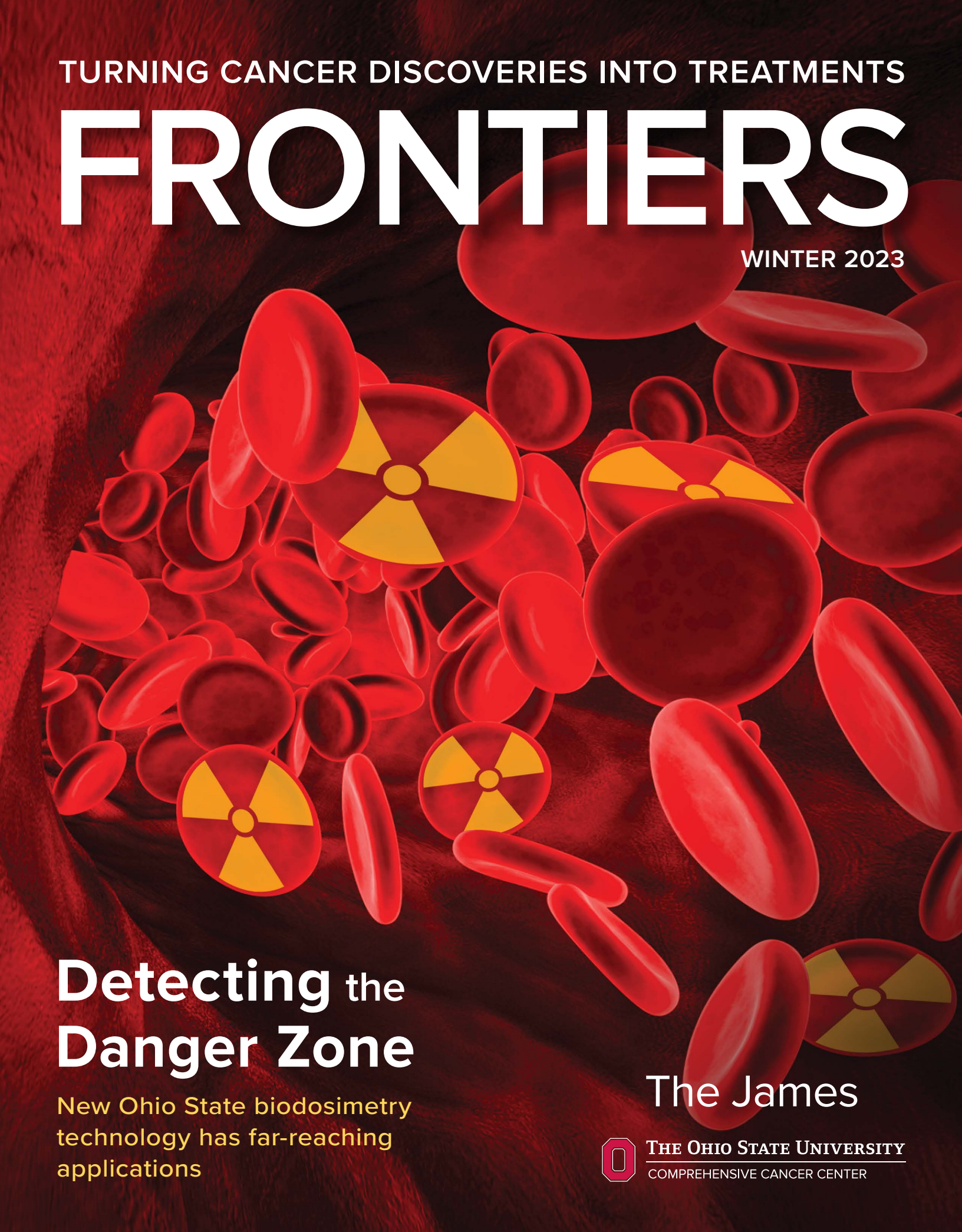
TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

WINTER 2023



Detecting the Danger Zone

New Ohio State biodosimetry technology has far-reaching applications

The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

UPFRONT

Coming full circle: Linking ibrutinib with Ohio State-discovered hairy cell leukemia

A study by researchers at the OSUCCC – James indicates that the oral targeted therapy drug ibrutinib, which was developed with major contributions from scientists at Ohio State, is an effective treatment option for patients with high-risk hairy cell leukemia (HCL), a disease first identified and described by Ohio State scientists.

HCL is a rare B-cell blood cancer diagnosed in 600 to 800 people annually in the United States. While it generally has a good prognosis, some patients with variants of the disease do not respond well to standard therapies or cannot tolerate side effects.

Principal investigator **Kerry Rogers, MD**, associate professor in the Division of Hematology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James, says this study shows that ibrutinib is a safe, effective and well-tolerated option for patients with relapsed or variant forms of HCL – an important discovery for people facing this diagnosis. The study was published in the journal *Blood*.

For this phase II clinical trial, a multi-institutional team led by the OSUCCC – James recruited 44 patients with high-risk HCL to test the effectiveness of ibrutinib. All participants had either classic HCL and had received other treatments, or they had the variant form, for which it is not likely that the standard chemotherapies, cladribine and pentostatin, would be effective.

Ibrutinib is in a class of drugs called Bruton's tyrosine kinase (BTK) inhibitors, which block chemical reactions in the body involved in cellular processes in the leukemia cells. Use of the drug for this study was experimental; however, ibrutinib is FDA approved for treating certain patients with mantle cell lymphoma and chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma. Scientists at the OSUCCC – James conducted much of the clinical and basic science that led to FDA approval.

HCL was initially identified in a landmark 1958 paper in the journal *Blood* by **Bertha Bouroncle, MD**, at Ohio State, in which she and Ohio State co-authors **Bruce Wiseman, MD**, and **Charles Doan, MD**, described a rare form of leukemia they originally called leukemic reticuloendotheliosis.

It later became known as hairy cell leukemia because of the ragged edges of the malignant cells, which display hair-like projections under a microscope. The paper characterized HCL as an independent form of chronic leukemia and provided the first comprehensive description of this disease. In the 1980s, Dr. Bouroncle and Ohio State scientists **Michael Grever, MD**, and **Eric Kraut, MD**, developed a drug called deoxycoformycin, or pentostatin, that helped change HCL from a uniformly fatal disease into one of the most treatable cancers.

To learn more about the OSUCCC – James, visit cancer.osu.edu.

***FRONTIERS*:**

TARA KUISICK
Editor

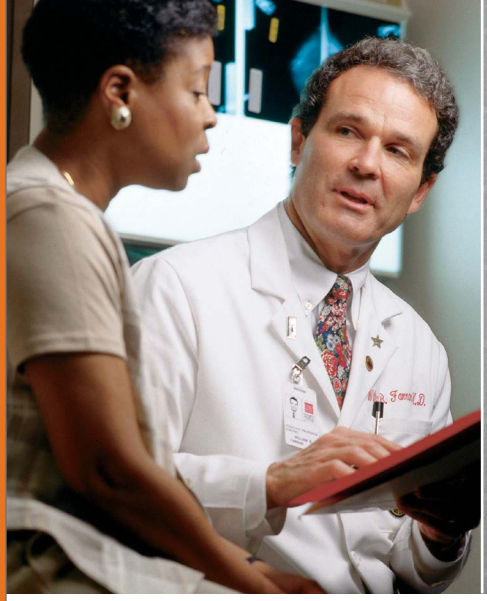
BOB HECKER
AMANDA HARPER
Writers

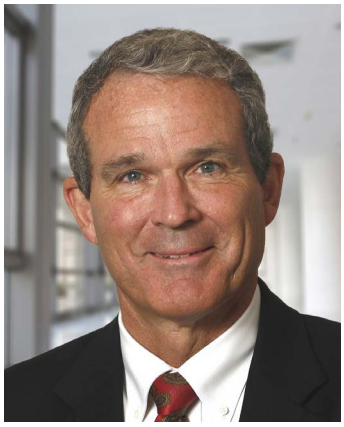
FRONTIERS

WINTER 2023

FEATURES

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





William B. Farrar, MD

Surgical oncologist William Farrar, MD, retires as CEO of The James

William B. Farrar, MD, a surgical oncologist at Ohio State for nearly five decades who also served as CEO of The James for the past few years, retired June 30 following a career in which he performed more than 20,000 surgeries on patients with nearly every kind of malignancy except brain cancer.

Beloved by patients and respected by colleagues, Dr. Farrar was the first surgical oncology fellow at Ohio State and the last medical trainee of the late Arthur G. James, MD, the hospital's namesake, known to be working in 2022.

Later in his 46-year tenure at Ohio State – which started when he arrived as a surgical resident in 1975 – Dr. Farrar began specializing in breast cancer care and conducting research and clinical trials at Ohio State's Comprehensive Cancer Center and The James (OSUCCC – James). His expertise in that specialty led to his appointment as medical director of the **Stefanie Spielman Comprehensive Breast Center** when it opened at the OSUCCC – James in 2011. He held that position until 2021.

"Dr. Farrar's surgical excellence has had an immeasurable impact on patients, their families, his colleagues and in our communities," says Ohio State University President Kristina M. Johnson, PhD. "He has seen our cancer program rise to national prominence and played an integral part in its development.

"When the original James Cancer Hospital opened to patients in July 1990," she adds, "Dr. Farrar was an inaugural member of the medical staff, and over the subsequent decades, he expertly held several top leadership positions while never losing his fervent passion for one-on-one patient care. We extend our sincerest gratitude and congratulations to him for an unmatched career in medicine."

Dr. Farrar held key administrative positions, including 28 years as director of the Division of Surgical Oncology in The Ohio State University College of Medicine, Department of Surgery. He also served for 22 years as director of medical affairs at the OSUCCC – James.

In 2017, he became interim CEO of the cancer hospital and was named to the full position in 2019. In addition, he held the Dr. Arthur G. and Mildred C. James – Richard J. Solove Chair in Surgical Oncology at the Ohio State College of Medicine.

"Dr. Farrar deeply cared about his patients. It was unequivocally clear from the get-go that this was his key motivation."

RAPHAEL E. POLLOCK, MD, PHD, FACS

Besides his clinical career, Dr. Farrar was a researcher in the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James. He authored or co-authored more than 100 clinical studies and reviews published in scientific journals, including studies on such subjects as genetic counseling and sentinel lymph node mapping/biopsy – a procedure to determine whether cancer cells have spread from the tumor to adjacent lymph nodes.

"Dr. Farrar helped define The James as we know it today. As a clinician, educator, researcher and leader, he helped evolve our nationally renowned cancer care through his expertise as much as the kindness he showed every patient," says **Andrew Thomas, MD**, interim co-leader and chief clinical officer at The Ohio State University Wexner Medical Center. "His legacy continues through the many physicians he has mentored and the patients who are living their best lives."

Dr. Farrar also served as president of the U.S. National Committee for the International Union Against Cancer, as principal investigator for the National Surgical Adjuvant Breast and Bowel Project Clinical Trial group at Ohio State, and on numerous national committees.

Colleagues note that his most lasting career legacy, however, is the genuine compassion he brought to the care of his patients.

"Dr. Farrar deeply cared about his patients. It was unequivocally clear from the get-go that this was his key motivation," says OSUCCC Director **Raphael E. Pollock, MD, PhD, FACS**. "He was a surgeon's surgeon who performed at the highest level of technical commitment, but equally important are his personal humility, his quiet and professional persona, his quick smile and his very big heart."

To read more about Dr. Farrar's career, visit **go.osu.edu/FarrarLegacy**.

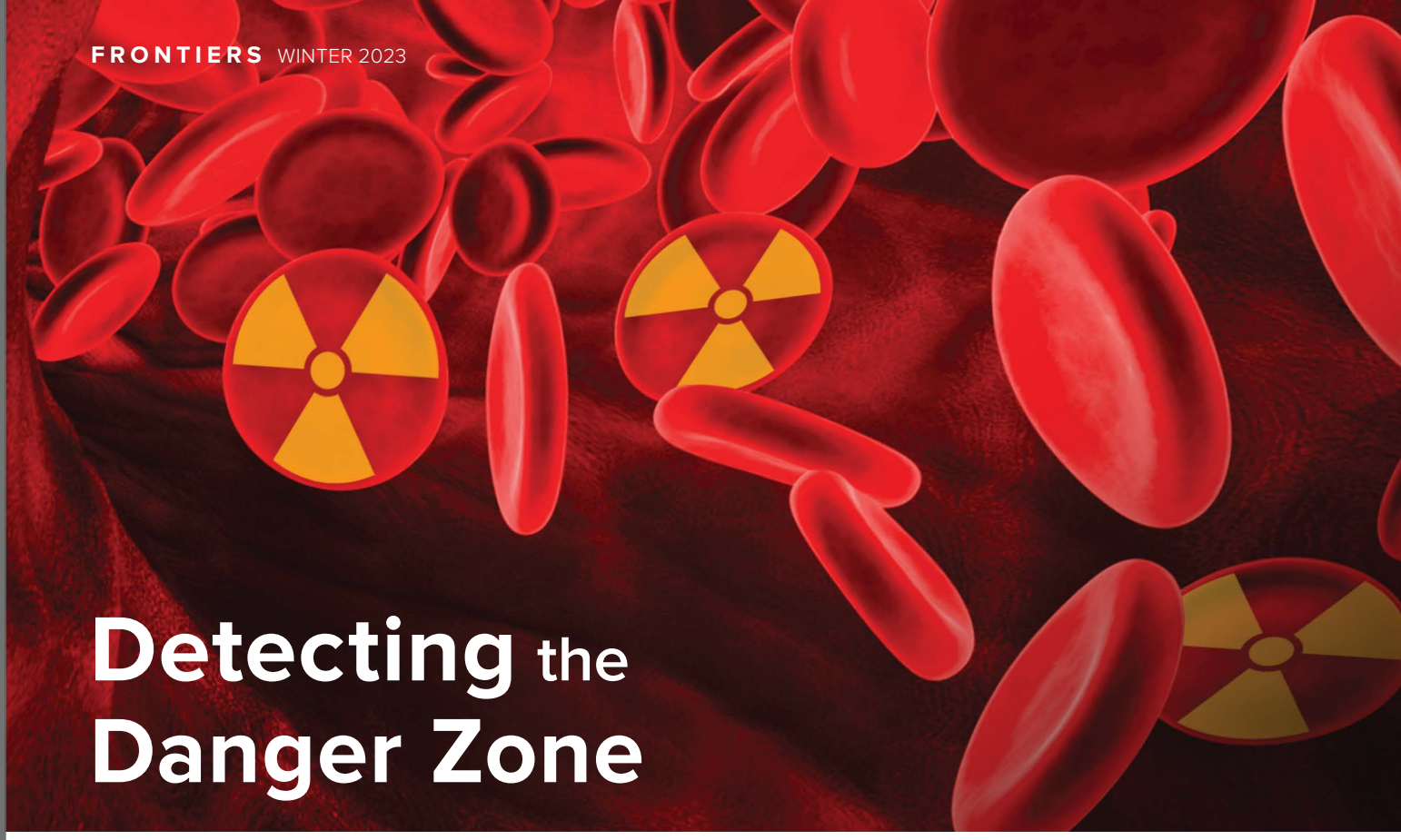
Dr. Cohn serves as interim CEO of The James

David E. Cohn, MD, MBA, chief medical officer at The James since 2018, was appointed as interim CEO of the cancer hospital effective July 1 following the retirement of former CEO **William B. Farrar, MD**. Dr. Cohn also assumed Dr. Farrar's role on The Ohio State University Wexner Medical Center Executive Committee.

