has received several other large grants to bolster its research. One is a $3.9 million award from the FDA that is enabling researchers to evaluate the effects of e-cig flavors on the smoking behaviors of current adult smokers. The grant is sponsored by the National Institute on Drug Abuse (NIDA).

This study, co-led by Dr. Wagener and Tracy Smith, PhD, of the Medical University of South Carolina Hollings Cancer Center, will be the first to provide definitive information about the impact of non-tobacco e-cig flavors for helping adult smokers quit.

Dr. Wagener says youth advocates have long objected to e-cigs with flavors such as mint, mango or strawberry that may be enticing young people to take up an addictive and potentially harmful habit, but he adds that flavors may also be more appealing to adult smokers who have been unable to quit.



A researcher observes someone using a tobacco product inside a state-of-the-art negative pressure lab at Ohio State's Center for Tobacco Research. This technology allows scientists to monitor biofeedback in real time to better understand the potentially harmful effects of vaping.

"The FDA is making regulatory decisions about e-cig flavors with incomplete scientific data," he says. "Existing data show that adult smokers also prefer flavored e-cigs, and while there are a few survey studies suggesting that flavored e-cigs may be more helpful for switching to vaping, those studies aren't rigorous enough for the FDA to base regulatory decisions on. Our study will provide the FDA with definitive information about the benefit, if any, of e-cig flavors to adult smokers."

While switching to e-cigs is not a completely healthy choice, he adds, it is thought to be better than continuing to smoke – a concept known as "harm reduction."

Other recent large funding awards to CTR scientists include:

- A five-year, $3.87 million NCI grant led by Principal Investigator (PI) **Alayna Tackett, PhD**, to study the abuse liability, topography and toxicology of ice flavors and non-menthol synthetic cooling agents in e-cigs;
- A five-year, $3 million NIDA grant led by PI **Ce Shang, PhD**, to examine the impact of excise tax structures for retail marijuana on marijuana consumption.

Dr. Tackett is a pediatric psychologist and assistant professor in the Division of Medical Oncology at Ohio State. Dr. Chang is an associate professor in the Division of Medical Oncology and a health economist with experience in regulatory science. Both are in the Cancer Control Program at the OSUCCC – James.

Global impact of CTR research

"We have an amazing team of scientists at the CTR who are clearly having a significant impact on the field of tobacco control in all areas, from basic and translational science to surveillance and policy research," Dr. Wagener says. "Internationally, we are a top center for conducting tobacco regulatory science research, with more than $40 million in new grants over the past several years.

"This work is having and will continue to have a strong impact on tobacco interventions and policy in Ohio, the United States and far beyond for years to come."

Ted Wagener, PhD

Center for Tobacco Research (CTR) Recent Study Highlights

Nearly two-thirds of youths would stop vaping with no added sweet flavors, menthol or cooling agents

Major progress could be made in fighting the youth vaping epidemic with a complete restriction on sweet flavorings and cooling agents in both cartridge and disposable e-cigarette devices, according to a study from the CTR at the OSUCCC – James. The current U.S. Food and Drug Administration flavor ban applies only to cartridge electronic cigarette devices.

Published in the *Journal of Studies on Addiction and Drugs*, the study suggests that sweet flavorings and cooling agents like menthol keep youth puffing e-cigarettes, and the majority indicate they would likely stop vaping if e-liquid flavors were limited to tobacco-flavor only.

Rates of e-cigarette use among young adults and adolescents remain high, despite federal restrictions that limit the availability and appeal to youths. This study sought to examine how restricting flavors could affect adolescent and young adult e-cigarette usage. The senior author was **Alayna Tackett, PhD**, a pediatric psychologist and researcher with the CTR and a member of the Cancer Control Program at the OSUCCC – James.

Oral pouch products do little to curb addictive nicotine cravings

Oral nicotine pouches, a tobacco-leaf-free product marketed as an alternative to cigarettes, do little to curb current smokers' nicotine cravings, according to a new study. Public health scientists with the CTR at the OSUCCC – James reported these findings in the medical journal *Addiction*.

Nicotine pouches are small pre-portioned bags filled with nicotine powder, flavorings, artificial sweeteners and other chemicals that extend shelf life. Marketed as a smoke-free, tobacco-free alternative to cigarettes, these products have become increasingly popular since entering the consumer market in 2016.

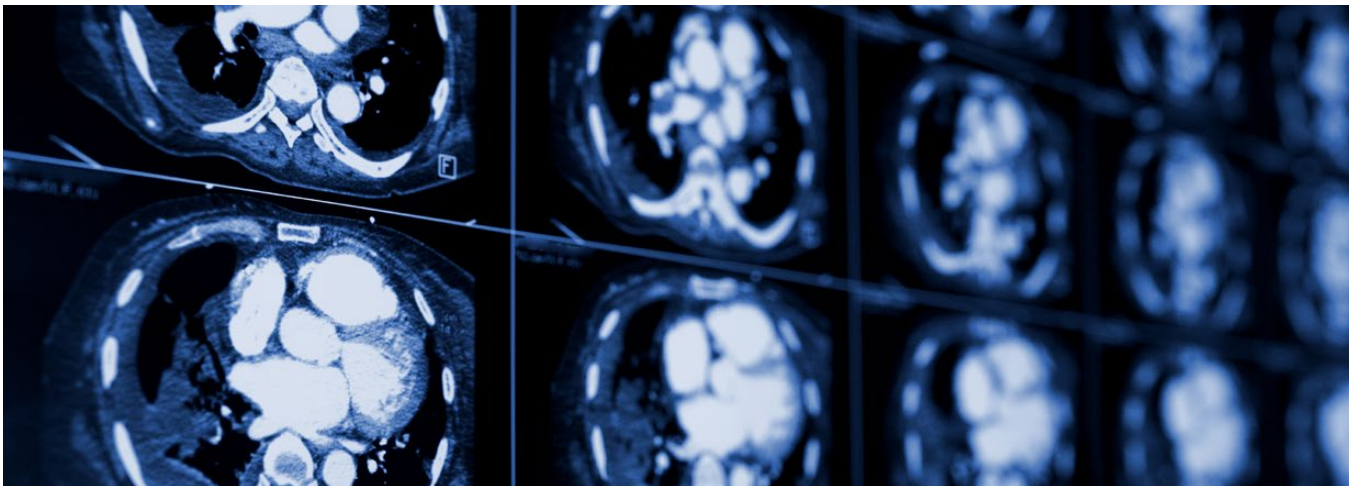
Lead author **Brittney Keller-Hamilton, PhD, MPH**, a researcher with the CTR and a member of the Cancer Control Program at the OSUCCC – James, says these products are appealing to current smokers because they contain fewer known carcinogens and toxins than other tobacco products and can be used indoors where smoking is banned. Researchers are concerned, however, that if not formulated and regulated very intentionally, these products could lead to an increase of nicotine product use among young people rather than reducing cancer risk among smokers.

Young vapers are at risk for respiratory symptoms, regardless of whether they smoke other products

Youths are at risk for lingering respiratory symptoms, including bronchitis symptoms and shortness of breath, after electronic cigarette (e-cigarette) use, regardless of whether they smoke other products or whether others smoke around them.

Reporting in the journal *Thorax,* researchers with the CTR at the OSUCCC – James and the Southern California Keck School of Medicine show that these negative health effects of e-cigarette use exist independent of cannabis or traditional cigarette use. Previous studies have looked primarily at dual-usage scenarios – for example, using e-cigarettes while also using cannabis or traditional cigarettes.

Researchers say these new data should be considered in ongoing regulatory decisions around the sale of e-cigarette products.



Prominent Studies

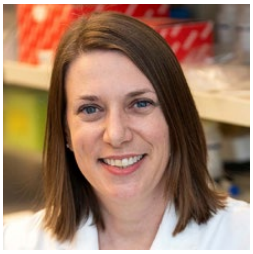
David Carbone, MD, PhD

Trial shows long-term survival for patients with metastatic non-small cell lung cancer

Data presented at the 2023 American Society of Clinical Oncology annual meeting in Chicago showed that patients with metastatic non-small cell lung cancer who were treated with a dual therapy-based combination experienced sustained clinical benefits after four years compared to chemotherapy.

The OSUCCC – James is a leading institution in the multi-center study, which is called CheckMate -9LA and is sponsored by Bristol Myers Squibb. After four years, the phase III trial demonstrated durable, long-term survival benefits with Opdivo (nivolumab) plus Yervoy (ipilimumab) with two cycles of chemotherapy compared to four cycles of chemotherapy in previously untreated patients with metastatic non-small cell lung cancer.

David Carbone, MD, PhD, director of the Thoracic Oncology Center and co-leader of the Translational Therapeutics Program at the OSUCCC – James, says the results seen with nivolumab plus ipilimumab with chemotherapy over four years, especially in patients typically facing a poor prognosis, demonstrate the sustained benefits of combining dual immunotherapy with limited chemotherapy for patients with advanced or metastatic non-small cell lung cancer. Dr. Carbone is an investigator in the trial.



