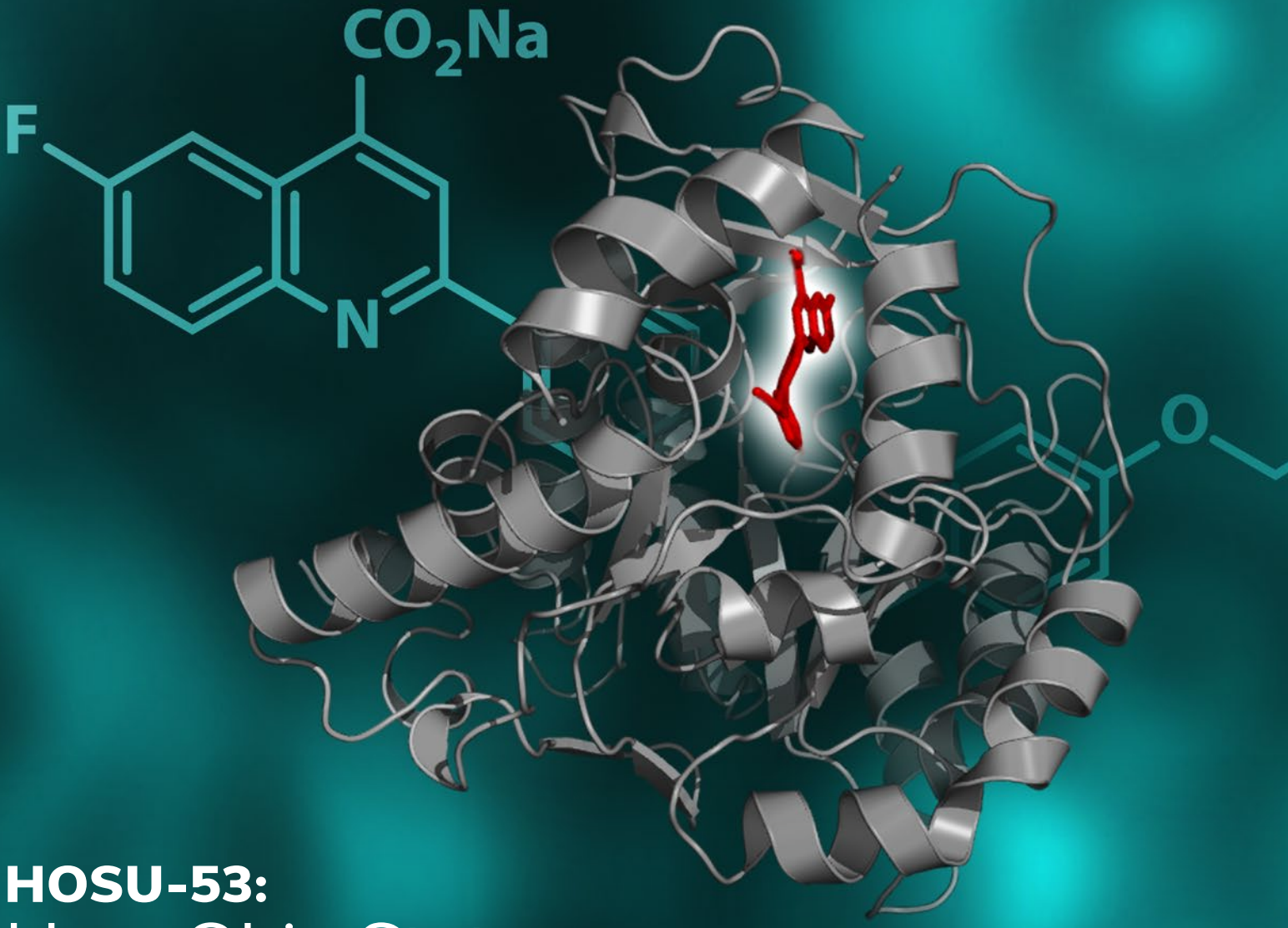
TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

WINTER 2025



HOSU-53:
How Ohio State created an original drug to fight cancer

Trial will test a best-in-class DHODH inhibitor that was discovered and developed entirely by Ohio State

The James

The Ohio State University
Comprehensive Cancer Center

Scientists find possible new therapy for some patients with non-small cell lung cancer

OSUCCC – James researchers have found a potentially effective drug-combination approach to treating certain patients with non-small cell lung cancer (NSCLC), a disease for which improved therapies are urgently needed.

Principal investigator and senior author of the study, which was published in the journal *Nature Communications*, was **Junran Zhang, MD, PhD**, professor in the Department of Radiation Oncology at Ohio State and a member of the Cancer Biology Program at the OSUCCC – James. Dr. Zhang, who also is a member of the **Pelotonia Institute for Immuno-Oncology** (PIIO) and the **Center for Cancer Metabolism**, and her team study DNA damage response in cells and how this natural process can be exploited for personalized cancer treatment.

In this new study, scientists show that a protein called checkpoint kinase 1 (CHK1) is critical for cell survival when the cells experience DNA replication stress. Drugs that inhibit CHK1 have been used with chemotherapy to kill cancer cells in preclinical studies, but this approach has been only minimally effective while causing substantial side effects in clinical trials involving humans.

To explore combination strategies that can overcome these limitations, the scientists studied an NSCLC cancer cell line, as well as tumors' response to CHK1 inhibitors, and found that blocking CHK1 can be more effective in killing NSCLC cells when combined with other proteins called thioredoxin1 (Trx1) and thioredoxin reductase (TrxR1) – important components of the body's antioxidant system. (The antioxidant system protects cells from damage caused by free radicals and regulates protein functions.)

"This combination targets the cancer cells' ability to manage replication stress, making them more vulnerable to the treatment," Dr. Zhang says.

Her team also found that a drug called auranofin, which is already used to treat rheumatoid arthritis, can enhance cancer cells' sensitivity to a CHK1 inhibitor drug that is being tested in a clinical trial for treating cancer patients.

"Our research results suggest a potential combinational approach to treating a subset of NSCLC patients and repurposing an existing drug (auranofin), originally used for treating rheumatoid arthritis, for use in oncology. Repurposing this drug in combination with CHK1 inhibitors for NSCLC treatment might be an area to focus on in future studies."

The scientists note that, although auranofin has a well-known toxicity profile, the dose used to achieve its anticancer activity in current preclinical studies is higher than the dose used for treating rheumatoid arthritis, so the next clinical steps may be to validate the drug's effectiveness and safety in NSCLC or other tumor models involving an immune component host.

The team says more specific and potent drug inhibitors targeting Trx1 or TrxR1 need to be developed.

Winter 2025 Frontiers

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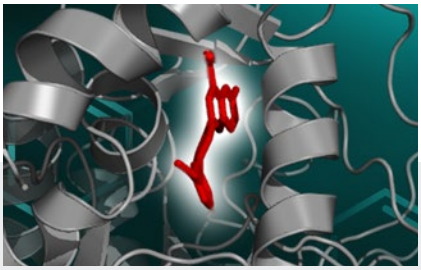
FRONTIERS

WINTER 2025

FEATURES



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With four decades of experience, the Blood and Marrow Transplant (BMT) Program at the OSUCCC – James has long been at the forefront of innovative care for patients with hematologic malignancies.

Read *Frontiers* online or download an issue at **cancer.osu.edu/Frontiers**.

The James

The Ohio State University
COMPREHENSIVE CANCER CENTER

Exemplifying Bench to Bedside: How Ohio State created an original drug to fight cancer

Patients with any solid cancer tumor or non-Hodgkin lymphoma who have few remaining treatment options may soon benefit from a phase I, first-in-human clinical trial available only at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (**OSUCCC – James**).

The single-center trial is now accruing patients and will test a best-in-class DHODH inhibitor that was discovered and developed for use in patients entirely by Ohio State.

The new oral drug, known as HOSU-53 while in testing, inhibits an enzyme called dihydroorotate dehydrogenase (DHODH), which is involved in cellular and metabolic processes that enable cancer cells to thrive. Specifically, the drug thwarts pyrimidine synthesis, a chemical process for producing precursors for new DNA and RNA molecules on which cancer cells heavily depend.

"Targeting pyrimidine synthesis stresses out the cancer cells and makes them more susceptible to other potential therapies."

Chad Bennett, PhD

Chad Bennett, PhD

Chad Bennett, PhD, senior director of chemistry for the OSUCCC – James **Drug Development Institute** (DDI) and co-lead investigator of the team that developed HOSU-53, explains that "targeting pyrimidine synthesis stresses out the cancer cells and makes them more susceptible to other potential therapies. The challenge is to starve the cancer cells by depriving them of pyrimidines while not disturbing healthy cells. Our molecule has been shown in preclinical and cell models to strike this careful balance."

Jabez Biosciences, a clinical-stage biopharmaceutical oncology company founded by industry veterans in 2024 and based in Zionsville, Indiana, has licensed HOSU-53, which has been renamed JBZ-001. As the clinical sponsor for the phase I trial, Jabez will work closely with principal investigator (PI) **Asrar Alahmadi, MBBS**, a thoracic oncologist in the Translational Therapeutics Program at the OSUCCC – James.

Asrar Alahmadi, MBBS

Landmark Achievement

OSUCCC – James researchers believe this marks the first time that Ohio State has developed a new molecule drug for cancer, shepherded it through the U.S. Food and Drug Administration's (FDA) rigorous commercial Investigational New Drug (IND) application process and then licensed it to bring it into the clinic. Delaying external sponsorship (or out-licensing) until it is a commercial IND is a difficult feat rarely accomplished at academic medical institutions due to the cost, work, time and complexity. And by doing so, Ohio State has added significant value, attractive to a licensee.

Jeff Patrick, PharmD

"It's extraordinary for an academic institution to not only make a promising drug discovery in the lab but also to have the in-house expertise and capabilities to then take that drug through the IND application process, build a business plan, secure a commercial clinical partner, and then open that trial to benefit patients," says **Jeff Patrick, PharmD**, a clinical pharmacist and senior director of the DDI.