A professor in the Department of Obstetrics and Gynecology, Division of Gynecologic Oncology at the Ohio College of Medicine, Dr. Cohn also holds the Stuart M. Sloan – Larry J. Copeland, MD, Chair in Gynecologic Oncology. Since joining the faculty at Ohio State in 2001, he has gained much experience collaborating with faculty and staff from across the cancer program, and the rest of the medical center, to ensure the delivery of safe, high-quality and patient-centered care.

Dr. Cohn maintains a clinical practice that includes both medical and surgical treatment of gynecologic cancers. He is also a member of the Translational Therapeutics Program in Ohio State's Comprehensive Cancer Center, where his research focuses on identifying biomarkers for early detection and prevention of ovarian cancer and the genetics of endometrial cancer.

Nationally, Dr. Cohn has served as co-chair of the National Cancer Institute NRG Oncology's Cancer Care Delivery Committee, and as president of the Society of Gynecologic Oncology (SGO). In January 2022, he became editor-in-chief of the journal *Gynecologic Oncology*, an international journal devoted to the publication of clinical and investigative articles about tumors of the female reproductive tract. He had been a deputy editor for that journal – the official publication of the SGO – since 2011.



Detecting the Danger Zone

New Ohio State biodosimetry technology has far-reaching applications

Radiation oncology researchers at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James) have good reason to believe their breakthrough work in biodosimetry is "out of this world" – it may soon be applied to deep space by the National Aeronautics and Space Administration (NASA).

And that isn't the only translational application for their biodosimetry expertise. Their work has also caught the attention of the U.S. government as a means of helping the intelligence community in matters of national security.

These cosmic and domestic applications of biodosimetry – which is defined as the use of physiological, biochemical or molecular techniques to analyze biological indicators for determining amounts of radiation exposure to individuals – are extensions of the OSUCCC – James' prowess in developing technology to save lives.

Here's how this work is unfolding.

"Our test uses a single drop of blood, collected from a simple finger prick, and results are ready in a few hours."

NADUPARAMBIL JACOB, PhD

NASA notices

In 2021, NASA selected 10 proposals led by agency employees for two-year projects that support development of space exploration capabilities under Project Polaris, an initiative to help the NASA workforce meet the challenges of sending humans back to the moon and to Mars.

One of those 10 projects utilizes a miRNA-based biodosimetry test devised by OSUCCC – James scientists to quickly diagnose radiation sickness based on biomarkers measured through a single drop of blood. The test is designed to save lives through early identification of acute radiation syndrome (ARS), a condition caused by the human body being exposed to a high dose of penetrating radiation in a short time. Without clinical intervention, ARS side effects can rapidly weaken a person and lead to death.

The NASA project that will utilize this biodosimetry test is titled "Radiation Assessment During Exposure and Long-Duration Spaceflight." The project will address how lengthy spaceflight missions pose a high risk of radiation exposure to crew members, potentially increasing their likelihood of developing cancer and degenerative diseases.

According to a NASA report from September 2021, a project team at NASA's Ames Research Center in California "will develop fast, easy-to-use, end-to-end radiation biodosimetry technology sensitive to levels expected of a solar particle event. This system will go from whole blood to quantitative, personalized results with less crew time and training than heritage polymerase

chain reaction (PCR) methods currently used on the International Space Station."

The report also states, "By understanding each person's effective dose through radiation, biodosimetry will reduce risk by guiding countermeasures or alterations in duty."

Naduparambil Jacob, PhD, led the OSUCCC – James study through which the original biodosimetry test was developed.

"Our test uses a single drop of blood, collected from a simple finger prick, and results are ready in a few hours," says Dr. Jacob, associate professor in the Department of Radiation Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James.

Dr. Jacob notes that the previous ARS diagnostic test, a dicentric chromosome assay, requires three to four days to get results. "Our test is rapid, scalable and can serve as a point-of-care-type diagnostic tool for real-time evaluation to screen a large number of individuals in a short time."

Dr. Jacob says the test can be applied to accidental radiation exposure of one or a small number of individuals, or to radiation exposure of many people in mass-casualty radiologic events, such as terrorist attacks or mishaps at nuclear reactor sites. It also has relevance for patients with cancer, especially blood and marrow transplant (BMT) patients and others who receive intense radiation therapy in which overdosing and underdosing are of concern.

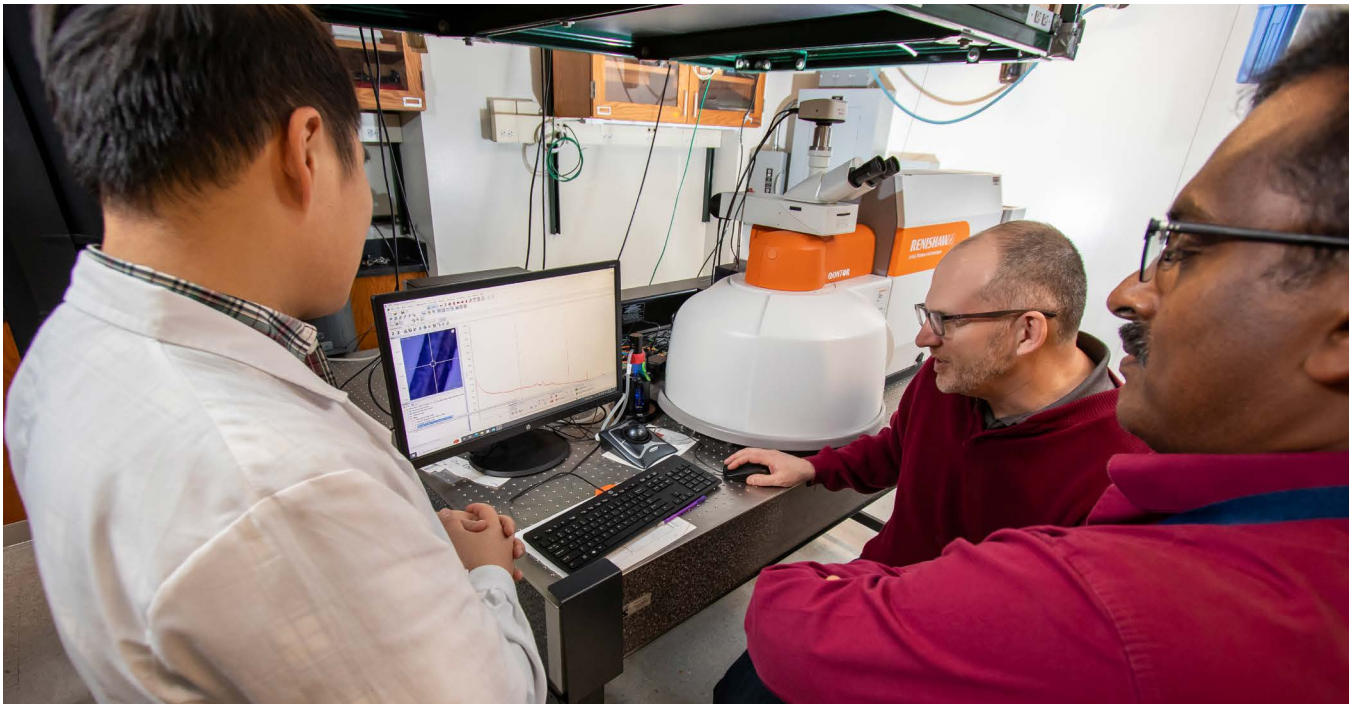
The test, he explains, compares the relative expression of two small microRNA molecules in the blood. One of those is microRNA-150, which his lab identified several years ago as a biomarker for measuring bone marrow damage. This microRNA decreases as a function of radiation dose while the normalizer, called microRNA-23a, does not change. Comparing those two molecular measures enables scientists to quantify the absorbed radiation and thus the overall risk to the person who was exposed.

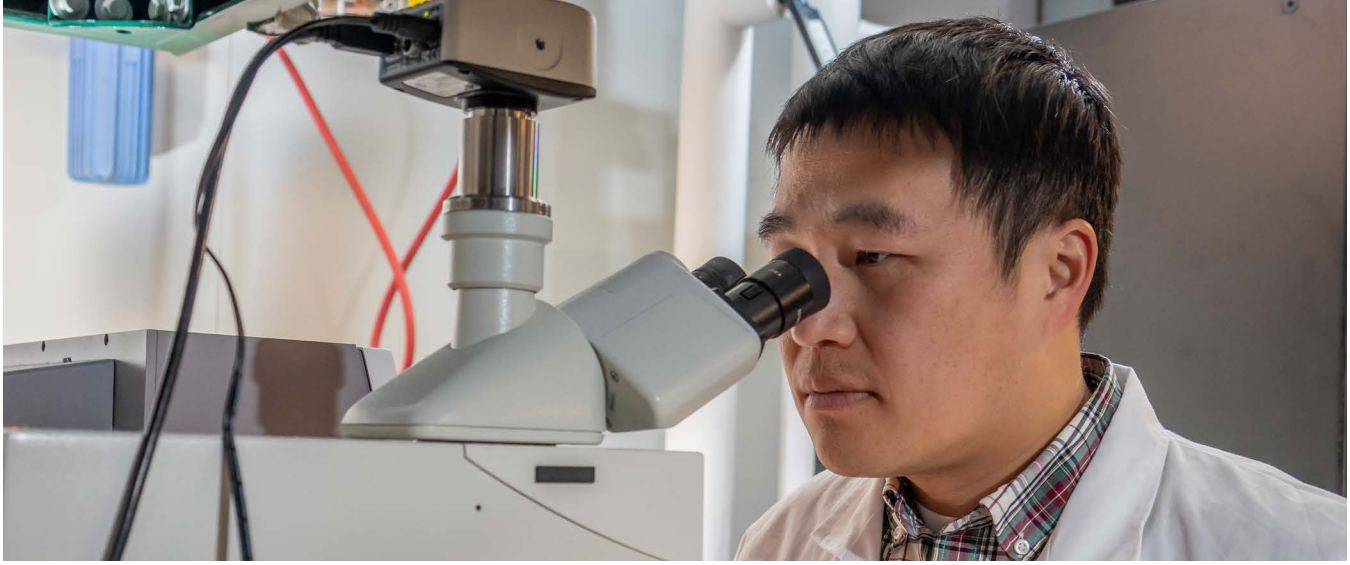
"We measure ionizing radiation in grays," he says. "People who are exposed to two grays need to be identified and treated. It is predicted that if a person is exposed to about four grays to the whole body, without timely treatment, there is only a 50% chance of survival."

As for the test's application to patients with cancer, Dr. Jacob notes that some patients who receive radiation therapy develop such serious conditions as thrombocytopenia and neutropenia. "We can't look at a patient and determine how much radiation he or she has absorbed, but the impact can be cumulative, and radiation sickness could occur weeks or months after their therapy," he says. "With additional research, our testing method could help oncologists measure, in real time, the amount of absorbed radiation and intervene before radiation sickness occurs."

Dr. Jacob and colleagues are happy that their testing technology is being applied to other areas of scientific interest. "We're pleased that NASA scientists and technology developers will be transitioning our miRNA-based biodosimetry test to space exploration," he says. "I have given them a letter of support. It's nice to see that the technology we developed has translational utility in multiple areas."

At the Raman microscope and spectrometer, (from left) Jiangjiang (Chris) Zhu, PhD, Zachary Schultz, PhD, and Naduparambil Jacob, PhD, discuss Raman data of an irradiated mouse hair, specifically looking at spatial changes in the chemical signals from melanon within the hair.





Chris Zhu, PhD

IARPA agreement

More recently, OSUCCC – James researchers entered a $9.42 million federal cooperative agreement that will help them further develop Ohio State's biodosimetry technology to discover noninvasive biomarkers – such as skin and hair – for radiation exposure.

Awarded by the Intelligence Advanced Research Projects Activity (IARPA), an organization within the Office of the Director of National Intelligence, and the Army Research Office (ARO), the agreement aligns with the IARPA's stated mission "to push the boundaries of science to develop solutions that empower the intelligence community to do its work better and more efficiently for national security."

This agreement comes through the IARPA's Targeted Evaluation of Ionizing Radiation Exposure (IARPA – TEI-REX) Program, which seeks "to establish novel biodosimetry approaches enabling improved quantification of lower-dose ionizing radiation exposures from samples that can be collected and tested minimally or non-invasively while also expanding quantitative and qualitative knowledge of the exposure environment."

Ohio State was selected based on broad agency announcement criteria to participate in this program.

Dr. Jacob, principal investigator (PI) for this project, says the work is particularly important because of the possible major health consequences of radiation exposure, including cancer and other illnesses. Being able to determine the amount and range of exposure would help clinicians more quickly and accurately mitigate the short- and long-term effects, he explains.

"We propose to develop rapid and accurate radiation biodosimetry solutions to human radiation exposure, based on biomarkers that are detectable in skin and hair, which can be collected non-invasively," Dr. Jacob says, adding that beneficiaries of this effort are broad: clinical, defense, academia, industry and intelligence.

Dr. Jacob says this project will complement the aforementioned efforts by OSUCCC – James scientists to develop blood biomarker-based mechanisms for early detection of acute radiation syndromes and delayed effects.

"While our previous studies focused on blood biomarkers, in this new program we will explore Raman spectroscopy- and mass spectrometry-based methods and changes in the microbiome," he says. "Specimens collected from laboratory models exposed to X-rays, gamma rays, neutrons, electrons and protons will be used for testing and validation."

Dr. Jacob says the IARPA funding will support a multidisciplinary team that includes Co-PIs **Zachary Schultz, PhD**, professor in the College of Arts and Sciences, Department of Chemistry and Biochemistry, and **Jiangjiang (Chris) Zhu, PhD**, associate professor in the College of Education and Human Ecology, Department of Human Sciences, Human Nutrition Program, and a faculty member of the Discovery Theme Food for Health Research Initiative. Both are members of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.

Dr. Schultz is an expert in Raman spectroscopy – a technique for determining vibrational modes of molecules – and Dr. Zhu is an expert in mass spectrometry, which measures mass-to-charge ratio of ions.

"We will collaborate with data scientists at Battelle Memorial Institute for artificial intelligence (AI)-assisted modeling," Dr. Jacob says, adding that the IARPA funding program will unfold in three phases over 42 months. "Once fully executed, we will have funding of $9.42 million, including a $1.63 million Battelle sub-award."

In their project abstract, the scientists state that exposure to radiation through unintentional contact with radioactive material (e.g., natural environmental or occupational settings) or through intentional release of a radioactive material (e.g., terrorist attack) could lead to serious health problems.

"The radioactive contamination released into the environment may consist of radionuclides that emit alpha, beta, gamma radiation, neutrons or a combination with

varying hazard levels," they write. "Some exposures may not present immediate visible clinical signs, especially at lower dose range, yet have significant delayed consequences. Early detection and risk assessment would allow timely mitigation."