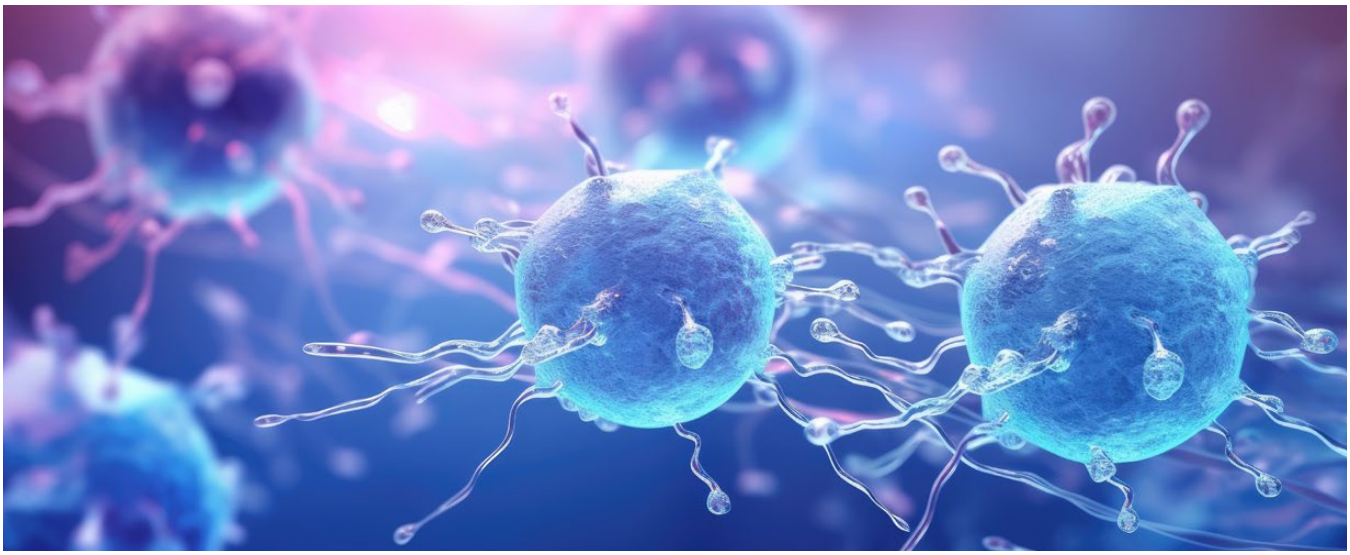
Jennifer Woyach, MD

Study finds potential therapy option for patients with CLL

Researchers continue to refine and improve targeted drug therapies that have changed chronic lymphocytic leukemia (CLL) – the most common form of adult leukemia – from an incurable to a chronic condition. New data published in the *New England Journal of Medicine* offer another treatment option for patients who have stopped responding to the first- and second-generation drugs.

In this study, co-led by the OSUCCC – James, researchers found that pirtobrutinib, a highly selective and reversible Bruton tyrosine kinase inhibitor (BTKi), showed efficacy in patients with CLL and small lymphocytic lymphoma who have become resistant to the first- and second-generation covalent inhibitors known as ibrutinib, acalabrutinib and zanubrutinib.

Jennifer Woyach, MD, professor in the Division of Hematology at Ohio State and co-leader of the Leukemia and Hematologic Malignancies Program at the OSUCCC – James, was co-first author of this study.



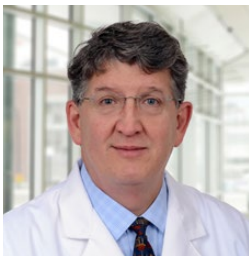
Sameek Roychowdhury, MD, PhD

‘Smart drugs’ give new hope to some patients with advanced pancreatic cancer

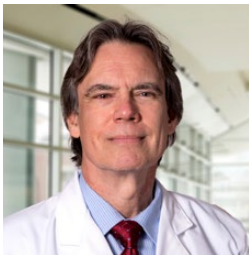
Promising new targeted cancer therapy will soon be available to certain patients with advanced pancreatic cancer from the comfort of their home through a first-of-its-kind, entirely telehealth-based cancer clinical trial at the OSUCCC – James.

Scientists led by **Sameek Roychowdhury, MD, PhD**, a medical oncologist at the OSUCCC – James and principal investigator in this study, say traveling for specialized cancer treatment is often cost-prohibitive for patients experiencing cancer – particularly for rare and aggressive types like pancreatic cancer, for which clinical trials may represent the most up-to-date and targeted treatment for advanced disease.

“Smart drugs” target only the genetic mutations that contribute to cancer cell growth, delivering precise treatment for each person’s disease characteristics. In this case, the genetic mutation is in the fibroblast growth factor receptors, or FGFRs, which are present in about 1% of pancreatic cancer patients.



James Rocco, MD, PhD



Ed Mroz, PhD

Study yields new way to determine genetic progression leading to cancer

A multi-institutional team of researchers co-led by the OSUCCC – James has demonstrated a way to infer early progression of genetic events leading to cancer in a type of head and neck malignancy for which this previously was not possible – an advance that could hold great clinical importance.

Reporting in the journal *Nature Cancer*, the researchers, including scientists at the Broad Institute of MIT and Harvard and at Massachusetts General Hospital Cancer Center, state that analysis of premalignant tissue has often identified the typical order of genetic changes leading to invasive tumors in several cancer types, helping clinicians determine better targeted treatments. However, premalignant tissue is unobtainable for some cancers, leaving genetic progression unknown and effective treatments less likely.

In this study – co-led by **James Rocco, MD, PhD**, chair of the Department of Otolaryngology – Head and Neck Surgery at Ohio State; **Ed Mroz, PhD**, of the same department; and by Gad Getz, PhD, and Ignaty Leshchiner, PhD, of the Broad Institute – researchers used a computational method called PhylogicNDT to infer genetic progression in primary tumors by sequencing the exome, or the protein-coding region of the human genome, in the absence of premalignant tissue.

Zihai Li, MD, PhD

Study: Loss of Y chromosome drives cancer growth but also sensitizes tumors to immunotherapy

A study published in the journal *Nature* shows that loss of the Y chromosome in males with bladder cancer correlates with poor prognosis but also makes tumors more susceptible to immunotherapy.

Researchers with the Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC – James were lead collaborators in the study, which was co-supervised by Dan Theodorescu, MD, PhD, director of Cedars-Sinai Cancer Center (CSCC) in Los Angeles, and **Zihai Li, MD, PhD**, director of the PIIO.

As men age, loss of the Y chromosome (LOY) occurs in many organs and cells. Many cancers also display LOY, including 10-40% of bladder cancers, but its clinical and biological significance is unknown. Dr. Li says this is the first study to make a connection between LOY and the immune system's response to cancer, explaining that loss of the Y chromosome allows bladder cancer cells to evade the immune system and grow more aggressively.

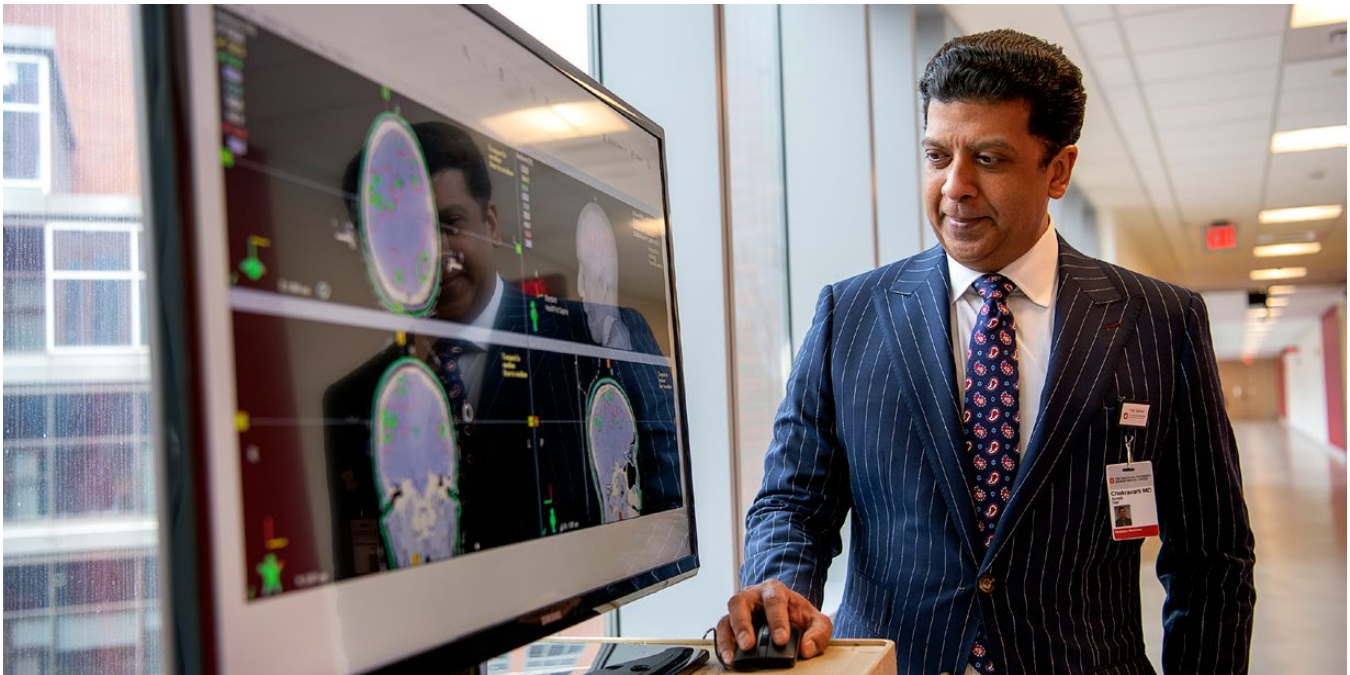
Arnab Chakravarti, MD

Loss of tumor-suppressor gene portends poor prognosis in brain tumors

A multi-institutional study has found that deletions of a certain tumor-suppressor gene in diffuse gliomas – the most common primary brain tumors – display distinct patterns, signify a poor prognosis in patients and should be included in models predicting the clinical behavior of these tumors.