> *"This is a testament to the investment in team, knowledge and infrastructure Ohio State has made to ensure we can propel promising discoveries from the lab to the clinic."*
>
> **Jeff Patrick, PharmD**

Bringing the drug from promising molecule to a clinical trial took vast resources of time, money (mainly through generous philanthropic support) and multidisciplinary collaboration from numerous clinicians, scientists and other experts across the university, including the OSUCCC – James, DDI, **College of Pharmacy**, **College of Medicine**, **Office of Innovation and Economic Development**, and **Enterprise for Research, Innovation and Knowledge**.

Sebastian Biglione, PhD, PharmD

Sebastian Biglione, PhD, PharmD, director of clinical and regulatory strategy for the DDI, says that, although other first-in-human phase I studies have started as investigator-initiated clinical trials using research INDs at the OSUCCC – James and the Ohio State Wexner Medical Center, none of those have run the full spectrum of development here as HOSU-53 has.

Although it's common for a new chemical entity (NCE) discovered by a university to be advanced to the clinic, Dr. Biglione says it's rare for a university or hospital to handle all of its development up to clinical testing.

"What is more common – and not as heavy of a lift – is to do studies on new indications of repurposed compounds already approved by the FDA," he says, adding that those studies take much less time and don't require the amount of documentation that he and Dr. Bennett compiled over several years in a 6,700-page report to gain FDA approval of HOSU-53 as an IND.

Long road to success

Despite the number of people involved along the way, Drs. Biglione and Bennett say the DHODH inhibitor discovery story had a humble start several years ago as a collaboration between former OSUCCC – James medical scientist John C. Byrd, MD, an internationally known specialist in hematologic malignancies, and his former mentor at Hendrix College in Arkansas, Thomas E. Goodwin, PhD, along with undergraduate students working under him who generated the prototype compound.

Noting that Dr. Byrd earned his undergraduate degree in chemistry at Hendrix, Dr. Bennett says Dr. Goodwin contacted Dr. Byrd at Ohio State and asked him if his lab team could test several molecules devised by Dr. Goodwin's chemistry undergraduate mentees to see if any of the molecules had clinical potential.

Dr. Byrd agreed, and in 2017 his team found one molecule that had promising activity, killing acute myeloid leukemia (AML) cells when tested against AML cell lines. The DDI became involved in late 2018, and the expanded team created and tested new molecules to improve upon the properties of the original molecule, with the goal of designing a new therapeutic.

Sandip Vibhute, PhD

In 2019, the compound known as HOSU-53 was made by **Sandip Vibhute, PhD**, in the OSUCCC – James Drug Discovery Shared Resource. DDI scientists aimed to characterize it, but their work was put on hold for a time during the COVID-19 pandemic that began in 2020.

"We had to learn how to work under COVID protection policies, but we were able to identify HOSU-53 had best-in-class potential in late 2020," Dr. Bennett says.

Gerard Hilinski, PhD

Gerard Hilinski, PhD, senior director of biochemistry for the DDI, spearheaded the expansion of the drug's indications to multiple myeloma, which triggered further expansion to non-Hodgkin lymphoma and many solid tumors, including small cell lung cancer, colorectal cancer and gastric cancers.

Then began the long process of documenting the safety and potential efficacy of the compound as part of the FDA's IND approval process that allows a new drug to be used in humans.

"That included learning how to manufacture the drug consistently while controlling its properties, and then making the capsules and doing the initial testing, including extensive safety testing in two preclinical models so we could determine which toxicities to expect," Dr. Bennett says.

Drs. Bennett and Biglione note that any new molecule dosed high enough will have toxicities; hence, the importance of their toxicity studies. "Our job was to find the dose levels that we thought would be efficacious but also safe to give to humans," Dr. Bennett says, explaining that phase I trials seek to determine safety and tolerability while looking for signals that the drug will work in future trials involving more patients and longer dosing periods.

Dr. Biglione emphasizes that the FDA approved the IND phase I trial as monotherapy to see how well it works as a single agent before it is combined with other therapies in future studies.

The researchers believe clinicians who enroll patients on the phase I trial will also be happy to have a blood test to guide them in assuring patient safety and efficacy, thanks to a pharmacodynamic biomarker meticulously studied by Dr. Bennett and **Chris Coss, PhD**, associate professor of Pharmaceutics and Pharmacology in the College of Pharmacy and member of the DDI.

"When we inhibit the DHODH enzyme, the chemical material that it uses – dihydroorotate, or the 'DHO' part of DHODH – builds up over time," Dr. Bennett says. "We've measured that in preclinical models and correlated it with efficacy and toxicity so we can get an optimal biological dose for each patient. We've spent years creating and evaluating data to correlate drug levels vs. DHO levels, efficacy and toxicity, so we should know when we approach dosing levels that are effective without harmful side effects.

"It can't be understated how excited our clinicians are to have a lab value they can look at for guidance, so they can tell their patients, 'We're going to stop here because we're getting into a danger zone,' or, 'We're in a safe zone where the drug will likely be effective,'" Dr. Bennett adds. "Every patient is different, and this pharmacodynamic data will offer a roadmap for success."

From idea to reality: Sandip Vibhute, PhD, with the original chemical building block and the final drug

Ohio State has opened the clinical trial for JBZ-001 in its state-of-the-art outpatient Clinical Treatment Unit (see feature on page 28).

Instant benefit, future promise

Investigators associated with the JBZ-001 clinical trial, which recently opened for patient accrual, are excited about its prospects for quick therapeutic results. Dr. Biglione says Jabez Biosciences has carefully "put into place all their clinical operations to work with our phase I unit, Dr. Alahmadi and our Clinical Trials Office" to ensure smooth coordination among all parties.

> *"This study has the potential to immediately help some patients for whom previous therapies have failed. This is the goal of clinical trials in medicine."*
>
> **Sebastian Biglione, PhD, PharmD**

"For many patients," adds Dr. Bennett, "standard therapy eventually fails, and there's a huge unmet medical need for additional treatments to help them. Our newly created DHODH inhibitor holds much promise as a therapeutic option that offers renewed hope for many patients, now and in the future."

To learn more about the JBZ-001 clinical trial or to refer a patient, contact Asrar Alahmadi, MBBS, or Cynthia Jenkins in the OSUCCC – James Clinical Trials Office.

Vital roles of support and collaboration

The investigators also stress the importance of the extensive philanthropic support they have received for large segments of this work from the **Harry T. Mangurian Jr. Foundation**, the **Paula and Rodger Riney Foundation** and **Pelotonia**, the community and annual cycling event series that raise millions of dollars for cancer research at the OSUCCC – James.

Nor can they overstate the contributions of many other collaborators at Ohio State, including **Mitch Phelps, PhD**; Min Hai; Joo Young Na, PhD; **Celeste Alverez, PhD**; Tyler Wilson, PhD; Janel Ezzell, PhD; **Alice Mims, MD**; **Uma Borate, MBBS**; **David Carbone, MD, PhD**; **Don Benson, MD, PhD**; and **Robert Wesolowski, MD**. They also acknowledge the contributions of Dr. Byrd and some of his colleagues formerly at Ohio State, (e.g., Erin Hertlein, PhD, and Ola Elgamal, PhD).

"This is a massive collaborative effort that has progressed over several years and is still unfolding," Dr. Bennett says. "It's exciting to think about where it might lead."

Institutional News

Paskett elected to AACR Board of Directors

Electra Paskett, PhD, MSPH, FACE

Electra Paskett, PhD, MSPH, FACE, deputy director for population sciences and community outreach at the OSUCCC – James, was elected to a three-year term on the American Association for Cancer Research (AACR) Board of Directors. Her term started April 8, 2024. The AACR includes more than 58,000 members in 141 countries.

Dr. Paskett also is founding director of the Center for Community Outreach and Engagement at the OSUCCC – James and holds the Marion N. Rowley Designated Chair in Cancer Research. She has made major contributions to improving public health and health care by conducting research that has enabled her and colleagues to design interventions that help people prevent or reduce the burden of cancer – particularly in racial and ethnic-minority groups and underserved populations.

Her heavily funded research program, which is nationally recognized for studying cancer health disparities, uses a team approach to understanding and intervening in improving cancer prevention and control interventions and concerns cancer survivors experience.

Nobel Prize laureate Sir Paul Nurse is recipient of 2024 Block Memorial Lectureship Award

Sir Paul Nurse, OM, CH, FRS

Sir Paul Nurse, OM, CH, FRS, a renowned geneticist and cell biologist who shared the 2001 Nobel Prize in Physiology or Medicine with two others for their discoveries of protein molecules that control cell division, received the 26th Herbert and Maxine Block Memorial Lectureship Award for Distinguished Achievement in Cancer in September 2024 and delivered the Block Lecture 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 a prominent researcher who then visits Ohio State to accept the honor, lecture about his or her work and select a junior faculty member to mentor for two years.

Li-Chun Tu, PhD

Sir Paul, founding director and chief executive of the Francis Crick Institute in London, England, selected **Li-Chun Tu, PhD**, an assistant professor in the Department of Biological Chemistry and Pharmacology and a researcher at the OSUCCC – James. Dr. Tu studies the origin and underlying physical principles of genetic mutations that lead to cancer.

Former AACR President receives OSUCCC – James Bloomfield Legacy Award

Electra Paskett, PhD, MSPH, FACE, presents the award to Elizabeth Jaffee, MD

Elizabeth Jaffee, MD, a globally renowned expert in cancer immunology and pancreatic cancer, received the **2025 Clara D. Bloomfield, MD, Legacy Award** and delivered a keynote address at a "Celebrating Women in Oncology" luncheon held by the OSUCCC – James in connection with the International Day of Women and Girls in Science, observed annually on Feb. 11.

Named in honor of an internationally renowned cancer researcher, clinician, educator and administrator who served Ohio State's cancer program for 23 years, the Bloomfield Legacy Award recognizes individuals dedicated to mentoring and development of the next generation of cancer researchers and clinicians. Dr. Bloomfield directed the OSUCCC from 1997-2003 and then served as cancer scholar and senior advisor until her death in 2020.

