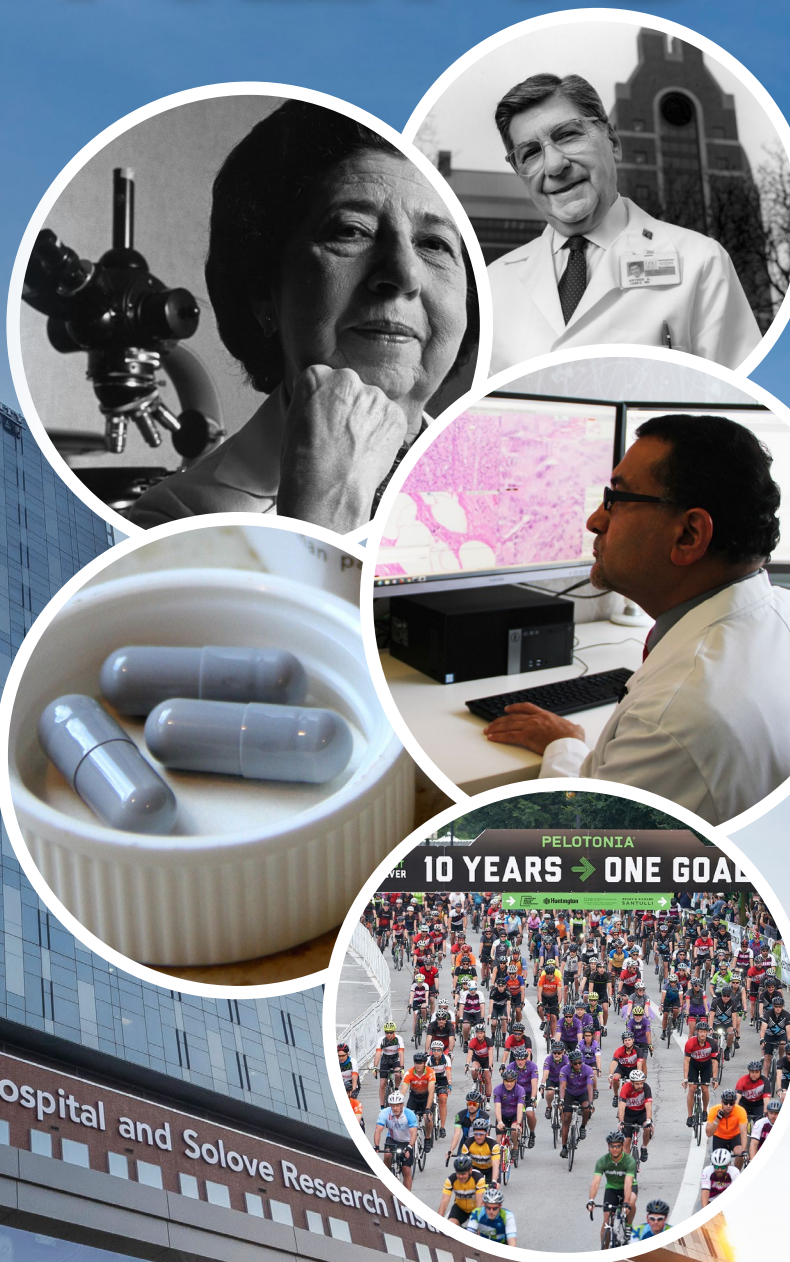
TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

SPRING EDITION 2021

Half a Century of Cancer Science at Ohio State: The National Cancer Act Turns 50



The James

The Ohio State University
COMPREHENSIVE CANCER CENTER

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

‘A source of hope’: President Biden touts support for cancer doctors, researchers during Ohio State visit

On March 23 President Joe Biden **brought his passion for cancer research to Ohio State**, where he met with doctors to discuss innovation at Ohio State’s Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James)—a “source of hope” that continues to break ground in the nationwide effort to create a cancer-free world.

Biden came to mark the 11th anniversary of the signing of the Affordable Care Act, the landmark legislation that transformed health coverage in the United States while also providing funds for advancements in medical technology, some of which are now in use at the OSUCCC – James, one of the nation’s leading comprehensive cancer centers.

The president was joined during his visit by James doctors, including **Arnab Chakravarti, MD, FASTRO, FACRO**, chair and professor of the Department of Radiation Oncology at Ohio State, who shared details about the impact of the ACA support on patients in central Ohio.

“I just concluded a tour of the radiation oncology department here, which was expanded thanks to a $100 million grant in the Affordable Care Act,” Biden said after speaking with Chakravarti and other Ohio State doctors. “Because of our investments, this department has gone from being able to treat 60 to 70 patients a day to nearly 300 a day. This place is a source of hope.”

That hope is evident on The James’ radiation oncology floor, where specialists work with patients representing nearly every cancer type.

“The ACA grant award expanded access to care—including historically underserved patient populations—and patient volumes at The James,” Chakravarti says. “It also led to the development of sentinel radiation oncology technologies at Ohio State that have already dramatically improved the safety and quality of care for our patients, and which also hold the potential to transform the future of cancer care, especially with the advent of proton therapy and FLASH (a highly targeted proton therapy scheduled to begin use at Ohio State in 2023).”

“We were excited to welcome President Biden to The James, and to discuss our shared vision for a cancer-free world,” says James CEO **William B. Farrar, MD**. “The president has long been a passionate advocate for cancer research, and we look forward to working with his administration to break new ground in cancer care and research right here at Ohio State.”

FRONTIERS

SPRING EDITION 2021

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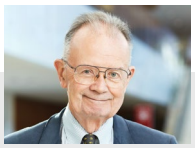

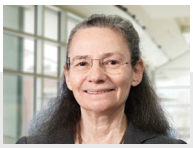

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Read *Frontiers* online or download an issue at **cancer.osu.edu/Frontiers**.

ON THE COVER:

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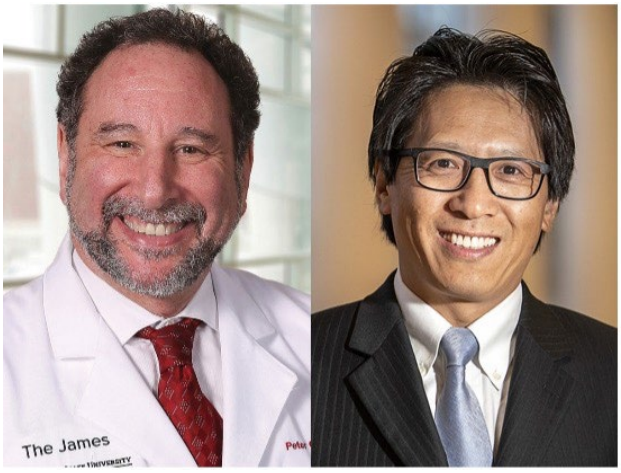
SIIREN STUDY

OSUCCC – James study seeks to understand effectiveness of COVID-19 vaccination in cancer patients, survivors

A large research study at the OSUCCC – James will evaluate how vaccination against SARS-CoV-2, the virus that causes COVID-19, impacts the immune system of cancer patients.

Project leaders believe the study will advance the scientific community's overall understanding of how effective the SARS-CoV-2 mRNA vaccine is in preventing COVID-19 infection, determine whether the vaccine is less effective in cancer patients receiving certain therapies and shed light on how long immunity lasts.

Many cancer therapies impact the immune system, which can leave it temporarily or permanently more susceptible to infection. These therapies could result in more severe infection and a higher chance of death from COVID-19 infections.



Co-principal investigators for the study, which is known as SIIREN (Study of Infections and Immune REspoNse), are **Peter Shields, MD** (left), deputy director of the OSUCCC – James, and **Zihai Li, MD, PhD** (right), director of the **Pelotonia Institute for Immuno-Oncology (PIIO)** at the OSUCCC – James.

When the study began, the researchers noted that there was no peer-reviewed published data on how cancer therapy affects the efficacy of the COVID-19 mRNA vaccine because cancer patients receiving active therapy were excluded from vaccine trials. Major trials had not specifically reported on outcomes in cancer patients not receiving active therapy; however, it is widely recommended that almost all cancer patients be vaccinated.

"This is a complicated study that our team developed in record time; from concept to our first patient was about eight weeks," says Shields, a professor in the Division of Medical Oncology at Ohio State and member of the Cancer Control Program at the OSUCCC – James. "This was hard work from more than 20 faculty and staff who were well-supported by leadership at all levels, and special credit also goes to the Ohio State Wexner Medical Center vaccine staff at the Schottenstein Center who made this happen with no slow-downs for overall vaccine patient flow."

"Our study will provide important data to confirm how effective the current COVID-19 vaccines are for preventing infection and transmission to others, which is a critical public health and economic question, especially for this high-risk population. It is also one of the largest prospective clinical trials to examine the immune response of cancer patients to the COVID-19 mRNA vaccines," says Li, a professor in the Division of Medical Oncology at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James.

SIIREN Study method and approach

OSUCCC – James researchers will enroll up to 450 cancer patients and 100 healthy volunteers aged 18 or older who are undergoing COVID-19 vaccination at the Ohio State Wexner Medical Center. The investigators will focus on how infection susceptibility and immunity change, based on the patient's stage of disease and treatment regimen.

Participants will provide weekly saliva samples by mail to test for SARS-CoV-2 infection and will provide periodic blood samples to comprehensively measure immune response. Patients will also complete periodic written questionnaires about the vaccine, any associated symptoms and potential COVID-19 exposures. Study investigators will monitor participants for a year.

As of mid-June, 28 individuals were enrolled in the trial, including 18 patients with cancer and 10 control individuals.

"Getting shots in arms to reach herd immunity so that—as a country—we can get back to some sense of normalcy is critical," Shields says. "Science has helped us rapidly mobilize to develop COVID-19 vaccines that are safe and effective at reducing severe illness and death in the adult general population, but there are substantial knowledge gaps we need to fill to provide the best protection to higher-risk populations, including the more than 17 million cancer survivors in the United States."

To learn more about participating in the SIIREN study, visit **cancer.osu.edu/SIIREN**. This study is supported by funds from the OSUCCC – James and from Pelotonia, the annual cycling event that raises millions of dollars for cancer research at Ohio State.

PROMINENT STUDIES

Preliminary results of two large immune therapy studies show promise in advanced ovarian cancer

Preliminary results from two independent phase II clinical trials investigating a new PD-1 (programmed cell death protein 1)-based immune therapy for metastatic cervical cancer suggest potential new therapies for a disease that has few effective treatment options and disproportionately impacts younger women.

David O'Malley, MD, director of the Division of Gynecologic Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, presented the preliminary study results last September at the European Society for Medical Oncology (ESMO) Virtual Congress 2020. O'Malley was the lead presenter for both trials, which were sponsored by Agenus Inc.

Each study involved more than 150 patients with recurrent or metastatic cervical cancer from cancer treatment centers across the United States and Europe. All patients had platinum-based chemotherapy as a first-line therapy. The two independent but consecutive phase II trials tested a new immune-based agent called balstilimab given alone or in combination with a second monoclonal antibody drug called zalifrelimab.

Balstilimab is part of a class of drugs called checkpoint inhibitors. These drugs target the PD-1 protein within cancer cells and act as an "on" switch to help the immune system recognize and destroy cancer cells that would otherwise go undetected. Zalifrelimab delivers engineered molecules (monoclonal antibodies) that allow for improved immune response to attack cancer cells.

For the first study, 160 patients were treated with single-agent balstilimab, resulting in a 14% response rate in all treated patients and a 19% response rate in PD-L1-positive patients.

For the second study, 155 patients were treated with balstilimab given in combination with zalifrelimab, resulting in a 22% response rate in all patients and a 27% response rate in PD-L1-positive patients.

"These studies represent the largest trials of immuno-oncology therapies in relapsed cervical cancer to date and show that balstilimab and zalifrelimab may present meaningful new therapies for patients with cervical cancer," O'Malley says. "Advances in these agents offer hope for patients who have limited treatment options. This is especially important because this disease disproportionately affects younger women."

Rubbery properties help RNA target tumors efficiently and quickly leave body

A study by researchers at the OSUCCC – James shows that RNA nanoparticles have elastic and rubbery properties that help explain why these particles target tumors so efficiently and why they possess lower toxicity in animal studies.

RNA nanoparticles show promise for the targeted delivery of anticancer drugs; understanding their structure and behavior is essential for their future use. This study, published in the journal *ACS Nano*, reveals that RNA nanoparticles' elastic and rubbery properties enable them to stretch and return to their normal shape. Researchers say these properties could help the particles target tumors by enabling them to slip through the poorly formed walls of tumor blood vessels and enter a tumor mass.