Currently, they add, there is no non-invasive biodosimetry assay or method approved for human use, but the Ohio State/Battelle team "offers development of rapid and accurate biodosimetry solutions, based on biomarkers detectable in skin and hair. (We) have complementary expertise in radiation biodosimetry, biomarker discovery, and validation using analytic platforms such as Raman spectroscopy, mass spectrometry, metagenomics, data science and AI-assisted modeling."

The scientists will irradiate cohorts of small laboratory models at recommended doses, collect skin and hair samples at specified intervals, and subject the samples in parallel to Raman spectroscopy, mass spectrometry and microbiome-based biomarker discovery to obtain information on exposure dose, duration, radiation types and dose-rate effects. They will gain further validation in larger laboratory models and in humans exposed to low doses of radiation during cancer therapy or scans.

Shown within the Small Animal Radiation Research Platform (SARRP) at Ohio State are (from left) Marshleen Yadav, PhD, research scientist; Naduparambil Jacob, PhD, associate professor; Lanchun Lu, PhD, associate professor and medical physicist; and Michael Geiman, program coordinator. All are in the Department of Radiation Oncology.

> *"Ideas may come from an investigator, and key data may come from a series of experiments in a single laboratory; however, for commercialization, we need partners and years of testing and validation supported by various stakeholders."*
>
> **NADUPARAMBIL JACOB, PhD**

"These will become the basis for development of end-to-end use diagnostic assays with integrated software and dose reconstruction and prediction," they write, noting that the characteristics tested will include readability even with intermittent exposure, considering the scenarios of unknown exposure that military personnel and civilians may encounter. "The combinatorial approaches will allow robust biodosimetry, days to months or even years after exposure."

Drs. Zhu and Schultz will play key roles in this project through their respective expertise in mass spectrometry (MS) and Raman spectroscopy.

"MS is a well-known analytical approach that can be used to understand the molecular composition in complex systems," Dr. Zhu says. "In this systematic study of radiation biomarkers, we expect to utilize MS-based techniques, in combination with other analytical methods such as high-performance liquid chromatography, to detect the changes in biological systems that can be detected in non-invasively collected samples of hair or skin."

He says his team's MS results "will be integrated with Raman spectroscopy and skin microbiome data for machine learning-based model constructions to evaluate and predict radiation-induced damage."

Dr. Schultz will oversee and direct the use of Raman spectroscopy to look for biochemical markers of ionizing radiation. "Raman spectroscopy uses a laser to investigate chemical properties, specifically the vibrations of chemical bonds, in samples," he explains. "We will use Raman to look for chemical changes in hair that can be related to the exposure dose and time since exposure."

He says a strength of this approach is the ability to correlate the molecules detected in mass spectrometry and other techniques with the chemical changes detected by Raman.

COVER STORY: DETECTING THE DANGER ZONE

"Raman can be performed on any sample that a laser can be shined on; thus, the chemical information in the Raman signal from hair – and potentially skin and nails – provides a non-invasive assessment of radiation exposure," Dr. Schultz says. "We aim to demonstrate the ability to measure even trace radiation exposure using this approach."

Drs. Jacob, Zhu and Schultz view the IARPA support for developing their biodosimetry technology as an important translational application of their work that also will benefit cancer treatment.

"The study should generate a diverse group of biomarkers and their related machine-learning models that are indicative and predictive to different types of radiation exposure," Dr. Zhu says. "The rapid and sensitive detection of these exposures could provide immediate response options in many application scenarios. These discoveries can also be translated to radiation studies or treatments for cancer patients to maximize the desired outcomes and minimize unwanted side effects."

"The project will provide a radiation dose at a level just above the environmental background, which in turn will produce new means of assessment for cancer patients undergoing radiation treatment," Dr. Schultz adds. "This also will have applications to nuclear forensics and security, as well as assessing exposure to astronauts and others with potential occupational hazards.

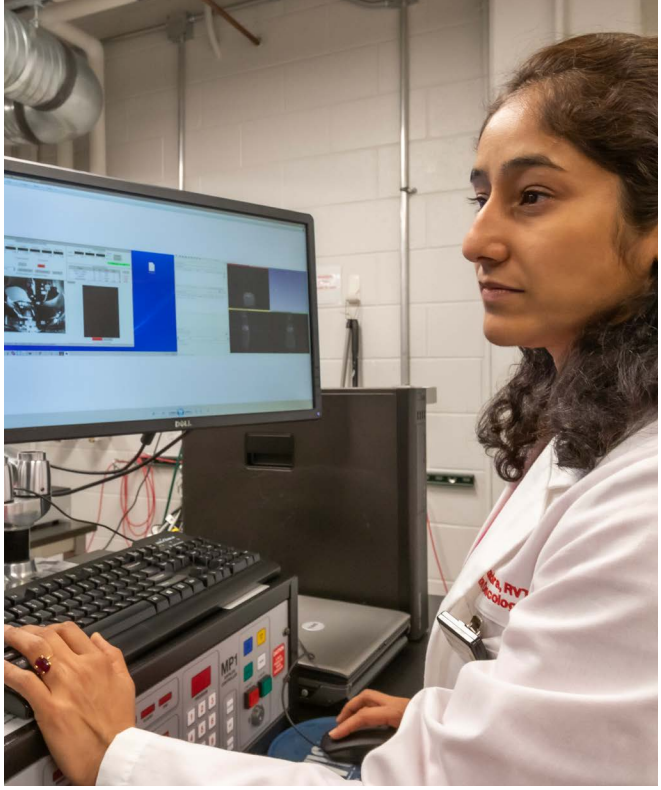
"Our work with Raman could enable a rapid, non-invasive diagnostic with the potential to be performed on-site with rapid results," he continues. "Fundamentally, we are enabling tracking of radiation exposure at levels and precision that have not been easily studied before."

Arnab Chakravarti, MD, professor and chair of the Department of Radiation Oncology at Ohio State, says receiving IARPA support is a credit to Ohio State's leadership in developing innovative technology.

"The IARPA funds high-risk, high-reward studies with significant impact," Dr. Chakravarti says. "With support from this large agreement, Dr. Jacob's team will develop rapid and accurate radiation biodosimetry solutions based on biomarkers detectable in skin and hair, with broad applications. This phenomenal achievement will have major impact in our field."

Commercialization via 'Capture Collective'

Capture Collective, Inc., which spun out of the Ikove Venture Partners Startup Nursery, licensed the biodosimetry technology in 2019, working with Ohio State's Office of Innovation and Economic Development (OIED), which handles technology licensing for the university. Ikove pursues early-stage investments with an emphasis on technology commercialization and worked with Dr. Jacob to gain a thorough understanding of the technology prior to licensing.



Marshleen Yadav, PhD

The technology was the basis to form Capture Collective, Inc., a start-up company whose mission is to maximize the safety and security of global citizens in the face of viral pandemic and radiological threats. Earlier engagement between Dr. Jacob and the U.S. Food and Drug Administration through a pre-submission process also facilitated the licensing path.

Sources of funding and expertise brought by entities like Ikove and IARPA are vital for advancing and translating science into market applications, says **Kevin Taylor**, senior associate vice president of technology commercialization at the university.

"Dr. Jacob's research and resulting inventions have significant potential to improve people's lives and benefit society," Taylor says. "The Technology Commercialization Office at Ohio State exists to accelerate the translation of cutting-edge science into the market, and we are excited to see the progress Capture Collective is making."

As an institution-approved faculty consultant, Dr. Jacob will support Capture Collective, Inc., aiding the transition of biodosimetry products from lab bench to clinic and market.

"Ideas may come from an investigator, and key data may come from a series of experiments in a single laboratory; however, for commercialization, we need partners and years of testing and validation supported by various stakeholders," Dr. Jacob says. "I'm humbled for the opportunity to work with such an exceptional team at Ohio State, and for the support we receive from government and industry partners."

Anna Vilgelm, MD, PhD

CDK inhibitors might improve immune therapy effectiveness for recurrent breast cancer

A class of drugs that inhibits breast cancer progression when used with hormonal therapy might also boost the effectiveness of immune therapy in cases of recurrent metastatic breast cancer, according to a study led by researchers at the OSUCCC – James.

Published in the journal *Cell Reports*, the findings of the animal study suggest that drugs called CDK4 and CDK6 (CDK4/6) inhibitors might improve the effectiveness of immune therapies for metastatic, estrogen-receptor-positive (ER+) breast cancer.

"We know that CDK4/6 inhibitors effectively slow the progression of newly diagnosed breast cancer, but they don't kill cancer cells," says principal investigator **Anna Vilgelm, MD, PhD**, assistant professor in the Department of Pathology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James. "Consequently, the disease often recurs, and then it is usually fatal because we have no effective therapies for recurrent disease.

"Our findings suggest that combining CDK4/6 inhibitors with immunotherapy might offer an effective treatment for recurrent, metastatic ER+ breast cancer," adds Dr. Vilgelm, whose research at the OSUCCC – James focuses on stress response phenotypes that enhance tumor cell immunogenicity.

Specifically, the study shows that CDK4/6 inhibitors can improve the efficacy of T-cell-based therapies, such as adoptive T-cell transfer or T-cell-activating antibodies in animal models of breast cancer.

Immune therapies are proving to be effective treatments for a variety of cancers but not for advanced breast cancer. One problem is that breast tumors often have low numbers of cancer-killing T lymphocytes within the tumor, and such tumors tend to respond poorly to immune therapies.

"In addition, breast cancer patients with low numbers of tumor-infiltrating lymphocytes often have worse survival compared to patients with high numbers of infiltrating lymphocytes in their tumors," Dr. Vilgelm says.

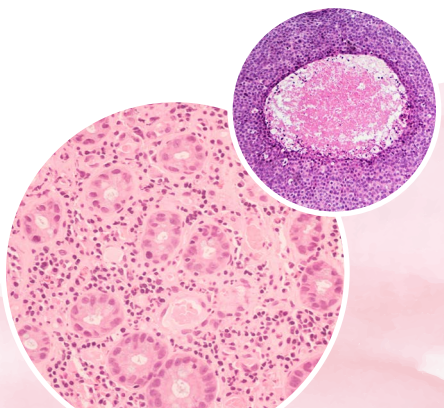
The new study shows that CDK4/6 inhibitors cause breast tumors to secrete small proteins called chemokines that attract T cells. This can help to improve patients' response to cancer immunotherapies.

For this study, Dr. Vilgelm and her colleagues used the oral CDK inhibitor palbociclib, mouse models, breast cancer cell lines and analyses of The Cancer Genome Atlas (TCGA) to study the influence of CDK4/6 inhibitors and chemokine production in the tumor immune microenvironment and on patient outcomes.

The study produced several key findings, including:

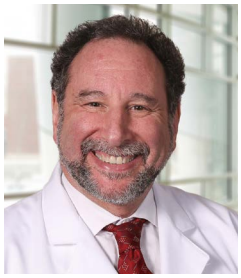
- Pre-treatment with a CDK4/6 inhibitor improved recruitment of T cells into tumors and the outcome of adoptive cell therapy in animal models;
- CDK4/6 inhibitor-treated human breast cancer cells produce T-cell-recruiting chemokines;
- TCGA analysis showed that chemokine expression is a favorable prognostic factor in breast cancer patients;
- mTOR-regulated metabolic activity is required for chemokine induction by CDK4/6 inhibition; and
- T-cell-recruiting chemokines may be useful prognostic markers for stratifying patients for immunotherapy treatment.

"Overall," Dr. Vilgelm says, "our findings suggest that CDK4/6 inhibitors may offer a therapeutic strategy that can attract T cells into breast cancer tumors, which may increase their sensitivity to immune therapies."



PROMINENT STUDIES

Zihai Li, MD, PhD



Peter Shields, MD

Shan-Lu Liu, MD, PhD

COVID booster shots likely provide increased, broad protection against Omicron variant in patients with cancer

New data show that booster vaccine doses provide stronger and broader protection for patients with cancer against SARS-CoV-2 (the virus that causes COVID-19) and its highly transmissible variant, Omicron. This protection is consistent for patients with solid tumors, regardless of treatment status.

Researchers at the Ohio State College of Veterinary Medicine and the OSUCCC – James report that the two-shot mRNA vaccination regimen against COVID-19 is "woefully inadequate" to provide durable protection in immune-compromised patients, and they urge cancer patients to get booster shots as soon as they're eligible.

Co-senior authors for the study (from top) are **Zihai Li, MD, PhD**, founding director of the Pelotonia Institute for Immuno-Oncology; **Peter Shields, MD**, deputy director of the OSUCCC; and **Shan-Lu Liu, MD, PhD**, professor in the Department of Veterinary Biosciences and associate director of Ohio State's Center for Retrovirus Research. The team reported its findings in the journal *Cancer Cell*. Dr. Liu was lead corresponding author.

In this study, OSUCCC – James researchers collected samples from 50 patients with solid tumors who had completed two- or three-dose COVID-19 vaccination. Samples were collected as part of an ongoing SIIREN research study looking at how COVID impacts patients with cancer.

The OSUCCC – James team collaborated with Dr. Liu's vet med lab team to measure the "neutralizing antibody response," or how well the body's immune system is triggered to respond to, recognize and fight infection once vaccinated – in this case against SARS-CoV-2 and its variants. "Although our sample size was small," Dr. Liu says, "the results show that a solid cancer diagnosis does not negatively impact adaptive immune response to booster-mediated protection against SARS-CoV-2 variants."

Sujit Basu, MD, PhD

Study identifies new molecular target for cancer therapy

Researchers at the OSUCCC – James have identified a new molecular drug target that could result in new cancer drugs with fewer side effects. Previous studies have shown that vascular endothelial growth factor-A (VEGF-A) – a potent cytokine (signaling protein) – and dopamine (a neurotransmitter/neurohormone) play essential roles in many physiological and pathological functions.

In this study, **Sujit Basu, MD, PhD**, of the Translational Therapeutics Program at the OSUCCC – James, and colleagues conducted further preclinical analysis of VEGF-A as a target for the development of cancer therapy approaches. They found for the first time that VEGF-A can increase expression of dopamine D2 receptors on endothelial cells that can then be stimulated to stop the growth of blood vessels that fuel the progression of several diseases, including colon cancer, endometriosis and ovarian hyperstimulation syndrome. The study appeared in *Journal of Cell Science*.

"This is a very compelling discovery that opens new pathways for developing effective anti-angiogenic therapy for the treatment of cancer and other diseases where VEGF-A is a known driver of disease growth and spread," says Dr. Basu, a professor in the Department of Pathology at Ohio State. He notes that, unlike the currently available anti-VEGF-A anti-angiogenic agents, selective dopamine D2 receptor agonists are inexpensive and have well-established and manageable side effects.

"These drugs are devoid of the serious side effects of the currently used anti-VEGF-A anti-angiogenic agents in the clinics," Dr. Basu says. "We believe they merit further investigation as a viable treatment approach in cancer and other diseases driven by the VEGF-A pathway."

Electra Paskett, PhD, MSPH

Study shows chronic lower extremity lymphedema has dramatic impact on physical function of older female cancer survivors

A study has found that nearly a third of older adult female survivors of colorectal, endometrial and ovarian cancer have quality-of-life-impacting challenges with physical activity due to lymphedema in the lower extremities. This was the first study to assess lower lymphedema in colorectal cancer survivors.