Dr. Jaffee, the third recipient of this award, is deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University and was president of AACR from 2018-19.

Appointments

Anil Parwani, MD, PhD, MBA

Anil Parwani, MD, PhD, MBA, was appointed as chair of the Department of Pathology in Ohio State's College of Medicine. Dr. Parwani is a Distinguished Professor and serves as vice chair and director of Anatomic Pathology, director of Pathology

Informatics and director of the Digital Pathology Shared Resource at the OSUCCC – James, where he is in the Molecular Carcinogenesis and Chemoprevention Program. An expert in genitourinary pathology, Dr. Parwani has focused his research on diagnostic and prognostic markers in bladder, prostate and renal cell carcinoma. He also is an internationally recognized leader in digital pathology and pathology informatics.

Amanda Toland, PhD

Amanda Toland, PhD, professor and interim chair of the Department of Cancer Biology and Genetics at Ohio State, was named as associate director for cancer research training and education coordination (CRTEC) and as director of the OSUCCC – James Center for Cancer Mentoring, Education, Leadership and Oncology-related Training (CAMELOT). CAMELOT is a hub for fostering cancer research and education for all levels of learners, and for disseminating those opportunities across the university. Its goal is to coordinate existing and develop new research training activities to prepare the next generation of cancer scientists. Dr. Toland also is a member of the OSUCCC – James Cancer Biology Program.

The OSUCCC – James appointed three deputy directors who will help elevate and align the goals, strategic priorities and operations within the CCC's organizational structure. The new deputy directors are: **Matthew Ringel, MD**, deputy director for basic research; **Electra Paskett, PhD, MSPH, FACE**, deputy director for population sciences and community outreach; and **Zihai Li, MD, PhD**, deputy director for translational research. They report to OSUCCC Director **Raphael E. Pollock, MD, PhD, FACS**.

Deputy Directors (from left) Li, Paskett and Ringel

Four of the five research programs within the OSUCCC – James have expanded from two to three co-leaders to reflect the ever-widening scope of research endeavors and funding. Below is the expanded leadership model, with new co-leaders denoted with an asterisk:

Cancer Biology (CB) Program
- **Matthew Ringel, MD**
- **Gina Sizemore, PhD***
- **Dawn Chandler, PhD***

Cancer Control (CC) Program
- **Theodore Wagener, PhD**
- **Diane Von Ah, PhD, RN**
- **Jesse Plascak, PhD, MPH***

Leukemia and Hematologic Malignancies (LHM) Program
- **Jennifer Woyach, MD**
- **Rosa Lapalombella, PhD**
- **Alice Mims, MD***

Molecular Carcinogenesis and Chemoprevention (MCC) Program
- **Steven Clinton, MD, PhD**
- **Richard Fishel, PhD**
- **Zobeida Cruz-Monserrate, PhD***

Translational Therapeutics (TT) Program
- **David Carbone, MD, PhD**
- **Blake Peterson, PhD**
- **Elaine Mardis, PhD**

2025 Institutional Events

OSUCCC – James experts participated or will participate in these national annual meetings/ conferences in the first half of 2025:

- Arab Health 2025, Jan. 27-30
- 2025 Catchment Area Data Excellence (CADEX) Conference, Jan. 29-31
- American Association for Cancer Research® (AACR) Special Conference in Cancer Research, March 11-13
- 2025 Society of Gynecology Oncology (SGO) Annual Meeting, March 15-18
- 2025 American Society of Preventive Oncology (ASPO) Annual Meeting, April 6-8
- 2025 American Association for Cancer Research® (AACR) Annual Meeting, April 25-30
- 2025 American Society of Clinical Oncology® (ASCO) Annual Meeting, May 30-June 3
- BIO International Convention/BIO 2025, June 16-19

Prominent Studies

Kai He, MD, PhD

Cell therapy approach harnesses the immune system in a different way to stop cancer

A new cancer treatment that uses a person's own immune cells has been approved by the U.S. Food and Drug Administration (FDA) for treating the most dangerous type of skin cancer. Now this form of cellular therapy (tumor-infiltrating lymphocyte, or **TIL therapy**) is showing promise in treating advanced lung cancers through clinical trials underway at the OSUCCC – James.

Kai He, MD, PhD, a thoracic medical oncologist and physician-scientist with the Pelotonia Institute for Immuno-Oncology at the OSUCCC – James, says TIL therapy boosts the immune system's ability to overcome the abnormal microenvironment inside a tumor that allows cancer to grow unchecked.

Robert Wesolowski, MD

Study finds triple-combination therapy effective in advanced breast cancer subtype

A study involving over 100 patients at 17 cancer centers across the United States, including the OSUCCC – James, has found that a triple combination of targeted drugs and endocrine (hormone) therapy is a promising treatment option for the most common subtype of advanced breast cancer.

The phase Ib study combined the targeted drugs gedatolisib and palbociclib with endocrine therapy in patients with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced cancer, and the investigators are encouraged by the results.

Robert Wesolowski, MD, associate professor in the Division of Medical Oncology at Ohio State and member of the TT Program at the OSUCCC – James, was senior author for the study, which was published in the journal *The Lancet Oncology*. Dr. Wesolowski and colleagues stated in their article that finding therapies with improved effectiveness versus available standards of care is paramount for breast cancer, the leading cause of cancer death among women worldwide.

Vaping and smoking together increases lung cancer risk fourfold

People who both vape and smoke are four times more likely to develop lung cancer than people who just smoke, according to a study published by the OSUCCC – James and College of Public Health. These findings were consistent across gender and race.

The researchers analyzed cigarette smoking and use of electronic cigarettes in 4,975 people with lung cancer compared to a control group of 27,294 people without cancer. All subjects were from the same general geographic location (treated in Columbus, Ohio).

This was the first study to provide evidence that smoking in combination with vaping increases cancer risk compared to smoking alone. It was published in the *Journal of Oncology Research and Therapy*. **Randall Harris, MD, PhD**, professor in the Division of Epidemiology at Ohio State, was corresponding author. **Marisa Bittoni, PhD**, a researcher in the Division of Medical Oncology, was lead author. **David Carbone, MD, PhD**, professor and director of the Thoracic Oncology Center at the OSUCCC – James, where he also co-leads the TT Program, was a co-author.

Naresh Bumma, MD

Study finds effective new therapy for patients with treatment-resistant multiple myeloma

Ohio State medical researchers took part in an international first-in-human clinical trial that demonstrated the effectiveness of a new antibody treatment for patients with relapsed/refractory multiple myeloma (RRMM), a blood cancer that remains incurable despite therapeutic advances.

Naresh Bumma, MD, assistant professor in the Division of Hematology at Ohio State, was first author of an article about the phase I/II study that was published in the *Journal of Clinical Oncology*. Madhav Dhodapkar, MD, of Emory University School of Medicine, was corresponding author.

The scientists state that, with repeated cycles of relapse and remission, RRMM patients face increasingly shorter periods of remission, and their disease becomes resistant to existing therapies. But through this study, they believe they have found an immunotherapy agent called linvoseltamab that is well tolerated and induces durable remissions.

Eric A. Singer, MD, MA, MS

International study reveals potential new treatment for high-risk bladder cancer

The OSUCCC – James participated in an international clinical trial that demonstrated a potentially suitable treatment option for certain patients with high-risk bladder cancer who were unresponsive to standard treatment and who declined or are ineligible for cystectomy (bladder removal).

The trial was an expansion of an earlier study (KEYNOTE-57, cohort A) that led to FDA approval of an immunotherapy drug called pembrolizumab for treating patients with a type of non-muscle-invasive bladder cancer known as carcinoma in situ with or without papillary bladder tumors. Marketed as Keytruda®, pembrolizumab works with the body's immune system to combat cancer.

Eric A. Singer, MD, MA, MS, professor of urology and director of the Division of Urologic Oncology at Ohio State, and a member of the TT Program at the OSUCCC – James, led the research at the OSUCCC – James for this phase II study, which involved patients at 54 hospitals or cancer centers in 14 countries. The study was published in the journal *The Lancet Oncology*.

David Carbone, MD, PhD

Radon gas likely linked to alarming rise in non-smoking lung cancer

Lung cancer is often considered a "smoker's disease," but 15-20% of newly diagnosed lung cancers occur in people who have never smoked, many in their 40s or 50s. Doctors say this rise in non-smoking lung cancer cases is likely linked to long-term, high exposures of radon gas.

This colorless, odorless gas is emitted from the breakdown of radioactive material naturally occurring underground that seeps through building foundations. It can accumulate in people's homes and lungs unless they know to test for it.

The U.S. Environmental Protection Agency recommends regular radon testing and taking corrective measures to reduce exposure levels in homes, but a consumer survey conducted on behalf of the OSUCCC – James showed that 75% of Americans have not had their homes tested for radon, and 55% are not concerned about exposure in their homes, community or schools. **David Carbone, MD, PhD**, director of the Thoracic Oncology Center at the OSUCCC – James, says everyone should be aware and concerned about radon exposure and ways to reduce it.

David Bond, MD

Study points to possible therapeutic option for patients with Richter transformation

An international study in which researchers at the OSUCCC – James played a lead role has shown the effectiveness of chimeric antigen receptor (CAR) T-cell therapy in treating patients with Richter transformation (RT), a blood cancer with poor prognosis and no standard therapies.

RT occurs when another blood cancer, chronic lymphocytic leukemia, transforms into an aggressive form of lymphoma, most commonly large B-cell lymphoma (LBCL). Although there is no standard of care for RT, treatment is usually modeled after LBCL therapy, but median overall survival after RT diagnosis ranges from three months to a year.

David Bond, MD, assistant professor in the Division of Hematology at Ohio State, was co-first author of the study, which was published in the *Journal of Clinical Oncology*. The study involved 12 cancer centers from around the world and sought to characterize the safety and effectiveness of anti-CD19 CAR T-cell therapy for patients with RT. CAR T-cell therapy involves removing a patient's T cells, modifying them in a laboratory to boost their ability to kill cancer cells, and returning them to the patient.