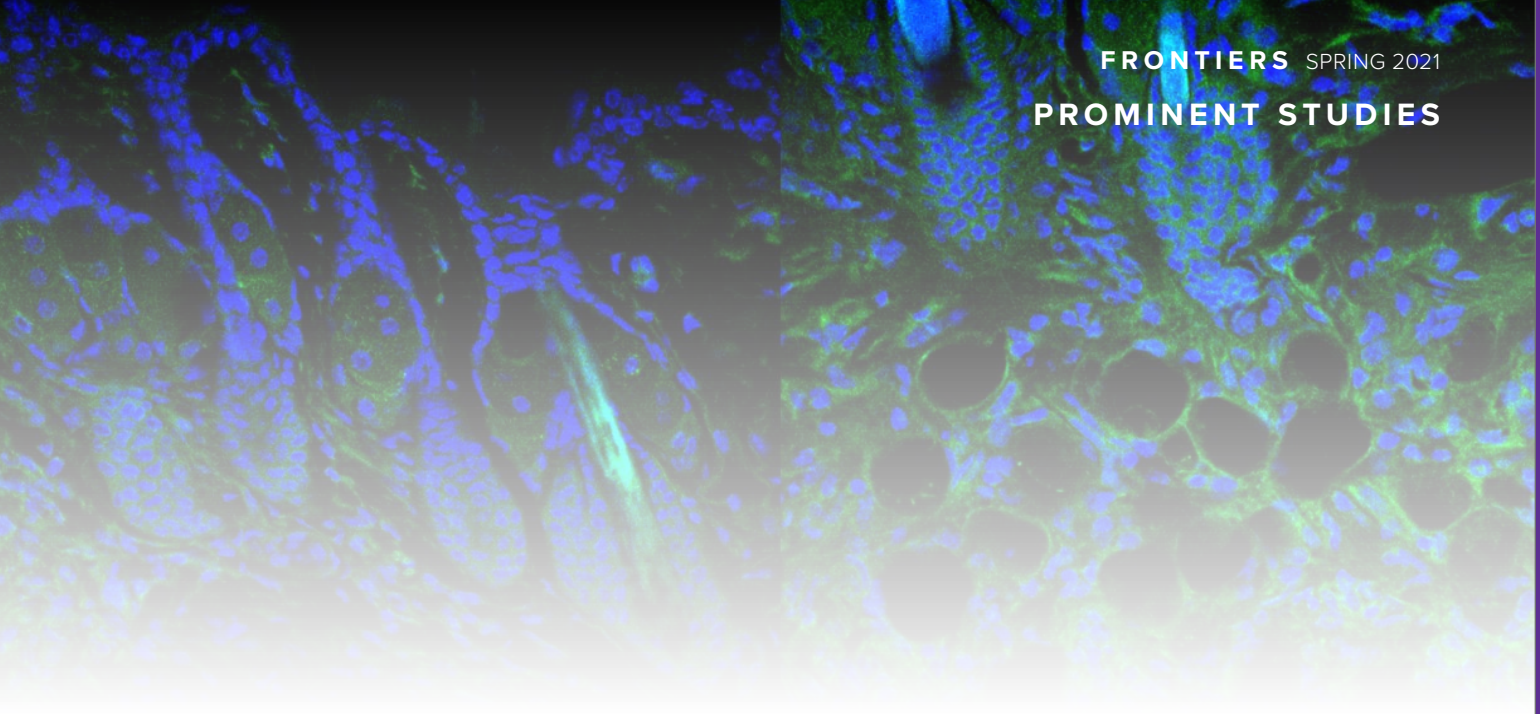
The researchers further proved that those rubbery properties enable the RNA nanoparticle to slip through the kidney to excrete into the urine a half-hour after systemic injection, thereby eliminating them from the body. That, in turn, could reduce retention of the anticancer agent in vital organs and lower the agent's toxicity.

"We show that RNA nanoparticles have a flexibility that allows for the assembly of molecular structures that have stretchable angles," says study leader and corresponding author **Peixuan Guo, PhD**, a professor in the College of Pharmacy and the Sylvan G. Frank Endowed Chair in Pharmaceutics and Drug Delivery. Guo is also in the Translational Therapeutics Program at the OSUCCC – James.

"These findings demonstrate the rubbery properties of RNA nanoparticles and why these molecules hold great promise for industrial and biomedical applications, especially as carriers for targeted delivery of anticancer drugs," says Guo, who directs Ohio State's Center for RNA Nanobiotechnology and Nanomedicine.

For this study, Guo and his colleagues tested the elasticity of nucleic acid polymers by stretching and relaxing individual RNA nanoparticles while subjecting them to elasticity studies using dual-beam optical tweezers built in the Guo lab. They then used animal models to study the biodistribution, excretion and retention of RNA nanoparticles. This included measuring excretion of the particles in urine and studying the effect of their shape and size.

"Overall," Guo says, "we believe these findings further support the development of RNA nanoparticles for targeted delivery of anticancer drugs or therapeutic RNA."



Study suggests common drug could be used to prevent certain skin cancers

New data published by researchers at the OSUCCC – James suggests that an oral drug used to treat neuromuscular diseases could also help prevent a common form of skin cancer caused by damage from ultraviolet-B (UVB) radiation from the sun.

Although this data was gathered from preclinical studies, senior author **Sujit Basu, MD, PhD**, of the Translational Therapeutics Program at the OSUCCC – James, says preliminary results in animal models are promising and worthy of further investigation through phase I human studies. Basu and colleagues in April reported their initial findings in the journal *Cancer Prevention Research*.

According to the American Cancer Society, more than 5.4 million basal and squamous cell skin cancers are diagnosed annually in the United States. The disease typically recurs throughout a person's lifetime, and advanced disease can lead to physical disfiguration. These cancers are linked to the sun's damaging rays, and despite increased public awareness of sun safety precautions, rates of the disease have been increasing for many years.

Previous peer-reviewed, published studies have shown that dopamine receptors play a role in the development of cancerous tumors; however, their role in precancerous lesions is unknown.

In this study, OSUCCC – James researchers report data showing that the neurotransmitter/neurohormone dopamine, by activating its D2 receptors, can stop the development and progression of certain UVB-induced precancerous squamous skin cancers. They also describe the molecular sequence of events that leads to cancer suppression.

"Cancer control experts have been stressing the importance of reducing exposure to the sun and practicing sun-safe habits for years, but scientific data shows us that cumulative damage of UV rays ultimately leads to skin cancer for many people," says Basu, a professor in the Department of Pathology at Ohio State. "Finding better ways to prevent these cancers from developing is critical to reduce the global burden of this disease.

"Our study suggests that a commonly used drug that activates specific dopamine receptors could help reduce squamous cell skin cancer recurrence and possibly even prevent the disease," he adds. "This is especially exciting because this is a drug that is readily used in clinical settings and is relatively inexpensive. We are excited to continue momentum in this area of research."

The OSUCCC – James is working on plans for further testing in a phase I clinical trial.

Therapeutic PD-1 cancer vaccine shown to be safe and effective in preclinical studies

A study led by researchers at the OSUCCC – James described a potential therapeutic anticancer vaccine that frees suppressed cancer-killing immune cells, enabling them to attack and destroy a tumor.

Published in the journal *Oncoimmunology*, the findings showed that the peptide called PD1-Vaxx, a first checkpoint inhibitor vaccine, was safe and effective in a colon cancer syngeneic animal model.

The researchers say the vaccine produced polyclonal antibodies that inhibit the programmed cell death receptor, PD-1, on cancer cells. The vaccine mimics the action of the PD-1 inhibitor nivolumab (Opdivo®), but it avoids triggering the innate and acquired

resistance associated with that and related agents, they add.

The study found that PD1-Vaxx was effective in inhibiting tumor growth. It was even more effective when used in combination with a second therapeutic peptide vaccine, one that targets two sites on the HER-2 receptor on colon cancer cells. The combination treatment produced complete responses in nine of 10 animals. That vaccine, called B-Vaxx, was developed earlier by the same research team.

"Our study is important for two key reasons," says first author and vaccine developer **Pravin T.P. Kaumaya, PhD**, a member of the OSUCCC – James Translational Therapeutics Research Program and a professor in Ohio State's College of Medicine. "First, PD1-Vaxx activates both B- and T-cell functions to promote tumor clearance. Second, the treatment is targeted to block signaling pathways that are crucial for tumor growth and maintenance.

"By giving this vaccine in combination with an immunotherapy drug," he explains, "we are super-charging and directing the immune system to target and kill cancer cells."

In November 2020, the U.S. Food and Drug Administration (FDA) granted investigational new drug (IND) approval to Imugene for clinical testing of PD1-Vaxx, an important milestone in the research collaboration between Ohio State and Imugene.

A first-in-human, phase I clinical trial to test the vaccine was expected to open at the OSUCCC – James in 2021 for certain patients with non-small cell lung cancer. Additional U.S. sites may be added to the trial later.

"We are excited to begin testing of this vaccine in the United States to offer new hope to patients with lung and other cancers," Kaumaya says.

Study: young Black patients with AML have worse treatment outcomes

Despite advances in treating acute myeloid leukemia (AML), Black patients below age 60 with this aggressive blood cancer have a 27% higher chance of dying compared with younger white patients.

When scientists at the OSUCCC – James explored factors that might contribute to this disparity, they found that, even when Black patients received the same treatment and follow-up care as their white counterparts, they still fared worse. This remained true in Black patients whose cancer carried genetic mutations that typically predict better prognosis and survival.

The researchers found that survival among young Black people with AML is "strikingly and unacceptably worse" than that seen in white patients with AML, particularly in younger patients. When the researchers looked at the mutations seen in AML, even Black patients with good prognostic risk factors experienced poorer outcomes.

The researchers presented their findings at the 2020 virtual annual meeting of the American Society of Hematology and published them in the journal *Cancer Discovery*.

For this study, they used the National Cancer Institute's Cancer Surveillance, Epidemiology and End Results (SEER) database to identify over 25,000 adults diagnosed with AML between 1986 and 2015. They found that, while survival for AML patients as a whole has improved, survival disparities between Black and white patients with AML have widened despite improved treatment and understanding of AML. They also identified a disparity in survival rates between young Black and white patients under age 60, who respectively had three-year overall survival rates of 34% and 43%.

Historically, the researchers stated, one of the biggest arguments for the poorer survival seen among Black AML patients has been challenges with access to treatment. However, the scientists found that even if patients have the same access and the same rates of remission, Black patients have significantly shorter survival time compared to white patients.

Study collaborator **Ann-Kathrin Eisfeld, MD**, and her team conducted genomic analyses to look at 81 genes commonly mutated in AML. Knowing whether a patient has these mutations helps clinicians customize treatment plans.

"We know that, when looking at the AML patient population, certain mutations are associated with better outcomes," Eisfeld says. "In this study, we showed this didn't hold true for all of them when we looked at Black patients alone. And when we analyzed factors that influence survival in all younger AML patients, Black race was an independent predictor of poor outcome. This suggests that Black race itself seems to be such a strong risk factor that it adds to the markers we rely on to risk-stratify patients."

National clinical trial led by Ohio State will test efficacy of immunotherapy plus radiation in reducing endometrial cancer recurrence

The OSUCCC – James is leading a multi-institutional phase III clinical trial to determine whether combining targeted immunotherapy with radiation therapy will reduce cancer recurrence in women with high intermediate-risk endometrial cancer.

The randomized clinical trial will compare whether the addition of a monoclonal antibody called pembrolizumab—a form of immunotherapy—to radiation therapy is more effective than radiation therapy alone in reducing the risk of cancer recurrence in patients with newly diagnosed stage I-II endometrial cancer characterized by mismatch repair-deficient (dMMR) tumors.

The national principal investigator for this trial, which is sponsored by the National Cancer Institute (NCI) in collaboration with NRG Oncology, is **Floor Backes, MD**, associate professor in the Division of Gynecologic Oncology at Ohio State and member of the Cancer Control Program at the OSUCCC – James. Patient accrual is under way with an anticipated enrollment of 168.

Backes says immunotherapy with monoclonal antibodies such as pembrolizumab may help the body's immune system attack the cancer and interfere with the ability of tumor cells to grow and spread, while radiation therapy uses X-rays to kill tumor cells and shrink tumors. The primary objective of this study, she adds, is to compare the three-year recurrence-free survival of women with high intermediate-risk stage I/II dMMR endometrial cancer who are treated with radiation and pembrolizumab versus those who are treated with radiation alone.

"Patients with early-stage endometrial cancer and a certain change in their tumor, called a mismatch repair deficiency or microsatellite instability (MSI-high), have a higher risk of cancer coming back," Backes says, explaining that MSI is a condition that predisposes to gene mutations and signifies that DNA mismatch repair is not functioning properly (deficient).

"These tumors appear less sensitive to chemotherapy but more sensitive to immunotherapy," she says. "This trial specifically enrolls this select population of endometrial cancer patients for personalized therapy involving targeted immunotherapy plus radiation, or just radiation."

She says the trial is "the first of its kind in randomizing a very specific population of patients for receiving targeted therapy. It will show whether this approach will change the standard of care and result in better outcomes and survival for these patients."

Finding a way to stop chemotherapy from damaging the heart

There could be an intervention on the horizon to help prevent heart damage caused by the common chemotherapy drug doxorubicin, new research suggests.

Scientists at the OSUCCC – James found that this drug, used to treat many types of solid tumors and blood cancers, can enter heart cells by hitchhiking on a specific protein that functions as a transporter to move a drug from the blood into heart cells.

By introducing another anticancer drug in advance of the chemo, the researchers were able to block the transporter protein, effectively stopping the delivery of doxorubicin to those cardiac cells. This added drug, nilotinib, has been previously found to inhibit activation of other related transport proteins.