OSUCCC – James researchers say these findings call attention to the importance of regularly assessing lower-extremity lymphedema in older survivors of cancer – something that's not part of current national clinical practice guidelines – so that effective and timely interventions can be given to preserve physical ability and independence.

They reported their findings in the journal *JAMA Network Open*. Senior author was **Electra Paskett, PhD, MSPH**, professor and director of the Division of Cancer Prevention and Control at Ohio State, and associate director for population sciences and community outreach at the OSUCCC – James.

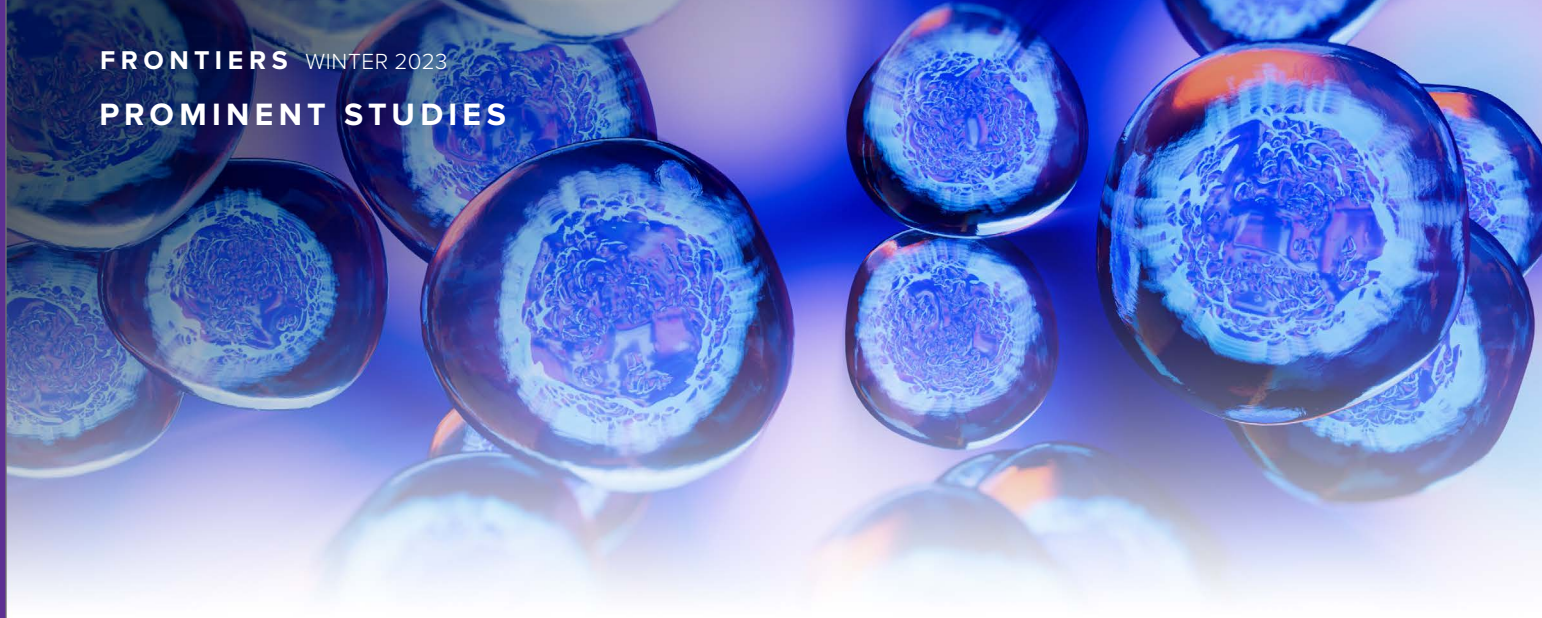
Often associated with side effects of cancer treatment, lymphedema impacts the ability to perform daily activities, such as walking, standing for long periods or lifting heavy objects. Unchecked, it can cause chronic infections in the affected area (often arms, pelvis or legs) that, in severe cases, can lead to limb loss.

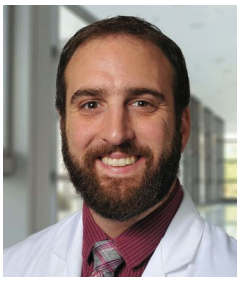
"Survivors of cancer continue to live longer thanks to early detection and more effective treatment, but long-term quality of life has become even more critical as a result," Dr. Paskett says. "Studies show that when a person has limited physical ability, it impacts both mental and physical health – and that impact layers over time to be even more challenging as individuals age."

For this report, researchers conducted a secondary analysis of 900 postmenopausal women previously diagnosed with endometrial, colorectal or ovarian cancer. Their average age was 78.5 years, and an average of 8.75 years had passed since each person's diagnosis.

When compared to similarly aged women who did not have lower-extremity lymphedema, all experienced decreased functional physical abilities. Survivors of colorectal cancer were disproportionally affected; 21.8% of these patients reported significantly declined physical function, as well as an increased need for help with daily activities. This association wasn't found in survivors of endometrial or ovarian cancer.

"Our data call attention to a significant challenge for a large portion of female cancer survivors that deserves attention from the medical community as part of long-term survivorship care," Dr. Paskett says.





Jonathan Brammer, MD

New three-drug combo stimulates 'master cancer killer' cells, boosts immune system of patients undergoing stem cell transplantation

A new three-drug combination could help patients with aggressive forms of blood cancer achieve longer cancer remission after undergoing allogeneic stem cell transplantation, according to preliminary clinical trial results presented by researchers at the OSUCCC – James.

For this phase I/II clinical trial, researchers evaluated a new stem cell transplant conditioning regimen designed to overcome the challenges of treating T-cell acute lymphocytic leukemia (ALL) and T-cell lymphomas. Initial study results showed that 88% of patients remained in remission a year after treatment completion, a dramatic increase in relapse-free survival compared to the expected 45%.

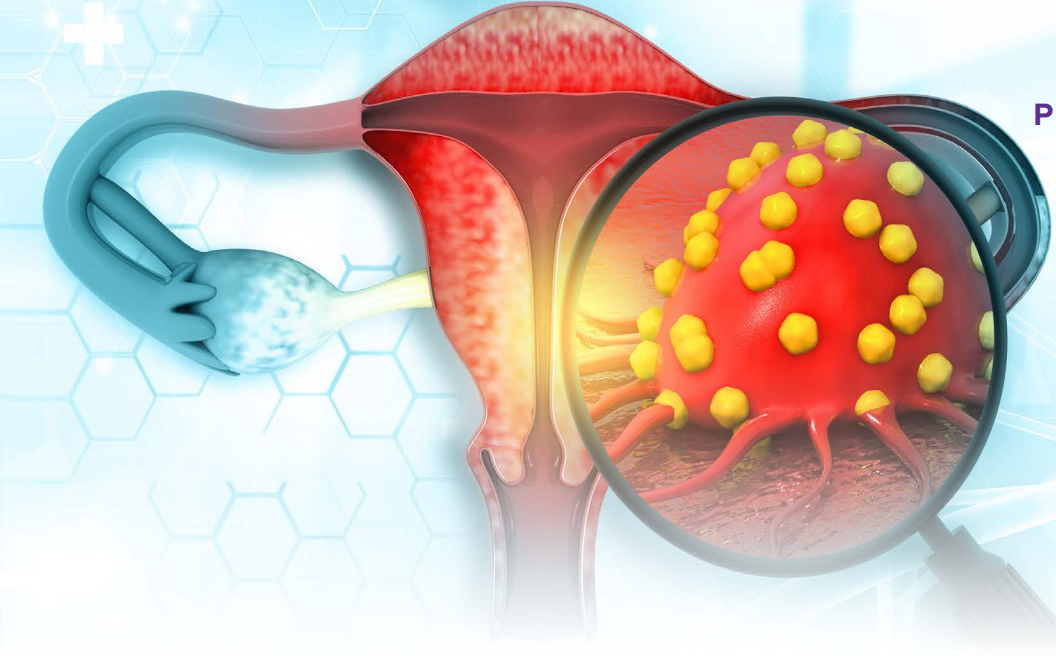
Principal investigator is **Jonathan Brammer, MD**, who is in the Leukemia Research Program at the OSUCCC – James. "This is a critical time when the patient's immune system is rebuilding strength to stop abnormal cell growth," Dr. Brammer says. "What is really promising is that the addition of the drug romidepsin as maintenance post-transplant appears to both reduce cancer relapse and activate natural killer (NK) cells in the immune system to eliminate any residual cancer cells."

In this OSUCCC – James investigator-initiated clinical trial, hematologists enrolled 21 patients with T-cell ALL or T-cell lymphoma who were in full or partial remission but required treatment with an allogeneic stem cell transplant. All patients were under age 70 with a matched sibling or unrelated donor and were treated at either Ohio State (15 patients) or MD Anderson Cancer Center (six patients) in Houston, Texas.

Patients received romidepsin (marketed as Istodax®) in addition to the standard conditioning chemotherapy agents busulfan (marketed as Busulfex™ and Myleran™) and fludarabine (marketed as Fludara). They continued to receive a maintenance dose of romidepsin every two weeks for a year post-stem cell transplant to decrease the chance of a relapse while their immune system regained strength.

"We know that even when people achieve full remission, there are likely some residual cancer cells that escape treatment and allow the cancer to recur," Dr. Brammer says. "It's exciting to see that the addition of romidepsin as a conditioning and maintenance medication appears to dramatically decrease the risk for relapse in the first year after stem cell transplantation."

Researchers expect final results from this study in 2023.



David O'Malley, MD

Immunotherapy drug shows promise against advanced endometrial cancer

A cancer immunotherapy drug approved by the U.S. Food and Drug Administration (FDA) to treat several forms of cancer is also effective for treating aggressive forms of endometrial (uterine) cancer, according to results from an international phase II clinical trial led by researchers at the OSUCCC – James.

For this study, researchers enrolled 90 women diagnosed with recurrent or advanced endometrial cancer to determine whether the drug pembrolizumab (marketed as Keytruda™) could be used to effectively treat this subset of patients with MMR-deficient (dMMR) or MSI-high tumors. The study included patients treated at 38 hospitals in 15 countries.

Pembrolizumab is a cancer immunotherapy drug that inhibits certain cellular receptors that prevent the immune system from recognizing and destroying cancer cells. The FDA has approved the drug for treating other cancers, including melanoma, lung, head/neck, cervical and stomach.

Researchers showed that 48% of patients with advanced endometrial cancer in this study experienced a complete or partial response. Two-thirds of the patients also had a response lasting over three years. Additionally, two-thirds of the patients had a clinical response. This trial was the longest follow-up reported to date, with a median follow-up of 42.6 months.

"These findings suggest a long-term benefit to patients. Even the potential for curative intent is now possible in patients with recurrent or metastatic uterine cancer," says **David O'Malley, MD**, director of the Division of Gynecologic Oncology at Ohio State and lead author of the study, which was published in *Journal of Clinical Oncology*.

Clinical trials are underway to evaluate pembrolizumab for treating earlier-stage disease.

Endometrial cancer is the second most common form of cancer in women worldwide, and incidence rates have been increasing. While platinum-based chemotherapy regimens can be effective, many patients experience a recurrence. Effective second-line therapies for recurrent or metastatic disease are limited, resulting in a 17% five-year survival rate for women with advanced or recurrent disease.

Darren Mays, PhD, MPH

Tailored mobile messaging reduces young adult water pipe tobacco use by 49%

Tailored mobile messaging is an effective intervention strategy to reduce tobacco water pipe smoking in young adults, according to a study published by researchers with the Center for Tobacco Research at the OSUCCC – James.

The researchers, who reported their findings in *American Journal of Public Health*, say this study demonstrates the effectiveness of a tailored mobile messaging intervention to support smoking cessation in youth tobacco hookah users. **Darren Mays, PhD, MPH**, of the Cancer Control Program at the OSUCCC – James, was the principal investigator.

"In the United States, hookah tobacco smoking is most prevalent among young adults," Dr. Mays says. "Our study is one of the first to demonstrate that a tailored mobile messaging intervention can motivate young adult hookah smokers to quit. This technology-based intervention is scalable to implement at the population level."

Between 2018 and 2020, the researchers recruited 349 water pipe (hookah) tobacco users between ages 18 and 30 and randomized them into one of three trial arms – two intervention arms and a control arm. Each participant underwent baseline evaluation prior to the beginning of the six-week intervention trial to gauge perceived associated riskiness of smoking, personal motivation to quit, water pipe smoking frequency and cessation.

Individuals in the intervention arms received six weeks of messaging via their mobile phones. The messages were designed to increase motivation to quit smoking via visual cues and information about long- and short-term health harms, toxicant exposure and addictiveness of water pipe tobacco use. Message content was developed to address misconceptions about risks of water pipe tobacco use in young adults.

Participants in the untailored intervention arm received the same message content, but messages in the tailored intervention arm were personalized to participants' frequency of water pipe tobacco use, how risky they believed water pipe smoking to be, and their responses to text messages during the intervention. The control arm received no intervention.

Participants were assessed again at the end of the intervention (six weeks), at three months and at six months. Study results showed that 49% of individuals who received tailored mobile messaging quit smoking water pipe tobacco at six months – 20% more compared to participants who did not receive any mobile intervention.

Zihai Li, MD, PhD

Study reveals male sex hormones are new targets for cancer immunotherapy

Patients with cancers stemming from non-reproductive organs, such as bladder and liver cancer, have striking discrepancies in incidence, progression, response to treatment and survival outcomes, depending on their sex. In almost all cases, male patients have worse prognoses and outcomes. This phenomenon has puzzled scientists for decades.

A study published in the journal *Science Immunology* and led by researchers at the Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC – James examined the differences in intratumoral immune responses between male and female cancers of non-reproductive origin. **Zihai Li, MD, PhD**, founding director of the PIIO, was the study's senior corresponding author.

This research focused on the T-cell immune response to malignancy, a key determinator of outcomes in cancer, and an important target that has contributed to the renaissance of cancer immunotherapy seen in recent years. The study reported a landmark finding that describes how male sex hormones contribute to cancer-related sex bias via the modulation of CD8+ T cells – a population of cells often referred to as "cancer-killer" cells, which mediate adaptive immunity and are critical for mounting an antitumor response.

"Collectively, these findings highlight androgen-mediated promotion of CD8+ T-cell dysfunction in cancer and suggest broader implications for therapeutic development to address sex disparities in health and disease," Dr. Li says.

This study revealed that CD8+ T cells from cancers in male subjects, including human patients and mice, are more likely to have characteristics of a weakened antitumor immune function, also known as "exhausted T cells." Androgen signaling promotes the progenitor-exhausted CD8+ T-cell phenotype via modulating the expression of TCF1, a master regulator of CD8+ T-cell function.

"Androgen-mediated promotion of CD8+ T-cell dysfunction results in faster tumor growth and worsened outcomes. Targeting of this signaling cascade holds a crucial key to improving current cancer immunotherapies," says Dr. Li, who is also a professor in the Ohio State College of Medicine, Department of Internal Medicine.

Samilia Obeng-Gyasi, MD, MPH

Chronic stress may impact treatment completion and survival outcomes in patients with breast cancer

A study at the OSUCCC – James shows that chronic physiologic wear and tear from stress, known as allostatic load, may be associated with a decreased likelihood of cancer treatment completion and lower overall survival. Research results also suggest that allostatic load appeared better than genetic ancestry at predicting chemotherapy completion and overall survival.