Ted Wagener, PhD

Ahmad El Hellani, PhD

Marielle Brinkman, BS

Ohio State researchers advise caution against possible tobacco industry tactics to offset proposed nicotine standard for cigarettes

Cancer researchers and public health officials should anticipate and work to prevent an array of tactics the tobacco industry could use to thwart a nicotine product standard for cigarettes that the U.S Food and Drug Administration (FDA) may implement to reduce smoking-related disease and death.

So say researchers with the OSUCCC – James Center for Tobacco Research (CTR) in a *New England Journal of Medicine* editorial titled "Reengineering Addiction – The Tobacco Industry's Potential Response to a Nicotine Standard for Cigarettes." The authors state that, to reduce the harm caused by cigarette smoking, the FDA is considering implementing a nicotine product standard under which cigarettes could contain only very low and possibly non-addictive levels of nicotine. But the scientists add that researchers and policymakers must be prepared for the tobacco industry's potential response to nicotine legislation.

Co-authors are CTR Director **Ted Wagener, PhD**, professor in the Division of Medical Oncology and co-leader of the OSUCCC – James CC Program; **Ahmad El Hellani, PhD**, assistant professor in the College of Public Health; and **Marielle Brinkman, BS**, research professor in the College of Public Health and member of the CC Program.

Kellie Archer, PhD

Ann-Kathrin Eisfeld, MD

Study shows effectiveness of new method for grouping certain acute myeloid leukemia patients

An international study led by researchers at the OSUCCC – James identified a new molecular signature that allows for more precise prognostic grouping of patients with cytogenetically normal acute myeloid leukemia (CN-AML).

The researchers achieved this by developing a mixture-cure model (survival analysis) to identify prognostically relevant genes that can help distinguish CN-AML patients who may be considered cured from CN-AML patients who are either at low or high risk of relapse following treatment. This information could help clinicians determine optimal individualized treatments for these patients.

Kellie Archer, PhD, professor and chair of the Division of Biostatistics in the College of Public Health at Ohio State, was study designer and corresponding author. **Ann-Kathrin Eisfeld, MD**, director of the Clara D. Bloomfield Center for Leukemia Outcomes Research at the OSUCCC – James, was senior author for the study, which was published in the *Journal of Hematologic Oncology*.

Jennifer Woyach, MD

Study sheds light on gene mutations that cause resistance to CLL therapies

OSUCCC – James researchers played a lead role in an international study that has provided a profile of genetic mutations that cause patients treated for chronic lymphocytic leukemia (CLL) to develop resistance to the drugs ibrutinib and acalabrutinib, enabling their cancer to recur.

The study will help researchers better understand mutational patterns commonly seen among patients treated with these drugs so physicians can adjust therapies and make them more effective. First author for this study, published in the journal *Blood*, was **Jennifer Woyach, MD**, professor in the Division of Hematology at Ohio State and co-leader of the LHM Program at the OSUCCC – James.

Ann-Kathrin Eisfeld, MD

Elaine Mardis, PhD

Study shows key role of genetics in identifying ancestry-based aspects of cancer, survival

Researchers at the OSUCCC – James led a global study that identified molecular predictors of survival among Black patients with acute myeloid leukemia (AML). The study suggests a need to modify current AML risk layers by including ancestry-specific genetic factors and testing those in clinical trials.

Co-corresponding authors for study, published in the journal *Nature Genetics*, are **Ann-Kathrin Eisfeld, MD**, director of the Clara D. Bloomfield Center for Leukemia Outcomes Research at the OSUCCC – James, and **Elaine Mardis, PhD**, co-leader of the OSUCCC – James TT Program.

The authors note that, while many genomic studies over the years have helped scientists classify AML subtypes, the genomic profiles and biomarkers among diverse patients with AML are under studied, resulting in sustained disparities in survival among patients with this disease. They hope their study highlights the need to have more diversity in clinical studies and subsequent biobanking.

Chyke Doubeni, MD, MPH

At-home colon cancer screening reduces risk of colorectal cancer death

A noninvasive colorectal cancer screening test that can be done at home could reduce the risk of colorectal cancer death by 33%, according to a study published in the journal *JAMA Network Open*. This is the first study to evaluate this tool's effectiveness in specific racial groups.

Researchers at the OSUCCC – James and Kaiser Permanente evaluated data from nearly 11,000 patients who underwent at-home fecal immunochemical testing (FIT) among Kaiser Permanente's members in California between 2002 and 2017. Kaiser Permanente has one of the largest at-home screening programs in the United States and has been a leader in implementing at-home colorectal cancer screening to increase screening guideline compliance and improve racial disparity gaps.

Chyke Doubeni, MD, MPH, chief health equity officer at the Ohio State Wexner Medical Center and associate director at the OSUCCC – James, was senior author.

Pelotonia-Funded Research

Pelotonia 2024

Pelotonia is a community and an annual cycling event series that raise millions of dollars for cancer research at the OSUCCC – James. On Aug. 3-4, 2024, some 7,000 Riders – including hundreds of survivors – from 44 U.S. states and seven countries participated in Ride Weekend, which was supported by 3,000 volunteers.

Complementing Ride Weekend was the second annual Gravel Day, a Sept. 21 event in which cyclists wheeled over the back roads of southeastern Ohio to raise additional funds for cancer research.

Altogether in 2024, the Pelotonia community **raised more than $26.2 million**, bringing the 16-year fundraising total to **over $309.8 million** since the first Ride Weekend was held in 2009. Every dollar raised by Riders, Challengers, Volunteers and Donors goes directly to cancer research at the OSUCCC – James thanks to Pelotonia's major funding partners. Read more about Pelotonia at **Pelotonia.org**.

"By harnessing the power of the Pelotonia community – which has raised an astounding $309 million in 16 years – we are able to build a world-class immuno-oncology team, turn innovative ideas into treatments, inspire the next generation, and more. It is truly helping us create a cancer-free world."

Raphael E. Pollock, MD, PhD, FACS

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 Nationwide Children's Hospital in Columbus, Ohio.

DELIVERING
NEW THERAPIES THAT GIVE HOPE

Strategic Research Investments
Pelotonia dollars support initiatives such as the Drug Development Institute, digital pathology, the Total Cancer Care® protocol, the Center for Cancer Engineering and proton therapy.

FUNDING
INNOVATIVE IDEAS

Idea Grants
Pelotonia-funded Idea Grants help teams of cancer researchers gather early data for innovative ideas so they can later apply for larger grants. The OSUCCC – James has awarded 220 Pelotonia Idea Grants since 2010 totaling $31.2 million.

INSPIRING
THE NEXT GENERATION OF CANCER RESEARCHERS

Pelotonia Scholars Program
The OSUCCC – James annually awards $2 million to train the next generation of cancer researchers. Since 2010, 712 scholarships have been awarded to Ohio State students from 53 countries and 36 U.S. states.

ADVANCING
NEW WAYS OF PREVENTION AND DIAGNOSIS

Instruments of Discovery
Pelotonia dollars provide sophisticated equipment to conduct cutting-edge cancer research, including for OSUCCC – James Shared Resources, which provide specialized, centralized services to cancer researchers.

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

CREATING
OPPORTUNITIES TO TRANSFORM CANCER CARE

Recruitment
Bringing the brightest minds in cancer research to Ohio State, the OSUCCC – James has recruited 296 top scientists since 2010 with Pelotonia support.

Pelotonia Institute for Immuno-Oncology (PIIO)
Established in 2019 through an initial pledge of $102 million from the Pelotonia community, the PIIO has recruited top tier faculty researchers, bringing the total number of PIIO faculty to 128 scientists who drive breakthroughs in immuno-oncology, a discipline that harnesses the body's immune system to combat cancer.

Read more at cancer.osu.edu/PelotoniaImpact.

Pelotonia Scholars Program awards funding to 32 student researchers in 2024

The OSUCCC – James announced two rounds of Pelotonia Scholar Awards in 2024 that will enable 32 Ohio State students to conduct cancer research in the labs of faculty mentors at the OSUCCC – James.

The 2024 Pelotonia Scholars include 13 undergraduate students, 14 graduate students, three postdoctoral researchers and two medical students. Since the program began in 2010, it has awarded 712 scholarships to students in many disciplines and all levels of study who are interested in cancer research and represent 53 countries and 36 U.S. states. The OSUCCC – James annually allocates $2 million to this program from funds generated by Pelotonia.

New Pelotonia-funded Idea Grants are helping cancer researchers pursue innovative studies

The OSUCCC – James in spring 2024 awarded two new Pelotonia-funded Idea Grants totaling $280,000 that will help teams of Ohio State faculty researchers produce early data for innovative cancer studies that could lead to 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 for two-year periods. Since 2010, the OSUCCC – James has awarded 220 Pelotonia-funded Idea Grants totaling $31.2 million.

Grant titles, names of awardees (an asterisk denotes principal investigator) and brief descriptions of the research projects are below:

"Targeting the DNA Damage Response in Mantle Cell Lymphoma (MCL)" (Lapo Alinari, MD, PhD*, Matthew Summers, PhD, Jack Yalowich, PhD, Ken Young, MD, PhD (of Duke University), Xiaoli Zhang, PhD) –This proposal will characterize the expression and function of the transducin ß-like protein 1 (TBL1) in MCL, determine the mechanism of MCL cell death induced by targeting TBL1, and establish TBL1 as a novel therapeutic target in MCL.

"Targeting Chromosomal Instability in Breast Cancer" (Steven Sizemore, PhD, and Matthew Summers, PhD*) – Researchers will extend their preliminary work to establish preclinical proof-of-concept evidence demonstrating the effectiveness of targeting the KIF20A protein – which is involved in cellular proliferation and is overexpressed in many cancers, including breast cancer – to impact the growth of breast cancer cells and tumors and enhance the efficacy of paclitaxel therapy.