The current findings are based on lab experiments in cell cultures and mice. The researchers are continuing studies and hope to start designing human trials of the drug intervention later in 2021.

PROMINENT STUDIES

"The proposed intervention strategy that we'd like to use in the clinic would be giving nilotinib before a chemotherapy treatment to restrict doxorubicin from accessing the heart," says first author **Kevin Huang**, who recently earned a PhD in pharmaceutical sciences at Ohio State and is a former Pelotonia Fellow. "We have solid preclinical evidence that this intervention strategy might work."

The study was published in January in the journal *Proceedings of the National Academy of Sciences*.

Doxorubicin is known for its potential to increase patients' risk for serious heart problems, with symptoms sometimes surfacing decades after chemo, but the mechanisms have been a mystery. The risk is dose-dependent—the more doses a patient receives, the higher the risk for future cardiac dysfunction, including arrhythmia and a reduction in blood pumped with each contraction, a symptom of congestive heart failure.

Huang worked in the lab of senior study authors **Shuiying Hu, PhD**, and **Alex Sparreboom, PhD**, faculty members in the Division of Pharmaceutics and Pharmacology at Ohio State, and members of the Translational Therapeutics Program at the OSUCCC – James. This research and other studies targeting transport proteins to prevent chemo-related nerve pain were also part of Huang's dissertation.

"Our lab works on the belief that drugs don't naturally or spontaneously diffuse into any cell they would like to. We hypothesize that there are specialized protein channels found on specific cells that facilitate movement of internal or external compounds into the cell," Huang says.

Older minority cancer patients experience worse surgical outcomes compared to white patients with similar socioeconomic factors

Older minority cancer patients with poor social determinants of health are significantly more likely to experience negative surgical outcomes compared to white patients with similar risk factors, according to a study by researchers at the OSUCCC – James.

In a retrospective analysis of more than 200,000 patients, minority patients living in high socially vulnerable neighborhoods had a 40% increased risk of a complication and a 23% increased risk of 90-day mortality compared to white patients for neighborhoods with low social vulnerability. The U.S. Centers for Disease Control and Prevention (CDC) defines social vulnerability as "potential negative effects on communities caused by external stresses on human health."

The study was selected for the 2020 Southern Surgical Association Program and published in the *Journal of the American College of Surgeons*.

"This study speaks to how health care and health outcomes extend beyond the doors of the hospital and even beyond the specifics of the disease the patient may have. Ultimately, theresources in the patient's community may be as important to the patient's health as what goes on in the hospital," says **Timothy Pawlik, MD, PhD, MPH**, senior author of the study and holder of the Urban Meyer III and Shelley Meyer Chair for Cancer Research at the OSUCCC – James. Pawlik is surgeon-in-chief at the Ohio State Wexner Medical Center and chair of the Department of Surgery in Ohio State's College of Medicine.

"This issue is not new, but the data strongly suggests we could significantly improve surgical outcomes by integrating vulnerability assessments into our national standard of care models. By doing so, we could help identify the most vulnerable among us—upfront—and provide additional supports as patients move through treatment and recovery," Pawlik adds. "The data emphasizes how efforts to improve outcomes for cancer patients need to extend beyond the hospital and address systemic health-related disparities within the communities in which patients live."

For this study, researchers used the social vulnerability index (SVI) risk-stratification tool, a composite measure of 15 social and economic factors. Although the CDC created the SVI using census data to identify communities needing greater support during disasters, researchers recently have applied it to medical studies.

They found that minority patients with high SVI scores had a 47% increased chance of an extended length-of-stay, 40% increased odds of a surgical complication and 23% increased odds of 90-day mortality.

Metastatic colorectal cancer phase Ib study

A phase Ib adaptive study of dasatinib for the prevention of oxaliplatin-induced neuropathy in patients with metastatic colorectal cancer

Patient accrual is under way at Ohio State for an interventional phase Ib clinical trial that will study side effects and best dose of the drug dasatinib in preventing oxaliplatin-induced peripheral neuropathy in patients with stage II, III and IV colorectal cancer and other gastrointestinal cancers who are receiving the FOLFOX regimen with or without bevacizumab.

Drugs used in chemotherapy, such as leucovorin, fluorouracil and oxaliplatin (the FOLFOX regimen), work to stop the growth of tumor cells by killing them, preventing them from dividing or keeping them from spreading. But a buildup of oxaliplatin in peripheral nerves can damage them and cause peripheral neuropathy, which results in numbness, tingling and pain, usually in the hands and feet. Dasatinib may prevent oxaliplatin from entering the nerve root and damaging it.

This study seeks to determine whether blocking the transporter of oxaliplatin using dasatinib will reduce oxaliplatin-induced peripheral neuropathy. The study was recently amended to allow inclusion of patients with stage II and III colon and rectal cancer or any other gastrointestinal cancers for which FOLFOX would be a suitable treatment.

Study design

Patients receive oxaliplatin IV over 2 hours, leucovorin IV over 2 hours, fluorouracil slow IV push over 2-4 minutes followed by continuous infusion over 46 hours on days 1 and 15. Patients also receive dasatinib PO QD on days 14, 15 and 28 of cycle 1 and day 1 of cycle 2. Patients may receive bevacizumab IV over 30 minutes on days 1 and 15. Treatment repeats every 28 days for up to cycle 3 day 1 in the absence of disease progression or unacceptable toxicity.

Primary objectives

To determine the recommended phase 2 dose of dasatinib in combination with oxaliplatin and fluorouracil (5FU) (modified version 6 regimen of leucovorin, fluorouracil and oxaliplatin [mFOLFOX6]) with or without bevacizumab in patients with metastatic colorectal cancer or other gastrointestinal cancers, defined as the lowest intermittent dose of dasatinib that affects serum biomarkers of OCT2 without influencing the pharmacokinetic properties of oxaliplatin.

To determine the toxicity profile (based on Chemotherapy-Induced Peripheral Neuropathy [CIPN]20 and Common Terminology Criteria for Adverse Events [CTCAE] version [v.] 5.0) of dasatinib in combination with oxaliplatin/5-FU/bevacizumab in patients with colorectal cancer and other gastrointestinal cancers.

Study leaders

Principal investigator is **Anne Noonan, MD**, associate professor in the Division of Medical Oncology at Ohio State and member of the Translational Therapeutics (TT) Program at the OSUCCC – James. Scientific lead is **Shuiying Hu, PhD**, assistant professor in the College of Pharmacy and a member of the TT Program.

At a glance

Trial No.: OSU-19067

ClinicalTrials.gov identifier: NCT04164069

PI: Anne Noonan, MD
Phone: 614-385-2039
Questions & referrals: anne.noonan@osumc.edu or danielle.trunzo@osumc.edu

Eligibility
Inclusion criteria: Men and women 18 years of age or older; patients with confirmed stage II, III or IV (advanced/metastatic) colorectal cancer or other gastrointestinal cancers who are candidates for mFOLFOX6, with or without bevacizumab therapy; pathological confirmation of gastrointestinal cancer; patients may have had prior therapy for metastatic colorectal or other gastrointestinal cancer; Eastern Cooperative Oncology Group (ECOG) performance status =< 2

Exclusion criteria: Pre-existing neuropathy of any type which is grade 2 or greater (grade 1 neuropathy is allowed), treatment with any other investigational agents within 4 weeks or 5 half-lives (whichever is longer) prior to the first dose of dasatinib; gastrointestinal (GI) disease or impairment of GI function that is likely to significantly alter the absorption of dasatinib.

Half a century of cancer science at Ohio State

The National Cancer Act turns 50

The Ohio State University's cancer program took root decades before the signing of the National Cancer Act in 1971, but it began to flourish soon after that historic event. Fifty years later, the OSUCCC – James remains focused on creating a cancer-free world. Here are a few of the program's milestones and research highlights of the past half century.

1976

- In April, the NCI designated Ohio State as a comprehensive cancer center (OSUCCC)—one of only 18 at the time—with **David Yohn, PhD**, as the first director. Yohn guided the OSUCCC through its early years and helped it start rising toward national prominence.

1980

- **Richard Olsen, DVM, PhD**, led an OSUCCC team in veterinary pathobiology—including **Larry Mathes, PhD**—that discovered and developed a vaccine for feline leukemia, helping to protect cats from their No. 1 killer.
- During the 1980s, **Bertha Bouroncle, MD**, **Eric Kraut, MD**, **Michael Grever, MD**, and colleagues developed the drug pentostatin for patients with hairy cell leukemia (HCL), a rare chronic leukemia that Bouroncle had identified in 1958. They showed that pentostatin induced over 90% complete remission in HCL patients. It became a standard therapy and changed the natural history of HCL from incurable to a disease for which patients regularly achieve remission.

1984

- The university broke ground for a new freestanding cancer hospital that would become the adult patient care component of the OSUCCC.

1987

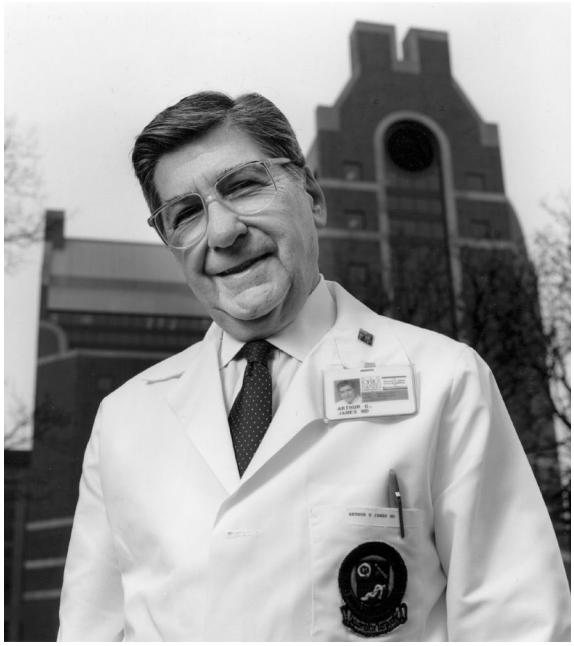
- During a ceremony at which the cornerstone was set, then-Ohio State University President Edward Jennings announced that the hospital would be named for **Arthur G. James, MD**, a surgical oncologist who had spent nearly 40 years leading the charge for a cancer hospital in central Ohio.

1988

- **David Schuller, MD**, a surgical oncologist and researcher in the Department of Otolaryngology – Head and Neck Surgery, was named as director of The James (two years before it opened) and also of the OSUCCC. His tenure saw enormous growth in the OSUCCC – James' ability to translate cancer research to innovative clinical care.

1990

- The original **James Cancer Hospital and Research Institute** opened on July 9, 1990. **Arthur G. James, MD**, accompanied the first patient to be wheeled into the new facility from the adjoining Ohio State University Hospitals. Dr. James would retire from seeing patients in this same year, but he had an office at the hospital and maintained an everyday presence in an emeritus role until 1996. He died in 2001.



1995

- The OSUCCC – James, under the leadership of **David Schuller, MD**, played a primary role in a multi-institutional phase III clinical trial demonstrating that chemotherapy plus radiation therapy improved survival of patients with advanced head and neck cancer compared with then-standard treatment of radiation therapy alone. This trial changed the standard of care for this disease.

1997

- A new era in cancer research began at Ohio State with the recruitment of internationally renowned medical scientists **Albert de la Chapelle, MD, PhD**, **Clara D. Bloomfield, MD**, and **Michael A. Caligiuri, MD**. Bloomfield became director of the OSUCCC and deputy director of The James; de la Chapelle founded and directed the human cancer genetics program; Caligiuri became associate director for clinical research at the OSUCCC. **David Schuller, MD**, remained as director of The James and became deputy director of the OSUCCC.

1998

- The OSUCCC – James contributed to a landmark national study, the Breast Cancer Prevention Trial, which over the past six years had shown a 45% reduction in breast cancer cases among women at high risk for the disease who took the drug tamoxifen vs. placebo. **William Farrar, MD**, and **David Schuller, MD**, discussed the breakthrough at a press conference in The James Lobby. Tamoxifen became the first drug known to prevent rather than just treat breast cancer.

- An international team led by **Clara D. Bloomfield, MD**, and **Michael A. Caligiuri, MD**, discovered a genetic marker for a novel mechanism of leukemogenesis that they called partial tandem duplication of the *MLL* oncogene. This was the first molecular marker discovered for patients with acute myeloid leukemia (AML) who have normal cytogenetics.

1999

- Community leader **Richard J. Solove**, a longtime friend of Dr. James and supporter of the cancer program at Ohio State, donated $20 million to the OSUCCC – James Threshold of Discovery campaign for human cancer genetics research. In honor of this donation, the hospital was renamed the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

2000

- OSUCCC – James researcher **Christoph Plass, PhD**, led an international team that discovered and described the non-random and tumor-type specific nature of DNA promoter methylation in cancer. This was the first time DNA methylation had been examined in human cancer on so large a scale and with comparisons of so many tumor types.

2001

- An OSUCCC – James team including **Michael Ostrowski, PhD**, **Gustavo Leone, PhD**, and **Charis Eng, MD, PhD**, presented one of the first microenvironment-based genetic models of the multi-step process leading to breast cancer. The model was based on their discovery that mutations in stromal cells (which surround or connect to tumors) are linked to cancer formation. They called the model "paradigm-shifting" because, previously, mutations leading to breast cancer were thought to occur only in epithelial cells, which line or cover organs.