Samilia Obeng-Gyasi, MD, MPH, a surgical oncologist and member of the Cancer Control Program at the OSUCCC – James, presented the findings in October 2021 at the American Association for Cancer Research Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved.

Allostatic load is defined as wear and tear on the body caused by lifelong exposure to such stressors as social isolation, poverty and racism, many of which are common among racial and ethnic minorities. Elevated allostatic load is associated with such health problems as high blood pressure, increased body mass index, kidney disease, inflammation and arthritis.

"Patient behavior and clinical outcomes can't be isolated from the effects of their social environment," says Dr. Obeng-Gyasi. "Allostatic load provides us with a way to evaluate the effects of social and environmental stressors on a patient's physiology."

She and her colleagues in the ECOG-ACRIN Cancer Research Group sought to understand whether allostatic load or genetic ancestry (identified by DNA) impacted patients' survival and likelihood of completing chemotherapy. This study represents a retrospective review of ECOG-ACRIN E5103, a clinical trial evaluating the inclusion of bevacizumab into adjuvant sequential anthracycline and paclitaxel in patients with lymph node-positive or high-risk lymph node-negative HER2-negative breast cancer.

Clinical spotlight: Expanding to better serve patients and learners through improved access and innovation

The James Outpatient Care: Centralizing outpatient cancer care and adding innovative proton therapy treatment capabilities to benefit patients

The James Outpatient Care, a 385,000-square-foot cancer-focused facility, is set to open in summer of 2023 in the new Carmenton community on Ohio State's west campus. It will include outpatient operating and interventional radiology rooms, an extended recovery unit, a pre-anesthesia center, a diagnostic imaging center, a pharmacy, hematology and genitourinary (GU) clinics, an infusion and medical office and support spaces, and a large parking garage. The facility also will include central Ohio's first proton therapy center, in partnership with Nationwide Children's Hospital, that will enable children and adult patients to receive the latest radiotherapy in one facility conveniently located in their community.

Proton therapy is a highly targeted form of radiotherapy that uses protons instead of X-rays to kill cancer cells. From outside the body, a cyclotron delivers a high-energy proton beam painlessly through the skin to the tumor, limiting radiation exposure and consequent damage to healthy surrounding tissue and organs. Limiting radiation exposure reduces the chance of short- and long-term side effects that could impact quality of life compared to conventional radiation.

The James Outpatient Care facility will feature sophisticated imaging and treatment technology made by Siemens Healthineers, including Varian, which has worked with the OSUCCC – James for nearly a decade.
The facility's advanced precision cancer care will include proton therapy, radiosurgery and oncology-focused interventional radiology.

The facility will build on this technology, including the current treatment planning capabilities, to offer the most advanced diagnostic and treatment-planning tools, such as Digital PET and Dual Source Dual Energy spectral imaging.

Working with Siemens Healthineers and Varian, the OSUCCC – James leads a university-based International Training Center of Radiation Oncology and Cancer Consortium with a training-dedicated linear accelerator and planning environment. The consortium uses big data approaches to advance education, research and patient care at 37 institutions around the world.

Researchers at the OSUCCC – James and Siemens Healthineers will explore opportunities in intelligent radiation dosimetric-contouring algorithms that are tailored to individual patients. One potential objective is to create a platform that combines clinical, imaging, pathology and genomic data with artificial intelligence to drive pathways of care in near-real time, enabling providers and patients to make well-informed, evidence-based decisions together.

Ohio State Outpatient Care New Albany

The Ohio State University Wexner Medical Center ushered in a new era of convenient access to primary and specialty services with the August 2021 opening of Ohio State Outpatient Care New Albany in northeast Columbus. The 251,000-square-foot building is the first of three outpatient care centers that are part of the medical center's strategic expansion of outpatient services into accessible locations where patients can have multiple appointments with different health care providers, often on the same day. Experts from 22 specialties, including cancer, diagnose and treat patients on site. The center offers advanced imaging services and diagnostic testing, as well as cancer screening and diagnosis from experts at the OSUCCC – James.

Ohio State Outpatient Care Dublin

The new Ohio State Outpatient Care Dublin facility, which opened for patients in August 2022, extends convenient access to many primary and specialty care services in central Ohio, including cancer services such as advanced imaging and diagnostic testing, screening and diagnosis, and mammography, all provided by experts from the OSUCCC – James. The 272,000-square-foot building is the second of three planned outpatient care facilities that offer patients access to Ohio State's nationally ranked experts and care in convenient community locations. A third suburban outpatient care facility, located just north of Columbus, is targeted to open in 2025.

Interdisciplinary Health Sciences Center

This center is a multiphase, 225,000-square-foot interprofessional learning facility on Ohio State's main campus. The innovative design integrates learning, studying and health and wellness spaces so learners can have the optimal education experience. Medical students will have collaborative multidisciplinary learning experiences with learners from other health science disciplines, such as nursing, dentistry, optometry, pharmacy, public health, veterinary medicine and health and rehabilitation sciences.

The Interdisciplinary Health Sciences Center will focus on inclusive and innovative learning environments that will include:

- 33 interdisciplinary, state-of-the-art classrooms
- The latest teaching technology, such as realistic virtual reality models to simulate patient care, emerging telehealth innovations, and enhanced anatomy and surgical practice labs
- Spaces for learners to meet and develop critical team-approach skills to patient care planning
- 6,000-square-foot student forum
- 300-person-capacity atrium
- 125-seat grand reading room

Wexner Medical Center Inpatient Hospital

Scheduled to open in 2026, the 1.9-million-square-foot inpatient hospital under construction on the Ohio State Wexner Medical Center campus will provide leading-edge research, outstanding clinical training and world-class patient care. The new hospital, located beside the James Cancer Hospital and Solove Research Institute that opened in 2014, is the largest single facilities project ever undertaken at Ohio State. It will contain more than 800 patient beds – including nearly 100 for cancer patients – in private room settings to elevate patient-centered care, patient safety and training for the next generation of health care providers. It also will feature state-of-the-art diagnostic, treatment and inpatient service areas (imaging, operating rooms, critical care and medical/surgical beds).

Destination Medicine Global Health Care

The Destination Medicine Global Health Care team at the OSUCCC – James is dedicated to ensuring that distance and language are not obstacles to receiving the care that makes Ohio State's cancer program a destination of choice for patients and families from around the world. Led by Director **Milly Valverde**, who also serves as co-chair of the Wexner Medical Center and Health Science Colleges Diversity Council, the program cares for patients in all 50 states, three U.S. territories and 85 countries.

Research spotlight: New interdisciplinary cancer research centers

Center for Cancer Metabolism (CCM)

The OSUCCC – James Center for Cancer Metabolism (CCM) at Ohio State aims to become a world-renowned research entity focused on basic and translational studies regarding cancer metabolism and the development of therapies targeting tumor metabolic pathways.

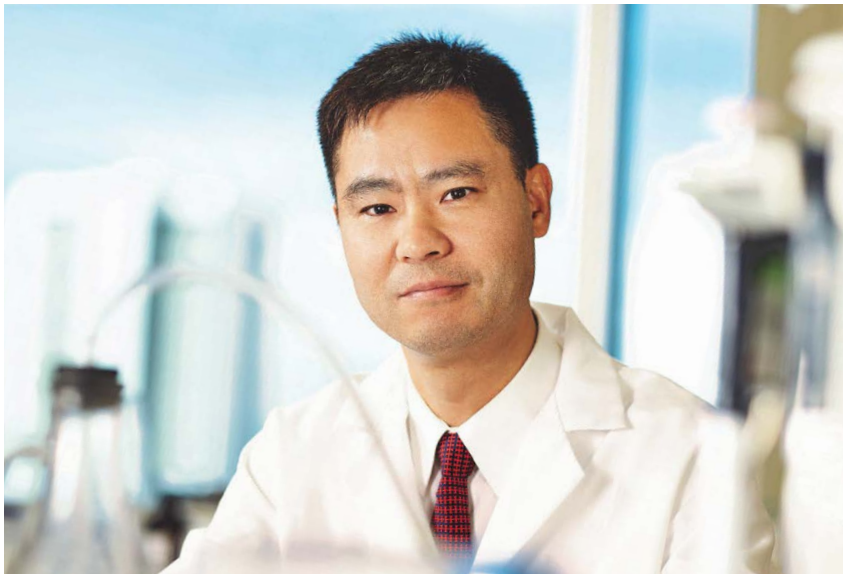
Researchers in the CCM, which is housed within the OSUCCC – James, apply multidisciplinary technologies and techniques to answer challenging questions, such as: How do tumor cells generate the lipids necessary for rapid growth and proliferation, and how can the biological mechanisms that underlie lipid production be exploited as a vulnerability in cancer treatments?

The CCM is led by Director **Deliang Guo, PhD**, professor, vice chair for clinical and basic research, and director of the Division of Cancer Metabolism in the Department of Radiation Oncology in the Ohio State College of Medicine, where he also serves as basic science director of the Center for Neurological Malignancies and Cancer Neurology. In addition, Dr. Guo holds the Urban and Shelley Meyer Professorship in Cancer, and he is in the Translational Therapeutics Program at the OSUCCC – James.

The more than 20 CCM research faculty have collective expertise in cancer metabolism, metabolomics and proteomics, cancer biology and other fields. Recent CCM publications in scientific journals include: (from Dr. Guo's lab) Cheng et al. 2022, *Nature Metabolism*; Cheng et al. 2022, *Genes and Diseases*; Kou et al. 2022, *Biomedicines*; (from the lab of Qingfei Zheng, PhD) Cai et al. 2022, *Microbiology Spectrum*; Ray et al. 2022, *ACS Chemical Biology*.

To learn more about cancer metabolism or to find a collaborator with cancer metabolism expertise, visit **cancer.osu.edu**.

Deliang Guo, PhD



Center for Cancer Engineering (CCE)

The OSUCCC – James Center for Cancer Engineering – Curing Cancer Through Research in Engineering and Sciences (CCE-CURES) bridges the medical and engineering fields to collaboratively design, develop and integrate innovative engineering technologies and data analytic approaches with cancer biology, biomechanics and fundamental science. The goal is to enhance cancer prevention, detection, diagnosis and treatment.

The CCE-CURES program – which has more than 50 members and offers training opportunities, collaborative research, cross-disciplinary funding, and technology development and transfer – is led by co-directors **Matthew Ringel, MD**, and **Jonathan Song, PhD**. Dr. Ringel, who holds the Ralph W. Kurtz Chair in Hormonology, is a professor and director of the Division of Endocrinology, Diabetes and Metabolism in the Ohio State College of Medicine and co-leader of the Cancer Biology Program at the OSUCCC – James. Dr. Song is an associate professor in the Department of Mechanical and Aerospace Engineering in the Ohio State College of Engineering and a member of the Cancer Biology Program at the OSUCCC – James.

The CCE-CURES program has three primary areas of emphasis supported by cross-cutting themes. Areas of emphasis are:

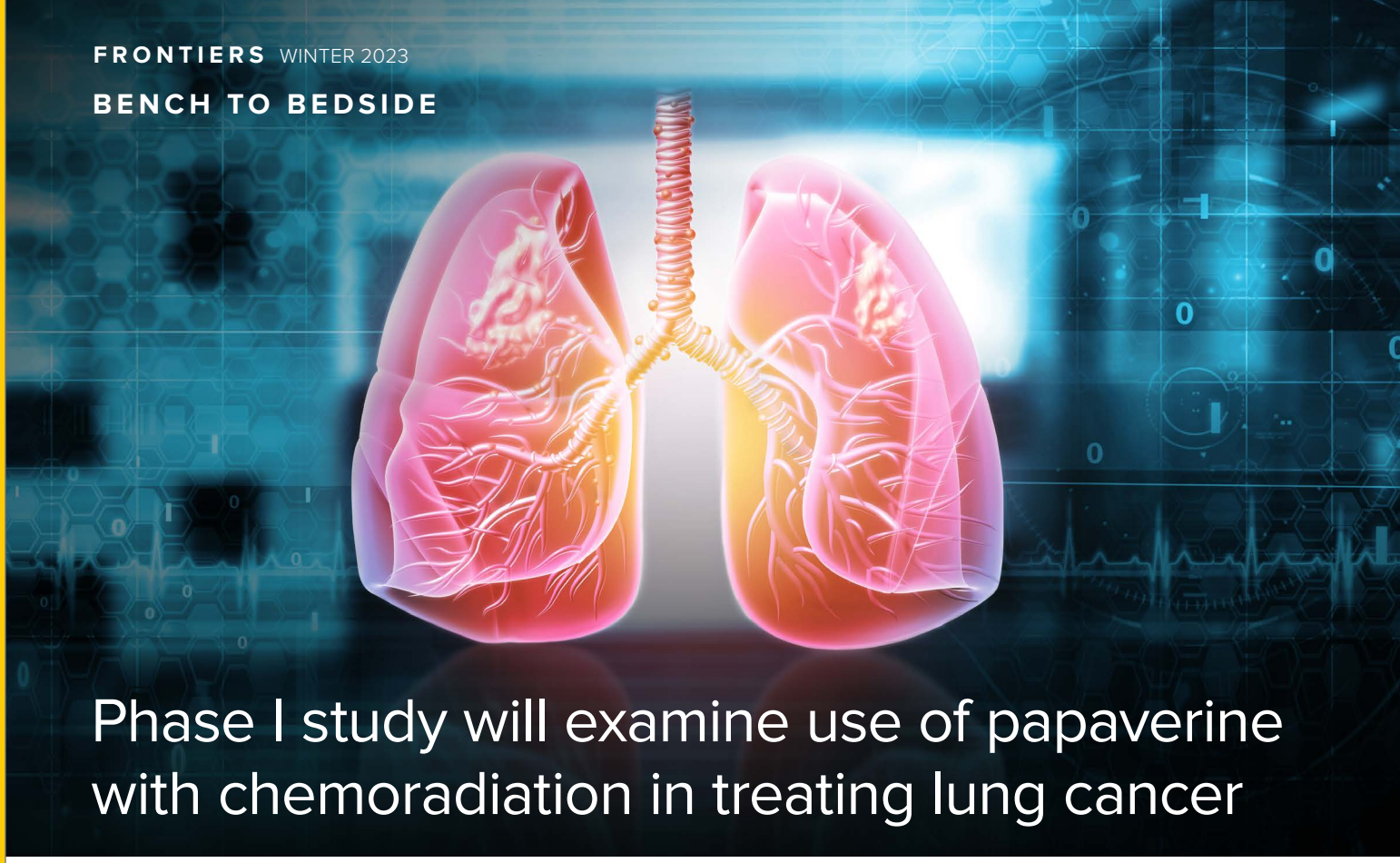
- Advance detection and fundamental knowledge using emerging imaging methods and technologies;
- Transform treatment using novel materials and drug-delivery approaches; and
- Enhance diagnosis and prediction using computation-enabled discovery.

Cross-cutting themes are:

- Mechanisms of cancer invasion and metastasis to target cancer progression;
- Biosensors and molecular imaging for cancer detection;
- Therapeutics to improve cancer care; and
- Data analysis and computing to link discovery to the cancer clinic.