In addition, the OSUCCC – James in spring 2024 awarded a two-year, $170,000 Clinical Trials Grant funded by Pelotonia to **Sameek Roychowdhury, MD, PhD***, and **Aharon Freud, MD, PhD**, for a study titled **"Defining FGR as an Actionable Precision Oncology Target for Pancreatic Cancer."** This project will bring personalized or precision medicine to patients with advanced pancreatic cancer. It includes a clinical trial, developed with **Zachary Risch, MD**, that uses telehealth to reach patients around the United States with pancreatic cancer and *FGFR* gene mutations.

Cottini awarded inaugural Mason Fisher Grant

Francesca Cottini, MD

Francesca Cottini, MD, assistant professor in the Division of Hematology at Ohio State and member of the TT Program at the OSUCCC – James, is the inaugural recipient of the recently established Mason Fisher Grant.

Funded entirely by Pelotonia dollars, the Mason Fisher Grant Program provides early-career faculty members or learners (students, residents, fellows) in Ohio State's College of Medicine or the OSUCCC – James with up to $50,000 to advance their research of genetic mutations that can lead to cancer. Dr. Cottini will apply her $50,000 grant toward understanding why patients with myeloma are at greater risk of developing a second hematologic malignancy, such as acute leukemia and myelodysplastic syndrome.

The grant program honors Mason Fisher, an Ohio State medical student who passed away following a medical event that occurred while he was riding in the 2022 Pelotonia. Mason, who wanted to be a cancer surgeon-scientist, was a passionate advocate for research and rode in Pelotonia for three years.

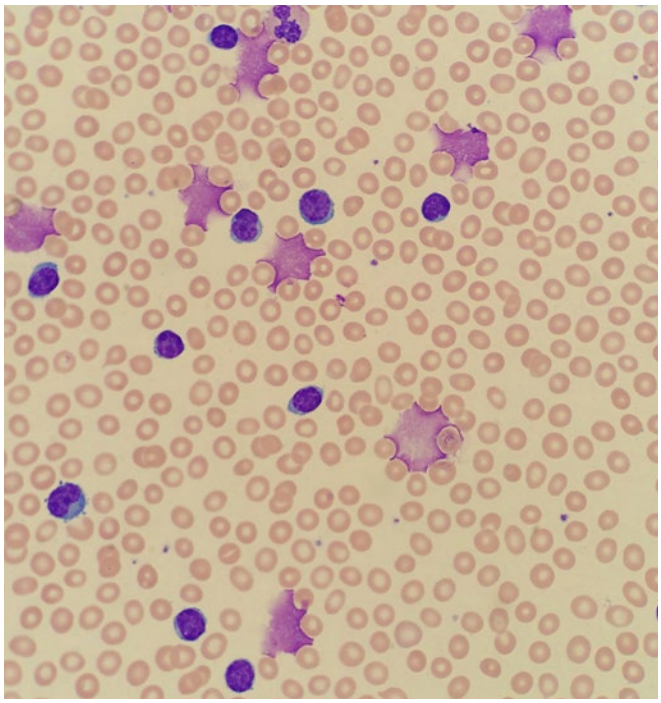
Study explores novel therapeutic treatment for glioblastoma

A study led by researchers at the OSUCCC – James has found that combining a brain-penetrating antipsychotic drug called pimozide with a clinically investigative glutamine metabolism inhibitor can suppress the growth of glioblastoma, the most lethal form of brain cancer.

Deliang Guo, PhD

Lead author for the study, published online in the journal *Cell Reports Medicine*, was **Deliang Guo, PhD**, founding director of the Center for Cancer Metabolism at Ohio State, where he also is a professor in the Department of Radiation Oncology and a member of the TT Program at the OSUCCC – James.

This study was supported in part by Pelotonia funding and the Urban and Shelly Meyer Fund for Cancer Research, as well as grants from the NCI and the National Institute for Neurological Disorders and Stroke.



Chronic lymphocytic leukemia blood smear

Tumor cell migration in CLL may be thwarted by intervention at protein receptor site

A study led by researchers at the OSUCCC – James has shown the migratory role of a protein called Siglec-6 in patients with chronic lymphocytic leukemia (CLL) and has revealed that blocking the protein's activity could stop the progression and spread of CLL cells.

CLL, a cancer of blood, bone marrow cells, is the most common form of leukemia in adults. B-CLL cells that are found in circulating peripheral blood migrate to bone marrow and secondary lymphoid tissues. OSUCCC – James scientists believe the role played by Siglec-6, which is found on CLL cells, makes it a promising target for therapeutic intervention.

Natarajan Muthusamy, DVM, PhD,

Natarajan Muthusamy, DVM, PhD, a professor in the Division of Hematology at Ohio State and member of the LHM Program at the OSUCCC – James, was corresponding author of the study, published in the journal *Nature Communications*. This work was supported in part by a Pelotonia Idea Grant to Dr. Muthusamy and a graduate Pelotonia scholarship awarded to first author Jessica Nunes.

Molecular findings could lead to new treatments for multiple myeloma

Researchers at the OSUCCC – James have reported molecular findings that could lead to new approaches for treating patients with multiple myeloma (MM), an incurable blood cancer that occurs when plasma cells multiply abnormally and build up in bone marrow.

Published in the journal *Leukemia*, the study was led by corresponding author **Francesca Cottini, MD**, assistant professor in the Division of Hematology at Ohio State and member of the TT Program at the OSUCCC – James.

The researchers state that more than 20 drugs have been approved for treating MM, but patients always relapse, largely because MM cells are able to escape the body's antitumor immune response even when patients are treated with immunomodulatory drugs, T-cell engagers and chimeric antigen receptor (CAR) T-cell therapies. This research, which enhances understanding of how cancerous MM cells evade the immune system, was supported in part by Pelotonia funding.

The Haslam 3 Foundation donates $2 million to Pelotonia for cancer research at the OSUCCC – James

In July 2024, Pelotonia announced a $2 million donation from Dee and Jimmy Haslam and The Haslam 3 Foundation to accelerate research on chronic lymphocytic leukemia (CLL) at the OSUCCC – James.

Dee and Jimmy are managing partners of Haslam Sports Group, a sports and entertainment group with ownership of the NFL's Cleveland Browns, operating rights to Major League Soccer's Columbus Crew, co-ownership of the NBA's Milwaukee Bucks and investors in the WNBA. The Haslam 3 Foundation is the family's philanthropic entity that gives to community organizations in Ohio and Tennessee.

Join us for Pelotonia 2025!

Ride Weekend → Aug. 1-3
Gravel Day → Oct. 4

PIIO Propels Immuno-oncology Research

In its first five years under the leadership of Founding Director **Zihai Li, MD, PhD**, the Pelotonia Institute for Immuno-Oncology (PIIO) – established in 2019 through an initial pledge of $102 million from the Pelotonia community – has worked to drive breakthroughs in immuno-oncology, a discipline that harnesses the body's immune system to combat cancer.

Here are examples of recent Pelotonia-supported studies conducted by members of the PIIO:

New cell-based immunotherapy offers hope for patients with metastatic lung cancer

Researchers at the OSUCCC – James say results of a phase II, multicenter clinical trial revealed that a new type of cell therapy is a promising potential treatment option for patients with stage 4 lung cancer who were previously treated but later developed resistance to other therapies. In the first global phase II clinical trial of lifileucel in lung cancer, oncologists showed the approach was safe and effective in treating metastatic non-small cell lung cancer. Study results were published in the journal *Cancer Discovery*. The lead author was **Kai He, MD, PhD**.

Study reveals GPR84 as a key metabolic switch for anti-tumorigenic macrophage polarization

A study led by **Gang Xin, PhD**, with first authorship by Jianying Li, a graduate research assistant in the labs of Drs. Xin and **Qin Ma, PhD**, shed light on a novel strategy for enhancing adaptive immunity against cancer. Tumor-associated macrophages (TAMs) play a crucial role in facilitating tumor escape from immune checkpoint blockade therapy. The study revealed that TAMs expressing elevated levels of the fatty acid receptor G-protein-coupled receptor 84 (GPR84) exhibit an anti-tumorigenic phenotype. Findings highlight GPR84 as a crucial metabolic sensing switch for orchestrating anti-tumorigenic macrophage polarization.

Targeting A2B adenosine receptor: Enhancing antitumor immunity through metabolic microenvironment modulation

PIIO investigators **Lai Wei, PhD**, **Dwight Owen, MD**, **Daniel Spakowicz, PhD**, **David Carbone, MD, PhD**, and **Mikhail Dikov, PhD**, along with other researchers, explored the role of the A2B adenosine receptor in regulating immunosuppressive metabolic stress within the tumor microenvironment. Their investigation included testing the novel A2B adenosine receptor antagonist PBF-1129 for its antitumor activity in mouse models and assessing its safety and immunologic efficacy in a phase I clinical trial involving patients with non-small cell lung cancer (NSCLC). Results show the potential of targeting the A2B adenosine receptor as a therapeutic strategy to enhance the effectiveness of immunotherapies.

PIIO by the Numbers

78 current IO clinical trials

29 scientists are pursuing IO-based clinical trials

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

Since 2019

1,340 published peer-reviewed articles

254 new IO trials

31 new faculty

35 Pelotonia Idea Grants

160+ new staff jobs

56 patents issued

73 technologies disclosed

Recent Recruits

The OSUCCC – James continuously works to bring the brightest minds in cancer research and clinical care to Ohio State. Here's a look at a few recently recruited renowned scientists who will play key roles in the cancer program.

Ravi V. Bellamkonda, PhD

Bellamkonda named Ohio State executive vice president and provost

Ohio State President Walter "Ted" Carter Jr. announced the selection of **Ravi V. Bellamkonda, PhD**, an accomplished scientist, higher-education administrator and cancer researcher, as The Ohio State University's next executive vice president and provost effective Jan. 14.

Dr. Bellamkonda was recruited from Emory University in Atlanta, where he was provost and executive vice president for academic affairs, as well as a member of the Discovery and Developmental Therapeutics Program at the Winship Cancer Institute. A bioengineer and neuroscientist, Dr. Bellamkonda focuses his research on the interplay of biomaterials and the nervous system for neural interfaces, nerve repair and brain tumor surgery. His lab has invented approaches to treat pediatric and adult brain tumors.