- The World Health Organization (WHO) classification of hematologic malignancies for the first time incorporated genetic studies rather than just morphology—particularly in AML—based in large part on the work of a WHO clinical advisory committee chaired by OSUCCC Director **Clara D. Bloomfield, MD**. Under her leadership, the WHO classification for AML was further revised over the years based on molecular studies at Ohio State and other institutions.

2002

- **Pierluigi Porcu, MD**, and **Michael A. Caligiuri, MD**, developed a therapy yielding the best reported survival to date for patients with post-transplant lymphoproliferative disorders (PTLD), an often lethal form of lymphoma associated with the Epstein-Barr virus. Of 11 patients on the therapy, 10 were alive nearly three years later with no sign of disease.

HALF A CENTURY

2002

In the early 2000s, **John C. Byrd, MD**, was the national study leader for clinical trials in which rituximab became the first modern therapy to show significant improvement in overall survival for patients with chronic lymphocytic leukemia (CLL). Researchers found that combining rituximab with the standard chemotherapy drug fludarabine increased progression-free survival by 22% and overall survival by 12% compared with fludarabine alone.

2003

Clara D. Bloomfield, MD, stepped down as director of the OSUCCC and deputy director of The James to focus more fully on her pioneering research in adult leukemia and lymphoma. **Michael A. Caligiuri, MD**, succeeded her in both roles. **David Schuller, MD**, remained as executive director of The James and deputy director of the OSUCCC; Bloomfield became an Ohio State University cancer scholar and senior adviser to the OSUCCC – James.

Researchers led by **Clara D. Bloomfield, MD**, and **Albert de la Chapelle, MD, PhD**, reported that overexpression of a gene called *BAALC*, which they and others at Ohio State had co-discovered, is linked to poor response to therapy and shorter survival for patients with AML. Researchers could thus identify a new subset of AML patients who previously were classified as standard risk but who actually are more likely not to respond well to standard treatments.

William Carson, MD, led a research team that demonstrated in laboratory studies and clinical trials the effectiveness of combining the drug Herceptin with a cytokine called interleukin-12 (IL-12) to boost the immune system's ability to fight breast cancers that overexpress the HER-2 protein.

2004

The first findings were reported from a long-term Ohio State study called the Stress and Immunity Breast Cancer Project led by **Barbara Andersen, PhD**, who started it in 1994 as a randomized clinical trial involving 227 women with stage II and III breast cancer. Findings indicated that a psychological counseling intervention for these patients can not only lower stress but also lead to healthier diets, reduced smoking and a stronger immune system.

2005

Scientists at the OSUCCC – James led the way in defining the role that microRNA may play in carcinogenesis. **Carlo Croce, MD**, and colleagues reported their discovery of how microRNA works in breast cancer and said the microRNA signature in this disease is linked to biological features that doctors may use for diagnosis and treatment.

Studies led by **Albert de la Chapelle, MD, PhD**, and **Heather Hampel, MS, LGC**, in 2005 and 2008 showed that one in 35 people with colon cancer also have Lynch syndrome (LS), an inherited condition that predisposes to colorectal, endometrial, ovarian and other cancers. The researchers recommended screening all newly diagnosed colon-cancer patients for LS.

Since 2005, OSUCCC – James researchers have worked with scientists, medical professionals and policy experts from eight colleges at Ohio State in the Center for Advanced Functional Foods Research and Entrepreneurship (CAFFRE). This collaboration has resulted in more than $19 million in nationally sponsored projects and over 300 publications on food and health. Led by Director **Yael Vodovotz, PhD**, and Associate Director **Steven Clinton, MD, PhD**, CAFFRE has commercialized several products, including soy-tomato juice, soy-almond bread and black raspberry confections—functional foods with anticancer properties that enhance human health.

2006

An international study led by OSUCCC – James researchers **Christoph Plass, PhD**, and **Albert de la Chapelle, MD, PhD**, discovered the first inherited gene mutation that increases risk for CLL. The mutation is in the *DAPK1* gene.

2006

- A team led by **Michael A. Caligiuri, MD**, discovered the site and stages of development for natural killer (NK) cells, the last major set of human immune cells to be biologically characterized. The findings opened doors to manipulating the human immune system, possibly leading to new therapies for cancer, infection and immune deficiencies.

- A study led by **John C. Byrd, MD**, revealed that a new strain of mouse offered the first real animal model for CLL. The TCL-1 transgenic mouse, originally engineered by Ohio State researcher **Carlo Croce, MD,** develops a malignancy that mimics CLL.

2007

- A team led by **David Schuller, MD**, reported that three phase II trials at the OSUCCC – James over the past 12 years had shown that "intensification therapy"—a complex regimen of surgery, radiation and chemotherapy developed at Ohio State in the 1990s—is a difficult but tolerable treatment that yields good overall survival rates for patients with advanced head and neck cancers.

2008

- The cancer program's research and clinical components were consolidated into one leadership position held by **Michael A. Caligiuri, MD**, who succeeded **David Schuller, MD**, as CEO of The James while retaining his post as director of the OSUCCC. Schuller was appointed vice president for medical center expansion and outreach.

2009

- A study at the OSUCCC – James indicated that some older AML patients (60 or above) whose cancer cells have mutations in the *NPM1* gene respond better to therapy and experience longer survival. Study leader **Clara D. Bloomfield, MD**, said researchers knew mutations in this gene signaled a favorable prognosis for younger AML patients, but this study's findings indicated the same is true for older patients, suggesting they should be offered stronger therapy.

2009

- The inaugural **Pelotonia**, an annual three-day cycling event that raises millions of dollars for cancer research at Ohio State, was held in August. Over the years (2009-21) Pelotonia has raised more than $224 million, with every dollar raised by riders, challengers, donors and volunteers going directly to cancer research.

2011

- A team of surgeons removed the left leg, hip and pelvis of a cancer patient and used the healthy bones from his amputated leg to rebuild the connection between his spine and remaining right pelvis to support a high-tech prosthetic leg. It was the first time the procedure had been performed in the United States, according to **Joel Mayerson, MD**, an orthopedic oncologist who worked with a team that included neurosurgeon **Ehud Mendel, MD**, and plastic surgeon **Michael Miller, MD**. Their work was voted "Reconstructive Surgery Case of the Year" by the American Society of Reconstructive Microsurgeons.

- A study at the OSUCCC – James showed that the loss of the *NFKBIA* gene promotes the growth of glioblastoma multiforme, the most common and deadly form of brain cancer. Published in the *New England Journal of Medicine*, the study suggested that therapies to stabilize this gene may improve survival for certain patients. Senior co-author **Arnab Chakravarti, MD**, said investigators showed the gene may be an independent predictor of survival in some patients.

HALF A CENTURY

2012

- A study led by **Clara D. Bloomfield, MD**, and published in the journal *Blood* found that older people with AML and normal-looking chromosomes in their cancer cells have a higher risk of recurrence if they have mutations in the *ASXL1* gene. The study was the first to investigate the influence of these mutations on prognosis in patents with cytogenetically normal AML and in conjunction with other prognostic gene mutations.

2013

- Clinical studies published in the *New England Journal of Medicine* suggested that the drug ibrutinib shows strong potential as a safe, effective, targeted treatment for patients with chronic lymphocytic leukemia (CLL) or mantle cell lymphoma (MCL). The studies, co-led by researchers at the OSUCCC – James and MD Anderson Cancer Center, resulted in FDA approval of ibrutinib for treating relapsed MCL. The CLL study leader was **John C. Byrd, MD**; the MCL study leader was **Kristie Blum, MD**.

- An OSUCCC – James study showed that women who wait more than 60 days to begin treatment for advanced breast cancer face a significantly higher risk of dying than women who start therapy shortly after diagnosis. A delay of more than 60 days among women with late-stage disease was associated with an 85% higher risk of breast cancer-related death. **Electra Paskett, PhD, MSPH**, was senior author of this study, published in the *Journal of Clinical Oncology*.

2014

- The FDA expanded the approved use of the drug ibrutinib (Imbruvica®) to treat certain patients with CLL. Ibrutinib was the first drug designed to target a protein that is essential for CLL cell survival and proliferation. Much of the clinical and basic-science research that led to FDA approval was performed by OSUCCC – James scientists, including **John C. Byrd, MD**, **Amy Johnson, PhD**, **Jason Dubovsky, PhD**, **Jeffrey Jones, MD, MPH**, **Joseph Flynn, DO, MPH**, **Jennifer Woyach, MD**, **Kami Maddocks, MD**, and **Kristie Blum, MD**.

2014

- In December, the **new James Cancer Hospital and Solove Research Institute** opened to replace the original James that had opened in 1990. With 1.1 million square feet and 356 beds, the new James is the third-largest cancer hospital in the United States—a transformational facility that integrates cancer research and clinical care more closely than ever.

2015

- A study published in the *New England Journal of Medicine* showed that the drug acalabrutinib promotes high and durable response rates in patients with CLL while producing minimal side effects. The drug is a second-generation Bruton tyrosine kinase (BTK) inhibitor. Preclinical and clinical efforts with acalabrutinib were led by **John C. Byrd, MD**, and **Amy Johnson, PhD**.

- The American Cancer Society featured a study by OSUCCC – James researchers as one of "10 Key Breakthroughs and Insights for 2015." Led by **Deliang Guo, PhD**, and published in the journal *Cancer Cell*, the study identified a pathway used by cancer cells to make lipids (fats) by integrating oncogenic signaling, fuel availability and lipid synthesis to support cell division and rapid tumor growth. They found a molecule in that pathway that, if blocked, could cripple lipid production by cancer cells and slow tumor growth.

2016

- A study conducted at Nationwide Children's Hospital (NCH) and led by **Timothy Cripe, MD, PhD**, of NCH and the OSUCCC – James, found that a new chemotherapy is effective against both pediatric and adult cancers, and that it allowed other chemotherapies to more readily reach their targets. Published in the journal *Pharmaceutical Research*, the study described a novel class of anticancer amphiphilic amines (RCn).

2016

- The OSUCCC – James assumed a lead role in a "Beat AML" clinical trial sponsored by the Leukemia & Lymphoma Society. The ongoing trial represents collaboration among leukemia researchers and medical centers, non-profit corporations, pharmaceutical companies and a genomics information company to advance treatment for AML.

2017

- A few weeks after the U.S. FDA permitted marketing of the first whole slide imaging (WSI) system for review and interpretation of digital surgical pathology slides from biopsied tissue, the OSUCCC – James initiated a comprehensive Digital Pathology Program to fully digitize anatomical pathology services using WSI technology under the leadership of Director **Anil Parwani, MD, PhD, MBA**.

- The FDA approved a breakthrough cancer treatment called chimeric antigen receptor T-cell (CAR T-cell) therapy for use in adults with advanced lymphoma and for treating a rare type of treatment-resistant childhood leukemia. **Samantha Jaglowski, MD, MPH**, tested the therapy in clinical trials at Ohio State.

- OSUCCC Director and James CEO **Michael A. Caligiuri, MD**, stepped down to embark on a new career opportunity in California. Surgical oncologist **Raphael E. Pollock, MD, PhD, FACS**, became director of the OSUCCC; surgical oncologist **William B. Farrar, MD**, became interim (and later permanent) CEO of The James.

2018

- A study by researchers at the OSUCCC – James and Ohio State's College of Pharmacy showed that attaching antibody-like RNA nanoparticles to microvesicles can deliver RNA therapeutics specifically to cancer cells. Researchers led by **Peixuan Guo, PhD**, used RNA nanotechnology to apply the RNA nanoparticles and control their orientation to produce microscopic, therapy-loaded extracellular vesicles that targeted three types of cancer in animal models.

2019

- OSUCCC – James researchers reported the first evidence of biological changes correlated with e-cig use in never-smokers in the journal *Cancer Prevention Research*. **Peter Shields, MD**, was senior author and **Min-Ae Song, PhD**, was first author of the study, which was one of the most highly cited articles published in 2019 in this journal.

- A pledge of $102,265,000 in funds from Pelotonia supported the establishment of the Pelotonia Institute for Immuno-Oncology (PIIO), a comprehensive bench-to-bedside research initiative focused on harnessing the body's immune system to fight cancer at all levels, from prevention to treatment to survivorship. Renowned immunologist **Zihai Li, MD, PhD**, is the founding director.

- The FDA approved the use of acalabrutinib for first-line therapy in chronic lymphocytic leukemia (CLL) and small cell lymphoma (SCL). This was the first full approval of the targeted drug therapy, which was developed and tested at the OSUCCC – James with Acerta Pharma. The basic science research, initial phase I clinical trial, and numerous sequential phase II and III trials that led to FDA approval were performed by Ohio State researchers led by **John C. Byrd, MD**, and colleagues, including **William Kisseberth, DVM, PhD**, and **Jennifer Woyach, MD**.

2020

- A study led by researchers at the OSUCCC – James identified a protein within certain immune cells that is required for optimal immune responses to cancer. The findings also suggest the protein, called PCBP1, might be useful for predicting which cancer patients are less likely to respond to immune checkpoint blockade therapy. **Zihai Li, MD, PhD**, was principal investigator; **Ephraim Abrokwa Ansa-Addo, PhD**, was first author.

These highlights are only a few of the many achievements by experts in Ohio State's cancer program over the past 50 years. Read a longer review of highlights in ***Half a Century of Cancer Science at Ohio State*** *at* **cancer.osu.edu/halfcentury**.

NCI again rates OSUCCC – James as 'exceptional' and renews CCC status

For the third consecutive time, the National Cancer Institute (NCI) in 2020 rated Ohio State's cancer program as "exceptional"—the highest rating provided—following a review of the OSUCCC – James' application for re-designation as a Comprehensive Cancer Center and a virtual site visit by a team of NCI surveyors.

The OSUCCC – James thus retains a designation it has maintained since 1976 through a competitive peer-review process that includes both written and on-site evaluation of the research program and infrastructure. The re-designation will extend for five years and will provide the cancer program with an estimated $33 million Cancer Center Support Grant (CCSG) from the NCI. The CCSG supports research programs, community outreach and engagement, education and training, clinical trial infrastructure, center senior leadership and administration, shared resource facilities, and program development.

NCI designation as a Comprehensive Cancer Center is the most prestigious recognition a cancer program can receive, providing an external and expert validation of the breadth and depth of an institution's cancer research efforts and of how the institution translates those discoveries into excellent patient care.

"This exceptional ranking from the NCI is a tribute to the dedication of our team of nearly 300 scientists and clinician-investigators working in laboratory, translational, clinical and population sciences to advance cancer discoveries that will improve care at the bedside," says OSUCCC Director **Raphael E. Pollock, MD, PhD, FACS**. "We are honored to continue this important work that will lead us toward a cancer-free world."

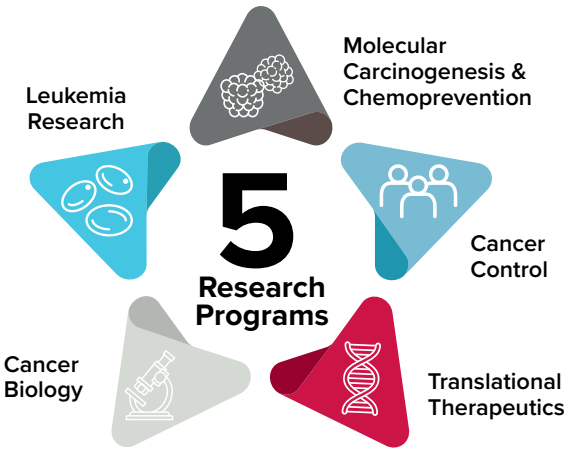
- 1971 – National Cancer Act signed into law and "War on Cancer" declared
- 1976 – Ohio State receives its first CCC designation
- 1990 – Opening of The James
- 2014 – Opening of the new home of The James
- 2021 – 50th anniversary of the National Cancer Act and most recent Ohio State CCC re-designation

OSUCCC Cancer Center support grant by the numbers, 2015-2020

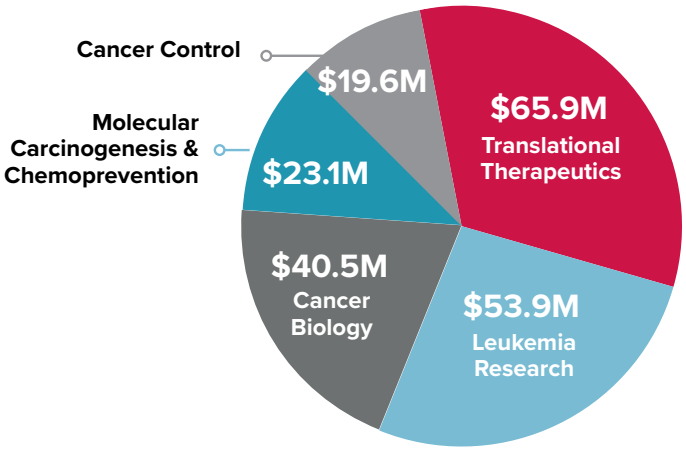
293 OSUCCC MEMBERS

48 DEPARTMENTS

11 COLLEGES



$203M OSUCCC Research Program Investment



Five-Year funding, grants & philanthropy

2015-2020 vs. 2010-2015

$75.4M Total cancer funding from all sources, a +16.4% increase

559 Total active grants, a +21.5% increase

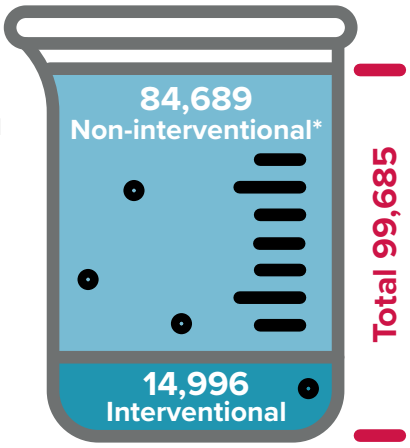
$338M Philanthropic support, a +46% increase

Clinical trial participation

Total Clinical Research Accruals 2015-2020

99,685 total clinical research accruals

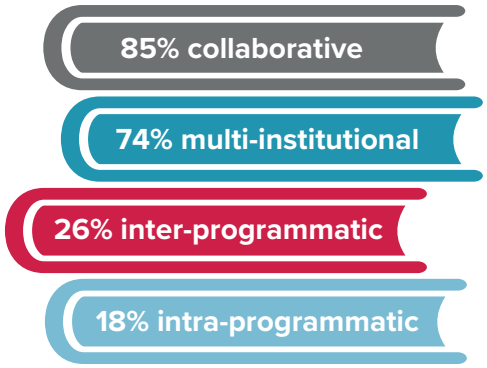
5,648 therapeutic accruals



*Includes 50,683 in ORIEN

Publications, 2015-2020

3,477 total publications



High Impact Factor Publications
497 publications with impact factor >10
+51% increase versus 2010-2015

TRIBUTE

Farewell to unforgettable figures in groundbreaking cancer research

Amid the turbulence of 2020, Ohio State's cancer program also marked the end of an era with the passing of two internationally renowned research titans—Clara D. Bloomfield, MD, and Albert de la Chapelle, MD, PhD—a married couple who came to the OSUCCC – James in 1997 and, over nearly a quarter century, helped it achieve acclaim as an elite cancer institution. On this and the next three pages are tributes to both.

Center for Leukemia Outcomes research will extend Bloomfield legacy at Ohio State

Clara D. Bloomfield, MD

Cancer had a formidable foe in **Clara D. Bloomfield, MD**, a determined medical scientist who was every bit as demanding as the discipline to which she devoted her life.

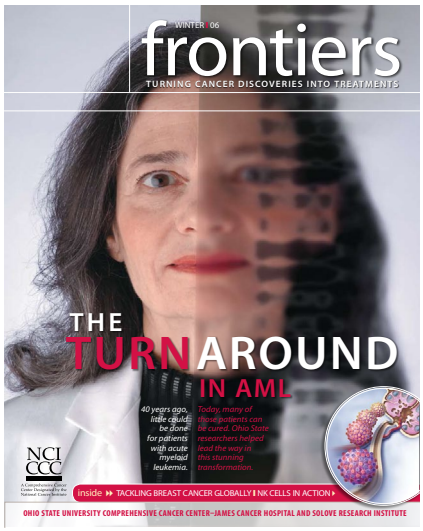
When, soon after her arrival at Ohio State in 1997 as director of Ohio State's Comprehensive Cancer Center and deputy director of The James, she was informed of her advance billing as a relentless researcher and leader, she didn't deny it.

"I am driven. I am a perfectionist," she told an interviewer, "but I consider myself a pragmatic perfectionist. I want things to be as good as they can be, but I don't wait until every 'i' is dotted and every 't' is crossed before proceeding."

And proceed she did, leading the cancer program to new heights in research-based patient care. Soon after her untimely death at age 77 in March 2020, the OSUCCC – James announced it will expand her legacy by establishing a center devoted to furthering her decades of groundbreaking research in hematologic malignancies—work that revolutionized treatment for patients with acute myeloid leukemia and acute lymphoblastic leukemia via a science-based, risk-stratified therapeutic approach.

The **Clara D. Bloomfield Center for Leukemia Outcomes Research** will continue the pursuit of studies in hematologic malignancies, including acute leukemias, myelodysplastic syndromes and clonal hematopoiesis. A Distinguished University Professor who most recently served as cancer scholar and senior adviser to the OSUCCC – James, Bloomfield was globally recognized for her many discoveries relating to those diseases. Her research led to her election to the Institute of Medicine (now the National Academy of Medicine) in 2001. Until she died, she continued her research as ardently as ever.

"This new center will be a worthy tribute not only to Dr. Bloomfield's achievements, but to all who were privileged to be mentored by her or to work with her during her years at Ohio State," says OSUCCC Director **Raphael E. Pollock, MD, PhD, FACS**. "She played an incalculable role in our shared vision of creating a cancer-free world."



Left: Clara D. Bloomfield, MD, speaking at the 35th anniversary of the OSUCCC event in 2011; Center: Cover from the Winter 2006 edition of Frontiers featuring Clara D. Bloomfield, MD; Right: Clara D. Bloomfield, MD, in her lab.

Bloomfield's work over half a century—including 23 years at Ohio State—had worldwide impact, resulting in the incorporation of cytogenetic and molecular genetic findings in the diagnosis of acute leukemias for the first time in the 2001 World Health Organization classification. Such findings also were incorporated into patient management of hematologic malignancies, including the clinical practice guidelines of the National Comprehensive Cancer Network.

Earlier, Bloomfield was the first to suggest and demonstrate that adults with acute leukemia, including the elderly, could be cured with chemotherapy, and to demonstrate that biomarkers, including chromosomal abnormalities, constitute independent prognostic factors that can be used to predict outcomes and to select treatment in adults with acute leukemia or lymphoma—a forerunner to personalized or precision medicine.

In the early 1980s, Bloomfield was instrumental in establishing Central Karyotype Review for trials conducted by Cancer and Leukemia Group B, which not only ensured a high quality of data for clinical and translational studies but also became the model for other cooperative groups and contributed substantially to improving the quality of leukemia karyotyping in this country. She also first identified several now-classic chromosome changes with prognostic significance in leukemia and lymphoma, and she was considered by most to be the world's authority on how chromosome changes, certain gene mutations and gene expression changes influence treatment and outcomes in adults with leukemia.

The new center dedicated to her lifework will build upon her prognostication research, with the goal to better classify and risk-stratify leukemia and associated diseases, including the identification of personalized treatments.

> *"This center will be a worthy tribute not only to Dr. Bloomfield's achievements, but also to all who were privileged to be mentored by her or to work with her during her many years at Ohio State."*
>
> **RAPHAEL E. POLLOCK, MD, PHD, FACS**

As Bloomfield and many other scientists at the OSUCCC – James were contributing over the years to advances in cancer research and care, she once described Ohio State as "an ideal academic climate for this type of exciting research. With results like these, we can all sense that we're doing some good in the world."

TRIBUTE

De la Chapelle placed Ohio State human cancer genetics research on new course

Albert de la Chapelle, MD, PhD

When asked several years ago what he had learned from more than four decades of work and discovery in science, **Albert de la Chapelle, MD, PhD**, replied, "Not much."

"Nature is always a step or two ahead of us," he explained. "In my world, we can hunt for a gene with a particular function for 10 years, and once we find it, it's just the beginning. We always know we have much more to learn about it."

An esteemed Finnish scientist who was recruited to Ohio State from the University of Helsinki in 1997, de la Chapelle devoted himself to lifelong learning until he died at age 87 in December 2020 after a 23-year tenure in which he developed and led the university's human cancer genetics program to prominence. His death came just nine months after the passing of his wife, Clara D. Bloomfield, MD. Both were Distinguished University Professors at Ohio State.

De la Chapelle was internationally renowned as a pioneer in the study of human cancer genetics. His research, which included more than 800 publications in scientific journals over nearly half a century, led to important seminal discoveries about the molecular and genetic nature of cancer, setting the stage for innovative treatments.

De la Chapelle received numerous accolades during his career, including his election to the National Academy of Medicine and a lifetime achievement award from the Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA-ICC). The CGA president at that time described de la Chapelle as "a giant in the field of genetics and specifically in colorectal cancer genetics" whose discoveries "paved the way for identification, diagnosis and cancer prevention in patients with mismatch repair mutations."

De la Chapelle began his career at the University of Helsinki. His early work on the analysis of human X and Y sex-determining chromosomes identified the region of the Y chromosome responsible for maleness. He co-initiated the International Workshops on Chromosomes in Leukemia, which resulted in a series of discoveries. With the use of linkage disequilibrium to find genes responsible for hereditary diseases in isolated populations, his laboratory discovered the region of chromosomes responsible for 14 human diseases. For seven of those, he found the gene responsible for the disease.

One of de la Chapelle's most important achievements was helping to identify and map four mismatch repair genes that cause Lynch syndrome (LS), an inherited disorder that makes certain families susceptible to colorectal cancer. By discerning that this susceptibility results from a damaged cell's inability to repair its DNA, he discovered a cancer-causing mechanism.

At Ohio State, de la Chapelle not only led the human cancer genetics program for the OSUCCC – James but also mentored students and continued his groundbreaking research on molecular causes of cancer. His focus was on the mapping, cloning and characterization of high- and low-penetrance genes for cancer predisposition.

"The OSUCCC – James benefited for nearly a quarter century from Dr. de la Chapelle's expertise and skills as a researcher, educator, administrator and friend."

RAPHAEL E. POLLOCK, MD, PHD, FACS

He emphasized applying laboratory discoveries to the development of diagnostic procedures and treatments, including a test to screen people for LS, and studies that led to recommendations for the universal screening of patients with colorectal cancer for LS so that, if they tested positive, their relatives could be screened for LS as well. His work led to the Ohio Colorectal Cancer Prevention Initiative, which involved 50 hospitals throughout Ohio.

He also contributed to the study of papillary thyroid cancer (PTC), acute myeloid leukemia and endometrial cancer.

"The OSUCCC – James benefited for nearly a quarter century from Dr. de la Chapelle's expertise as a researcher, educator, administrator and friend to all who worked with him or were mentored by him," says OSUCCC Director **Raphael E. Pollock, MD, PhD, FACS**. "His 1997 recruitment to Ohio State with Dr. Bloomfield was a momentous occasion for our program."

Despite his many achievements, de la Chapelle once said he had no high aspirations for being remembered.

"I did not win the Nobel Prize, I did not detect the structure of DNA like (James) Watson and (Francis) Crick—those are the sorts of highly visible things that people remember," he said. "But there will always be those who want to know how things evolved in certain academic disciplines, and there I hope I'll have my little slot."

Mission accomplished.

Top: Albert de la Chapelle, MD, PhD, in his lab; Center L-R: Rachel Pearlman, MS, LGC; Albert de la Chapelle, MD, PhD; and Heather Hampel, MS, LGC, in the lobby of The James; Bottom L-R: Clara D. Bloomfield, MD, and Albert de la Chapelle, MD, PhD, at Pelotonia 11.

Recent recruits

Recognition of nationally renowned oncology experts recently recruited to the OSUCCC – James

Marcos de Lima, MD

Marcos de Lima, MD, came to Ohio State from Case Western Reserve University to serve as a professor in the Division of Hematology and as director of both the Blood and Marrow Transplant (BMT) and Cellular Therapy programs at the OSUCCC – James. His appointments were effective April 1. Previously, de Lima was co-leader of the Hematopoietic and Immune Cancer Biology Program at Case Comprehensive Cancer Center, director of the Bone Marrow Transplant Program at University Hospitals Cleveland Medical Center, and director of the Hematologic Malignancies and Stem Cell Transplant Program at University Hospitals Seidman Cancer Center. He has years of experience in developing and conducting clinical trials involving stem cell transplantation for cancers originating in blood-borne tissue, bone marrow or immune system cells.

Christa Nagel, MD

Christa Nagel, MD, has joined Ohio State's College of Medicine as an associate professor in the Division of Gynecologic Oncology. Nagel was recruited from Case Western Reserve University School of Medicine, where she had been an assistant professor in the Division of Reproductive Biology since 2014. She was also an attending physician in the Division of Gynecologic Oncology at University Hospitals Cleveland Medical Center and on the Gynecologic Cancer Care Team at University Hospitals Seidman Cancer Center. She's a national leader in minimally invasive surgery, including laparoscopic and robotic surgery. Nagel has served on National Comprehensive Cancer Network guidelines committees for endometrial cancer, gestational trophoblastic disease, and cervical, vaginal and vulvar cancers. She earned her MD and served her residency at Ohio State before doing fellowship training at The University of Texas Southwestern Medical Center.

Mark Rubinstein, PhD

Mark Rubinstein, PhD, was recruited from the Medical University of South Carolina (MUSC) and the Hollings Cancer Center to serve as an associate professor in the Division of Medical Oncology at Ohio State and as a researcher in the Pelotonia Institute for Immuno-Oncology at the OSUCCC – James, where he's also in the Translational Therapeutics Program. Rubinstein's NIH-funded research program focuses on understanding how the immune system functions and on applying this knowledge to the development of immune-based therapies to treat cancer. As part of this effort, his laboratory is working to develop improved adoptive cell therapy and immune checkpoint therapy strategies. Rubinstein earned his bachelor's degree at the University of Virginia and his PhD at MUSC. He completed his postdoctoral studies at the University of California, San Diego, and the Scripps Research Institute in La Jolla, Calif.

Large grants and gifts

Recognition of significant grants and gifts for Ohio State's cancer program

$10 million gift will help establish Riney Family Foundation Myeloma Center For Advanced Research Excellence

A $10 million gift from the Paula and Rodger Riney Foundation will help the OSUCCC – James establish the **Riney Family Foundation Myeloma Center for Advanced Research Excellence (Myeloma CARE)**, a center that will focus on accelerating myeloma drug discovery and development projects. The center is a collaboration between the OSUCCC – James Drug Development Institute (DDI) and the Division of Hematology at Ohio State. The Riney gift, provided over two years, will boost drug discovery research designed to explore potential new treatments using specific molecular targets, including some identified by OSUCCC – James scientists. Leading the center is **Don Benson, MD, PhD**, a professor in the Division of Hematology at Ohio State, director of the Myeloma Program, and member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.

Mangurian Foundation $10 million gift supports six diverse Ohio State areas

A $10 million gift to Ohio State from The Harry T. Mangurian, Jr. Foundation is supporting six diverse areas at the university, including leukemia research and cancer drug development. The Mangurian Foundation was established in 1999 by Harry and Dorothy Mangurian to support medical, educational and environmental organizations nationally and internationally. The gift includes $5 million for construction of the anchor to the university's new Innovation District, the Interdisciplinary Research Facility, a project that will provide space for the OSUCCC and its Pelotonia Institute for Immuno-Oncology (PIIO). The remaining $5 million will be divided equally among: Drug Discoveries at the OSUCCC – James' **Drug Development Institute (DDI); leukemia research**, including clinical trials, developing synthetic microRNAs and purchasing equipment; **neurological disease research**; the **MBA program** at the Max M. Fisher College of Business; and **student-athlete health and wellness initiatives**.

NCI awards $10 million grant to study COVID-19 impact on first responders

Researchers at The Ohio State University College of Medicine and the Ohio State Wexner Medical Center received a five-year, $10 million grant from the National Cancer Institute (NCI) to study the long-term, longitudinal impact of COVID-19 on first responders, health care workers and the general population. The grant will fund the Center for Serological Testing to Improve Outcomes from Pandemic COVID-19 (STOP-COVID) at Ohio State, a new Serological Center of Excellence. With this funding, researchers will learn more about the interactions among exposure risks, transmission, immune responses, disease severity, protection and barriers to testing/vaccination, with the goal of improving population health and clinical outcomes in the face of COVID-19. Lead co-investigator for the study is **Eugene Oltz, PhD**, chair of the Department of Microbial Infection and Immunity at Ohio State and member of the Cancer Biology Program at the OSUCCC – James.

NCI renews longstanding grant for studying retrovirus models of cancer

The NCI renewed a longstanding Program Project Grant that will enable researchers at Ohio State's College of Veterinary Medicine (CVM), the OSUCCC – James, and the Washington University CCC in St. Louis to continue studying retrovirus models of cancer. The $9.1 million, five-year grant renewal was awarded to principal investigator **Patrick Green, PhD**, associate director for basic research at the OSUCCC – James and director of the Center for Retrovirus Research in the CVM. The goal of this PPG, which has been operational at Ohio State since 2003 and is the longest-running P01 PPG at the university, is to use a human T-cell leukemia virus type 1 (HTLV-1) T-cell immortalization model to gain an understanding of the microenvironmental, cellular and viral factors that lead to adult T-cell leukemia.

NCI grant renewal supports cancer drug discovery research based on natural compounds

The OSUCCC – James and the Ohio State College of Pharmacy received a five-year, multidisciplinary, $7 million Program Project Grant (PPG) renewal from the NCI that will allow teams at Ohio State, the University of Illinois – Chicago and University of North Carolina – Greensboro to keep investigating potential anticancer drug leads based on compounds from tropical plants, coastal lichens, cultured cyanobacteria and filamentous fungi. The grant is led by principal investigator **A. Douglas Kinghorn, PhD, DSc**, professor and Jack L. Beal Chair of the Division of Medicinal Chemistry and Pharmacognosy at Ohio State's College of Pharmacy. Since the grant was first funded in 2007, over 180 research and review articles have been published based on findings from the three collaborating institutions.

Ohio State receives $5.5 million grant to study health impact of youth vaping

Ohio State researchers are studying health effects of e-cigarettes and nicotine on youth and helping to develop vaping-cessation programs via a $5.5 million grant awarded by the American Heart Association as part of its End Nicotine Addiction in Children and Teens (ENACT) research initiative. Ohio State's trans-institutional work is led by scientists in the Center for Tobacco Research at the OSUCCC – James, including: **Theodore Wagener, PhD**; **Loren Wold, PhD**; **Liz Klein, PhD, MPH**; **Megan Roberts, PhD**; and by **Peter Mohler, PhD**, chief scientific officer for the Ohio State Wexner Medical Center. Wagener directs the Center for Tobacco Research. The scientists are working with colleagues in the colleges of Medicine, Nursing, Public Health and Engineering on a two-year project called Vaping's End through Research and Innovation for Youth (VERIFY).

Ohio State patients to benefit from NCI grant renewal for studying experimental therapeutics agents

The NCI awarded a five-year, $5.3 million grant renewal to help a consortium of academic institutions led by the OSUCCC – James continue conducting phase I and II clinical trials involving targeted experimental agents that provide patients with the latest treatments. The consortium is led by principal investigator **William Carson, MD**, associate director for clinical research at the OSUCCC – James, and is staffed by the Clinical Trials Office. The award, a UM1 grant, will allow the integration of Ohio State's experimental therapeutics efforts with three sub-site institutions: University of Kentucky, University of Utah and University of North Carolina. The entire grant amount comes to Ohio State; distribution of funds to the sub-sites is based on accrual of patients to the study.

$5 million NIH award to address disparities in COVID-19 testing among vulnerable

The Ohio State University received a two-year, $5 million grant from the National Institutes of Health RADx-UP program to support projects designed to rapidly implement COVID-19 testing strategies in populations disproportionately affected by the pandemic. Ohio State was among 32 institutions to receive awards to help African Americans, American Indians/Alaskan Natives, Latinos/Latinas, Native Hawaiians, older adults, pregnant women, and people who are homeless or incarcerated. Multiple-principal investigators are **Electra Paskett, PhD, MSPH**, associate director for population sciences at the OSUCCC – James; and **Rebecca Jackson, MD**, director of Ohio State's Center for Clinical and Translational Science.

Researchers awarded federal grant to lead multi-center study of stem cell transplant complication

The National Heart, Lung and Blood Institute awarded a five-year, $3.87 million grant to help OSUCCC – James researchers lead a multi-center study of thrombotic microangiopathy, a severe and life-threatening complication in patients undergoing hematopoietic stem cell transplant as treatment for blood cancers. Principal investigator for the study, titled MIDAS: Microangiopathy, Endothelial Damage in Adults Undergoing Stem Cell Transplantation is **Sumithira Vasu, MBBS**, of the Leukemia Research Program at the OSUCCC – James. **Spero Cataland, MD**, a professor in the Division of Hematology, is co-investigator.

Grant will help researchers gauge psychosocial risk in young survivors of early onset pediatric cancer

The NCI awarded a five-year, $3.5 million grant to help researchers at the OSUCCC – James and Nationwide Children's Hospital (NCH) lead a multi-site study of psychosocial risk in young survivors of early-onset pediatric cancer. Principal investigator is **Cynthia Gerhardt, PhD**, a psychologist and

director of the Center for Biobehavioral Health at NCH. She and colleagues state in their project abstract that, despite increased survival, over two-thirds of children with cancer experience late effects such as sensorimotor deficits, neurocognitive impairment and psychosocial difficulties.

NCI grant study will test strategy to improve therapy for hypoxic tumors

A five-year, $2.9 million NCI grant will help a team of OSUCCC – James researchers test a strategy for overcoming low levels of oxygen in tumors—a condition called hypoxia that reduces the effectiveness of anticancer treatment with radiotherapy, some chemotherapy and immune checkpoint blockade therapy. The study is led by principal investigators **Nicholas Denko, MD, PhD**, of the Cancer Biology Program at the OSUCCC – James, and **Zihai Li, MD, PhD**, director of the Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC – James.

NCI grant supports study of novel genetic counseling approach for high-risk breast cancer patients

An interdisciplinary team of OSUCCC – James researchers will use a five-year, $2.8 million NCI grant to conduct a randomized clinical trial on a novel genetic counseling patient preference (GCPP) intervention that may better suit the needs of women who have an elevated risk of breast cancer. The researchers—led by principal investigators **Kevin Sweet, MS, LGC**, professor in the Division of Human Genetics, and **Mira Katz, MPH, PhD**, professor in the College of Public Health—say their study will compare conventional genetic counseling with a GCPP intervention integrated within an electronic health record patient portal for women with elevated risk. They hope to show the efficacy of their approach.

Researchers will use NCI grant to probe mechanics of metastatic progressive thyroid cancer

The NCI awarded a five-year, $2.25 million grant to OSUCCC – James researchers who identified a new pathway that inhibits thyroid cancer metastasis so that therapeutic targets and/or biomarkers can be devised. In previous studies the researchers, led by principal investigator **Matthew Ringel, MD**, co-leader of the Cancer Biology Program at the OSUCCC – James, identified a gene called *RCAN1.4* as a metastasis suppressor. They found that the loss of this gene results in cancer progression by inducing a transcription factor known as Nrf3 that promotes thyroid cancer cell growth and invasion, and is associated with poor prognosis. In their new project abstract, the researchers state that thyroid cancer provides an outstanding model to identify regulators of late-stage cancer progression.

Grant study evaluates approach to abrogating acute graft-versus-host disease in stem cell transplant patients

OSUCCC – James researchers will use a five-year, $2.07 million grant from the NCI to evaluate an innovative approach to abrogating acute graft versus-host disease (aGVHD) in patients who have received allogeneic stem cell transplants (alloSCT) as treatment for hematologic malignancies. The principal investigators are **Hannah Choe, MD**, (study leader), and **Parvathi Ranganathan, PhD**, members of the Leukemia Research Program at the OSUCCC – James. In their project abstract, they state that aGVHD, which occurs when donor T cells react against host tissues, is the major cause of non-relapse mortality after alloSCT. They note that 50% of patients don't respond to front-line corticosteroid therapy and have limited treatment options. This study is designed to improve outcomes for these patients.

NCI grant to help researchers explore biology and targeting of non-coding RNAs in AML

A five-year, $1.95 million NCI grant will help an OSUCCC – James research team study how a certain long non-coding RNA (lncRNA) contributes to a common form of cytogenetically normal acute myeloid leukemia (CN-AML) and determine whether blocking the lncRNA is a viable targeted therapy. Some 45-50% of AML cases are cytogenetically normal, meaning they have no chromosomal abnormalities. However, novel recurrent gene mutations recently have been identified in CN-AML. The most common among those are mutations in the *NPM1* gene, and researchers at the OSUCCC – James have discovered that abnormally high levels of a lncRNA called HOXB-AS3 in the leukemic cells of patients with *NPM1*-mutated AML enables the rapid growth and proliferation of malignant blast cells. Principal investigator **Ramiro Garzon, MD**, co-leader of the Leukemia Research Program at the OSUCCC – James, and colleagues want to learn how this works and whether they can stop it.

Ohio State to lead national consortium coordinating center to boost junior faculty cancer research careers

OSUCCC – James scientists **Claire Verschraegen, MD**, and **Rebecca Jackson, MD**, are playing a lead role in establishing and coordinating a federally funded national consortium that will help junior faculty grant awardees maintain independent academic cancer research careers. The NCI awarded a three-year grant of more than $1.63 million to support an NCI Awardee Skills Development Consortium (NASDC) in a project titled "Enhancing Cancer-Focused Education for Tomorrow's Workforce – Coordinating Center." Located at Ohio State, the coordinating center will provide infrastructure enabling four other consortium institutions to offer courses to mentor junior faculty who have received NCI R-series (research) and K-series (career development) grants. The other consortium members are University of Pennsylvania, Memorial Sloan Kettering Cancer Center, University of Utah and Dana-Farber Cancer Institute.

BCRP grant to aid study of breast cancer initiation, progress and metastasis

A three-year, $1.56 million grant from the U.S. Department of Defense Breast Cancer Research Program (BCRP) will help OSUCCC – James scientists study a component of the tumor microenvironment that promotes primary breast tumor growth and metastasis. Principal investigator **Gina Sizemore, PhD**, of the Cancer Biology Program at the OSUCCC – James, says this project could change the way women with breast cancer are screened and treated for their disease.

Researchers gain grant to study prediction of chemoresistance in ovarian cancer

A two-year, $1 million federal grant will support an OSUCCC – James study that could lead to improved detection of chemotherapy resistance and allow for more targeted treatments in patients with high-grade serous ovarian carcinoma (HGSOC). The U.S. Department of Defense awarded the grant to a team led by principal investigator **Selvendiran Karuppaiyah, PhD**, of the Translational Therapeutics Program at the OSUCCC – James. In their project abstract, the researchers cite the need for evaluating cancer biomarkers that help predict which patients will develop chemotherapy resistance so clinicians can devise more targeted treatments.

Grant will assist development of therapy to inhibit gastric cancer progression and spread

The U.S. Department of Defense awarded a three-year, $780,000 grant to help OSUCCC – James researchers study the therapeutic role of dopamine receptor agonists in preventing progression and metastasis of gastric cancer. The study will be led by principal investigator **Sujit Basu, MD, PhD**, of the Translational Therapeutics Program at the OSUCCC – James. Basu says researchers will explore the ability of dopamine receptor agonist therapy to inhibit gastric cancer progression and lymph node metastasis in preclinical mouse models simulating human patients with the intestinal form of this disease.

Achievements, awards and honors

Institutional

Following an unannounced full resurvey, **The Joint Commission granted a three-year reaccreditation** to all James Cancer Hospital and Solove Research Institute locations until Feb. 12, 2024. The Joint Commission conducted the resurvey to assess compliance with the Medicare conditions for hospitals through the commission's deemed status survey process. The Joint Commission also recommended The James for continued Medicare certification effective last Feb. 12. Because the resurvey was virtual due to COVID-19 restrictions, The James will undergo a full on-site survey once conditions are appropriate to resume on-site activity, in accordance with CMS directives.

The OSUCCC – James has earned two more national awards for excellence in patient care delivery from Press Ganey, a health care performance-improvement organization that works with more than 41,000 health care facilities to improve the overall safety, quality and experience of care. 2020 marked the fifth consecutive year the OSUCCC – James has received the **Press Ganey® Guardian of Excellence Award®**, which recognizes top-performing health care organizations that have achieved the 95th percentile or above for performance in patient experience. Also in 2020, the OSUCCC – James received for the second consecutive year the **Press Ganey Pinnacle of Excellence Award®**. This honor goes to top-three performing organizations in each award category—in this case, recognizing the OSUCCC – James for consistently high levels of excellence in patient experience over three years.

The Multinational Association of Supportive Care in Cancer (MASCC) has certified the OSUCCC – James as an **MASCC-Designated Center of Excellence in Supportive Care in Cancer** for 2021 to 2024. The OSUCCC – James is only the second institution in the United States to receive this certification, which recognizes oncology centers that demonstrate best practices in supportive cancer care. Certification by the MASCC, an international multidisciplinary organization, honors oncology centers that uphold high standards and provide comprehensive services in supportive cancer care. MASCC members hail from more than 70 countries and represent many specialties.

OSUCCC – James caregivers will work with staff at a large hospital in Germany as part of **Magnet4Europe**, a randomized trial funded by the European Commission to determine the feasibility of redesigning hospital work environments in six European nations under principles of the American Nurses Credentialing Center Magnet Recognition Program®. Magnet recognition is the highest honor a U.S. health care organization can receive for quality patient care and professional nursing practice. Through the Magnet4Europe initiative, over 70 hospitals in Belgium, England, Germany, Ireland, Sweden and Norway will be supported by one-to-one "twinning" with an experienced U.S. Magnet-recognized hospital to promote capacity building through transfer of knowledge, skills, tools, technology and best practices. The OSUCCC – James, an ANCC Magnet-designated hospital since 2013, is paired with Klinikum Bremerhaven-Reinkenheide GmBH, a 723-bed hospital in Bremerhaven, Germany.

An OSUCCC – James **multidisciplinary pancreatic cancer clinic** opened in May at Martha Morehouse Outpatient Care, 2050 Kenny Road, in Columbus, Ohio, to provide patients with diagnostic testing, education and multi-provider assessment—all in one visit. Health care professionals at the full-day clinic can quickly diagnose and establish treatment plans for patients, and ensure their involvement in their care. The clinic is open by referral to patients with non-metastatic pancreatic adenocarcinoma, as well as those with resectable or border-line resectable or locally advanced pancreatic cancer. Services include diagnostics (CT scan), lab work and individual assessment by experts in multiple disciplines. Patients also receive a personalized treatment plan. For referrals, call The James Line at 800-293-5066 or visit go.osu.edu/patientreferral.

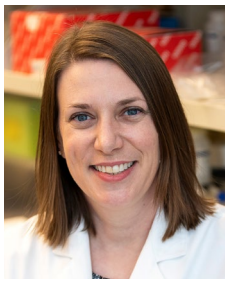
The OSUCCC – James has **added two Ohio hospital systems to The James Cancer Network (JCN)**—a system of collaborations among many institutions in cancer care. Memorial Health in Union County, a not-for-profit community hospital serving Union and five surrounding counties, joined on Feb. 1. With cancer services primarily in Marysville and Urbana, Memorial Health has a robust and growing cancer program. Mercy Health – Lorain, which opened June 1, is part of Mercy Health, the largest health care provider in Ohio. The JCN affiliation is part of a larger alliance between the Ohio State Wexner Medical Center and Mercy Health. Mercy Health – Lorain has an exceptional cancer program that offers therapies and surgical technologies for several cancer types.

The Division of Palliative Medicine in Ohio State's College of Medicine achieved re-designation as a European Society of Medical Oncology (ESMO) Designated Centres of Integrated Oncology and Palliative Care Programme. The Division of Palliative Medicine, led by associate professor and director **Jillian Gustin, MD**, first earned this designation in 2016 and regained it in February 2021. The program includes more than 225 institutions from 49 countries. ESMO's mission is to improve the quality of cancer care, from prevention and diagnosis to palliative care and patient follow-up, and to educate doctors, cancer patients and the public about the best practices and latest advances in oncology while promoting equal access to optimal cancer care for all.

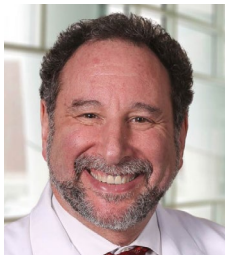
Ohio State's colleges of Medicine, Nursing, Optometry and Veterinary Medicine received the 2020 Health Professions Higher Education Excellence in Diversity (HEED) Award from *INSIGHT into Diversity* magazine, the oldest and largest diversity-focused publication in higher education. This is the second consecutive year that four health science colleges at Ohio State have earned this honor, and the fifth year for the College of Nursing. Ohio State is the only academic institution in the country to have four colleges receive this 2020 designation.

Pheo Para Alliance, a patient advocacy organization that supports patients with pheochromocytoma (pheo) and paraganglioma (para)—rare neuroendocrine tumors that can be benign or malignant—has **designated The Ohio State University Wexner Medical Center as a Center of Excellence** for treating and studying these and related genetic illnesses. The Center of Excellence Program recognizes institutions worldwide for providing quality multidisciplinary care for patients with these diseases and for participating in research on the underlying molecular causes. The centers of excellence also provide professional and lay education about pheo and para in the areas they serve. Physicians from several specialties treat these patients at the Ohio State Wexner Medical Center and the OSUCCC – James, including specialists in the departments of Surgery, Internal Medicine (divisions of Medical Oncology; Endocrinology, Diabetes and Metabolism; Human Genetics) and Otolaryngology – Head and Neck Surgery, as well as the new Comprehensive Adrenal Program.

Team and individual



Jennifer Woyach, MD, a professor in the Division of Hematology at Ohio State, has agreed to serve as co-leader of the Leukemia Research (LR) Program at the OSUCCC along with current co-leader **Ramiro Garzon, MD**, who is also a professor in the Division of Hematology. Woyach, a longstanding member of the LR Program, is a hematologist-oncologist who specializes in treating patients with blood cancers, particularly chronic lymphocytic leukemia (CLL) and B-cell lymphomas. Her research focuses on targeted therapies for CLL and on strategies to overcome resistance to those therapies. She led a collaborative effort that identified the mechanism of resistance to the BTK inhibitor drug called ibrutinib in CLL, and she has led preclinical and clinical studies to identify drugs that can help patients with CLL overcome ibrutinib resistance.

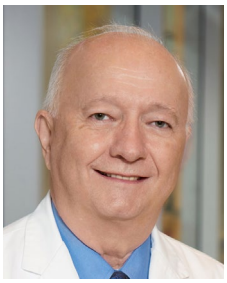


A report by OSUCCC – James researchers on data suggesting that even short-term e-cig use can cause cellular inflammation in never-smoker adults was one of the most highly cited articles published in 2019 in the journal *Cancer Prevention Research*. The American Association for Cancer Research (AACR) highlighted the 2019 most-cited research articles, also known as The Best of the AACR Journals, prior to the AACR Virtual Annual Meeting in May 2021. **Peter Shields, MD** (top), deputy director of the OSUCCC, was senior and corresponding author of the article, titled "Effects of Electronic Cigarette Constituents on the Human Lung: A Pilot Clinical Trial." **Min-Ae Song, PhD** (bottom), a member of the Cancer Control Program at the OSUCCC – James and an assistant professor in Ohio State's College of Public Health, was first author. They and their colleagues reported the first evidence of biological changes correlated with e-cig users who had never previously smoked.

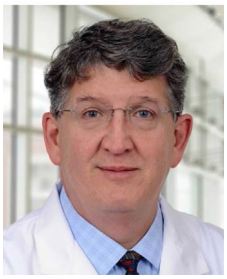
Yiping Yang, MD, PhD, professor and director of the Division of Hematology at Ohio State, and a member of the Leukemia Research Program at the OSUCCC – James, was inducted into the Association of American Physicians (AAP). Yang was nominated for his pioneering studies on the critical role of the CD40 co-stimulating protein in initiating T cell-dependent immune responses, and for his work on Toll-like receptors in overcoming immune tolerance, which has served as a guiding principle in cancer immunotherapy.

The Lymphoma Research Foundation (LRF) elected **Kami Maddocks, MD**, associate professor in the Division of Hematology at Ohio State, as clinical mentoring co-chair for the 2021-2022 cohort of the Lymphoma Scientific Research Mentoring Program. In this national role, she will direct curriculum and mentoring for LRF clinical track scholars for two years. In addition, Maddocks, who also is in the Leukemia Research Program at the OSUCCC – James, was selected to serve on the American Society of Hematology's (ASH) new Subcommittee on Clinical Trials for a three-year term.

Matthew Ringel, MD, professor and director of the Division of Endocrinology, Diabetes and Metabolism at Ohio State, where he also co-leads the Cancer Biology Program at the OSUCCC – James, was appointed editor-in-chief of the journal *Endocrine-Related Cancer*. A thyroid cancer specialist, Ringel co-directs the Center for Cancer Engineering and serves as deputy director of Ohio State's Center for Clinical and Translational Sciences. His lab focuses on molecular mechanisms of thyroid cancer invasion and metastasis, with a special interest on pathways that regulate cancer progression.



Larry Copeland, MD, a professor in the Division of Gynecologic Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, received a 2020-21 Distinguished Service Award from the Society of Gynecologic Oncology (SGO). This award recognizes individuals who, over an extended period, display continuous outstanding meritorious service in the field of gynecologic oncology. The award was presented at the SGO's 2021 Virtual Annual Meeting on Women's Cancer.



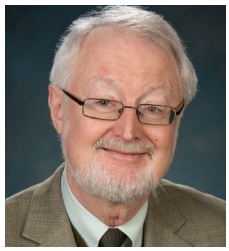
James Rocco, MD, PhD, professor and chair of the Department of Otolaryngology – Head and Neck Surgery at Ohio State, was included on *Becker's ASC Review's* 10 More ENT Physicians to Know for his work in head and neck cancer, including parotid, tongue, laryngeal and HPV-related oropharyngeal cancers. Rocco also is in the Translational Therapeutics Program at the OSUCCC – James and serves as director of the Head and Neck Disease-Specific Research Group.

Robert Merritt, MD, associate professor and director of the Division of Thoracic Surgery at Ohio State, was chosen as a recipient of the 2021 Leonard Tow Humanism in Medicine Award from the The Arnold P. Gold Foundation. These awards recognize graduating students and faculty members who demonstrate clinical excellence and outstanding compassion in the delivery of care, and who show respect for patients, families and health care colleagues.

Sharla Wells-Di Gregorio, PhD, assistant professor in Ohio State's College of Medicine, Department of Internal Medicine, Division of Palliative Medicine, and a member of the Cancer Control Program at the OSUCCC – James, received the American Psychosocial Oncology Society (APOS) Outstanding Education and Training Award for 2021. The award goes to an APOS leader who has enhanced the field of psychosocial oncology through the education and training of new investigators and/or clinicians and fostered the professional development of psychosocial oncologists.

Payal Desai, MD, associate professor in the Division of Hematology at Ohio State, where she also serves as director of sickle cell research and co-director of the Sickle Cell Program, was selected as co-chair of the Sickle Cell Disease Coalition's (SCDC) Research & Clinical Trials Working Group. In this role, Desai will help lead the group's strategy and guide the national clinical research conversation. At the OSUCCC – James, she is part of a multidisciplinary team that treats patients with sickle cell disease and provides them with opportunities for clinical trials on alternative therapies to treat their illness.

Heather Hampel, MS, LGC, professor and associate director of the Division of Human Genetics at The Ohio State University College of Medicine, was elected secretary/treasurer-elect for the National Society of Genetic Counselors (NSGC). Hampel is a cancer genetic counselor at the OSUCCC – James, where she also is associate director for biospecimen research. The NSGC is the only professional organization that promotes the professional interests of genetic counselors. Hampel's two-year term began in January. She'll serve the first year as secretary/treasurer-elect and become secretary/treasurer in 2022.



The *Journal of Natural Products* honored **A. Douglas Kinghorn, PhD, DSc**, a member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James, in a special issue highlighting his impact on the field of natural products and his career accomplishments in the academic, private and public sectors, including

14 patents, 430 research articles, 80 book chapters and more. Kinghorn is a professor and the Jack L. Beal Chair in Medicinal Chemistry and Pharmacognosy for Ohio State's College of Pharmacy. The special issue is a well-deserved recognition for a remarkable career.

Mary Dillhoff, MD, associate professor in the Division of Surgical Oncology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, was one of six physicians named to the inaugural class of the Americas Hepato-Pancreato-Biliary Association (AHPBA) Academy. The AHPBA is a non-profit organization devoted to relieving human suffering caused by HPB disorders by improving education, training, innovation, research and patient care. The association cultivates leadership skills among HPB surgeons to help build a pipeline for the future of AHPBA. Its more than 1,250 members are also members of the International Hepato-Pancreato-Biliary Association (IHPBA).

Sarah Wall, MD, MPH, assistant professor in the Division of Hematology at Ohio State, was accepted into the 2021 American Society for Transplantation and Cellular Therapy (ASTCT) Clinical Research Training Course held in Park City, Utah. She is one of 12 fellows and/or junior faculty selected competitively for the course, which enhances participants' skills in formal presentations, research subject eligibility and recruitment, clinical trial design, data management and quality control, grant writing and more.

Peter Kneuertz, MD, **Desmond D'Souza, MD**, and **Robert Merritt, MD** (shown respectively from left), produced an abstract titled "National Trends and Outcomes of Segmentectomy in the Society of Thoracic Surgery Database" that was selected for inclusion among the 2021 Society of Thoracic Surgeons (STS) Richard E. Clark Memorial Papers for General Thoracic Surgery. The Clark Memorial Papers represent some of the top-rated abstracts at the STS annual meeting, held last January. Their abstract was presented during the session on General Thoracic Top-Scoring Abstracts. All three physicians are faculty members in the Division of Thoracic Surgery at Ohio State. Merritt serves as division director.

Clinical Translational Science Shared Resource helps improve cancer diagnosis, treatment strategies

The OSUCCC – James Clinical Translational Science Shared Resource (CTSSR) team works with clinical and translational researchers to design and develop customizable portfolio validation assays that provide correlative science studies for early-phase solid tumor oncology clinical trials.

Under the direction of **Pravin Mishra, PhD, MBA**, a member of the Translational Therapeutics Program at the OSUCCC – James, this shared resource helps researchers translate basic science findings to the clinical setting and vice-versa to improve diagnosis and treatment strategies for patients with cancer.

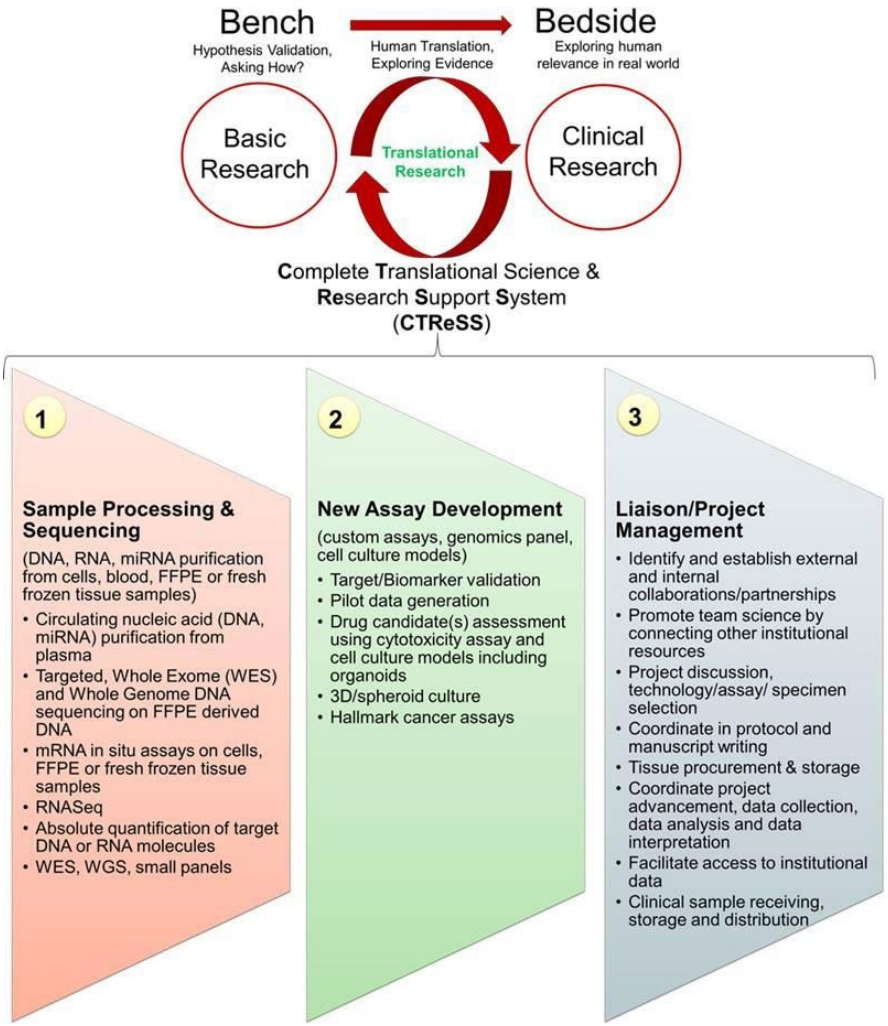
Toward this goal, the CTSSR offers multiple laboratory services, including clinical sample receiving, processing, storage and distribution; automated DNA, RNA, miRNA purification from cells, blood, FFPE or fresh frozen tissue samples; circulating nucleic acid (DNA, miRNA) purification from plasma, urine and other bodily fluids; and many others.

The CTSSR serves as a central repository for specimens collected from patients on clinical trials and is responsible for processing the tissue for any number of downstream analyses. In addition to developing novel assays, the CTSSR partners with other OSUCCC shared resources to utilize available technologies such as next-generation sequencing, RNA expression analysis and proteomics. In these situations, the CTSSR obtains and prepares the patient samples for downstream analyses and then collects and organizes the data.

This shared resource also helps identify and develop partnerships among investigators and pharmaceutical companies to gain access to new drugs and compounds, and to provide corresponding correlative testing and analyses for cancer studies.

For more information about services available through the CTSSR, call 614-366-9041 or email Pravin.Mishra@osumc.edu.

NOTE: The Shared Resources and core facilities at the OSUCCC – James constitute a National Cancer Institute-recognized network of specialized service facilities that enhance an investigator's ability to conduct cancer research by offering: expert multidisciplinary leadership and training; clinical, administrative and technical support; and state-of-the-art instrumentation. The CTSSR highlighted here is one of 20 OSUCCC – James Shared Resources.



New diagnostic center accelerates diagnosis, provides immediate access

In June 2020, the James Cancer Hospital and Solove Research Institute opened a James Cancer Diagnostic Center to give patients direct, expedited access to diagnostic testing for cancer.

David E. Cohn, MD, MBA, chief medical officer at The James, says the diagnostic center offers immediate community-wide patient access to cancer providers for anyone with a suspected cancer, especially those in communities where access to health care is limited and has become even more challenging due to the COVID-19 pandemic.

Open daily, the center provides a platform for expert evaluation and access to the appropriate diagnostic testing so that a timely and precise cancer diagnosis can be made in a low-risk environment. Patients may self-refer to the center or be referred by a physician, and visits can be virtual or in-person, depending on the patient's preference.

The center is staffed by a team of advanced practice professionals and nurses who have expertise in oncology. The team is overseen by physicians with oncology experience and expertise. Center staff first identify and prioritize patient needs and concerns, and then coordinate appropriate testing and evaluation on behalf of the patient at facilities within The James and the Ohio State Wexner Medical Center. Follow-up care is also coordinated with a specialized, multidisciplinary team at The James if a cancer diagnosis is made.

"COVID-19 has limited and changed access to health care across the country and the world," says Cohn, who also is a gynecologic oncologist and member of the Translational Therapeutics Program at the OSUCCC – James. "Having timely access to providers is a very real concern. We want to ensure that anyone with a suspected cancer can get a timely, accurate diagnosis so potentially life-saving care is not delayed unnecessarily.

"Navigating a cancer diagnosis and treatment can be stressful enough during 'normal' times—adding the uncertainty and fear of the COVID-19 pandemic threatens to make it truly overwhelming," he adds. "We want the community to know we are here to help, and patients should feel safe turning to us for testing and cancer care. That starts with being connected to the right experts and the right tests to get answers to guide treatment."

To connect with the Cancer Diagnostic Center or schedule another appointment, call The James Line at 614-293-5066.

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COMPREHENSIVE CANCER CENTER –
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