Gliomas, which include several subtypes such as astrocytoma, oliogodendroglioma and glioblastoma, typically spread quickly and are highly resistant to therapy. Understanding their normal and abnormal molecular mechanisms can help scientists devise therapies that better target the malignancies.

Researchers at the OSUCCC – James were key collaborators in this study, which was published in the journal *Cell Reports Medicine*. Senior author **Arnab Chakravarti, MD**, chair of the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, says the researchers believe findings from this study bring them closer to deciphering the mechanisms behind the aggressive behavior of certain brain tumors.



Pelotonia-Funded Research

Pelotonia 2023

Pelotonia is a community determined to help bring about the end of cancer by raising money to support cancer research at the OSUCCC – James. The centerpiece of this massive effort is a cycling event held every August that draws thousands of people from around the world to Columbus, Ohio, for a weekend of riding, volunteering, entertainment and shared devotion to a common cause.

Every dollar raised by Pelotonia Riders, Challengers, Volunteers and Donors goes directly to cancer research thanks to the event's major funding partners. Pelotonia dollars support seven major areas at the OSUCCC – James. **Read about the impact** of money raised by Pelotonia.

The 2023 Ride Weekend took place on Aug. 4-6, and a newly added event, Gravel Day, took Riders along unpaved roads of beautiful southeastern Ohio on Sept. 30. These events **raised more than $25 million** combined, bringing the **15-year Pelotonia fundraising total to over $283 million**. More than 11,000 Riders, Volunteers and Challengers from 41 states and 10 countries participated in Pelotonia 2023.

Read more about Pelotonia at **pelotonia.org**

Pelotonia dollars support seven major areas

Pelotonia research funding has been allocated to researchers in 10 of the 15 colleges at The Ohio State University, as well as at Nationwide Children's Hospital in Columbus.

Idea Grants

Pelotonia-funded Idea Grants help cancer researchers accelerate innovative ideas. The James has awarded 213 Pelotonia Idea Grants totaling $29.9 million

Statewide Initiatives

Four statewide initiatives funded by Pelotonia have promoted early detection and better outcomes for colorectal, endometrial, lung and breast cancer patients in Ohio.

Pelotonia Institute for Immuno-Oncology (PIIO)

The PIIO is a research initiative focused on harnessing the body's immune system to fight cancer.

Pelotonia Scholars Program

$2 million is awarded annually to train the next generation of cancer researchers. The James has issued 680 Pelotonia Scholar Awards since 2010.

These scholars have come from 52 countries and 35 states.

Recruitment

Bringing the brightest minds in cancer research to Ohio State, the OSUCCC – James has recruited 271 top scientists with Pelotonia support.

Strategic Research Investments

Pelotonia dollars support such OSUCCC – James initiatives as the Drug Development Institute, digital pathology and the Total Cancer Care® protocol.

Instruments of Discovery

Pelotonia dollars provide sophisticated equipment for cutting-edge cancer research.

Zihai Li, MD, PhD

Pelotonia-supported PIIO advances immuno-oncology research

Since an initial pledge of $102 million from the Pelotonia community helped launch the **Pelotonia Institute for Immuno-Oncology (PIIO)** at the OSUCCC – James in 2019, the PIIO has been growing rapidly and is making an impact on cancer research and treatment.

Here are examples of recent Pelotonia-supported studies conducted by members of the PIIO, which is led by Founding Director **Zihai Li, MD, PhD**, and has 118 members:

Deciphering the Role of CD28 Co-Stimulation for Tumor-Specific, Stem-Like Cells in Humans – Andreas Wieland, PhD, MSc, is the principal investigator for this project supported by a Pelotonia Idea Grant. Immunotherapies involving immune checkpoint inhibitors (ICI) – which release the "brakes" on antitumor immune responses – can be effective, but most patients don't respond to ICI therapy. Dr. Wieland and PIIO colleagues have shown in preclinical models that successful ICI therapy depends on additional positive signals that act as "gas pedals" to boost antitumor responses. In this study, they aim to identify the positive signals that tumor-specific immune cells from cancer patients require to best respond to tumor antigens.

Selective Targeting of GARP-LTGFß Axis in the Tumor Microenvironment Augments PD-1 Blockade via Enhancing CD8+ T Cell Antitumor Immunity – Anqi Li is a graduate student who received a Pelotonia Scholarship for this study and was first author on an article published in the *Journal for Immunotherapy of Cancer* about this work, which like the above study is also aimed at improving ICI immunotherapy. Li and colleagues reported that a cell surface receptor known as glycoprotein-A repetitions predominant (GARP) contributes to multiple aspects of immune resistance in cancer. However, they found that an anti-human GARP antibody they call PIIO-1 is a safe and effective strategy to offset GARP activity and overcome resistance to ICI therapy. PIIO-1, therefore, warrants clinical development as a novel cancer immunotherapeutic.

PIIO By the Numbers

81 current IO clinical trials

34 scientists are pursuing IO-based clinical trials

$39M in annual grant funding ($22 million from the NCI)

Since 2019

1,180 published peer-viewed articles

230 new IO trials

29 new faculty

35 Pelotonia Idea Grants

160+ new staff jobs

56 patents

73 technologies

OSUCCC – James awards new Pelotonia-funded Idea Grants to help cancer researchers pursue innovative studies

The OSUCCC – James in 2023 awarded seven new **Pelotonia-funded Idea Grants** totaling over $1.4 million that will enable teams of Ohio State faculty researchers to gather early data for innovative cancer studies that could later receive external funding from sources such as the NCI.

Idea Grants must include at least two investigators from different scientific disciplines. The awards are typically funded at $200,000 over two years. Since 2010, the OSUCCC – James has awarded 213 Pelotonia-funded Idea Grants.

Grant titles, names of awardees (an asterisk indicates principal investigator) and brief descriptions of the seven projects are shown below and include members from three research programs: Cancer Control, Leukemia and Hematologic Malignancies, and Translational Therapeutics.

Naxitamab (Danyleza), Gemcitabine and Ex-Vivo Expanded Allogeneic Universal Donor, TGFß-Imprinted Natural Killer Cells. (Margaret Gatti-Mays, MD, MPH*; Dean Lee, MD, PhD; Zihai Li, MD, PhD; Daniel Stover, MD; Sumithira Vasu, MBBS) – Immunotherapy has limited success against breast cancers because breast tumors use tactics to inactivate immune cells, including natural killer (NK) cells. These scientists will conduct a clinical trial to test whether combining NK cells from healthy patients with an antibody against a protein found in many breast cancers (naxitamab) and a chemotherapy drug (gemcitabine) will improve clinical responses.

Trispecific CAR T Cells Targeting CD19, CD20 and CD22 to Treat B-Cell Malignancies. (Lapo Alinari, MD, PhD*; Wing Chan, PhD*; Marcos de Lima, MD*; Sumithira Vasu, MBBS*; Bradley Blaser, MD, PhD; Nathan Denlinger, DO, MS; Aharon Freud, MD, PhD; Xiaoli Zhang, PhD, MS) – These researchers propose a first-in-human clinical trial involving chimeric antigen receptor (CAR) T cells manufactured at Ohio State that target three proteins in patients with B-cell malignancies in hopes of improving the results of single-protein (antigen) CAR T cells.

Deciphering the Role of CD28 Co-Stimulation for Tumor-Specific, Stem-Like Cells in Humans. (Andreas Wieland, PhD*; Zihai Li, MD, PhD; James Rocco, MD, PhD; Mark Rubinstein, PhD) – Immunotherapies involving immune checkpoint inhibitors (ICI) – which release the "brakes" on antitumor immune responses – can be effective,

but most patients don't respond to ICI therapy. These researchers have shown that successful ICI therapy depends on additional positive signals that boost antitumor responses. In this study, they will identify the positive signals that tumor-specific immune cells from cancer patients require to best respond to tumor antigens.

RAMP1-CGRP Axis Shapes Immune Responses in Glioblastoma. (Nandini Acharya, PhD*; Maciej Pietrzak, PhD*; Erica Bell, PhD; Zihai Li, MD, PhD; Pierre Giglio, MD; Benjamin Segal, MD; Ramesh Ganju, PhD) – These researchers have identified a neuropeptide called CGRP as a potential therapeutic target in glioblastoma. Previously, they found that blocking the CGRP pathway can boost antitumor immunity. Here, they will determine how CGRP impairs the antitumor effectiveness of immune cells so they can better thwart this neuropeptide. Since CGRP antagonists are already FDA-approved, this work could quickly improve glioblastoma treatment.

Examining the Safety, Acceptability and Preliminary Efficacy of Psychedelic-Assisted Therapy for Lung Cancer Patients With Depression: A Proof-of-Concept Trial. (Theodore Wagener, PhD*; Barbara Andersen, PhD*; Alan Davis, PhD*) – Patients with lung cancer are more likely than other cancer patients to experience depression, anxiety and despair. Current talk therapies and medications are limited, require intensive therapy or cause significant side effects, but research shows that psychedelic medicines combined with talk therapy may relieve cancer-related depression. These researchers will test the safety and acceptability of two psychedelic medicines and see how they affect depression and anxiety in patients with lung cancer.

Developing a Novel Chimeric Antigen Receptor Therapy for CTCL. (Wing Chan, PhD*; Walter Hanel, MD, PhD*; Ian Hout; Pushpa Lata; John Reneau, MD, PhD, co-investigator; Anna Vilgelm, MD, PhD, co-investigator) – Cutaneous T-cell lymphoma (CTCL) is a type of non-Hodgkin lymphoma (NHL) generally localized to the skin. In chimeric antigen receptor (CAR) T-cell therapy, a patient's T cells are removed from the body and engineered in a lab to attack cancer cells before being returned to the patient. Scientists in this study will further develop a CAR T-cell therapy specific for patients with CTCL in hopes of better treating them for this devastating disease, which often involves persistent itching and pain, life-threatening infections and spread to vital organs.

Discovering Novel Therapeutics and Immune Checkpoints for Rare Aggressive Sinonasal Malignancies. (Dukagjin Blakaj, MD, PhD*; Esmerina Tili, PhD, co-investigator; Priya Dedhia, MD, PhD; Ricardo Carrau, MD, co-investigator; Daniel Prevedello, MD, co-investigator) – Sinonasal undifferentiated carcinoma (SNUC) and olfactory neuroblastoma (ONB) are rare and aggressive cancers found in the nose and in the soft tissue and bone near the nose. Many of these tumors have a poor prognosis despite treatment with chemotherapy, surgery and radiation, so new therapeutic options are needed to improve the outlook for these patients. In this study, scientists will work to uncover the biological origins of these cancers and develop therapies that target the underlying causes.

In addition, the OSUCCC – James recently awarded a $250,000 Clinical Trials Grant, partially funded by Pelotonia, that will help investigators test the effectiveness of an FDA-approved anti-inflammatory drug in preventing blood cancers:

Targeting the Inflammasome Via IL-1b to Prevent Leukemic Progression of High-Risk Clonal Cytopenias. (Uma Borate, MBBS*) – Clonal hematopoiesis (CH) is a precancerous condition caused by blood cells with specific genetic mutations. A type of CH that carries a particularly high risk of progressing to blood cancers is called clonal cytopenias of undetermined significance (CCUS). Studies have shown that the progression of CCUS to cancer is driven by inflammation via the interleukin 1b (IL-1b) protein. In this study, scientists will target this inflammatory pathway with the drug canakinumab and study its effectiveness in preventing advanced blood cancers.

Tasleem Padamsee, PhD

Daniel Stover, MD

Electra Paskett, PhD, MSPH

Statewide Initiatives update: 'Turning the Page on Breast Cancer' addresses breast cancer disparities among Black women

Turning The Page On Breast Cancer

An OSUCCC – James statewide initiative that is partially supported by Pelotonia is demonstrating the potential effectiveness of multiple methods of community-, clinic- and web-based engagement for addressing persistent disparities in breast cancer outcomes among Black women.

Researchers in the "Turning the Page on Breast Cancer (TPBC)," which was launched in 2021, recently published an article in the journal **Cancer** to explain how it works and demonstrate its early progress. First authors were **Tasleem Padamsee, PhD**, and **Daniel Stover, MD**. **Electra Paskett, PhD, MSPH**, who leads the TPBC initiative, was senior author.

The article states that compared with their white peers, Black women across the United States are more often diagnosed with late-stage breast cancer, less often receive stage-appropriate treatment, and have lower survival rates at more advanced disease stages.

It also notes that Ohio had the nation's second-worst mortality rate for breast cancer in 2015, with 35% higher mortality among Black women compared with white women. These disparities exist despite Black and white women's similar rates of screening mammograms and breast cancer incidence.

Now in its third year, TPBC provides targeted interventions in 12 Ohio counties with high breast cancer rates among Black women. The initiative works to improve local health care facilities' ability to conduct effective breast cancer screening, follow-up and treatment; enlists the involvement of community-based organizations and social media to enhance awareness of these services; and provides education and personal-risk information through a **culturally relevant website**.

The site is targeted toward Black women aged 25-70 years and promoted through social media and community events. To date, more than 4,100 users have visited the website, and nearly 16% have completed the risk assessment.

TPBC has provided tailored information packets, evidence-based interventions and systematic support for improving the tracking and follow-up of breast health care among patients in 10 clinical partnerships.

Deliang Guo, PhD

Could disrupting the cholesterol supply to brain cancer cells suppress their growth?

A study led by researchers at the OSUCCC – James sheds light on how tumor cells maintain the balance of cholesterol in their membranes and provides a promising avenue for developing treatments for glioblastoma, the most lethal form of brain cancer.

In certain cancers, including glioblastoma, excess cholesterol is stored in lipid droplets within the cells. Since tumors grow rapidly and need proper levels of cholesterol in their cell membranes to survive, targeting cholesterol could be a strategy for antitumor therapy. Researchers examined clinical human glioblastoma specimens and cells for this study, which was published in the journal *Cell Reports*.

Deliang Guo, PhD, a professor in the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was lead author. He is also founding director of the Center for Cancer Metabolism at the OSUCCC – James. This work was supported by the National Institute of Neurological Disorders and Stroke, the National Cancer Institute, the American Cancer Society, a **Pelotonia Idea Grant** and the Urban and Shelly Meyer Foundation.

Institutional News & Events

Walter 'Ted' Carter Jr. begins his tenure as the new president of The Ohio State University

The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) is excited to welcome **Walter "Ted" Carter Jr.** as Ohio State's 17th president, a role he assumed on Jan. 1.

President Carter has a passion for Ohio State's mission to shape the future of research and innovation, workforce development, the arts, health care, college affordability and athletics. The OSUCCC – James shares in his belief that Ohio State is ready and well positioned to be the best in higher education in the United States and the world.

President Carter formerly served as president of the University of Nebraska System, where he oversaw four campuses of almost 70,000 students, faculty and staff, including their academic medical center. Before that, he led the U.S. Naval Academy as its longest continuously serving superintendent since the Civil War.

John J. Warner, MD, marks first year as Wexner Medical Center CEO and Ohio State executive vice president

On April 1, 2024, nationally recognized clinician and health care leader **John J. Warner, MD**, completed his first year as CEO of The Ohio State University Wexner Medical Center and executive vice president at Ohio State after coming to the university in 2023 following five years as CEO of The University of Texas Southwestern Health System. A national leader in academic medicine, Dr. Warner is dedicated to improving health care quality, safety and experience by putting patients and their families first. He also is a former president of the American Heart Association (2017-18).

At the Wexner Medical Center, Dr. Warner leads efforts to advance and pioneer interdisciplinary approaches to health care delivery, research and teaching across seven hospitals, an expansive and growing network of outpatient care centers, a nationally ranked College of Medicine, more than 20 research institutes, a faculty group practice, an accountable care organization and a health plan.

Cancer innovation moves forward with opening of new Pelotonia Research Center

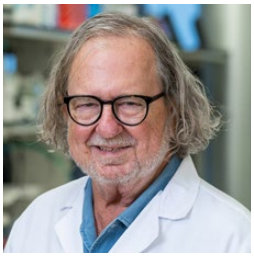
In May 2023, the OSUCCC – James celebrated the opening of the new Pelotonia Research Center, a five-story, 305,000-square-foot laboratory building that is named in recognition of Pelotonia's partnership and philanthropic support for cancer research at the OSUCCC – James. Since 2008, the Pelotonia community has raised more than $283 million.

The Pelotonia Research Center is equipped with the spaces, technologies and resources needed for researchers to work across disciplines to accelerate discoveries in multiple areas, including cancer, gene-and cell-based therapies, cardiovascular and pulmonary medicine, neurological disease, microbiome, food systems and health, artificial intelligence, sensory biology, and social and environmental determinants of health.

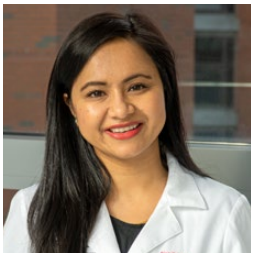
The center's location in Ohio State's Carmenton innovation district – which is connected to the university's academic and medical campuses – will strengthen collaborative, curiosity-driven and solution-oriented research designed to improve the lives of millions of people with cancer and other diseases.

Two floors are devoted entirely to cancer research, including one for the OSUCCC – James **Pelotonia Institute for Immuno-Oncology (PIIO)**, providing a state-of-the-art location for dozens of principal investigators who are leaders in their respective areas of immuno-oncology.

Another floor provides a new home for the **Center for Cancer Engineering – Curing Cancer through Research in Engineering and Sciences**, a multidisciplinary program in which investigators collaborate to develop and integrate engineering technologies and data science with cancer biology to enhance cancer prevention, diagnosis and treatment.



James P. Allison, PhD



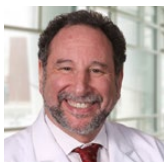
Nandini Acharya, PhD

Nobel Prize-winning expert in immuno-oncology receives 25th Block Memorial Lectureship Award

James P. Allison, PhD, co-winner of the 2018 Nobel Prize in physiology or medicine and a pioneer in groundbreaking immunotherapy research, received the **25th Herbert and Maxine Block Memorial Lectureship Award for Distinguished Achievement in Cancer** in April 2023 at Ohio State and delivered the Block Lecture the next day at the OSUCCC – James.

Funded by proceeds from the Herbert J. Block Memorial Tournament, an annual golf outing started in 1982 by the Block family of Columbus, the $50,000 award is given by the OSUCCC – James to an esteemed cancer researcher who then comes to Ohio State to accept the honor, lecture about his or her work and select a junior faculty member to mentor for two years. The **2023 Block Lectureship Junior Faculty Award recipient** is **Nandini Acharya, PhD**, assistant professor in the Department of Neurology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James.

OSUCCC – James faculty news



Peter Shields, MD

Peter Shields, MD, a tenured professor in the College of Medicine and the College of Public Health at Ohio State, **has retired as deputy director of the OSUCCC** – a title he had held since he came to Ohio State in 2011 – and has begun a new phase of his career as a medical oncologist and researcher within the cancer program. Now an emeritus professor, Dr. Shields focuses on patient care and cancer-prevention research. He sees patients in the clinic at The James, remains the principal investigator of his current grants, continues to co-lead the NCI T32 postdoctoral training program in Cancer Prevention and Control, and retains his membership in the Cancer Control Program at the OSUCCC – James.

Diane Von Ah, PhD, RN, FAAN

Ted Wagener, PhD

Diane Von Ah, PhD, RN, FAAN, a distinguished professor of cancer research in the College of Nursing at Ohio State, was named as **co-leader of the Cancer Control (CC) Program at the OSUCCC – James**, sharing that title with CC Program co-leader **Ted Wagener, PhD**, a professor in the Division of Medical Oncology and director of the Center for Tobacco Research. Dr. Von Ah, who is also director of cancer research in the College of Nursing's Center for Healthy Aging, Self-Management and Complex Care, has been a member of the CC Program since 2021.

Matthew Ringel, MD

Matthew Ringel, MD, was appointed as **chair of the newly established Department of Molecular Medicine and Therapeutics (MMT)** in The Ohio State University College of Medicine. Dr. Ringel also serves as co-leader of the Cancer Biology Program and co-director of the Center for Cancer Engineering at the OSUCCC – James. The MMT department fosters translational research and education in foundational therapeutics, regenerative medicine and molecular medicine.

Susan Tsai, MD, MHS, FACS

Susan Tsai, MD, MHS, FACS, became **director of the Division of Surgical Oncology** and professor in the Department of Surgery at Ohio State in November 2023. Previously an endowed professor in the Division of Surgical Oncology at the Medical College of Wisconsin (MCW), Dr. Tsai is a recognized leader in gastrointestinal oncology with a focus on pancreatic cancer. On a national level, she is a past president (2022-23) of the Society of Asian Academic Surgeons and a member of several prestigious surgical associations, including the American Surgical Association and the Society of Clinical Surgeons.

Regina Crawford, MD

Regina Crawford, MD, became **director of Ohio State's Sickle Cell Program** and clinical associate professor in the Division of Hematology in early 2023. She oversees all clinical and operational aspects of the Sickle Cell Program while maintaining the division's three-part mission of teaching, research and patient care. Dr. Crawford was recruited from Duke University Medical Center, where she was a benign hematologist, therapeutic apheresis specialist and sickle cell specialist who led the Duke Adult Sickle Cell Program.

2024

OSUCCC – James experts participated or will participate in these annual meetings/conferences in 2024:

- Society of Gynecologic Oncology (SGO), March 16-19
- American Society of Preventive Oncology (ASPO), March 17-19
- American Association for Cancer Research® (AACR) Annual Meeting 2024, April 5-10
- American Society of Clinical Oncology (ASCO), May 31-June 4
- BIO International Convention, June 3-6
- American Society for Radiation Oncology (ASTRO), Sept. 29-Oct. 2
- Association of American Cancer Institutes (AACI) Cancer Center Administrators Forum, Oct. 20-22
- Society for Immunotherapy of Cancer (SITC), Nov. 6-10
- American Society of Hematology (ASH), Dec. 7-10

Diversity, Equity & Inclusion (DEI) Spotlight

Remote outreach yields six-fold increase in rural cancer screenings

Rural women are six times more likely to get timely breast, cervical and colorectal cancer screening with remote outreach that involves interactive education and follow-up support by telephone, according to a new study.

Through the **Rural Interventions for Screening Effectiveness (RISE) study**, researchers at the OSUCCC – James and Indiana University compared the effectiveness of outreach methods designed to increase cancer screening adherence among women (biologically female) living in rural areas with limited access to health care services. They recruited 983 women between the ages of 50-74 from 98 rural counties in Ohio and Indiana. The women had no previous cancer diagnoses and were not up to date on one or more of the evidence-based cancer screenings recommended by the **U.S. Preventive Services Task Force**. Study participants were randomly assigned to one of three intervention groups:

- Usual care (no intervention except for study newsletters);
- A mailed interactive DVD with prompts to personalize educational information for recipients about screening tests, as well as information to schedule screenings;
- The same mailed interactive DVD with additional follow-up support calls from a patient navigator to answer questions, address barriers to screening and directly assist with scheduling.

While evidence-based screening tests exist for breast, cervical and colorectal cancer, adherence with these tests remains lower than expected – particularly among historically at-risk populations, including rural communities, minorities and people of lower education and income.

Electra Paskett, PhD, MSPH

"Women are dying every day of cancers that could have been prevented or detected in precancerous stages with timely cancer screening. This is not a new problem – but it is one of paramount importance to reduce the burden of cancer in our country, especially among those who are historically at increased risk due to socioeconomic factors," says **Electra Paskett, PhD, MSPH**, co-principal investigator of the RISE study and deputy director for population sciences and community outreach at the OSUCCC – James.

Study data suggest combining a remotely delivered interactive DVD and patient navigation services is an effective and relatively low-cost way to improve cancer screening rates among rural women. Specifically, while all women who received the DVD intervention were twice as likely to become up to date with all screenings, women who also received patient-navigation support in addition to the DVD were almost six times more likely to obtain all three screenings compared to women in the usual-care arm. This was the first large-scale evaluation of a remote intervention approach focused on multiple screenings.

Clinical Spotlight

Ohio State opens large cancer-specific outpatient care facility that also holds region's first Proton Therapy Center

Far more than a formality, a June 9 ceremony marked the opening of **The James Outpatient Care (JOC)** in Ohio State's Carmenton innovation district and started a new chapter in cancer care at the OSUCCC – James.

On Dec. 20, another ceremony was held to observe the opening of central Ohio's first **Proton Therapy Center**, which is housed within the JOC and is a collaboration between the OSUCCC – James and Nationwide Children's Hospital to provide adult and pediatric patients with access to the latest radiation oncology treatments in one location closer to their homes.

The 385,000-square-foot JOC, which is entirely devoted to cancer treatment, contains the OSUCCC – James' first free-standing outpatient surgery center, several specialty clinics and a clinical trials treatment unit. The facility focuses on cancers that affect blood, kidneys, bladder, prostate, and bone and soft tissue (sarcomas) – cancers for which therapies have advanced to the point that outpatient care is a highly effective option.

Notably, it contains the hospital's eight outpatient operating rooms designed for cancer surgeries that require no more than a short stay of less than one night after surgery, including such procedures as prostate surgery, kidney surgery, hysterectomies and breast lumpectomies.

It also includes interventional radiology rooms, an extended recovery unit, a pre-anesthesia center, a diagnostic center, an outpatient pharmacy, an oncology rehabilitation facility, chemotherapy infusion areas and such specialty facilities as a Chronic Hematology Clinic, a Genitourinary Clinic, and a **Cancer and Aging Resiliency (CARE) Clinic** to accommodate the needs of older patients with cancer.

Occupying 55,000 square feet of the JOC is the Proton Therapy Center, which offers an advanced form of radiation treatment that uses protons, or positively charged particles found within atoms, instead of X-rays to precisely target tumors. This limits radiation exposure and consequent damage to nearby healthy tissue and organs, reducing the chance of short- and long-term side effects that impact quality of life.

And because proton therapy results in fewer complications and side effects, clinicians can sometimes deliver higher doses of radiation to tumors, enhancing curative potential.