As Ohio State's provost, Dr. Bellamkonda will oversee a university-wide portfolio of programs and initiatives in the Office of Academic Affairs that support faculty and student success across the university's campuses. The deans of all 15 academic colleges and University Libraries report to the provost, who also serves on the President's Cabinet, which includes leaders of the Ohio State Wexner Medical Center and key administrative units.

Glen Barber, PhD, FRS

Barber directs Center for Innate Immunity and Inflammation at Ohio State's PIIO

Glen Barber, PhD, FRS, was recruited from the University of Miami (Florida) to serve as director of the Center for Innate Immunity and Inflammation in the OSUCCC – James Pelotonia Institute for Immuno-Oncology (PIIO). Dr. Barber also is associate director of entrepreneurship and technology commercialization.

He focuses his research on cellular sensing mechanisms that trigger the body's defense measures against microbial infection, and he has pioneered the use of viruses as cancer therapeutics and vaccines. Dr. Barber also is one of three recipients of the 2025 Paul Ehrlich and Ludwig Darmstaedter (PELD) Prize, Germany's highest medical award, for outstanding contributions to research in hematology, immunology or chemotherapy.

Christian Rolfo, MD, PhD, MBA

Ohio State appoints Rolfo to lead Division of Medical Oncology

Christian Rolfo, MD, PhD, MBA, is a renowned cancer researcher and physician who was recruited from the Mount Sinai Health System in New York to become director of the Division of Medical Oncology at Ohio State and associate director for early-phase clinical trials at the OSUCCC – James.

Dr. Rolfo's research focuses on drug development, immunotherapy and molecular oncology. As a clinical investigator in the Spanish Lung Cancer Group, he helped identify *EGFR* gene mutations in non-small cell lung cancer (NSCLC) in the Caucasian population. These findings, together with his studies of the drug erlotinib as first-line chemotherapy for patients with NSCLC with *EGFR* mutations, have fundamentally impacted treatment standards for this disease.

Clinical Spotlight

Blood and Marrow Transplant Program celebrates 40 years of service to patients

With four decades of experience in bone marrow transplants and peripheral blood stem cell transplants (PBSCTs), the Blood and Marrow Transplant (BMT) Program at the OSUCCC – James has long been at the forefront of innovative care for patients with hematologic malignancies and other blood disorders.

Since the first BMT was performed at Ohio State in February 1984, the program's internationally recognized specialists have completed more than 6,500 transplants using patient or donor cells. The BMT program is the longest-running in central Ohio and one of the most experienced in the nation.

Marcos de Lima, MD, director of both the BMT and the Cellular Therapy programs at the OSUCCC – James, says BMTs and PBSCTs are most often used for treating patients with leukemia, lymphoma or multiple myeloma, but they can also be used to treat other cancers, such as neuroblastoma and several additional malignant and nonmalignant conditions.

"These procedures restore or replace blood-making stem cells that were destroyed by high doses of chemotherapy or radiation therapy in patients being treated for certain cancers or other blood disorders," Dr. de Lima says. "Most blood-making cells are in bone marrow, but some, called PBSCs, are in the bloodstream or in umbilical cord blood."

Dr. de Lima says clinicians can harvest these cells from any of those locations for use in three types of transplant: autologous (patients receive their own stem cells that were removed before chemotherapy or radiation therapy); syngeneic (patients receive stem cells from their identical twin) or allogeneic (patients receive stem cells from a sibling, parent or unrelated donor).

OSUCCC – James BMT Program

40 years

6,500+ transplants

35 years as a National Marrow Donor Program member

Top 5 in clinical trial accruals

BMT Clinical Trials Network
Core Clinical Center

Because BMTs and PBSCTs are performed with needles or apheresis – and with later intravenous reinfusion of stem cells – no surgery is involved, but bone marrow harvests are performed in an operating room with the use of anesthesia. However, the preparatory process and the subsequent recovery period can be complex, requiring the care and guidance of providers with extensive experience, such as those at the OSUCCC – James.

Since it began in 1984, the BMT program has become the largest adult BMT program in Ohio in terms of patient volume. It has been a member of the National Marrow Donor Program for 35 years, and it has been accredited by the Foundation for the Accreditation of Cellular Therapy since 2003. In 2011, it became a BMT Clinical Trials Network (CTN) Core Clinical Center; per BMT CTN metrics, the OSUCCC – James consistently ranks among the top five in clinical trial accrual through this network of centers.

"BMT care is rapidly evolving with new options and recovery protocols," Dr. de Lima says.

"Our subspecialists are not only abreast of these advancements, but we are helping to define them through our BMT clinical trials and research programs."

Macros de Lima, MD

He adds that transplantation has evolved to also use genetically modified cells that target cancer cells and are individualized to a patient's type of leukemia or lymphoma, for example.

"The broader name of 'cell therapy' is now used to encompass these treatments and also other forms of cancer and non-cancer treatments, such as gene therapy for sickle cell anemia," he explains.

"Our multidisciplinary team understands that every patient's cancer is biologically unique and requires individually tailored treatments," Dr. de Lima says. "That's why we conduct research that translates to personalized care and leads to faster patient responses, fewer side effects and better outcomes."

Clinic focuses on immunotherapy side-effect management to give patients best quality of life

Immunotherapy extends life for many patients with cancer, but the treatments often come with side effects that diminish quality of life. A new clinic at the OSUCCC – James and the Pelotonia Institute for Immuno-Oncology helps manage autoimmune side effects of immunotherapy cancer treatment, allowing patients to live the fullest life possible during cancer treatment and long-term as a survivor.

Led by **Alexa Meara, MD**, the OSUCCC – James Immunotherapy Management Clinic was created to lessen the harm of cancer treatment. A rheumatologist who helps cancer survivors manage side effects of cancer treatment, Dr. Meara specializes in autoimmune diseases, which occur when the body's immune system attacks healthy cells.

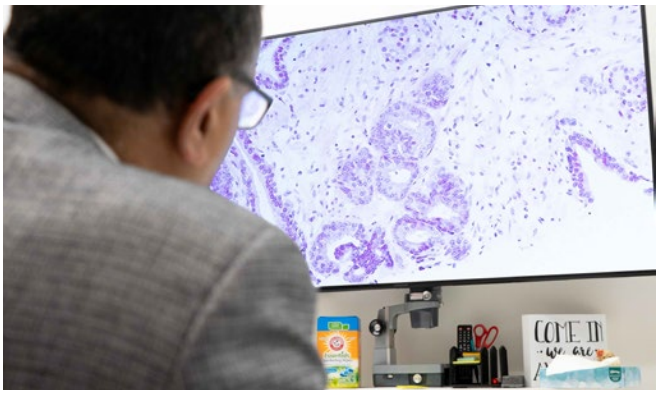
Alexa Meara, MD

OSUCCC – James offers online second opinions for select specialties in cancer care

Anyone diagnosed with cancer can gain clarity and confidence with an online second opinion from experts at the OSUCCC – James, who can provide insight on the diagnosis and recommend the best treatment options.

The second-opinion team works closely with patients and loved ones to review medical and imaging records, answer questions and prepare a written care plan. Second opinions may be appropriate for those who want to confirm a diagnosis or learn more about it, make decisions about the next medical steps, or discuss possible alternative treatments, including some that may be available only at the OSUCCC – James.

Click or scan the QR code to learn more



AI tools see beyond the human eye to better diagnose cancer

Digital pathology has both sped up and increased the accuracy of cancer diagnosis in the past 10 years, and now artificial intelligence (AI) could improve these tools even more. Most people think of AI as someone teaching a computer to recognize and respond (known as "supervised learning") to perform a specific task automatically; unsupervised learning involves teaching the computer to recognize and respond to certain things, but then allowing it to evolve to learn beyond what it was taught.

Though scientists are nowhere near unsupervised AI use in diagnosing cancer, **Anil Parwani, MD, PhD, MBA**, chair of the Department of Pathology at Ohio State, and member of the MCC Program at the OSUCCC – James, says these tools are becoming a powerful decision-support resource to confirm diagnoses made by trained pathologists. Long-term, they could address a global shortage of pathologists and fill gaps in care.

Ohio State among first in United States to perform surgery using next-generation robotic surgery

In April 2024, a surgical team at the OSUCCC – James was among the first in the United States to perform a surgery using the da Vinci 5 robotic system, which was recently approved by the U.S. Food and Drug Administration (FDA).

The 40-minute surgery, a gastric devascularization, was led by **Robert Merritt, MD**, director of the Division of Thoracic Surgery at Ohio State, and a team of operating room staff.

Surgeons with the OSUCCC – James and The Ohio State University Wexner Medical Center were involved in both preclinical and clinical trials used to test and validate the da Vinci 5 robotic system, including Dr. Merritt, who served as principal investigator of the studies at the OSUCCC – James, and **Michael Meara, MD**, medical director of robotics for Ohio State's hospitals.

Program helps kids understand loved one's cancer diagnosis, reduce fear of visiting hospital

When someone is diagnosed with cancer, their first thought is often not of themselves – but how to tell their loved ones about their diagnosis. This is especially the case for parents or grandparents of young children, for which the hospital can be an especially scary place to visit.

The OSUCCC – James is among a few hospitals in the country to offer certified child life specialists to support families experiencing a cancer diagnosis and prepare kids for what they will experience when visiting their loved one in an adult hospital.

Director of Survivorship in Cancer Support Services **Denise Schimming, APRN-CNP**, says when working with patients, their team recognized how important it was to offer this full spectrum of support to families and launched the Child Life Services program in collaboration with Nationwide Children's Hospital. Since then, the team has helped dozens of families navigate the physical and emotional transitions associated with navigating a cancer diagnosis and treatment process.