Matthew Ringel, MD

Jonathan Song, PhD



Phase I study will examine use of papaverine with chemoradiation in treating lung cancer

Patient accrual is underway for a phase I clinical trial at the OSUCCC – James (OSU-20327) to determine the best dose and possible benefits and/or side effects of the drug papaverine (PPV) when given in combination with chemoradiation therapy (CRT) and immunotherapy to patients with unresectable, locally advanced, stage II-III non-small cell lung cancer (NSCLC).

Papaverine targets mitochondrial metabolism to lower oxygen consumption and decrease tumor hypoxia. Principal investigator **Jeremy Brownstein, MD**, assistant professor in the Department of Radiation Oncology at Ohio State, and his colleagues hypothesize that giving papaverine with CRT may work best to treat patients with NSCLC.

The clinical trial also will: estimate the rates of primary tumor control, local control, time to local-regional progression, disease-free survival and overall survival; assess whether blood oxygen level determination (BOLD) functional magnetic resonance imaging (MRI) studies can predict which patients may respond best to PPV + CRT; detect changes in oxygenation before and after PPV administration; and assess whether blood-based and tissue-based biomarkers can predict which patients may respond best to PPV + CRT.

This dose-escalation trial is open to all patients 18 years or older with histologically or cytologically proven NSCLC that is considered unresectable or medically inoperable. Participants receive PPV intravenously or subcutaneously and undergo five fractions of radiation therapy per week.

> *"It is our hope that papaverine will allow radiation to better eradicate lung cancer without increasing damage to nearby healthy tissues."*
>
> **JEREMY BROWNSTEIN, MD**

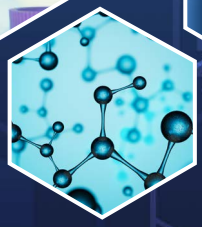
They also receive paclitaxel IV over one hour and carboplatin IV once weekly over one to six weeks in the absence of disease progression or unacceptable toxicity. When they are within one month of completing CRT, patients with PD-L1-positive disease receive durvaumab IV every two weeks for 12 months.

After completion of study treatment, all patients are followed for two years at one, three, six, nine, 12, 16, 20 and 24 months, and then periodically for up to five years.

"Hypoxia within tumors makes radiation less effective, which may be why some lung cancers recur after treatment," Dr. Brownstein says. "By decreasing tumor hypoxia, it is our hope that papaverine will allow radiation to better eradicate lung cancer without increasing damage to nearby healthy tissues."

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: Medicinal Chemistry

The **Medicinal Chemistry Shared Resource (MCSR)** integrates the expertise of scientists in multiple disciplines, including medicinal, synthetic and process chemistry, instrumental analysis, chemical biology and molecular pharmacology, to provide medicinal chemistry and high-throughput screening support to investigators at the OSUCCC – James and other academic and commercial institutions.

In collaboration with other **OSUCCC – James Shared Resources**, the MCSR translates basic science findings from investigators into small-molecule agents for testing individual hypotheses, adding an important dimension in translating basic science to the clinic.

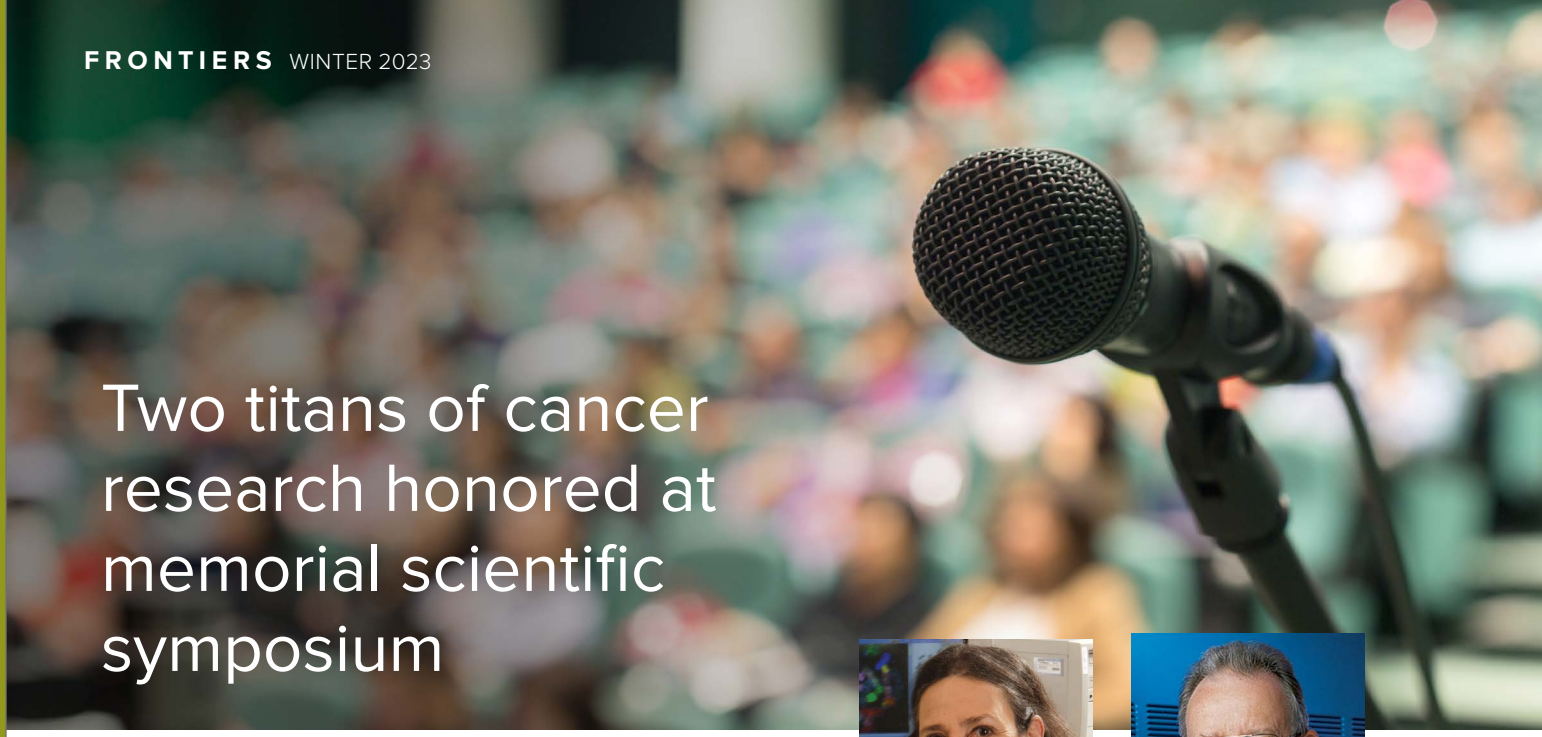
The MCSR achieves this by providing investigators with multiple aspects of medicinal chemistry and small-molecule screening services, such as chemistry feasibility consultation, design and synthesis of new molecules of biological interest, sample purity analyses and custom syntheses of known agents. This resource also offers high-throughput screening and high-content screening of small-molecule libraries against a wide range of biological assays and targets.

The MCSR has two cores:

The **synthetic core (MCSR-SC)** offers consultation and several services relating to synthetic medicinal chemistry. Staff working in this core help researchers design derivatives of lead structures to improve biological properties such as potency, efficacy and bioavailability. Services also include custom synthesis of agents not available from commercial sources, and consultations with investigators about commercially available small molecules.

The **high-throughput screening core (MCSR-HTSC)** offers libraries of diverse small molecules integrated with sophisticated instrumentation for automated liquid handling and detection of interactions with biological pathways and proteins on multiwell plates. This core offers cell-based high-content screening by confocal imaging and flow cytometry, and biochemical/biophysical high-throughput screening using luminescence-based and thermal ramping methods. Services include assay adaptation and development, high-throughput screening, high-content screening, verification of compound activity, collections of plated compounds, analysis of HTS data and high-content imaging data, grant-writing assistance, support services and project management.

The MCSR is led by Co-Directors **Chad Bennett, PhD** (synthesis); **Blake R. Peterson, PhD** (synthesis/HTSC); and **Meng Wu, PhD** (HTSC).



Two titans of cancer research honored at memorial scientific symposium

Clara D. Bloomfield, MD

Albert de la Chapelle, MD, PhD

Medical scientists from the United States, Germany, Finland and Spain lectured on cancer-related topics held dear by two titans of cancer research – **Clara D. Bloomfield, MD**, and **Albert de la Chapelle, MD, PhD** – at a June 1 memorial symposium held for them at The Ohio State University, where they played key leadership roles from 1997 until they died only eight months apart in 2020.

The symposium, which took place at The Ohio Union and was livestreamed to an even wider audience, was a gathering of friends, colleagues and trainees of these two internationally renowned scientists, a husband-and-wife duo whose groundbreaking studies in hematologic malignancies and human cancer genetics helped change the landscape of science-based cancer care.

Raphael E. Pollock, MD, PhD, FACS, director of The Ohio State University Comprehensive Cancer Center (OSUCCC), said in his opening remarks that their contributions to a broad spectrum of cancer issues "is matched only by their remarkable mentoring impact and development of cancer programs that continue to thrive on the basis of what they accomplished."

Among the guests was Michael A. Caligiuri, MD, former director of the OSUCCC and former CEO of Ohio State's James Cancer Hospital and Solove Research Institute, who said Dr. Bloomfield "put her money where her heart was and probably remains" by bequeathing $4 million to establish the **Clara Derber Bloomfield Research Endowed Fund** to provide research support to senior cancer researchers in acute leukemia at Ohio State. Dr. Caligiuri said his former mentor and colleague wanted "to see to it that we continue to work hard to cure not only acute leukemia, but other cancers as well."

Reflecting on the long-term impact Drs. Bloomfield and de la Chapelle had on Ohio State's cancer program, Dr. Pollock referenced a recent conversation he had with **David Schuller, MD**, who was director of both the OSUCCC and The James until 1997, when Dr. Bloomfield became director of the OSUCCC and deputy director of The James. (Dr. Schuller remained as director of The James and deputy director of the OSUCCC.)

"Dave pointed out to me that the smartest thing he ever did in his role as director was to help recruit Clara and Albert, and I think we can all agree with that assessment," Dr. Pollock said, referring not only to how they helped the OSUCCC – James' research programs grow and thrive, but also to how they "propagated through the next several generations of investigators and clinician-investigators who have participated in moving these programs forward on an ever-expanding basis.

"We're just extremely fortunate that Clara and Albert – without sounding too smarmy – graced us with their presence and helped us in so many ways to 'up the ante' and markedly increase the visibility of the university as a whole, and of our cancer program specifically, to its current level of international impact."

The symposium included lectures by prominent scientists on such topics as "microRNA Dysregulation in Cancer Causation and Progression" (**Carlo Croce, MD**, professor in the Department of Cancer Biology and Genetics at Ohio State), "Clara and Albert and the Rise of Cancer Epigenomics" (Christoph Plass, PhD, professor at The German Cancer Research Center in Heidelberg);

"From Years of Cytogenetics to Reprogramming Early Cells" (Juha Kere, MD, PhD, of the University of Helsinki in Finland); and "Sisterhood of the Core Binding Factor: Rowley and Bloomfield" (Tim Ley, MD, of Washington University School of Medicine).

Also on the agenda were tribute videos and breakout sessions on hematology and genetics, with the speakers in each session also presenting scientific talks.

The hematology session featured Hartmut Doehner, medical director of the Department of Internal Medicine at Ulm University in Germany; John C. Byrd, MD, chair of the Department of Internal Medicine at the University of Cincinnati; and Dr. Caligiuri, president of City of Hope National Medical Center in Duarte, California.

The genetics session featured Sanford Markowitz, MD, PhD, professor of cancer genetics at Case Western Reserve University; Laura Valle, PhD, principal investigator of the Hereditary Cancer Program at Catalan Institute of Oncology in Barcelona, Spain; and Luis Diaz Jr., MD, head of the Division of Solid Tumor Oncology at Memorial Sloan Kettering Cancer Center in New York City.

Dr. Croce said he had known Drs. Bloomfield and de la Chapelle for many years before he was recruited to Ohio State in 2004, and that he had collaborated with Dr. Bloomfield on breakthrough studies of hematologic malignancies.

"I was always impressed by her drive," Dr. Croce said. "She was chair of the scientific advisory committee of the cancer center in Philadelphia where I was the director, and I loved to interact with her because she knew how a cancer center works, and she gave me some of her knowledge about that.

"I knew Albert for over 40 years and was impressed by his knowledge of human genetics and cancer genetics. It is a great pleasure to be here to celebrate these two people who contributed so much to the study of leukemias and solid tumors, and to the reputation of Ohio State's cancer program."

Dr. Plass, who worked with Drs. de la Chapelle and Bloomfield when he was at the OSUCCC – James from 1997-2007, expressed a sentiment echoed by many of the day's speakers when he spoke of "how their support of young scientists has impacted their careers."

Dr. Doehner called Dr. Bloomfield "one of the most remarkable people I've ever met" and added that she was "probably the most important mentor and supporter of my career."

Dr. Valle said Dr. de la Chapelle "was not only my mentor but a role model and someone I looked up to. I learned many things from him, both personally and professionally."

Ohio State scientists **Ann-Kathrin Eisfeld, MD**, assistant professor in the Division of Hematology, and **Amanda Toland, PhD**, associate professor in the Department of Cancer Biology and Genetics, moderated the two breakout sessions. Both expressed gratitude for their mentors.

> *"Dave pointed out to me that the smartest thing he ever did in his role as director was to help recruit Clara and Albert, and I think we can all agree with that assessment."*
>
> **RAPHAEL E. POLLOCK, MD, PHD, FACS**

"Albert was a very big influence on my career," Dr. Toland said. "From the beginning, he was always open to sit down and talk about what your experiments were, what you were thinking about doing, and he would ask the pivotal question, the one that nobody else asked, but as soon as he asked it, you were like, 'Of course! I should think about this!' or "Why didn't I think about this?' or 'That's such a great insight!'"

Dr. Eisfeld, who also directs the **Clara D. Bloomfield Center for Leukemia Outcomes Research** at the OSUCCC – James, spoke of how she benefited from the influence of both scientists – Dr. de la Chapelle in the study of cancer genetics, and Dr. Bloomfield in the realm of hematologic malignancies. "I would hope that their legacies will extend beyond science," she said. "They were such good scientists because they were such good people."

The day's final speaker was Charles Derber, PhD, a professor in the Department of Sociology at Boston College and Dr. Bloomfield's younger brother. In a virtual address, he thanked Ohio State and the OSUCCC – James for hosting the memorial symposium, which he called "a really creative way to celebrate their contributions."

Dr. Derber said he was moved by hearing the speakers' memories, feelings and appreciation of Drs. Bloomfield and de la Chapelle.

"I'm speaking as a representative of the family, but really, as was very clear today, Clara and Albert had two families: their families of origin, and all of you who are a huge central part of a second family," Dr. Derber said, adding that, from the day's heartfelt tributes, he had learned even more than he knew before about these two individuals "and how remarkable they were as people and academicians and scholars."

"Their relationship itself needs to continue to be celebrated," he said. "Freud said there are two important things in life: work and love. Usually, these are separated into different compartments of people's lives, but in the case of Clara and Albert, they melded. Their relationship was a fusion of these incredibly powerful forces of passion for work, and passion for love and life."