The Proton Therapy Center is also equipped to deliver an even newer form of radiotherapy called FLASH, which is being studied in preclinical models and has not yet been approved by the FDA. Preclinical data have demonstrated that FLASH could reduce a typical weeks-long treatment regimen to a single treatment delivered in less than a second. FLASH will be studied at the Proton Therapy Center in clinical trials involving patients with certain newly diagnosed, recurrent or advanced cancers.

Ashley Rosko, MD

Carolyn Presley, MD, MHS

Nicole Williams, MD

CARE Clinics at OSUCCC – James address health needs of older patients with cancer

Older adults undergoing cancer treatment often face challenges unique to aging. Because more than 50% of patients with cancer are over the age of 65, these challenges can be difficult to overcome. At the OSUCCC – James, experts in the Oncogeriatrics Program provide care that is designed to offer comprehensive treatment for older adults with cancer.

The Oncogeriatrics Program has created the **Cancer and Aging Resiliency (CARE) Clinics** to provide multidisciplinary care for patients at The James, The James Outpatient Care in Ohio State's new Carmenton innovation district, and the Stefanie Spielman Comprehensive Breast Center. The CARE Clinics are led by Co-Directors **Ashley Rosko, MD**, professor in the Division of Hematology, and **Carolyn Presley, MD, MHS**, associate professor with tenure in the Division of Medical Oncology. The CARE Clinic at the Breast Center, led by **Nicole Williams, MD**, associate professor in the Division of Medical Oncology, is specific to patients with breast cancer.

The CARE Clinics provide each patient with a multidisciplinary treatment plan that addresses quality of life, optimized nutrition, sensory loss, cognition, mental health and wellness, medication management, symptom management, physical function needs, home-safety and caregiver support.

The oncogeriatrics program also helps patients overcome obstacles to care, such as medication interactions, travel, transportation, financial barriers, food access, physical changes and psychological issues related to coping. In addition, the clinics offer strategies to reduce treatment side effects.

"Health changes with aging, and creating a cancer care plan personalized to each individual's unique disease and health status is important," says Dr. Rosko, who also serves as medical director of the Oncogeriatrics Program. She notes that the CARE Clinics are among only a few programs nationally that are dedicated to addressing the health needs of elderly patients with cancer.

"By working closely with each patient's primary physician, our program and CARE Clinics streamline care so that communication among the multidisciplinary team is prioritized and each patient's progress is tracked throughout treatment and beyond," adds Dr. Presley. "Our goal is to provide the highest quality of care while also ensuring there are no barriers to receiving it."

OSUCCC – James leads international clinical trial comparing open vs. minimally invasive surgery for early-stage cervical cancer

OSUCCC – James gynecologic surgeons are leading an international clinical trial to determine whether minimally invasive robotic surgery is better or worse than open surgery when performing a radical hysterectomy to treat cervical cancer.

Although minimally invasive and robotic-assisted surgery techniques have become the standard approach for many surgeries, in gynecologic cancer open surgery – which involves one large incision versus several keyhole-sized incisions – has remained the standard practice for radical hysterectomy.

The preference for an open approach to radical hysterectomy is in direct response to a 2018 study published in the *New England Journal of Medicine* – known as the Laparoscopic Approach to Cervical Cancer (LACC) trial – which reported concerns over increased risk for cancer recurrence and death in women undergoing minimally invasive surgery for cervical cancer.

Kristen Bixel, MD

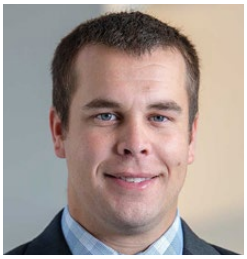
Allison Quick, MD

In this new **study** sponsored by the **Gynecologic Oncology Group**, researchers hypothesize that minimally invasive, robotic-assisted radical hysterectomy is not inferior to open surgery when appropriate tumor-containment methods are utilized and intrauterine manipulators are avoided. If proven, this would refute the LACC trial that led to a dramatic shift away from minimally invasive surgery.

Kristen Bixel, MD, a gynecologic oncologist at the OSUCCC – James, believes minimally invasive surgery should be re-evaluated as an option for patients with early-stage cervical cancer. She notes that this approach could be especially impactful for young women living with the long-term impact of treatment for cervical cancer.

"Studies have proven that robotic surgery results in less pain, fewer deaths and fewer surgical complications. We have greater knowledge now of how to reduce the risk of recurrence through standardized tumor-containment techniques, introduction of preoperative imaging and other standardized methodologies. Women deserve a better option than open surgery," says Dr. Bixel, who is one of four international co-principal investigators along with colleague **Allison Quick, MD**, a radiation oncologist at the OSUCCC – James.

"Results of this trial could alter the surgical approach to treatment of early-stage cervical cancer," Dr. Bixel says. "With strict patient-selection criteria and protective surgical maneuvers to prevent tumor exposure to the peritoneal cavity at the time of minimally invasive radical hysterectomy, we may be able to optimize oncologic outcomes, reduce complications and improve perioperative recovery."



Kyle VanKoevering, MD

3D modeling lab helps personalize and improve cancer reconstructive surgery

3D printing is improving functional and cosmetic treatment outcomes for patients with difficult-to-treat head and neck cancers at the OSUCCC – James, which has used this approach since 2021 in the surgery planning and treatment of over 200 patients with complex head and neck cancer surgeries impacting the jaw.

These surgeries are especially delicate and precise, says **Kyle VanKoevering, MD**, a head and neck surgeon and member of the Translational Therapeutics Program at the OSUCCC – James. Dr. VanKoevering is clinical director of the **Medical Modeling, Materials and Manufacturing (M4) Lab**, a partnership of the OSUCCC – James and the Ohio State College of Engineering.

"We want to make sure our patients can talk, chew, eat, swallow, breathe and function normally as much as possible after surgery," says Dr. VanKoevering. "As a surgeon, I've trained over the years to take all these two-dimensional pictures and mentally create a 3D roadmap in my head about where all this anatomy and the tumor are located. To see that come together in a real 3D model is incredible because it is not only a guide to use in the operating room, but also an important educational tool for our residents and patients."

The M4 Lab is a collaborative initiative through which engineers and surgeons work together to create custom 3D anatomical models based on a patient's collective 2D and 3D imaging tests to guide medical interventions.

In the M4 Lab housed in the Pelotonia Research Center, Lab Director Kyle VanKoevering, MD, holds a 3D anatomic model of the right pelvis of a patient with a pelvic tumor. The bony pelvis structure is gray, the tumor is yellow, the femoral artery is red and the femoral vein is blue.

Research Grant Highlights

Ann-Kathrin Eisfeld, MD

Elaine Mardis, PhD

Large NCI grants will support innovative studies of acute myeloid leukemia

Two five-year grants totaling more than $6 million from the NCI will help OSUCCC – James researchers and colleagues at other institutions better understand acute myeloid leukemia (AML) genetics and the role of inflammation in regulating immune response to this disease.

Ann-Kathrin Eisfeld, MD, assistant professor in the Division of Hematology at Ohio State and director of the Clara D. Bloomfield Center for Leukemia Outcomes Research at the OSUCCC – James, is principal investigator (PI)/project leader for a $3.43 million grant that will help researchers delineate genetic and genomic contributors that are currently missing in clinical risk-stratification tools and in the growing landscape of potential druggable and disease-modifying targets for AML.

Other PIs for this study are **Elaine Mardis, PhD**, professor in the Department of Pediatrics at Ohio State and co-leader of the Translational Therapeutics Program at the OSUCCC – James, and Leighton Grimes, PhD, professor in the Department of Pediatrics at the University of Cincinnati and co-leader of the Program in Hematologic Malignancies of Cincinnati Children's Hospital Medical Center, Cancer and Blood Diseases Institute.

Dr. Eisfeld is also a PI for a $2.85 million grant study that she and colleagues believe will provide, for the first time, information to help clinicians better target aberrant inflammation as an immune response in patients with AML, the most common form of acute leukemia in adults. Iannis Aifantis, PhD, chair of the Department of Pathology at New York University Grossman School of Medicine, is PI/project leader for this study.

Diane Von Ah, PhD, RN, FAAN

Ohio State leads NCI grant-funded study to improve cognitive functioning in breast cancer survivors

A five-year, $2.76 million grant from the NCI will fund a multi-center clinical trial led by the OSUCCC – James that is designed to help improve self-reported and objective cognitive functioning in breast cancer survivors with cancer-related cognitive impairment (CRCI).

The grant was awarded to **Diane Von Ah, PhD, RN, FAAN**, co-leader of the Cancer Control Program at the OSUCCC – James and a professor at the Ohio State College of Nursing, where she also is director of cancer research in the Center for Healthy Aging, Self-Management and Complex Care. The study, a collaboration with the NCI's National Community Oncology Research Program, will compare a computerized cognitive training program with a computerized active attention control program. Findings will provide evidence to guide clinicians' recommendations and survivors' treatment selections for managing CRCI.

Lalit Sehgal, PhD

NCI grant will help researchers develop novel therapy for patients with MCL

Researchers at the OSUCCC – James will use a **five-year, $2.03 million grant** from the NCI to develop a novel therapy for improving outcomes in patients with mantle cell lymphoma (MCL), a currently incurable form of non-Hodgkin lymphoma.

Principal investigator for the grant is **Lalit Sehgal, PhD**, assistant professor in the Division of Hematology at Ohio State and member of the Leukemia and Hematologic Malignancies Program at the OSUCCC – James. Dr. Sehgal and colleagues will examine the role of the fibroblast growth factor receptor-1 *(FGFR1)* gene in the biology of MCL and develop therapeutic strategies for this disease, which has a median progression-free survival of only four years after first-line treatment.

Priya Dedhia, MD, PhD

Researchers land DOD grant to study metastatic progression in medullary thyroid cancer

The U.S. Department of Defense (DOD) has awarded a four-year, $1.15 million grant to help OSUCCC – James researchers use biologic structures called organoids to study how medullary thyroid cancer (MTC) progresses so they can better treat patients who have advanced MTC and limited therapeutic options.

Organoids are 3-dimensional, mini-organ-like structures made by growing a person's tumor cells or stem cells in the laboratory. They closely mimic the structure, organization and functions of human tissues and organs and are thus helpful in studying how normal tissues and diseases form so drugs can be developed and tested. Principal investigator for this new study is **Priya Dedhia, MD, PhD**, assistant professor in the Division of Surgical Oncology at Ohio State and member of the Translational Therapeutics Program and **Center for Cancer Engineering** at the OSUCCC – James.

Kristy Townsend, PhD

Keck Foundation issues research award to study brain and fat tissue connections

Researchers at The Ohio State University College of Medicine and Wexner Medical Center are leading a multi-center team that received $1.2 million from the W.M. Keck Foundation to explore the neural feedback loop between the brain and adipose (fat) tissue.

This team, led by **Kristy Townsend, PhD**, associate professor in the Department of Neurological Surgery at Ohio State and a member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James, will employ advanced techniques to evaluate how and which lipids are communicated to the brain by nerves in adipose tissue in mouse models. The team, which includes experts in neuroscience, lipid biochemistry and metabolic health, will collect foundational data about the function of adipose sensory nerves and the diversity of information they communicate to the brain.

Monica Venere, PhD

NCI grant will aid study of lethal pediatric brain tumor in quest for therapies

Researchers at the OSUCCC – James and St. Jude Children's Research Hospital will use a five-year, $3.5 million grant from the NCI to study the causes of a highly lethal pediatric brain tumor and determine therapeutic options that can be moved to clinical trials.

Multiple principal investigators for the project are **Monica Venere, PhD**, assistant professor in the Department of Radiation Oncology at Ohio State and member of the Cancer Biology Program at the OSUCCC – James, and Stephen Mack, PhD, of the Developmental Neurobiology Department at St. Jude and the St. Jude Comprehensive Cancer Center. The researchers will focus on an interacting protein that is elevated in a subtype of ependymoma called ZFTA-RELA and could be a therapeutic target.

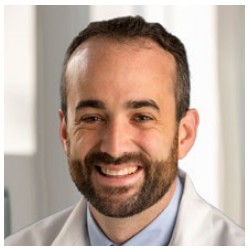
Somashekar Krishna, MD, MPH

NCI grant-funded study will evaluate novel method for early detection of pancreatic cancer

The NCI has awarded a five-year, $2.2 million grant to help OSUCCC – James researchers evaluate a novel method for more accurate risk stratification and earlier detection of pancreatic ductal adenocarcinoma arising from pancreatic cystic lesions (PCLs).

The study is led by principal investigator **Somashekar Krishna, MD, MPH**, professor and director of advanced endoscopy in the Division of Gastroenterology, Hepatology and Nutrition at Ohio State. Dr. Krishna also is a member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James. He and colleagues have utilized and demonstrated a high accuracy (97%) for a novel diagnostic method of endoscopic ultrasound (EUS)-guided needle-based confocal laser endomicroscopy, a technology that they say provides *in vivo*, real-time optical biopsies of PCLs.

Ann Scheck McAlearney, ScD, MS



James Burke, MD, MS

Daniel Jonas, MD, MPH

ACCELERATE program established with grant for health services research training

A novel Ohio State program designed to prepare the next generation of health services researchers (HSR) has been established with a $1.7 million Institutional Training Grant from the Agency for Healthcare Research and Quality (AHRQ).

The grant was awarded to principal investigators **Ann Scheck McAlearney, ScD, MS**, professor in the Department of Family Medicine and member of the Cancer Control Program at the OSUCCC – James; **James Burke, MD, MS**, professor in the Department of Neurology; and **Daniel Jonas, MD, MPH**, professor in the Division of General Internal Medicine and Geriatrics. "ACCELERATE: Accelerating HSR at OSU" will increase accessibility to high-quality health care by developing diverse and exceptional postdoctoral trainees.

Gina Sizemore, PhD

NCI grant will support study of breast cancer metastasis to the brain

OSUCCC – James researchers will use a five-year, $2.34 million grant from the NCI to further their studies of how breast cancer metastasizes to the brain so they can devise targeted therapies that improve patient outcomes. Principal investigator for this grant is **Gina Sizemore, PhD**, associate professor in the Department of Radiation Oncology at Ohio State and member of the Cancer Biology Program at the OSUCCC – James.

Dr. Sizemore and colleagues say this work will be the first to test the hypothesis that a protein called platelet-derived growth factor B (PDGFB), which is secreted by breast cancer cells, and its cell receptor (PDGRFß) work to alter the brain microenvironment and precondition it to allow for metastasis. They note that patients diagnosed with breast cancer-associated brain metastases have a median survival rate of only 10-11 months.

Julie Johnson, PharmD

Ohio State receives $37.9 million CTSA Award, appoints new leader of translational research

The Ohio State University has received a seven-year, $37.9 million Clinical and Translational Science Award (CTSA) from the National Institutes of Health (NIH) to support the university's **Center for Clinical and Translational Science** (CCTS). Principal investigator for this award is **Julie Johnson, PharmD**, who recently was recruited from the University of Florida as director of the CCTS.

The award, which represents the fourth cycle of NIH funding that the CCTS has received since 2008, supports the center's work to turn scientific discoveries into clinical therapies that improve human health. Besides directing the CCTS, Dr. Johnson serves as associate dean for clinical and translational research and holds the Dr. Samuel T. and Lois Felts Mercer Professorship of Medicine and Pharmacology in the Ohio State College of Medicine. She also is associate vice president for research at Ohio State.

Kari Kendra, MD, PhD

Grant will boost study of novel treatment for melanoma brain metastases

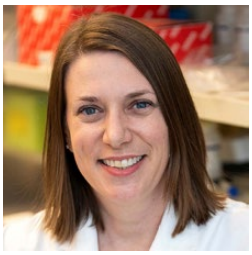
Kari Kendra, MD, PhD, professor in the Division of Medical Oncology at Ohio State and chair of the Melanoma Disease-Specific Research Committee at the OSUCCC – James, received a two-year, $200,000 award from the Melanoma Research Foundation for a first-of-its-kind immunotherapy study that will use universal donor (UD) TGFß natural killer (NK) cells to help patients with melanoma that has metastasized to the brain.

Dr. Kendra and colleagues state that brain metastases are a leading cause of death among patients with metastatic melanoma. They also note that the body's NK cells are the first line of defense against tumors. Dr. Kendra's collaborative team has developed a method to collect NK cells from donors and grow them in large numbers for storage in a cell bank available for multiple treatments. They also have devised a technique used when expanding the UD NK cells that provides those cells with resistance to TGFß, a cytokine (small protein) that impairs the function of NK cells.

Dr. Kendra's team will recruit melanoma patients with brain metastases and treat them with TGFßi NK cell infusions to generate preliminary data about how these cells travel in the body, enter the brain, attack malignant cells and interact with the immune system. They also will assess preliminary effectiveness of this treatment against melanoma metastases in the brain and outside of the brain.

Bench To Bedside: Featured Clinical Trial

Phase II clinical trial gauges effectiveness of drug combination for treating Richter's syndrome



Jennifer Woyach, MD

Patient accrual is underway for a phase II clinical trial at the OSUCCC – James (**OSU-22157**) that is testing how well zanubrutinib and lisocabtagene maraleucel (liso-cel) work together in treating patients with recurrent or refractory Richter's syndrome (RS).

RS occurs when chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL) transforms into an aggressive lymphoma.

Zanubrutinib is a kinase inhibitor that prevents abnormal proteins from inducing cancer cells to multiply, which helps stop the spread of cancer. Liso-cel is a chimeric antigen receptor (CAR) T cell therapy in which a patient's T cells are removed from the blood and altered in a laboratory so they will more potently attack cancer cells.

In the laboratory, the gene for a CAR receptor that binds to a certain protein in the patient's cancer cells is added to the T cells. Large numbers of CAR T cells are then grown and given to the patient by infusion. In this trial, researchers hypothesize that administering zanubrutinib and liso-cell together may kill more cancer cells in patients with recurrent or refractory RS.

The trial is led by principal investigator **Jennifer Woyach, MD**, professor in the Department of Hematology at Ohio State and co-leader of the Leukemia and Hematologic Malignancies Program at the OSUCCC – James.

The trial is open to patients age 18 or older who have been diagnosed with RS (occurrence of diffuse large B-cell lymphoma in patients with antecedent or concurrent CLL) and who have relapsed/refractory disease after one prior line of therapy (complete inclusion and exclusion criteria may be viewed in the OSU-22157 link shown above). Importantly, patients can enroll if they developed RS on preceding CLL-directed therapy.

The trial's primary objective is to evaluate the efficacy of combining zanubrutinib and liso-cel for treating RS. Secondary objectives are to describe the safety profile of this combination and to evaluate the duration of its efficacy for patients with RS.

After study completion, patients are followed for 24 months and then every six months until disease progression or death.

To search for cancer clinical trials at Ohio State, visit **cancer.osu.edu/clinicaltrials**. To receive a monthly e-newsletter with information on newly opened cancer clinical trials at the OSUCCC – James, send an email to cancerclinicaltrials@osumc.edu.

Featured Shared Resource

Clinical Translational Science

Wancai Yang, MD

The Clinical Translational Science Shared Resource (CTSSR) team at the OSUCCC – James works with clinical and translational scientists to develop a customizable portfolio of biomarker assays that provide correlative science studies associated with early-phase solid tumor oncology clinical trials.

The CTSSR is a central repository for specimens collected from patients in clinical trials and is responsible for processing the samples for downstream analyses. Besides developing assays, this resource partners with other OSUCCC – James shared resources in the use of such technologies as next-generation gene sequencing, RNA expression analysis and proteomics. In these situations, the CTSSR obtains and prepares patient samples for analysis, and then collects and analyzes the data.

The CTSSR also helps foster partnerships among investigators and biotech/pharmaceutical companies to gain access to new drugs and compounds, and to provide corresponding correlative testing and analyses for cancer studies.

All these services facilitate the translation of basic science research to the clinic to improve diagnosis strategies and design better treatment modalities for patients with cancer.

Located in Room 240 of Ohio State's Biomedical Research Tower, the CTSSR is led by Director **Wancai Yang, MD**.

Institutional Achievements

The OSUCCC – James was highlighted by the Gynecologic Oncology Group (GOG) Partners/National Research Group (NRG) Oncology for having **the highest patient accrual to gynecologic oncology clinical trials of any site in the nation**. According to GOG Partners/NRG Oncology combined accrual data for the top 50 sites, the OSUCCC – James enrolled 171 patients in gynecologic oncology clinical trials over the past three years; only three other institutions had more than 100 accruals.

The Ohio State **Department of Radiation Oncology ranked No. 1 in NRG (National Research Group)-National Cancer Institute clinical trials activity** in the United States in 2022 based on NCI-Cancer Therapy Evaluation Program data, and the department ranked **No. 5 in the country in NIH Radiation Oncology funding** in 2022.

The 2023 Blue Ridge Institute for Medical Research, an independent non-profit organization founded in 2006, **ranked the Ohio State Department of Surgery No. 11 in the country** based on NIH funding for fiscal year 2023.

The OSUCCC – James has joined the **Radiosurgery Society® (RSS) Sponsorship Alliance**, a medical professional non-profit organization representing over 800 members in 45 countries.

The Ohio State Division of Thoracic Surgery earned a **distinguished 3-star rating for all composites** from The Society of Thoracic Surgeons (STS). The rating, which denotes the highest category of quality, places Ohio State among the elite for general thoracic surgery in the United States and Canada.

OSUCCC – James accreditations/reaccreditations/designations:

- Reaccreditation for three years by the **American College of Surgeons – Commission on Cancer:** A hallmark of excellence, the survey found no deficiencies.
- Reaccreditation of the **Stefanie Spielman Comprehensive Breast Center** for three years by the **National Accreditation Program for Breast Centers (NAPBC)**. The site visit found no deficiencies.
- **Comprehensive Radiopharmaceutical Therapy Center of Excellence** designation by the Society of Nuclear Medicine & Molecular Imaging – one of only 31 sites worldwide.
- **Excellence in Evidence-Based Practice and Outcomes in Healthcare Designation (Gold)** from the Helene Fuld Health Trust National Institute for Evidence-Based Practice (EBP) in Nursing and Healthcare.
- Reaccreditation of the Advanced Practice Provider (APP) Fellowship Program for four years by the **American Nurses Credentialing Center's (ANCC) Practice Transition Accreditation Program® (PTAP)**. The James Oncology and Critical Care Advanced Practice Fellowship was previously accredited in 2016 and 2019. In 2019, the university's APP fellowship programs combined into one **Health System Fellowship**.

Institutional Achievements (continuted)

Castle Connolly accolades for the OSUCCC – James and Ohio State Wexner Medical Center:

- 450 physicians on the **2023 Top Doctors list**
- 33 of the 114 **Top Black Doctors 2023** roster
- 110 named **2023 Exceptional Women in Medicine**
- 37 listed as **Top Asian American and Pacific Islander (AAPI) Doctors**
- 15 listed as **Top Hispanic and Latino Doctors**
- 11 highlighted as national **2023 "Rising Stars"** – five specific to the OSUCCC – James: **Brittany Dulmage, MD**, **Stephanie Trovato, MD**, **Catherine Ulman, MD**, **Bradley Nesemeier, MD**, and **Kerry-Ann Mitchell, MD, PhD**.

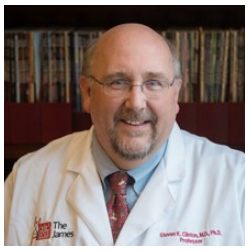
Individual Achievements

Fred Tabung, PhD, MSPH

Fred Tabung, PhD, MSPH, was **appointed by President Joe Biden to a multi-year term on the National Cancer Advisory Board**. The board guides the director of the NCI in setting the course for the national cancer research program and will complement the Cancer Moonshot initiative that Biden reignited in 2022.

Julia Agne, MD

Julia Agne, MD, is one of four winners of the **2023 National Comprehensive Cancer Network (NCCN) Foundation Young Investigator Award**, which provides up-and-coming leaders in oncology research with money for two-year projects. Recipients will present study results at an NCCN Annual Conference.



Steven Clinton, MD, PhD

Steven Clinton, MD, PhD, was inducted as a **Fellow of the American Society for Nutrition (FASN)**, the ASN's highest honor, which recognizes individuals for lifetime achievement and distinguished careers in nutrition. Dr. Clinton also has served the National Academy of Sciences to establish dietary reference intakes for nutrients and has served the U.S. Department of Health and Human Services to establish Dietary Guidelines for Americans.

Amy Rettig, DNP, MALM, MSN

Amy Rettig, DNP, MALM, MSN, was one of three national recipients of the Oncology Nursing Foundation's **2023 Mara Mogensen Flaherty Memorial Lectureship Award**. Recipients of the award, which recognizes leading voices in managing psychosocial aspects of cancer, served as panelists for a discussion at the Oncology Nursing Society's 48th Annual ONS Congress.

Raphael E. Pollock, MD, PhD, FACS

Raphael E. Pollock, MD, PhD, FACS, was appointed **chair-elect of the Big Ten Cancer Research Consortium (CRC) Foundation**, a research collaboration among cancer centers at institutions in the Big Ten Conference. Dr. Pollock also presented "New Directions in Retroperitoneal Liposarcoma" as the **63rd Annual Samuel Clark Harvey Memorial Lecture** co-hosted by the departments of Surgery and Neurosurgery at Yale University School of Medicine.

David Carbone, MD, PhD

David Carbone, MD, PhD, was among 12 scientists worldwide to be named as inductees in the 11th annual class of **Giants of Cancer Care®** by OncLive®, one of the nation's leading multimedia resources for oncology professionals. He was inducted as a ***Giant in Lung Cancer.***

Barbara Andersen, PhD

Barbara Andersen, PhD, chaired a **national review panel that updated the American Society of Clinical Oncology (ASCO) guideline** on the management of anxiety and depression in adult cancer survivors. Results were reported in an article in *Journal of Clinical Oncology* for which Andersen was first author. ALSO, Andersen received the **Distinguished Scientist Award** at the 44th annual meeting of the Society of Behavioral Medicine.

Carolyn Presley, MD, MHS

Carolyn Presley, MD, MHS, received the **Rising Star Award from Women Leaders in Oncology (WLO)**, which recognizes and empowers women who have dedicated their careers to advancing oncology research. ALSO, Dr. Presley was selected to present the annual **Jimmie Holland Lecture at the Alliance for Clinical Trials** in Oncology's fall 2023 meeting in Chicago.

Cheryl Lee, MD

Cheryl Lee, MD, the first Black female chair of a urology department in the country, received a **Distinguished Service Award from the American Urological Association (AUA)** for her outstanding commitment to patients with bladder cancer and for fostering a culture of inclusivity.

David Gosky, MA, MBA

David Gosky, MA, MBA, was elected as the inaugural **treasurer of the Association of Cancer Center Administrators,** which helps professionally develop staff who lead cancer centers that are designated or working toward designation by the NCI. Gosky also was re-appointed as **treasurer of the Association of American Cancer Institutes**.

Read about additional OSUCCC – James awards and honors at cancer.osu.edu/news.

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