Research Grant Highlights

NIDCR grant: Study of modulating biologic pathway to improve oral cancer treatment

Oral cancer remains a major public health concern, but OSUCCC – James researchers have received a five-year, $3.2 million grant to study how the body's oral glucocorticoid system affects oral carcinogenesis and how this biologic pathway can be modulated to improve treatment outcomes.

Steve Oghumu, PhD

The grant was awarded by the National Institute of Dental and Craniofacial Research to principal investigator **Steve Oghumu, PhD**, associate professor in the Department of Pathology at Ohio State and a member of the MCC Program at the OSUCCC – James.

Glucocorticoids are naturally occurring steroids that have many functions throughout the body, including the oral cavity. Because of this, synthetic glucocorticoids have been developed for various treatments, including adjuvant therapy for patients with oral cancers. However, Dr. Oghumu and colleagues say recent evidence indicates synthetic glucocorticoids may promote tumor progression in some cases, thus challenging the use of these compounds in patients with premalignant and malignant oral disease.

NCI grant: Awarded to establish course in effective oncology clinical trial design

The National Cancer Institute (NCI) has awarded OSUCCC – James researchers a five-year, $1.57 million grant to establish a course that will educate oncology trainees and junior faculty from any cancer specialty in applying Good Clinical Practice (GCP) and scientific reasoning to clinical trial design.

Titled "Clinical Trial Concept in the Oncology Landscape (CTC)," the virtual and in-person course will address a nationwide need for thorough training on clinical trial design and execution to eventually benefit patients with cancer and support the professional development of junior oncology faculty.

Claire Verschraegen, MD

Dwight Owen, MD

Robert Wesolowski, MD

Principal investigators are **Claire Verschraegen, MD** (project leader), and **Dwight Owen, MD**. Both are medical oncologists in the TT Program at the OSUCCC – James. The course curriculum director will be **Robert Wesolowski, MD**, also a medical oncologist in the TT Program and co-investigator on this grant. Dr. Wesolowski is an expert in phase I clinical trial research.

NCI grant: Study of novel therapeutic approach to colorectal cancer lung metastasis

A five-year, $2.48 million grant from the NCI will help researchers at the OSUCCC – James and other institutions study a method of silencing a genetic mutation in colorectal cancer that has metastasized to the lungs.

Peixuan Guo, PhD

The project leader is **Peixuan Guo, PhD**, professor and director of the Center for RNA Nanobiotechnology and Nanomedicine in Ohio State's colleges of Pharmacy and Medicine. Dr. Guo, who also is a Fellow of the National Academy of Inventors and is in the TT Program at the OSUCCC – James, is one of three principal investigators for this multi-institutional grant.

The researchers state that colorectal cancer is the second-leading cause of cancer death, due primarily to *KRAS* gene mutations and subsequent lung metastasis. They note that the *KRAS* gene is considered "undruggable," but through RNA nanotechnology and exosomes, which enable scientists to create products with new structural attributes by engineering molecular features, this team has created a fusion ribonucleoprotein complex that can be transported into cancer cells to silence mutated *KRAS* genes.

NIH grant: Study to conduct trial of cancer symptom management app after successful pilot

Sharla Wells-Di Gregorio, PhD

A pilot trial led by **Sharla Wells-Di Gregorio, PhD**, a psychosocial oncology specialist at Ohio State, recently suggested that use of a new intervention could drive clinically significant improvements in a symptom cluster (sleep difficulties, anxiety, fatigue, depression) experienced by patients with advanced cancer.

Now, Dr. Wells-Di Gregorio, associate professor in the Division of Palliative Medicine and a member of the CC Program at the OSUCCC – James, has received a five-year, $3.8 million NIH grant to conduct a larger randomized, blinded trial of the FOCUS (Finding Our Center Under Stress) app that will include 120 participants with advanced lung cancer, prostate cancer, breast cancer, myeloma or melanoma.

She says there is strong evidence that cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT) can help with symptom control, but these interventions generally take 12-20 sessions and aren't designed for advanced cancer patients. This app incorporates elements of both therapies but is tailored to this population.

NCI grant: Study of CD200R blockade for cancer immunotherapy

The NCI awarded researchers at the OSUCCC – James a five-year, $3.26 million grant to study whether blocking a molecular pathway called CD200R enhances the immune system's ability to combat cancer.

Sujit Basu, MD, PhD

Principal investigator **Sujit Basu, MD, PhD**, of the TT Program at the OSUCCC – James, says the study also will explore whether simultaneously inhibiting angiogenesis – or thwarting formation of blood vessels that help sustain tumors – will improve the effectiveness of CD200R blockade therapy. CD200R is an immune checkpoint protein found on myeloid cells and certain T cells.

Dr. Basu, a professor in the Department of Pathology and the Division of Medical Oncology (Internal Medicine) at Ohio State, says information generated by this study will not only advance understanding of cancer pathogenesis but will also pave the way for human clinical trials of CD200R blockade-based novel combination therapies.

NCI grant: Study to explore if ligand molecules can enhance immunotherapy via protein activation

Susheela Tridandapani, PhD

Susheela Tridandapani, PhD, and **Jonathan Butchar, PhD**, both of the LHM Program at the OSUCCC – James, received a five-year, $3.1 million NCI grant for a ligand study that may enhance immunotherapy in patients with chronic lymphocytic leukemia (CLL). A ligand is a molecule that binds to another molecule.

Jonathan Butchar, PhD

Specifically, they and their colleagues seek to turn monocytes/macrophages that are immunosuppressive in CLL into allies in the fight against tumor cells. Current immunotherapy is hindered by the fact that macrophages, including nurse-like cells (NLC) and natural killer (NK) cells – which are immunosupportive in healthy people – are subverted in patients with CLL, protecting and nurturing tumor cells instead.

They hope the end result of this study will be a novel mechanism for activating monocytes and NK cells in CLL, enhancing monoclonal antibody-based therapies.

NCI grant: Study to examine novel approach to immunotherapy in non-small cell lung cancer

Zihai Li, MD, PhD

OSUCCC – James researchers will use a five-year, $3 million NCI grant to test the effectiveness of a monoclonal antibody they have developed as an immunotherapeutic agent in mouse models of non-small cell lung cancer (NSCLC).

Principal investigator is **Zihai Li, MD, PhD**, founding director of the PIIO at the OSUCCC – James, who says his team's study of the novel antibody, called PIIO-1, could lead to a phase I clinical trial to see if the agent will enhance the efficacy of standard immunotherapy known as immune checkpoint blockade (ICB) for NSCLC patients.

The scientists hypothesize that disrupting the glycoprotein-A repetitions predominant (GARP)-TGFβ

axis within the tumor microenvironment by using their PIIO-1 anti-GARP antibody will augment the antitumor immunity of CD8+ T cells and overcome resistance to ICB therapy in patients with NSCLC.

NCI grant renewal: T32 training grant for cancer prevention and control

Peter Shields, MD

The NCI awarded the OSUCCC – James and the Ohio State College of Medicine a five-year, approximately $2 million renewal of a T32 Institutional Training Grant to support postdoctoral researchers in cancer prevention and control.

Chyke Doubeni, MBBS, MPH

Program directors for the grant are **Peter Shields, MD** and **Chyke Doubeni, MBBS, MPH**. Associate program director is **Ce Shang, PhD**. All three are members of the CC Program at the OSUCCC – James.

Ce Shang, PhD

The T32 program helps institutions develop or enhance cancer research training opportunities for pre- and postdoctoral fellows.

NCI grant: Study to explore potential treatment target for patients with glioblastoma

Matthew Summers, PhD

A research team at the OSUCCC – James is probing a novel approach to the treatment of glioblastoma, the most common brain cancer in the United States. The median length of survival following diagnosis is 15-18 months, and the five-year survival rate is only 10%.

Monica Venere, PhD

Cancer biologists **Matthew Summers, PhD**, and **Monica Venere, PhD**, are working under a two-year, $405,000 NCI grant to investigate a potential treatment target called KIF20A, a protein that is essential in cytokinesis, the final step of mitosis.

Elevated KIF20A is associated with chromosomal instability and a poor prognosis in many tumor types, including glioblastoma.

NCI grant: Study to determine if dietary influences on gut microbiomes can impact colorectal cancer survival outcomes

Fred Tabung, PhD, MSPH

Researchers at the OSUCCC – James have received a two-year, $405,316 grant from the NCI to help determine whether a proinflammatory diet increases the risk of developing aggressive colorectal cancer (CRC) that leads to death.

Daniel Spakowicz, PhD

Principal investigator **Fred Tabung, PhD, MSPH**, assistant professor in the Division of Medical Oncology at Ohio State and a member of the MCC Program at the OSUCCC – James, says results of this project will help researchers design larger studies of dietary strategies for mitigating molecular disruption in the gut and tumor tissue that is associated with proinflammatory dietary patterns and CRC progression.

Xiaokui (Molly) Mo, PhD

Other Ohio State investigators in this project include **Daniel Spakowicz, PhD**, assistant professor in the Division of Medical Oncology and member of the MCC Program; and **Xiaokui (Molly) Mo, PhD**, associate professor in the Department of Bioinformatics and leader of statistical support for the MCC Program.

NCI grant: Study to examine new approach to reduce smoking in rural Appalachia

Brittney Keller-Hamilton, PhD, MPH

Researchers at the OSUCCC – James Center for Tobacco Research (CTR) will use a five-year, $3 million grant from the NCI to study the effectiveness of oral nicotine pouches in reducing tobacco use among smokers in rural Appalachia, which has the highest cancer incidence and mortality rates in the United States.

Ted Wagener, PhD

Principal investigators **Brittney Keller-Hamilton, PhD, MPH** (project leader), and **Ted Wagener, PhD**, director of the CTR, propose a new approach to reduce the high prevalence of cigarette smoking in that region: oral nicotine pouches, which contain nicotine but no tobacco and have a similar toxicant profile to medicinal nicotine replacement therapy.