KEY RESEARCH GRANTS

Eugene Oltz, PhD

Prestigious MERIT Award boosts study of DNA break repair mechanisms

The National Institute of Allergy and Infectious Disease (NIAID) has issued a 10-year, $4.7 million Method to Extend Research in Time (MERIT) Award to help Ohio State researchers continue studying repair mechanisms for DNA double-strand breaks in lymphocytes (immune cells in the blood and lymph tissue). Faulty repair of these breaks can lead to genomic aberrations that cause cancer, especially leukemia and lymphoma. Principal investigator (PI) is **Eugene Oltz, PhD**, professor and chair of the Department of Microbial Infection and Immunity at Ohio State, and a member of the Cancer Biology Program at the OSUCCC – James. The MERIT Award goes to investigators with a stellar research record in immunology and infectious disease. It allows for significant freedoms and advances in research.

Ann-Kathrin Eisfeld, MD

Alice Mims, MD, MSCR

Elaine Mardis, PhD

NCI grant will fund study of treatment patterns in subset of patients with AML

A team of OSUCCC – James researchers will use a five-year, $3.32 million grant from the National Cancer Institute (NCI) for a study that will help them understand treatment response patterns and therapy resistance in a subset of patients with acute myeloid leukemia (AML). Multiple PIs are **Ann-Kathrin Eisfeld, MD** (project leader and contact PI), **Alice Mims, MD, MSCR**, and **Elaine Mardis, PhD**. Drs. Eisfeld and Mims serve respectively as assistant and associate professor in the Department of Internal Medicine, Division of Hematology at Ohio State and are also in the Leukemia Research Program at the OSUCCC – James. Dr. Mardis is a professor in the Department of Pediatrics at Ohio State and co-leader of the Translational Therapeutics Program at the OSUCCC – James. Dr. Mims also is clinical section head for the Acute Leukemia Program in the Division of Hematology, and Dr. Eisfeld is director of the Clara D. Bloomfield Center for Leukemia Outcomes Research.

Ce Shang, PhD

Cancer researcher gains federal grant to study impact of retail marijuana excise tax structures on marijuana consumption

Ce Shang, PhD, assistant professor in the Department of Internal Medicine, Division of Medical Oncology at Ohio State and a member of the Cancer Control Program at the OSUCCC – James, received a five-year, $3.3 million grant from the National Institute on Drug Abuse for a project titled "The Impact of Excise Tax Structures for Retail Marijuana on Marijuana Consumption." Dr. Shang says this project will evaluate how excise tax structures impact marijuana consumption and product choices among marijuana forms and between legal and illegal products. The empirical evidence will inform how to set excise tax structures to mitigate harms for states contemplating taxation policies as they legalize marijuana, and for states and localities with legal retail sales considering reforms to their current tax structures. Dr. Shang is a health economist with extensive experience in regulatory science. Her research evaluates the effectiveness of policies regulating tobacco, alcohol and recreational marijuana, with a focus on taxation.

Lapo Alinari, MD, PhD

Scientists receive NCI grant to develop therapy against rare large B-cell lymphoma

The National Cancer Institute (NCI) awarded a five-year, $2.9 million grant to help researchers at the OSUCCC – James study a rare form of large B-cell lymphoma (LBCL) and develop a targeted therapy for patients with this currently incurable cancer. The PI is **Lapo Alinari, MD, PhD**, assistant professor in the Department of Internal Medicine, Division of Hematology at Ohio State, and a member of the Leukemia Research Program at the OSUCCC – James. In their project abstract, Dr. Alinari and colleagues state that patients with LBCL that overexpresses the c-Myc protein have a significantly worse prognosis than patients with the cMyc-negative form of the disease – highlighting the need for novel therapeutic strategies.

Zihai Li, MD, PhD

NCI grant will help researchers target molecular pathway for cancer immunotherapy

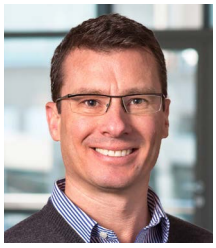
A five-year, $2.82 million grant from the NCI will enable OSUCCC – James investigators to study how a chaperone molecule called GRP94 controls cancer and to determine the best strategy to target this molecule for cancer immunotherapy. The PI is **Zihai Li, MD, PhD**, founding director of the Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC – James and professor in the Division of Medical Oncology at Ohio State. In the project abstract, Dr. Li states that his lab team has demonstrated that GRP94 "is a strategically important target for cancer, because it controls multiple key molecular pathways in cell growth, migration, immune tolerance and differentiation."

Selvendiran Karuppaiyah, PhD

Federal grants will aid efforts for earlier detection of endometrial and ovarian cancer

The U.S. Department of Defense (DOD) has awarded a pair of grants totaling approximately $2.65 million to help OSUCCC – James researchers identify cellular biomarkers that could lead to earlier detection of endometrial and ovarian cancer. A four-year, $1.94 million grant from the DOD Peer-Reviewed Cancer Research program will address gaps in the early detection and diagnosis of endometrial cancer. A three-year, $710,000 grant from the DOD Ovarian Cancer Research Program will enhance efforts for earlier detection of high-grade serous ovarian cancer (HGSOC). The PI for both is **Selvendiran Karuppaiyah, PhD**, associate professor in the Department of Obstetrics and Gynecology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James.

Bethany Mundy-Bosse, PhD

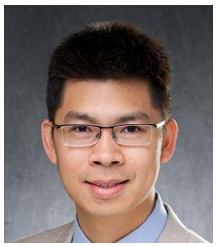


Christopher Oakes, PhD

Researchers land grant to study innate immune dysfunction in patients with AML

OSUCCC – James researchers will use a five-year, $2.54 million grant from the NCI to study a mechanism of innate immune dysfunction in acute myeloid leukemia (AML) and to explore a therapeutic combination that may repair this defect and improve immune cell responses in patients with cancer. The NCI awarded the grant, titled "Dysregulation of Lymphoid Immunity in Acute Myeloid Leukemia," to multiple PIs **Bethany Mundy-Bosse, PhD**, and **Christopher Oakes, PhD**, both of whom are assistant professors in the Division of Hematology at Ohio State and members of the Leukemia Research Program at the OSUCCC – James.

KEY RESEARCH GRANTS



Kin Fai Au, PhD

NIH grants to help bioinformatics studies with applications to developmental and stem cell biology

The National Human Genome Research Institute of the NIH has awarded a four-year, $2.4 million grant to help Ohio State researchers produce the first bioinformatics platform for comprehensively studying repetitive genes and gene isoforms in a complex biomedical context. Also, the National Institute of General Medical Sciences at the NIH has awarded an associated four-year grant of $1.79 million for a project that will use another set of bioinformatics and an innovative epigenome assay called MeSMLR-seq that the researchers developed by using nanopore sequencing. The PI for both grants is **Kin Fai Au, PhD**, associate professor in the Department of Biomedical Informatics and member of the Translational Therapeutics Program at the OSUCCC – James. Dr. Au says the grants will be applied to developmental and stem cell biology; the methods and results could extend to cancer research.

Yiping Yang, MD, PhD

Xiaopei Huang, PhD

Researchers awarded NCI grant to study regulation of tumor-infiltrating T cells by macrophages

A five-year, $2.2 million grant from the NCI will help investigators at the OSUCCC – James study how tumor-associated macrophages (TAMs) disrupt immune cells (particularly CD8 T cells) and contribute to cancer development and progression. Multiple PIs **Yiping Yang, MD, PhD** (left), and **Xiaopei Huang, PhD** (right), both of the OSUCCC – James Leukemia Research Program, hope their study will lead to therapeutic strategies that target TAMs for treating cancer. Dr. Yang is a professor and director of the Division of Hematology at Ohio State. Dr. Huang is an associate professor in the division.

Sakima Smith, MD, MPH, FAHA

Scientists garner large NIH grant to study cancer treatment links to heart disease

A five-year, $2 million grant from the National Heart, Lung and Blood Institute at the NIH will help Ohio State researchers probe a relatively new area of medical science that works to link certain cancer treatments to heart failure. In their project abstract, the scientists state that the 14 million cancer survivors in the United States "demonstrate continued improvements in anticancer treatment efficacy; yet, this success has been tempered by a parallel rise in the incidence of cancer treatment-related cardiotoxicity, leading to morbidity and mortality." The team is led by PI **Sakima Smith, MD, MPH, FAHA**, associate professor in the Department of Internal Medicine, Division of Cardiovascular Medicine, and holder of the Bob Frick Research Chair in Heart Failure and Arrhythmia.

Krishna Chinthalapudi, PhD, MSc

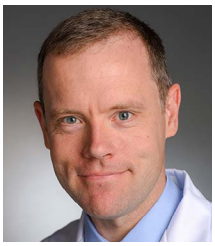
NIH grant-funded study may shed light on defective cellular processes that lead to cancer and other diseases

Researchers at Ohio State received a $1.89 million, five-year grant from the NIH to study the structure and function of nonmuscle myosin motors and how defects in the natural processes of these motor proteins can lead to a variety of human diseases, including cancer. The PI for the grant, awarded by the NIH's National Institute of General Medicine Sciences, is **Krishna Chinthalapudi, PhD, MSc**, assistant professor in the Department of Physiology and Cell Biology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James.

Adrienne Dorrance, PhD

NIH grants to help bioinformatics studies with applications to developmental and stem cell biology

OSUCCC – James researchers who have discovered that a protein called EGFL7 promotes acute myeloid leukemia (AML) will use a five-year, $1.5 million grant from the NCI to study how the protein facilitates AML and develop combination therapies to combat it. The PI is **Adrienne Dorrance, PhD**, assistant professor in the Department of Internal Medicine, Division of Hematology at Ohio State, where she also is in the Leukemia Research Program at the OSUCCC – James. In their project abstract, the researchers state that AML is a heterogeneous malignancy of the blood and bone marrow and note that, along with genetic mutations within the leukemic cells themselves, alterations in the bone marrow microenvironment play an important role in leukemia transformation, therapy resistance and relapse.



Bradley Blaser, MD, PhD

Federal grant will support study of hematologic regeneration after chemotherapy or stem cell transplantation

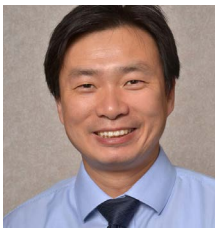
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) awarded OSUCCC – James researchers a five-year, $1.26 million grant for a study of hematopoiesis (blood cell production) that could lead to therapies to improve this process in leukemia patients following chemotherapy or stem cell transplantation. Led by PI **Bradley Blaser, MD, PhD**, assistant professor in the Division of Hematology at Ohio State and a member of the Leukemia Research Program at the OSUCCC – James, the basic-research study will explore the biological mechanisms involved with epigenetic control of vascular niche capacity to support hematopoiesis.

Kenneth Pitter, MD, PhD

Maria Mihaylova, PhD

Ohio State scientists land NIH high-risk, high-reward research grants

Two scientists in Ohio State's cancer program landed large grants from the NIH Common Fund's High-Risk, High-Reward Research Program, which supports scientists pursuing innovative research with the potential for broad impact in biomedical, behavioral or social sciences within the NIH mission. **Kenneth Pitter, MD, PhD**, assistant professor in the Department of Radiation Oncology, received a five-year, $1.25 million Early Independence Award, and **Maria Mihaylova, PhD**, assistant professor in the Department of Biological Chemistry and Pharmacology, received a five-year, $1.5 million New Innovator Award. Dr. Mihaylova also is in the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.



Lang Li, PhD

Grant-funded study will help scientists build informatics bridge over 'valley of death'

The NCI awarded a three-year, $1.16 million grant to help Ohio State investigators create a translational drug interaction knowledge base (TDCKB) that will provide an informatics bridge over the "valley of death" for multi-drug cancer therapies. **Lang Li, PhD**, chair of the Department of Biomedical Informatics at Ohio State and a member of the Cancer Biology Program at the OSUCCC – James, is the PI for the project. Dr. Li says the new TDCKB will integrate multi-drug exposure and toxicity data from various data sources.

Achievements, awards and honors

Institutional

The OSUCCC – James earned three national awards for excellence in patient care delivery from Press Ganey, a health care performance-improvement organization that works with more than 41,000 facilities. For the *seventh consecutive year*, the OSUCCC – James **received the Press Ganey Guardian of Excellence Award® for Patient Experience** for sustaining excellence in patient experience over a single year. The institution also **received its *fourth straight* Press Ganey Pinnacle of Excellence Award® for Patient Experience in Inpatient Care** (with regard to the non-Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) sections of the hospital's inpatient survey) for maintaining excellence over consecutive years. In addition, it **received its *third straight* Press Ganey Pinnacle of Excellence Award® for Patient Experience in HCAHPS** for maintaining excellence over consecutive years.

The Blood and Marrow Transplant (BMT) unit at the OSUCCC – James has again received national recognition for exceptional patient care and professional nursing practice with a **three-year Silver Beacon Award for Excellence** from the American Association of Critical-Care Nurses (AACN). This award – which provides gold, silver and bronze levels of recognition – honors hospital units that employ evidence-based practices to improve patient and family outcomes and that exemplify excellence in professional practice and patient care. This is the third Beacon Award of Excellence Award for the 36-bed BMT unit; the team previously received a bronze award in 2015 and a gold award in 2018.

The Board of Directors for the International Cardio-Oncology Society (IC-OS) has **designated The Ohio State University Cardio-Oncology Program as one of a limited number of Centers of Excellence (Gold Standard)** in recognition of the program's outstanding professional contributions to cardio-oncology. The three-year designation extends through July 2025. The Cardio-Oncology Program is led by Director **Daniel Addison, MD**, associate professor in the Division of Cardio-Vascular Medicine at Ohio State and a member of the Cancer Control Program at the OSUCCC – James.

The OSUCCC – James Acute Leukemia Program **received a disease-specific care re-certification from The Joint Commission**, the nation's top hospital-ranking organization. The Acute Leukemia Program is one of only three programs in the United States to have earned this advanced-level certification. It initially received Joint Commission certification in 2020. Joint Commission disease-specific certification means that the Acute Leukemia Program complies with the highest national standards for safety and quality of care and is committed to continually improving patient care.

The OSUCCC – James Sickle Cell Program **received a disease-specific care re-certification** from The Joint Commission following a review in which surveyors issued no findings or recommendations. In 2018, the OSUCCC – James became the only institution in the

United States to have the Joint Commission's sickle cell disease-specific certification, which involves evaluation of clinical programs across the continuum of care for compliance with standardized requirements and expectations for ensuring quality care and patient safety.

The OSUCCC – James has **joined the Caris Life Sciences® (Caris) Precision Oncology Alliance™ (POA)**, an international network of leading cancer centers that collaborate to advance precision oncology and biomarker-driven research. POA members work together to establish and optimize standards of care for molecular testing through research focused on predictive and prognostic markers that improve clinical outcomes for cancer patients. The Caris POA comprises 59 cancer centers and academic institutions.

Dayton Physicians – Hematology and Medical Oncology **has affiliated with The James Cancer Network (JCN) of the OSUCCC – James** to enhance cancer care services for cancer patients in five southwestern Ohio counties (Butler, Darke, Miami, Montgomery and Warren) and beyond. The JCN is a system of collaborations among the OSUCCC – James and many other institutions in cancer care. These regional connections not only improve care coordination but also enhance access to cancer expertise, clinical research and the latest developments in cancer treatment.