Featured Clinical Trial

Study examines effectiveness of de-intensified radiotherapy in HPV-associated oropharyngeal cancer

Patient accrual is underway for a phase II clinical trial (**OSU-23083**) at the OSUCCC – James that will examine the effectiveness of using circulating DNA to guide lower-dose radiation therapy in patients with oropharyngeal cancer that is associated with the human papillomavirus (HPV).

Principal investigator **Sujith Baliga, MD**, associate professor in the Department of Radiation Oncology at Ohio State, says radiation therapy in this study uses high-energy X-rays or particles to kill cancer cells and shrink tumors. Recently, he adds, a blood test has been developed to detect HPV in the blood and determine how many viral particles are present.

"We want to compare tumor response and disease outcomes of using lower-dose radiation therapy with chemotherapy to the usual standard-of-care-dose radiotherapy in patients who rapidly clear the HPV particles from their blood during treatment," Dr. Baliga says.

Patients in this trial undergo external beam radiotherapy for five days a week for four weeks. They also receive cisplatin intravenously (IV) weekly or every three weeks, or carboplatin/paclitaxel IV weekly at the discretion of the treating physician for four weeks. Patients undergo blood sample collection for circulating tumor DNA testing at week four, and then are assigned to one of two study arms based on results.

After completion of study treatment, patients are followed every three months for up to 24 months. For more information, email Dr. Baliga at **sujith.baliga@osumc.edu**.

To search for cancer clinical trials at Ohio State, visit **go.osu.edu/cancerclinicaltrials**. 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 Treatment Unit and Clinical Trials Processing Laboratory

The Clinical Treatment Unit and the Clinical Trials Processing Laboratory Shared Resource (CTU/CTPLSR) enable OSUCCC – James investigators to conduct phase I and II clinical translational research in a sound, expedient and cost-effective manner.

The CTU is an ambulatory phase I unit in the OSUCCC – James that specializes in treating early clinical trial patients who require intense monitoring or complex correlative sample collection and processing. The CTPL enhances research quality by providing staff for high-volume procurement, processing, storage, delivery and shipment of research specimens for the correlative studies component of clinical trials. As part of the OSUCCC – James Clinical Trials Office (CTO), the CTU/CTPLSR supports all new CTO-managed oncology trials with a correlative specimen component.

Experts in the CTU/CTPLSR work closely with other OSUCCC – James Shared Resources, including the Pharmacoanalytical, Hematology, Tissue Bank, Clinical Translational Science, and Biorepository and Biospecimen Shared Resources. These collaborations provide protocol review and feasibility assessment, as well as specimen distribution to internal and external research laboratories.

The CTU/CTPLSR is led by Director **Dwight Owen, MD**; CTU Nurse Manager **Carrie Hennelly, MSN, BSN, RN**; and Assistant Director for Clinical Research **Megan Jukich, MA**.

Institutional Achievements

The National Cancer Institute Cancer Consortium, known as NRG Oncology, **ranked Ohio State No. 3 in the country in NCI-NRG-Clinical Trials Evaluation Program (CTEP) clinical trials activity** through the NCI Consortium in 2023-24. NRG Oncology is the world's largest and oldest NCI-based consortium in radiation oncology, breast cancer and gynecologic-oncology. The cancer program's CNS Radiation Oncology, Breast Radiation Oncology, Head and Neck Radiation Oncology and Gynecologic-Oncology teams had the largest contributions in that order. Ohio State also ranked No. 1 for national accruals on NRG Brain Tumor Radiation Oncology trials in 2024.

U.S. News & World Report listed the James Cancer Hospital and Solove Research Institute among **America's Best Hospitals for cancer care for the 26th straight year**. The James first appeared on the *U.S. News* list in 1999, less than a decade after opening in 1990, and has remained there since.

Becker's Hospital Review, a medical industry trade magazine that offers news and insights for hospital and health care system executives, included the OSUCCC – James on its **2024 list of 100+ hospitals and health systems recognized for excellence in oncology.**

The American Association of Critical-Care Nurses again awarded the James Surgical and Neurological Intensive Care Unit (JSNICU) at the OSUCCC – James with a **Beacon Award for Excellence**. This is the third time the JSNICU has earned this designation, given to only a select few nursing units in the United States each year based on rigorous standards in professional practice, patient care and outcomes in six categories. The JSNICU achieved this award at the silver level.

The College of American Pathologists Biorepository Accreditation Program **has accredited the OSUCCC – James Leukemia Tissue Bank (LTB) within the Division of Hematology** at Ohio State. Accreditation means the LTB, led by Director **Lapo Alinari, MD, PhD**, and Assistant Director **Christopher Manring, MBA**, complies with the highest national standards for safety and quality for biorepositories, and ensures that ethical and legal frameworks are in place for using biospecimens in cancer research.

For the **ninth consecutive year**, the OSUCCC – James has received the **Press Ganey HX Guardian of Excellence Award® for Patient Experience in Inpatient Care**, which recognizes the top 5% of health care facilities in the nation for sustained patient experience excellence during a single year.

The HX Guardian of Excellence Award for Patient Experience goes to organizations that have achieved the 95th percentile or higher for any of a set of designated Healthcare Providers and System (HCAHPS) measures, including likelihood to recommend, overall rating and/or teamwork.

Individual and Team Achievements

Glen Barber, PhD

Glen Barber, PhD, is one of three scientists awarded the **Paul Ehrlich and Ludwig Darmstaedter Prize**, an international award given annually by the Scientific Council of the Paul Ehrlich Foundation in Frankfurt, Germany. The prize honors scientists who have made outstanding contributions in fields of research represented by the late Paul Ehrlich, a German medical scientist and pioneer in hematology, immunology and chemotherapy. It's considered the most prestigious medical prize given in Germany.

Ann-Kathrin Eisfeld, MD

Ann-Kathrin Eisfeld, MD, was appointed **vice chair of the Alliance for Clinical Trials in Oncology Leukemia Correlative Science Committee**. The Alliance is one of four adult network groups that constitute the National Cancer Institute's National Clinical Trials Network (NCTN), along with one pediatric group and one Canadian group. As a vice chair, Dr. Eisfeld helps lead the committee's research, clinical trials and studies of acute and chronic leukemia.

Asrar Alahmadi, MBBS

Asrar Alahmadi, MBBS, received the **Robert A. Winn Excellence in Clinical Trials Career Development Award**, a two-year program that supports early-stage investigator physicians who are transforming and expanding access to the clinical research landscape.

Cheryl Lee, MD

Cheryl Lee, MD, received the **2024 Society of Urologic Oncology (SUO) Medal** at the annual meeting of the American Urological Association in San Antonio. The SUO Medal is presented to an individual for a specific achievement or significant contributions in the field of urologic oncology.

Kami Maddocks, MD

Kami Maddocks, MD, was named to the **Executive Committee of the Mantle Cell Lymphoma Consortium** (MCLC), which is a part of the Lymphoma Research Foundation. The MCLC contains nearly 150 international laboratory and clinical scientists whose research is focused on MCL.

Alexa Meara, MD

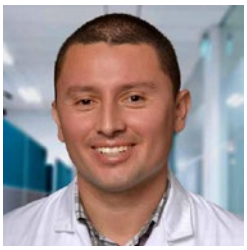
Alexa Meara, MD, was nominated to serve on an **American Society of Clinical Oncology (ASCO) expert panel** that will help update the Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy Guideline. Dr. Meara is a rheumatologist who directs the Immunotherapy Management Clinic at the OSUCCC – James.

Raphael E. Pollock, MD, PhD, FACS

Raphael E. Pollock, MD, PhD, FACS, was named as recipient of the **2024 Society of University Surgeons (SUS) Trailblazer Award**. The SUS presents this award each year to a surgeon who has made "trailblazing" contributions to surgery and meaningful impacts in academic surgery. Dr. Pollock accepted his award at the SUS 20th Academic Surgical Congress.

Matthew Kalady, MD

Matthew Kalady, MD, was appointed to a two-year term as **vice president of the board of trustees for the Research Foundation of the American Society of Colon and Rectal Surgeons**. The Research Foundation raises and awards funds to support research related to colorectal disease.



Daniel Gallego-Perez, PhD

Daniel Gallego-Perez, PhD, was inducted into the **American Institute for Medical and Biological Engineering's (AIMBE) College of Fellows** "for outstanding contributions to the development of nanotechnology-based platforms for non-viral gene delivery, tissue reprogramming, regenerative medicine and cancer therapies."

Carol R. Bradford, MD, MS, FACS

Carol R. Bradford, MD, MS, FACS, received the **2024 Margaret F. Butler Outstanding Mentor of Women in Head and Neck Surgery Award** from the American Head and Neck Society (AHNS). This award goes to those who demonstrate leadership in promoting gender diversity in head and neck surgery, and who encourage further training and mentorship of women leaders in this specialty.

Jessica Fleming, PhD

Jessica Fleming, PhD, was a recipient of a **2024 Annual Meeting Resident Recognition Award from the American Society for Radiation Oncology** (ASTRO). She was one of only 12 recipients of the award, which highlighted her work at the ASTRO Annual Meeting.

Ashley Cetnar, PhD

Ashley Cetnar, PhD, received the **2024 Karen Doppke Award for Women in Medical Physics**, an international award presented by the Division of Physics in the Department of Radiation Oncology at Massachusetts General Hospital and Harvard Medical School. The award honors mid-career, female-identifying physicists from all areas of medical physics for their contributions to the discipline. Dr. Cetnar is an associate professor in the Department of Radiation Oncology.

Russell Lonser, MD

Russell Lonser, MD, was elected as **chair of the American Board of Neurological Surgery** (ABNS), which works to encourage the study, improve the practice, elevate the standards and advance the science of neurological surgery. The ABNS conducts examinations of candidates who seek certification and issues certificates to those who meet board requirements and pass the exam.

Elaine Mardis, PhD

Elaine Mardis, PhD, was named **one of Research.com's Best Female Scientists**, ranking No. 35 in the United States and No. 56 in the world. Dr. Mardis is additionally ranked No. 42 in the world and No. 25 nationally for genetics. The Research.com rankings are based on publication data from sources such as OpenAlex and Crossref.

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

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