The 2022 Castle Connolly Top Doctors list contains almost 350 Ohio State physicians, including more than 100 who treat patients with cancer at the OSUCCC – James. The total is more than at any other hospital facility in central Ohio. Each year, *Columbus Monthly* magazine partners with Castle Connolly, a health care research company, to evaluate physicians based on their education, research leadership, interpersonal skills, professional success and disciplinary history. The newest list of more than 650 central Ohio top physicians appeared in the August issue of *Columbus Monthly*.

The nurse residency programs for the James Cancer Hospital and Solove Research Institute and for Health System Nursing **earned their second American Nurse Credentialing Center (ANCC) Practice Transition Accreditation Program® (PTAP)**. Both programs earned accreditation with distinction. The ANCC PTAP sets the global standard for residency or fellowship programs that transition registered nurses (RNs) and advanced practice registered nurses (APRNs) into new practice settings that meet evidence-based standards for quality and excellence.

The James Oncologic Physical Therapy (PT) Residency Program became the first oncology PT residency in Ohio – and the sixth in the United States – **to gain accreditation by the American Board of Physical Therapy Residency and Fellowship Education (ABPTRFE)**.

The residency provides extensive training for the successful treatment of patients with cancer. **Karen Hock, PT, MS, CT-LANA**, associate director of ambulatory oncology rehabilitation at The James, says the residency is a collaboration between The James and the Clinical Doctorate in Physical Therapy Program in the Ohio State College of Medicine's School of Health and Rehabilitation Sciences.

For demonstrating an outstanding commitment to diversity and inclusion, five health sciences graduate programs at Ohio State **received the 2022 Health Professions Higher Education Excellence in Diversity (HEED) Award** from *INSIGHT Into Diversity* magazine, the oldest and largest diversity-focused publication in higher education. The colleges of Medicine, Nursing, Optometry, Public Health and Veterinary Medicine were recognized. Ohio State was the only academic institution in the country to have five colleges honored.

The James, the Ohio State Wexner Medical Center and Nationwide Children's Hospital are among 17 health care entities in Ohio that were recognized by the Human Rights Campaign Foundation as **2022 LGBTQ+ Healthcare Equality Index (HEI) Leaders**. The HEI is a national LGBTQ+ benchmarking tool that evaluates health care facilities' policies and practices related to the equity and inclusion of their LGBTQ+ patients, visitors and employees. The HEI evaluates more than 1,700 health care facilities nationwide.

The OSUCCC – James has for the ***third time*** **achieved Magnet® recognition from the American Nurses Credentialing Center (ANCC)**. The Magnet Recognition Program® recognizes health care organizations for quality patient care, nursing excellence and innovations in professional nursing practice. The renewed Magnet® status, which included nine exemplars for nursing care, will extend for four years. The OSUCCC – James initially achieved Magnet® recognition in 2013 and regained it in 2018.

A brand storytelling website called **Ohio State Health & Discovery** located at **health.osu.edu** has been launched to showcase innovations in clinical care, health and wellness, science, research and education at The Ohio State University, the Ohio State Wexner Medical Center and the OSUCCC – James. The site is designed to serve as health news consumers' trusted source for stories behind the headlines from experts across the medical center, the OSUCCC – James and health science colleges. It includes a cancer topic section.

ACHIEVEMENTS, AWARDS AND HONORS

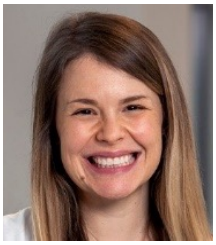
Team and individual

Corrin Steinhauer, DNP, RN, NEA-BC, CPPS

Corrin Steinhauer, DNP, RN, NEA-BC, CPPS, became the **chief nursing officer** (CNO) at the James Cancer Hospital and Solove Research Institute on May 9. She succeeded **Kris Kipp, MSN, RN**, executive director of clinical services, who had also served as CNO since 2013. Dr. Steinhauer, who reports to Kipp, came to the OSUCCC – James from the University of Chicago Medicine Ingalls Memorial Hospital, where she was vice president of patient care services and CNO. She has a strong academic medical center background and proven experience in leading a cancer service line.

Arnab Chakravarti, MD

Arnab Chakravarti, MD, professor and chair of the Department of Radiation Oncology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James, received the inaugural **Louis B. Harrison Award Lectureship at Moffitt Cancer Center** in Tampa, Florida. The award recognizes his outstanding leadership in radiation oncology on the international level, including securing some of the highest levels of federal funding; directing the most expansive growth in clinical volume and the highest patient quality and safety nationally; leading innovation in proton and FLASH therapies and translational research; and being the first Indian-American to chair a radiation oncology department among the top comprehensive cancer centers in the country.



Laura Chambers, DO

Laura Chambers, DO, assistant professor in the Division of Gynecologic Oncology at Ohio State, received the **2022 Gynecologic Oncology Group (GOG) New Investigator Award** from the GOG Foundation Education/Mentoring Committee, the NRG Oncology Early Career New Investigator Committee and the Society of Gynecologic Oncology (SGO). The three-year award is for young investigators who want to engage more with the GOG Foundation and NRG Oncology and learn more about the gynecologic cancer clinical trial process.

David Carr, MD, MPH, FAAD

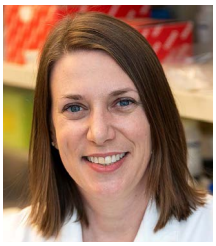
David Carr, MD, MPH, FAAD, clinical associate professor in the Department of Dermatology at Ohio State and Mohs micrographic surgery program director, received the **Making a Difference Award from the American Academy of Dermatology (AAD)**. Recipients are selected for the significance of their work and the uniqueness of their volunteer activity with exceptional service to the community, the underserved, the local dermatology society, academics and the AAD. Dr. Carr is a dermatologist primarily focused on cutaneous oncology.

Zihai Li, MD, PhD

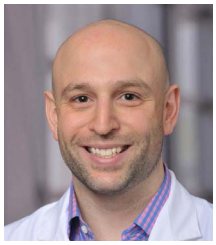
Announced in 2022, **Zihai Li, MD, PhD**, professor in the Department of Medical Oncology at Ohio State and founding director of the **Pelotonia Institute for Immuno-Oncology (PIIO)** at the OSUCCC – James, was among seven scientists from Ohio State who were elected to the 2021 class of **Fellows of the American Association for the Advancement of Science (AAAS)**. The AAAS Fellowship, which recognizes individuals for scientifically or socially distinguished efforts to advance science or its applications, is one of the most prestigious honors a U.S. scientist can receive. Dr. Li was elected for contributions to molecular immunology.

ACHIEVEMENTS, AWARDS AND HONORS

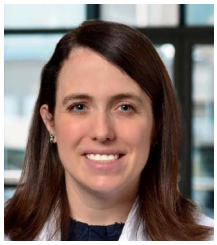
Seema Bhat, MD



Jennifer Woyach, MD

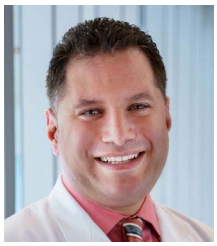


Adam Kittai, MD



Kerry Rogers, MD

Seema Bhat, MD, **Jennifer Woyach, MD**, **Adam Kittai, MD**, **Kerry Rogers, MD** and **Alison Neal, MPH, MSL** (not shown), all of the Division of Hematology at Ohio State, were **published in an Association of Community Cancer Centers (ACCC) report** titled "*Multidisciplinary Chronic Lymphocytic Leukemia Care: Quality Improvement Case Studies*." The ACCC, an education and advocacy organization for the cancer care community, invited the OSUCCC – James to join ACCC cancer program members in tailored quality-improvement workshops. The OSUCCC – James chronic lymphocytic leukemia (CLL) team completed a project to improve the care of hypertension in CLL patients on BTK inhibitors.



Dukagjin Blakaj, MD, PhD

Daniel Prevedello, MD

Brad Otto, MD

Matthew Old, MD

Ricardo Carrau, MD

The North American Skull Base Society (NASBS) designated The Ohio State University Skull Base Surgery team as an **NASBS Multidisciplinary Team of Distinction (MTD)**. This designation is based on having at least four NASBS members with specific multidisciplinary expertise. The five NASBS members who made Ohio State eligible are **Dukagjin Blakaj, MD, PhD** (Radiation Oncology); **Daniel Prevedello, MD** (Neurological Surgery); and **Brad Otto, MD**, **Matthew Old, MD**, and **Ricardo Carrau, MD**, (Otolaryngology – Head and Neck Surgery). Drs. Prevedello and Carrau lead the Skull Base Surgery team.

Sumithira Vasu, MBBS

Sumithira Vasu, MBBS, associate professor in the Division of Hematology at Ohio State and a member of the Leukemia Research Program at the OSUCCC – James, was invited to be a **co-chair of the Scientific Organizing Committee** for the 2023 Tandem Meetings of the American Society for Transplantation and Cellular Therapy and the Center for International Blood and Marrow Transplant Research.

ACHIEVEMENTS, AWARDS AND HONORS

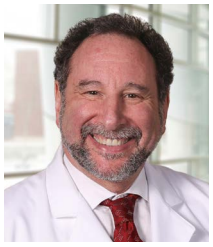
James L. Chen, MD

Wendy Frankel, MD

James L. Chen, MD, and **Wendy Frankel, MD**, were selected as two-year recipients of the **Alliance for Clinical Trials in Oncology Foundation Special Project Allocation**. Dr. Chen is a member of the Translational Therapeutics (TT) Program and an associate professor in the Division of Medical Oncology and the Department of Biomedical Informatics. Dr. Frankel is a member of the TT Program and serves as professor and chair of the Department of Pathology. The Alliance for Clinical Trials in Oncology accepts proposals to support research on high-priority areas every two years. Dr. Chen's allocation title is "Alliance Harmonized and Unified Biodashboard (HUB) Initiative"; Dr. Frankel's is "Automatic Detection of Tumor Buds in Colorectal Cancer Patients From H&E Images."

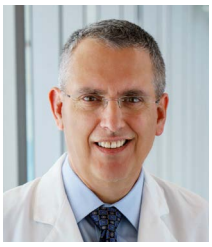
Robert Wesolowski, MD

Robert Wesolowski, MD, associate professor in the Division of Medical Oncology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James, was elected as a **co-chair of the Correlatives Clinical Trial Working Group Committee at the Big Ten Cancer Research Consortium**. Dr. Wesolowski treats patients with all types of breast cancer.



Peter Shields, MD

Peter Shields, MD, deputy director of the OSUCCC and a thoracic oncologist at The James, was one of two scientists nationally who received the 36th annual **Alton Ochsner Award Relating Smoking and Disease,** which celebrates individuals who have made major contributions regarding the relationship between smoking and disease along with the development of innovative treatment modalities. Ochsner Health is a not-for-profit system that delivers health care to people in Louisiana, Mississippi and the Gulf South.



Douglas Martin, MD

Douglas Martin, MD, a radiation oncologist and vice chair of clinical operations for the Department of Radiation Oncology at Ohio State, was selected to receive the **American Society for Radiation Oncology (ASTRO) Fellow designation (FASTRO)** at the ASTRO 64th Annual Meeting in October 2022. The ASTRO Fellows program recognizes individuals who have made substantial contributions to the society and radiation oncology through research, education, patient care and service. Since its inception in 2006, the FASTRO designation has been awarded to just 421 of ASTRO's 10,000 members worldwide.

Chyke Doubeni, MD, MPH

Dr. Doubeni begins new DEI leadership roles at Ohio State

Chyke Doubeni, MD, MPH, was named associate director for diversity, equity and inclusion (DEI) at the OSUCCC – James effective July 1, when he also became chief health equity officer and leader of the Office of Health Equity, Diversity and Inclusion at The Ohio State University Wexner Medical Center. He holds a faculty appointment in the Department of Family and Community Medicine at the Ohio State College of Medicine.

Dr. Doubeni succeeds **Cheryl Lee, MD**, who had served as interim director for diversity, equity and inclusion since July 2021 and is credited with launching the Office of Health Equity, Diversity and Inclusion. Dr. Lee continues to chair the Department of Urology in the College of Medicine.

Nationally recognized for his work in cancer prevention and public health, Dr. Doubeni came to Ohio State from the Mayo Clinic, where he directed the Center for Health Equity and Community Engagement Research. Besides his roles within the OSUCCC – James and the medical center, he will work with The Ohio State University Office of Academic Affairs on the RAISE initiative, which focuses on recruiting faculty who have a research emphasis on health-equity topics.

Working with the Office of Academic Affairs and the health science colleges at Ohio State, he also will lead the development and implementation of a new Center for Health Equity, an interdisciplinary incubator for health equity research collaboration across campus on research and training in the field.

A clinical epidemiologist, Dr. Doubeni focuses his research on evidence-based interventions to improve cancer screening and other preventive interventions to eliminate disparities in communities that are underserved with health care services.

At-home screening program aims to reduce colorectal cancer rates in Black community

Colorectal cancer experts have launched an initiative to improve the early detection and prevention of colorectal cancer in the Black community, which historically has been placed at increased risk for this disease by a lack of timely screening and because of barriers to receiving health care services.

Previous studies suggest that Black patients are 20% more likely to be diagnosed with colorectal cancer and 40% more likely to die of it than non-Hispanic white patients. In Ohio, it is estimated that more than 22% of Black patients diagnosed with colorectal cancer die of the disease.

"This is tragic and unacceptable in a disease with a highly effective and available screening tool for finding it in a precancerous and treatable stage," says **Subhankar Chakraborty, MD, PhD**, a gastroenterologist at the OSUCCC – James. "As we navigate year three of a global pandemic that continues to cause disruptions to both life and medical treatment access, it is even more critical that we find ways to increase timely cancer screening adherence. We want to catch the disease at its precancerous stage."

Through this initiative, The Ohio State University Wexner Medical Center, working in partnership with the Center for Cancer Health Equity at the OSUCCC – James, mailed at-home colorectal cancer screening kits to 400 patients who qualified for – but had not yet received – a colorectal cancer screening exam.

The initiative makes it easier for disproportionately affected groups to receive timely colorectal cancer screening tests. Black men and women between ages 45 and 75 who are treated at Ohio State and meet medical criteria for colorectal cancer screening were invited to receive one of the at-home colorectal cancer screening kits. They also received a letter describing how to complete the test and a follow-up call from the medical facility to answer questions.

Known as the "FIT kit," this test can detect microscopic amounts of blood in the stool that can be an early sign of colorectal cancer. The kit includes materials to collect and return a stool sample for medical evaluation. All participating individuals who have an abnormal finding are contacted by a nurse at Ohio State who explains the test results and may schedule a colonoscopy that can identify colorectal cancer and precancerous polyps.

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

460 W. 10th Ave.
Columbus, OH 43210-1240

NCI Designated Comprehensive Cancer Center

Non-Profit
U.S. Postage
P A I D
Columbus, OH
Permit No. 711

Opening in *2023*

The James Outpatient Care

Exceptional evidence-based cancer care and
central Ohio's only proton therapy treatment center

#ChooseTheJames
cancer.osu.edu

The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER