

University of
CINCINNATI
CANCER CENTER[™]

University of Cincinnati • UC Health • Cincinnati Children's



COLLABORATING TO FIND CURES

2023 REPORT TO THE COMMUNITY

At the University of Cincinnati Cancer Center, our vision is both simple and ambitious: to reduce the suffering and mortality caused by cancer. Achieving this vision is complex and multifaceted, which is why we're attacking cancer at every level possible.

In our laboratories, we're delving into the molecular level to uncover the biological origins and evolution of cancer. In our clinics and hospitals, we're implementing innovative treatments and conducting clinical trials to improve patient outcomes. And in our community, we're educating people about cancer prevention and reduction initiatives.

We have come a long way, but there's still much work to be done. Cancer rates in our city and the region remain higher than the national average. Too many people in our community do not understand what causes cancer or how to reduce their risk. And far too many lack access to the care and support they need.

At the University of Cincinnati Cancer Center, we're committed to fighting for every person affected by cancer, and we won't stop until cancer does.



Photos throughout provided by University of Cincinnati, UC Health and Cincinnati Children's.



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Transforming Cancer Research and Care

To our community and readers of this report,

When the University of Cincinnati, UC Health and Cincinnati Children's came together in January 2020 to form the University of Cincinnati Cancer Center, we unified cancer research under one umbrella to break down barriers and accelerate cancer discoveries. As we enter just our fourth year as a formal center, we are exceedingly proud of the work we are doing as an organization to provide the infrastructure and collaborative opportunities that our members need to make tomorrow's transformative discoveries possible.

In 2022, we concentrated our organizational work in four areas:

PEOPLE

Over the past year, we focused on recruiting key researchers and clinicians to propel our research forward and expand our capacity to serve patients. Every new employee — at all levels — is mentored by senior leaders to understand our values of outstanding care, community and teamwork.

COLLABORATION

Through ongoing communications and in-person professional events, we are connecting researchers from different organizations, colleges and disciplines to foster inter-programmatic collaborations.

RESOURCES

Cancer research and therapeutic development are expensive, complex processes. In 2022, we created shared resource programs in biospecimen collection and storage as well as biostatistics and informatics to make these tools accessible to all of our cancer researchers.

FUNDING

In 2022, we increased grant funding by more than 34%, revamped our pilot project awards process and awarded 12 pilot grants for early stage investigators to further their research.

In addition to our research accomplishments, the clinical program continues to grow and improve. Every member of the team understands the great privilege that we have in caring for patients and families at such an important time in their lives. Our community of providers, researchers, patients and advocates together embrace the challenge of making Greater Cincinnati a destination for superb cancer care.

We know there is more to do, and our results will be seen in the discoveries from our labs and in the care delivered to patients. We are committed to continuing to build a place where discoveries are made possible to reduce the burden of cancer on our community and beyond.

Sincerely,



Syed A. Ahmad, MD

Co-Director, University of Cincinnati Cancer Center
The Hayden Family Endowed Chair for Cancer Research
Professor of Surgery
Chief, Division of Surgical Oncology



William L. Barrett, MD

Co-Director, University of Cincinnati Cancer Center
Professor and Chair, Radiation Oncology
Medical Director, Barrett Center for Cancer Prevention,
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Syed A. Ahmad, MD
Department of Surgery
Medical Oncology

Syed A. Ahmad, MD

UCHealth
UNIVERSITY OF CINCINNATI PHYSICIANS

William L. Barrett, MD

2022 ACCOMPLISHMENTS

- Increased research funding by 34%
- Increased research membership by 22%
- Hosted 25 professional education events
- Increased active research grants by 73%

TRANSFORMATIVE

UNIVERSITY OF CINCINNATI CANCER CENTER > BY THE NUMBERS

DATA PROVIDED BY: University of Cincinnati > UC Health > Cincinnati Children's

10 Multidisciplinary Disease Centers

1. Transplant and Cellular Therapy
2. Brain & Nervous System
3. Breast
4. Gastrointestinal
5. Genitourinary
6. Gynecologic
7. Head & Neck
8. Lung
9. Ocular
10. Skin Cancer & Sarcoma

2020 PATIENT CARE

3,402

Analytic cases (patients)

34

Types of
cancer treated



Cancer Center Members

214 members representing
8 UC Colleges and
Cincinnati Children's

Clinical/Translational

Basic Science

Population Science

91

96

27

CANCER CARE



16 Cincinnati Children's Centers & Programs

- Advanced Cancer Therapies
- Brain Tumor
- Cancer Survivorship
- Cardio-Oncology
- Comprehensive Fertility Care & Preservation
- Hereditary Cancer
- Kidney Tumor
- Leukemia & Lymphoma
- Liver Tumor
- Neuroblastoma
- Neurofibromatosis
- Pediatric Cancer Rehabilitation
- Proton Therapy
- Retinoblastoma
- Sarcoma
- Young Adult Cancer

2022 ADULT CLINICAL TRIALS

752

Patients participated in a clinical trial

168

Interventional treatment clinical trials open to accrual

18.3%

Estimated overall clinical trial accrual rate

*Lymphoid leukemia was the No. 1 type of cancer for patients at Cincinnati Children's.

TOP 10 Most Common Cancer Cases

1. Breast	408	6. Lymphoid Leukemia*	193
2. Lung	340	7. Brain & Nervous System	146
3. Prostate	297	8. Pancreas	127
4. Lip, Oral Cavity & Pharynx	235	9. Colon	123
5. Melanoma, Skin	213	10. Corpus Uteri	115

2022 FUNDING

140 Active research grants **\$24.4M** Research funding

2022 Research Grants (Direct Costs)

Basic Science	Clinical/Translational	Population Science
81 awards	52 awards	7 awards
\$16.6 million	\$7.8 million	\$1.1 million

COMMUNITY SUPPORT



Nearly **\$1.6 million** raised through community events



One Gene at a Time

Researcher identifies function of GNAS mutation in evolution of pancreatic cyst into pancreatic cancer, establishing important biomarker identification and potential therapeutic target.

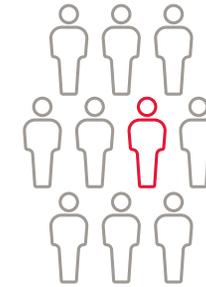
Identifying a genetic mutation that affects fewer than one in 10 cancer patients may not sound monumental. That is unless you're talking about pancreatic cancer, which kills 90% of patients within five years.

"One of the biggest problems is that pancreatic cancer is detected very late stage, when it has already metastasized," says Krushna Patra, PhD, University of Cincinnati Cancer Center member and assistant professor in the Department of Cancer Biology. "There are no early detection markers for pancreatic cancer, but there is a group of pancreatic cancers that develop from cysts that can be detected by imaging modalities."

Patra has been studying KRAS and GNAS mutations in pancreatic cancer and believes that the presence of these two mutations is a worrisome genetic makeup of precancerous cysts. While it is well-known that KRAS mutation is present in most pancreatic cancers, Patra's lab is working on showing how the GNAS mutation is the conduit from cyst to cancer. The fact that this particular genetic mutation occurs in fewer than 10% of cases doesn't deter him.

"My work is understanding pancreatic cancer, one gene at a time," Patra says.

Currently, clinicians can analyze the fluid inside the cyst to detect the genetic mutation and based on this, determine if the cyst is precancerous and if it needs to be removed. However, because these cysts develop in elderly patients, surgery may not be feasible, or surgery may not remove all cancerous cells. Understanding how the GNAS mutation facilitates the growth of pancreatic cancer could lead to the first targeted therapy for pancreatic cancer.



8-10% of Americans over 60 develop pancreatic cysts. About 1% of these become cancerous, accounting for 10% of all pancreatic cancer cases.

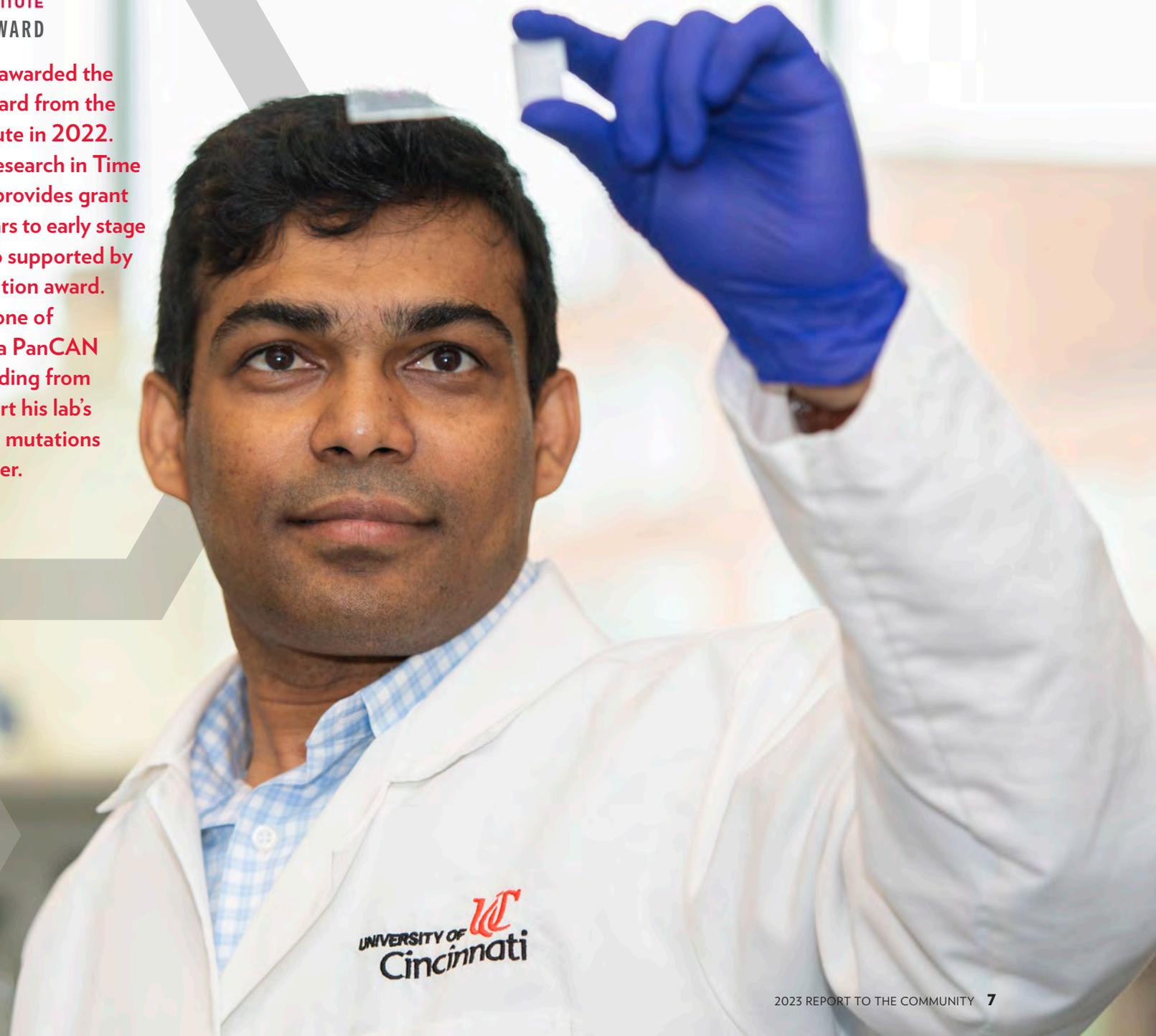


PANCREATIC CANCER IS NOT ONE TYPE OF DISEASE. WE NEED TO UNDERSTAND THE DISEASE BETTER, NOT AS A WHOLE BUT SLICE BY SLICE."

~ Krushna Patra, PhD



Dr. Krushna Patra was awarded the prestigious MERIT Award from the National Cancer Institute in 2022. The Method to Extend Research in Time (MERIT) Award (R37) provides grant support for up to seven years to early stage investigators. His lab is also supported by an NCI-K22 career transition award. In 2020, Patra was one of 10 researchers to receive a PanCAN award plus additional funding from BSI Engineering to support his lab's work on KRAS and GNAS mutations in pancreatic cancer.





Lipid Profile May Signal Breast Cancer Recurrence Risk

While 93% of breast cancer patients survive 10 years, that rate falls to 27% when the cancer comes back and just 7% if it metastasizes. Researchers hope lipid pathways can serve as biomarkers of recurrence risk and perhaps even treatment.

It's long been known that lipids are essential contributing factors to cardiovascular disease and, as a result, more than 60% of Americans over the age of 60 take a cholesterol-lowering medication. Now, two researchers at the University of Cincinnati Cancer Center are looking at how these same metabolites are involved in breast cancer recurrence.

"The area of lipids has been understudied because they are hard to detect," says Susanne Wells, PhD, a basic science researcher at the Cancer Center and director of the Epithelial Carcinogenesis and Stem Cell Program at Cincinnati Children's. "We got curious because this field is so ripe for exploitation as markers and as targets."

Wells and Susan Waltz, PhD, associate director for cancer research training and education coordination at the Cancer Center, have identified what they believe to be key lipid pathways in breast cancer recurrence and the genes that regulate these pathways. The duo believes that these genes can serve as biomarkers for recurrence, and that lipids could be a potential target for new therapies.

"We can use metabolic pathways to understand how we might be able to better treat cancer patients so that they're less susceptible to breast cancer

recurrence," Waltz says. "It could be dietary; it could be different ways of treating patients, compared to the toxic drugs that we give patients now."

The idea to research lipids as a biomarker and potential treatment for recurrent breast cancer didn't happen overnight. Wells and Waltz and their teams have been collaborating for 15 years to study the impact of Ron and DEK genes on breast cancer. Their work has shown that both oncogenes are independently associated with breast cancer recurrence and poor overall survival.

Targeting these genes, however, was proving elusive, so the researchers began looking at their role in breast cancer metabolites. "The science was telling us to go in that direction," Waltz says. The team identified the enzymes involved in regulating those metabolites and then looked deeper at lipids specifically.

To conduct the lipid research, which is now being considered for a patent before the work will be published, they partnered with NMR spectroscopy experts Sara Vicente-Muñoz, PhD, at the NMR-based Metabolomics Core at Cincinnati Children's, and Andrew Lane, PhD, at the University of Kentucky College of Medicine.



"WE CAN USE METABOLIC PATHWAYS TO BETTER TREAT BREAST CANCER PATIENTS SO THAT THEY'RE LESS SUSCEPTIBLE TO BREAST CANCER RECURRENCE."

- Susan Waltz, PhD (right), with Susanne Wells, PhD



Committed to Change

Local Cincinnati attorney beats breast cancer and takes her fight to the Ohio legislature to get insurance coverage for additional breast cancer testing for women with dense breast tissue.

Since high school, Michele Young has been advocating for causes she's passionate about, from environmental justice to social justice.

"I didn't plan for breast cancer but when I was diagnosed, I used the opportunity to save my life and help all women by changing the law," says Young, a mother of five and a Cincinnati attorney recognized for speaking out against injustice.

Despite getting breast cancer screenings using the latest 3-D technology, Young's annual mammograms likely missed the breast cancer because she is one of the 50% of women who have dense breast tissue. It wasn't until Young was diagnosed with late-stage cancer in 2018 that she learned that supplemental screening with breast MRI and ultrasound is recommended for women with dense breast tissue. These tests, which traditionally are not covered by insurance, could have caught her cancer earlier.

"Seventy-five percent of the women who receive a breast cancer diagnosis have no family history. Most women don't realize that having dense breast tissue is a strong risk factor for developing breast cancer. Through more advanced screening tools such as FAST MRI, we can make early detection a reality for women with dense breasts and this can save lives," says Ann Brown, MD, clinical/translational researcher at the University of Cincinnati Cancer Center and associate professor at the UC College of Medicine.

Young is now among the 3% of women in long-term complete remission, thanks to treatment at the University of Cincinnati Cancer Center from Elyse Lower, MD, former director of the Cancer Center's Breast Cancer Program and a UC Health physician.

While undergoing chemotherapy, Young focused not only on her own survival but also on how her experience could help other women. Working with Lower and Brown, Young took her story to the Ohio legislature to push passage of HB 371. The bill, which passed and took effect in September 2022, expands insurance coverage for annual 3-D mammography (tomosynthesis) for all women, regardless of breast density. It also mandates coverage for supplemental screenings like breast MRI or ultrasound for women with dense breast tissue or those with increased risk for breast cancer.



Michele Young used her story to help more women get the appropriate breast cancer screenings.



Tracing the Origins of Aggressive Medulloblastoma

Data from a new fetal brain atlas has helped a scientific team discover a collection of progenitor cells that give rise to aggressive “Group 3” medulloblastomas. Findings include identification of two genes that may serve as therapeutic targets. Mice with these tumors lived longer when bred to express reduced levels of these genes.

Medulloblastoma (MB) is the most common malignant childhood brain tumor, with one type — Group 3 — being the most deadly.

Until now, very little was known about the origins of Group 3 MB. University of Cincinnati Cancer Center researchers along with colleagues from three other countries were able to identify a specific type of progenitor cell responsible for tumor formation. The findings were published in November 2022 in *Nature*.

“We identified a progenitor cell population in the early developing cerebellum,” says Qing Richard Lu, PhD, basic science researcher at the Cancer Center and scientific director of the Brain Tumor Center at Cincinnati Children’s. “These progenitor cells are highly abundant in aggressive medulloblastomas with excessive MYC gene copies, which drive tumor formation. This progenitor population may serve as a potential cell of origin for the aggressive medulloblastomas.”

Even more promising, the researchers also identified two specific marker genes that activate the MYC oncogene to drive tumor cell growth: SOX11 and HNRNP1.

“These markers can be used in the clinic for disease prognosis,” Lu explains. Once they identified these biomarkers, the team used mouse models to discover if they were targetable. “We found that targeting those two genes can inhibit the growth of medulloblastoma tumor cells with excess MYC gene copies that we interpret as being the progeny of the progenitors.”

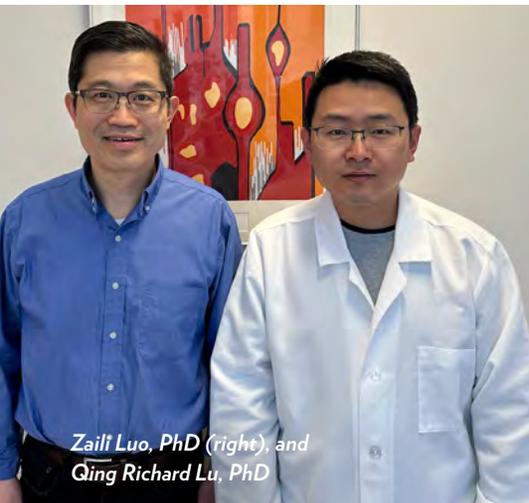
This discovery was made after the multinational team of scientists led by Lu and other experts at Cincinnati Children’s developed an “atlas” of human brain development so detailed that it tracks growth steps down to changes at the single-cell level.

“This study took the effort of 40 experts for nearly three years to complete,” Lu says. “It was worth so much effort because this new map guided us to a potential target for therapeutic intervention of aggressive medulloblastomas.”

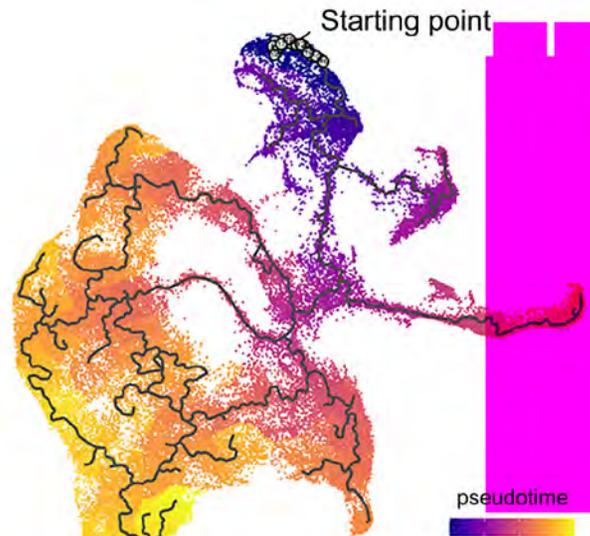
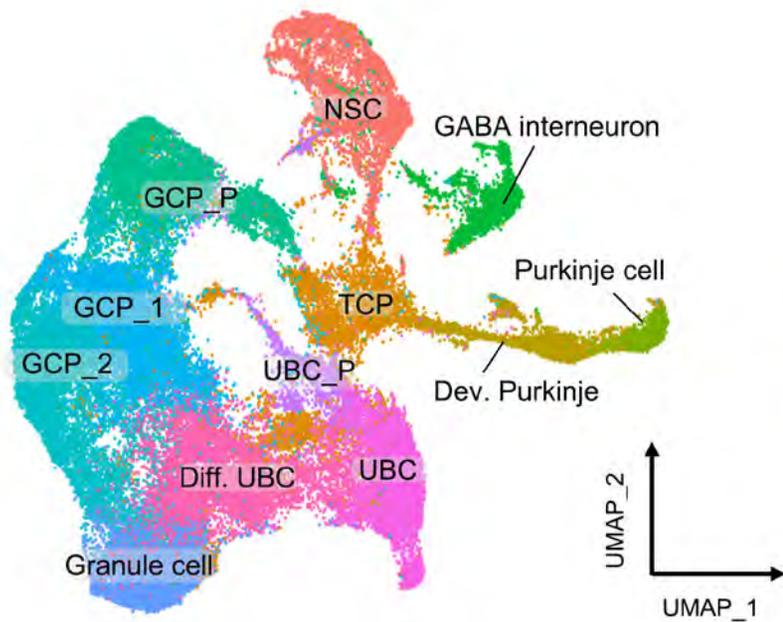
In addition to Lu, 15 other researchers at Cincinnati Children’s and University of Cincinnati co-authored the study, including Zaili Luo, PhD, a researcher in Dr. Lu’s lab and first author on the *Nature* publication. International collaboration came from researchers at the Children’s Hospital of Fudan University, Xinhua Hospital, the Shanghai Jiao Tong University School of Medicine and Westlake University in China; the University of Cambridge in the UK; the University of Toronto in Canada; and Northwestern University in Evanston, Ill.

Medulloblastoma accounts for 64.3% of all embryonal tumors in pediatric patients 0-19 years old.

Source: Central Brain Tumor Registry of the U.S.



Zaili Luo, PhD (right), and Qing Richard Lu, PhD



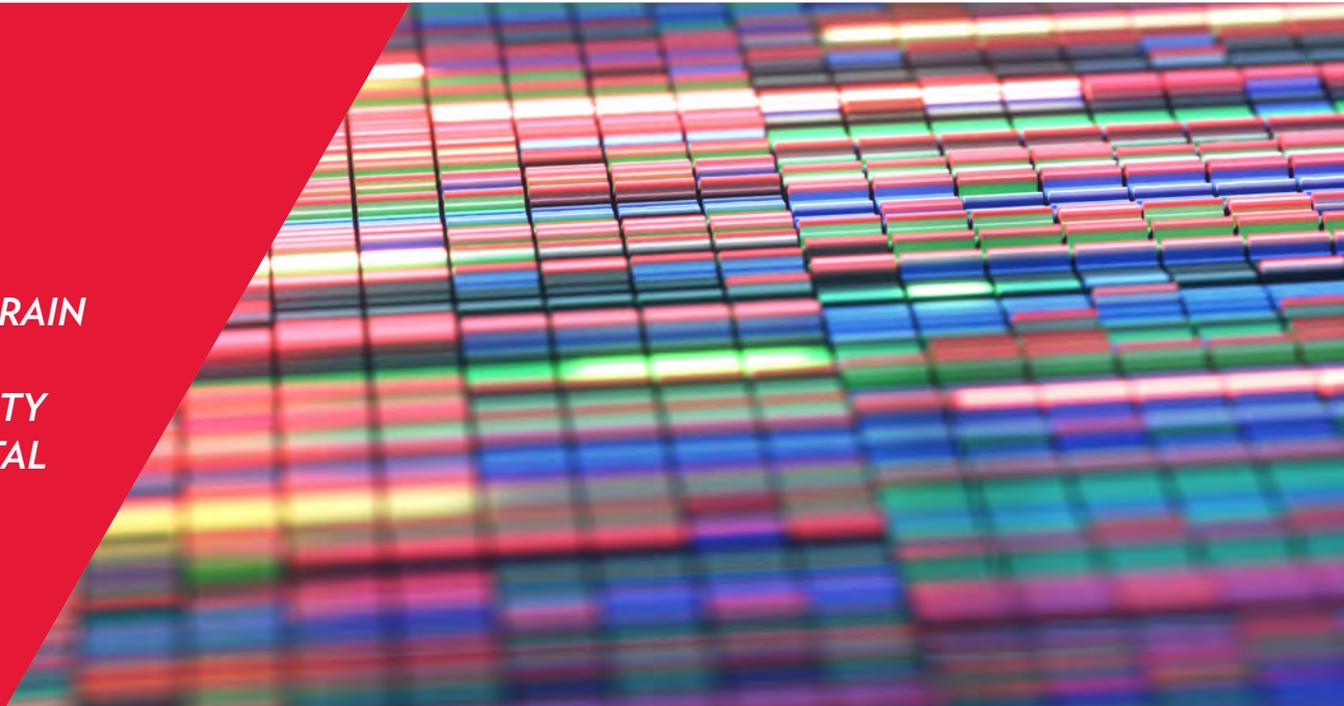
Left: UMAP visualization of neural cell types from the developing human cerebella.

Right: Predicted trajectories of neural cell-type fate transitions.



WHILE THIS STUDY FOCUSES ON MEDULLOBLASTOMA, THE NEW ATLAS WILL HELP ACCELERATE UNDERSTANDING OF OTHER CONDITIONS THAT RESULT FROM DISRUPTIONS IN HEALTHY EARLY BRAIN DEVELOPMENT, SUCH AS AUTISM, ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD), DEVELOPMENTAL DYSLEXIA AND PEDIATRIC CEREBELLAR DAMAGE.”

- Qing Richard Lu, PhD





Translating Targets Into Therapies

University of Cincinnati Cancer Center labs are working to bridge the chasm between identifying novel targets in cancers and developing the precision drugs that disrupt these molecular pathways. One lab — just months away from in-human trials for a drug that targets signaling pathways in AML — faces that challenge again after identifying new potential target.

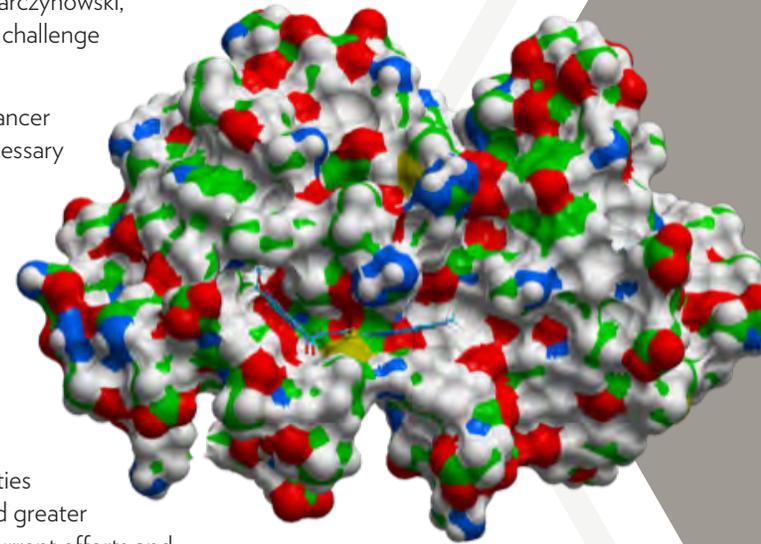
Daniel Starczynowski, PhD, and his research team at Cincinnati Children's are fervent in their efforts to discover new signaling pathways that contribute to the growth of acute myeloid leukemia (AML). But even when they are successful, they know their work is far from done.

"What we do well at the Cancer Center is understanding the complex mechanisms of cancer biology," says Starczynowski, associate director for basic science research for the University of Cincinnati Cancer Center. "What always is a challenge is now taking that information and translating it into a drug that patients will benefit from."

With the advent of computational chemistry and artificial intelligence, the Cancer Center is also looking at the possibility of developing the infrastructure necessary to develop drugs itself.

"There is a need and desire to provide new therapies for our patients," he says. "The conventional approach is not feasible because of the huge investment required, but there are cutting-edge and contemporary approaches that can be implemented to allow us to be successful at moving therapies into the clinic."

Some research groups at the Cancer Center are already pilot testing the new platforms. "We have some capabilities that are leading us in the right direction, but we still need greater investment," Starczynowski says. "If we can consolidate current efforts and investment in novel platforms, we can provide the type of support to investigators who might not have an appetite for drug discovery, but they have a really important mechanism and target that should be invested in and developed into a drug."



Daniel Starczynowski, PhD



my green lab
certification.

The Starczynowski Lab is the first in Ohio to earn the "My Green Lab" certification.

SMALL MOLECULE BLOCKS PROTEIN CRITICAL TO AML CELL SURVIVAL

The Starczynowski Lab in 2022 identified a protein — UBE2N — that appears crucial to multiple pathways that contribute to AML cell survival. The team also found a class of small molecules that block the protein's function. The discovery was published in *Science Translational Medicine*.

"We published proof of concept studies that this enzyme is indeed druggable and that you can use small molecules to inhibit its catalytic activity and target the function of these leukemic cells," Starczynowski says.

The Starczynowski Lab focuses on identifying altered genes and signaling pathways that contribute to the development of AML and myelodysplastic syndromes (MDS). Previously, the lab identified the role of two proteins, IRAK1 and IRAK4, in a signaling pathway that helps MDS and AML cells survive as well as a molecule that could inhibit those proteins. In addition, the team showed the same inhibitor could improve the potency of a common AML treatment, venetoclax, which could reduce the required dosage and accompanying side effects.

Working with Cincinnati Children's Innovation Ventures, Starczynowski founded a biotech startup (Kurome Therapeutics) to develop those discoveries into a drug. That drug is expected to enter Phase I trials in 2024, he says.

The new UBE2N inhibitor could follow the same path to drug development. Cincinnati Children's has filed a patent on the discovery.

New Drug Shows Promise for B-ALL

Phase II trial of inotuzumab ozogamicin (InO) showed a 58% remission rate in children with relapsed/refractory B-ALL. An international Phase III study is now underway to evaluate the drug's safety and efficacy.

Researchers at Cincinnati Children's completed a Phase II clinical trial showing that inotuzumab ozogamicin (InO), a drug well-tolerated in adults, is safe and effective in treating children and adolescents with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL).

"InO as a single agent led to remission in 28 patients (58.3%), many of whom went on to receive subsequent curative therapy," says Maureen O'Brien, MD, MS, clinical/translational researcher at the Cancer Center, director of the Leukemia/Lymphoma Program at Cincinnati Children's and principal investigator of the study. The study, sponsored by the Children's Oncology Group (COG), was published in the *Journal of Clinical Oncology* in March 2022.

InO targets CD22, a surface protein that is expressed on the leukemic blasts in about 95% of B-ALL cases. Study participants included 48 patients (ages 1 to 21 years) with CD22-positive relapsed/refractory B-ALL who had received prior treatment, such as intensive chemotherapy or immunotherapy.

"Patients who participated in this trial had experienced multiple relapses or did not respond to other therapies," O'Brien says. "They had few available treatment options."

In addition to resulting in remission in 58.3% of participants, the study showed:

- **InO was well-tolerated with minimal side effects reported during treatment.**

However, of the 21 patients who received hematopoietic stem-cell transplantation (HSCT) after InO, six (28.6%) developed sinusoidal obstruction syndrome (SOS), which is a serious toxicity of the liver.

"InO is one of the most effective single-agent therapies available for B-ALL, but we have to figure out how to use it safely, given the risks," O'Brien says.

To that end, O'Brien is co-principal investigator for an international Phase III COG-sponsored trial evaluating the safety and efficacy of InO when combined with chemotherapy for patients (ages 1 to 25 years) with newly diagnosed high-risk B-ALL. This trial has completed two safety phases that included 100 randomized patients and is being modified to reopen in the summer of 2023. Roughly 2,100 patients will ultimately participate in the trial and be randomized to either standard chemotherapy or chemotherapy plus two cycles of InO.



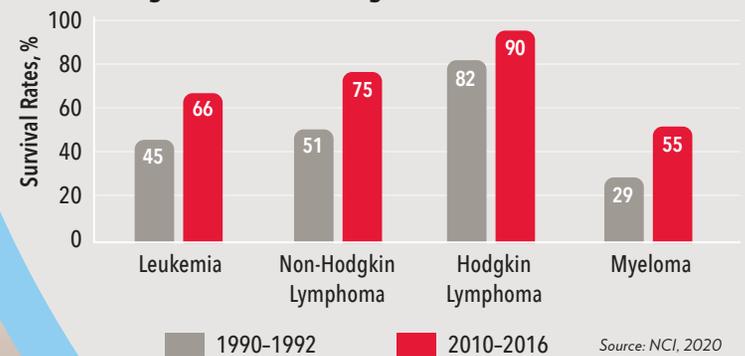
**Maureen O'Brien,
MD, MS**



Building a Leukemia Destination Program

Strategic recruitment of clinical faculty and investigators, coupled with technological and infrastructure investments, continue to build Cincinnati's blood cancer expertise.

Survival rates for the most common hematological malignancies have surged since 1990.



Over the past decade, five-year survival rates for people with leukemia, lymphoma and other hematological malignancies have greatly improved. New treatments are being developed at a record pace, and the University of Cincinnati Cancer Center's leukemia destination program is contributing to this work. In 2022, the Cancer Center continued to expand its expertise in hematological malignancies to provide the most advanced care to patients with leukemia in Ohio and surrounding regions while also supporting basic science and clinical/translational research in the field. Hematologic malignancy was once a diagnosis that led patients to leave town for care. But with recent investments, the University of Cincinnati Cancer Center has quickly become a destination for patients seeking the best care.

The Cancer Center recruited seven new team members, including Edward Faber Jr., DO, MS, a CAR T-cell therapy expert; Zulfa Omer, MD, a chronic lymphocytic leukemia expert; and Hira Shaikh, MD, a multiple myeloma and transplant expert. They join an existing cadre of experts, including Bryan Hambley, MD, MPH; Emily Curran, MD; Tahir Latif, MBBS, MBA; and Pier Paolo Scaglioni, MD. It also began development of a new Blood Cancer Healing Center, as well as continuing to move forward with basic and clinical research. (See stories next page.)

These new additions join the critical elements already in place at the University of Cincinnati, UC Health and Cincinnati Children's. The Cancer Center's leukemia program now offers:

1

Access to advanced diagnostic tests and technologies, including molecular profiling, flow cytometry, cytogenetics and immunohistochemistry, to accurately identify the type and subtype of leukemia and guide treatment decisions.

2

Access to a wide range of treatments, including chemotherapy, targeted therapy, immunotherapy, radiation therapy, bone marrow transplant and cellular therapies, including CAR T-cell therapy.

3

Clinical trials that offer new and promising therapies for patients who do not respond to standard treatments or who have relapsed or have refractory disease.

4

A Cancer Wellness Center that provides supportive care services, including management of coexisting health conditions, access to integrative therapies (such as acupuncture and yoga) and survivorship care.

"We have quickly built a nidus to support early drug development and leading-edge treatments," says John C. Byrd, MD, senior advisor to the Cancer Center and the Gordon and Helen Hughes Taylor Endowed Chair of the Department of Internal Medicine in UC's College of Medicine. "The people in the tristate area deserve to have empathetic, state-of-the-art care for leukemia. We seek to serve them while also helping patients from all over the world."





Leukemia Advancements

The Transplant and Cellular Therapy Center at the University of Cincinnati Cancer Center is undergoing a growth spurt and evolving into a comprehensive leukemia treatment program that will attract and treat patients from around the country.

CAR T-Cell Expert Joins Cancer Center

In 2022, the Division of Hematology and Oncology recruited five clinical faculty members and two lab-based investigators. It plans to recruit 18 additional clinical faculty members in the next 2-3 years and 12 more lab-based investigators by 2028, says Pier Paolo Scaglioni, MD, associate director for translational research at the Cancer Center and director of the Division of Hematology and Oncology at the UC College of Medicine.

“I joined the UC College of Medicine and Cancer Center in 2018 because I was given the task and resources of building and developing the academic mission of the Division of Hematology and Oncology,” Scaglioni says. “That mandate has even become stronger after the appointment of Dr. Ahmad as co-director of the Cancer Center and Dr. Byrd as chair of the Department of Internal Medicine. We have made significant progress toward our goal to be a leading academic division and cancer center, but the job is not done. I believe that the division should double in size with the recruitment of additional clinical investigators and lab-based scientists to be competitive nationally.”

One notable recruit in 2022 was the addition of Edward Faber Jr., DO, MS. Faber, a clinical/translational researcher and director of the Transplant and Cellular Therapy Center at the Cancer Center, specializes in the use of cellular therapies in blood diseases.

Faber’s appointment reflects the Cancer Center’s emphasis on treating blood cancers with precision, says John C. Byrd, MD, the Gordon and Helen Hughes Taylor Endowed Chair of the Department of Internal Medicine in UC’s College of Medicine. The focus is to advance the development and clinical use of cellular therapies beyond hematopoietic stem cell transplantation to newer cellular therapies that involve immune system cells. These types of cells are collected from the patient’s own blood, modified in the laboratory to produce a more vigorous attack on the patient’s cancer cells, and then re injected into the patient. Cellular therapy using chimeric antigen receptor T-cell therapy (CAR T), Faber’s area of interest, is already being used to treat certain types of leukemia, lymphoma, myeloma and solid tumors.

As the division continues its recruitment drive, it is placing special emphasis on diversity, equity and inclusion, Byrd says. In 2022, leadership formed a Diversity and Belonging Council that made significant changes in hiring, promotion and pay practices.



*Edward Faber Jr., DO, MS,
specializes in CAR T therapy.*



Megan Johnstone, PhD, is a clinical research director in the Leukemia and Drug Development Lab.

LP-168 Clinical Trial

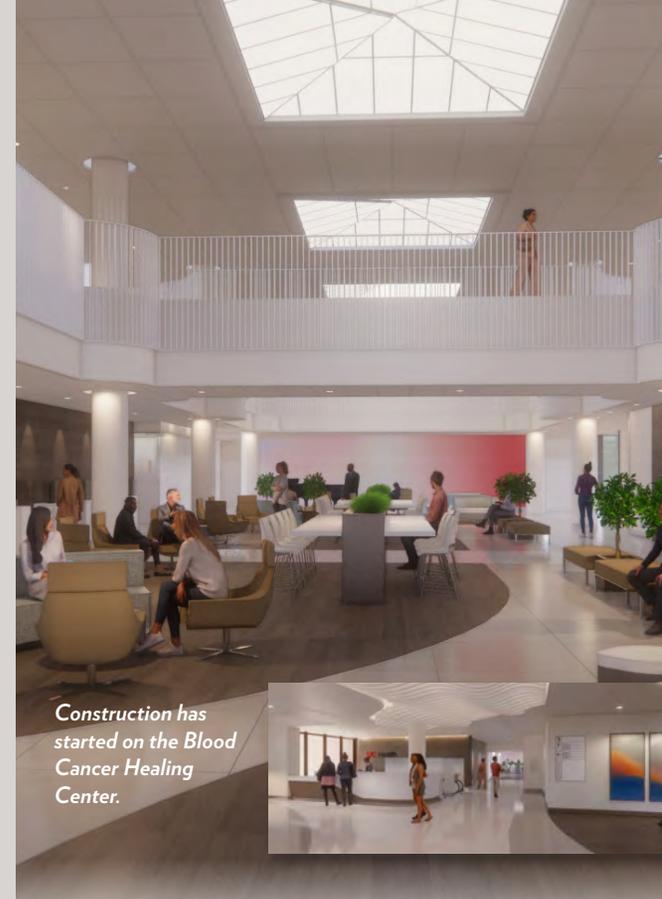
The University of Cincinnati Cancer Center is one of four U.S. sites conducting a clinical trial of a new drug for patients with B-cell lymphomas or chronic lymphocytic leukemia (CLL) that have grown resistant to standard treatments.

The Phase I trial is studying the safety and efficacy of a new drug called LP-168, a fourth-generation small molecule inhibitor. The first and second generations of this type of small molecule inhibitors were effective, but the cancer could develop resistance through a mutation that broke the gene, making it harder for the drug to reach its target, says John C. Byrd, MD, a senior advisor at the Cancer Center and the trial's principal investigator. These inhibitors "changed the natural history of these diseases" by creating the mutation, which only exists in patients who have been treated with the drug, he says.

LP-168 addresses the problem of resistance with a new design that could get around the mutation. "It takes the third-generation molecule and the first-/second-generation molecule, and it glues them together," Byrd says. "If the cancer cell develops a resistance to one part, you have the other part there that kills it."

Blood Cancer Healing Center

In 2022, the University of Cincinnati completed the purchase of the former Cincinnati Shriners' Hospital and began renovations to transform the building into the Blood Cancer Healing Center. The multimillion dollar renovation will create a dedicated blood cancer clinic, an inpatient unit for blood cancer and cellular therapy, a 24/7 infusion center, and a dedicated Phase I clinical trial unit. Additional areas will be designated for translational and fundamental blood cancer research and integrative medicine. The new center also will include hotel-type rooms located within the building that will be available for outpatients who require close observation but not inpatient care. UC anticipates the center will open in 2024.



Construction has started on the Blood Cancer Healing Center.

FACT Accreditation

The George L. Strike Bone Marrow Transplant Center at the University of Cincinnati was accredited by the Foundation for the Accreditation of Cellular Therapy (FACT) in 2022. The Bone Marrow Transplant Center joins two of its sister institutions in being accredited: Cincinnati Children's Cancer and Blood Diseases Institute, Bone Marrow Transplantation and Immune Deficiency Program; and the Hoxworth Blood Center at the University of Cincinnati. Founded in 1996, FACT establishes standards for high-quality medical and laboratory practices in cellular therapies. FACT accreditation is a voluntary program that requires a rigorous and comprehensive inspection by international experts in cellular therapy practices.





First-in-Human FLASH Radiation Therapy Trial Deemed a “Breakthrough”

***Physics World* names FAST-01 trial a Top 10 Breakthrough, and *USA Today* proclaims it one of the Top 3 Advances in Cancer Treatment.**

Research findings from the world’s first-in-human clinical trial of proton FLASH therapy, which was conducted at the Cincinnati Children’s/University of Cincinnati Medical Center Proton Therapy Center, indicate the clinical feasibility and preliminary efficacy and safety of an experimental treatment for cancer patients that delivers radiation therapy at ultrahigh dose rates in less than 1 second.

FLASH radiotherapy induces a phenomenon known as the FLASH effect, which reduces harm to normal tissue surrounding a tumor during conventional radiation therapy while still killing the cancer cells at the tumor site.

“Our unique FLASH research has far-reaching implications for how we treat cancer in kids and adults,” says John Perentesis, MD, senior advisor at the University of Cincinnati Cancer Center, research director for the Proton Therapy Center, and co-director of the Cancer and Blood Diseases Institute at Cincinnati Children’s. “It’s important because radiation is one of the most effective tools for treating cancer and is used for nearly half the cancer patients in the U.S. FLASH holds promise to become a paradigm-shifting technology by potentially providing more effective cancer treatment with fewer side effects.”



John Perentesis, MD

The FAST-01 study was led by Cancer Center members John Breneman, MD, medical director of the Proton Therapy Center, and Emily Daugherty, MD, a clinical/translational researcher at the Cancer Center and assistant professor in the UC College of Medicine. Findings were published in *JAMA Oncology* and presented Oct. 23,



The Proton Therapy Center, which opened in 2016, is the first proton therapy center in Ohio and one of only 39 in the U.S. It incorporates a \$24 million, one-of-a-kind research facility that includes a fully operational proton treatment room dedicated to research along with integrated laboratories. The unique capabilities of the research center were instrumental in developing the world’s first and only clinical trials of FLASH proton therapy.



John Breneman, MD

2022, at the American Society for Radiation Oncology (ASTRO) annual meeting. Anthony Mascia, PhD, chief physicist at the Proton Therapy Center, is the principal author of the landmark *JAMA Oncology* paper.

Data from FAST-01 has already led to the approval of FAST-02. The FAST-02 clinical trial (FeAsibility Study of FLASH Therapy for the Treatment of Symptomatic Bone Metastases) is expected to enroll 10 patients with painful bone metastases. The study aims to evaluate treatment-related side effects and efficacy of treatment, which will be assessed by measuring trial participants' pain relief.

"Our study shows FLASH radiotherapy with protons is a practical modality to reduce pain," says Daugherty. "It deserves further exploration because of its potential to decrease the side effects associated with conventional radiation treatments."

* FLASH RT vs. Conventional Radiotherapy for Bone Metastases

Most early research on FLASH RT used electron beams to deliver radiation, but electron beams don't penetrate deeply into tissue, limiting its applicability. Proton beams for ultrahigh-dose radiation allow for penetration sufficient to reach tumor locations in most people.

	FLASH RT	Conventional Radiotherapy
 Radiotherapy Dosage	FLASH-enabled (≥ 40 Gy/sec) proton radiotherapy system using a single-transmission proton beam	Conventional dose rate is approximately 0.03 Gy/sec but can vary by patient
 Time on Treatment Table	15.8 minutes per treated site	15-30 minutes
 Delivery Time of Treatment	3/10 of a second	A few minutes
 Number of Treatments	1	Can be 1, but often requires treatment 5 days a week for 2-3 weeks, depending on the size, type and location of the cancer
 Side Effects	Mild with most common being transient mild skin hyperpigmentation	Varies by location of radiation but can include damage to nearby cells and tissue, fatigue, skin changes and issues like weight loss and hair loss
 Pain Reduction	8 out of 12 treatment sites for an overall response rate of 67%	65% overall response rate achieved in the RTOG 9714 trial



Physics World recognized the FAST-01 trial as a Top 10 Breakthrough of the Year for 2022.



FLASH radiation could mean cancer treatment in seconds, not weeks, proclaims **USA Today** as it announces FLASH radiation therapy as one of the Top 3 Advances in Cancer Treatment.



Linking Gut Health to Cancer Survival

Increased presence of *Faecalibacterium prausnitzii* in gut microbiome of pancreatic cancer survivors is the same species shown to improve immunotherapy response in melanoma patients.

How the gut microbiome affects health is a hot topic and no less so when it comes to cancer. After researchers again and again hit a dead end in trying to identify genetic differences in people who survive pancreatic cancer, one University of Cincinnati Cancer Center researcher decided to take a look inside the gut.

“There really hasn’t been much difference in a (pancreatic cancer) survivor, compared to a patient who didn’t survive, in terms of the genetics of the patient or the genetics of the tumor,” says Jordan Kharofa, MD, a clinical/translational researcher and co-director of the Gastrointestinal Disease Center at the Cancer Center. “There is emerging science suggesting that pancreatic cancer survivors have a robust immune response in their tumors and data suggesting the gut microbiome can influence immune response. We wondered if there was a relationship with the gut microbiome in pancreatic cancer survivors.”

After collecting and analyzing stool samples from 16 pancreatic cancer survivors (more than four years from surgery without signs of recurrence) in 14 states, Kharofa and his co-researchers found that these patients had an increased presence of *Faecalibacterium prausnitzii*. This is the same species that has been shown in melanoma patients to increase the response to immunotherapy. The link between bacteria in the gut and the immune system seems to



Jordan Kharofa, MD



make sense, Kharofa says, because pancreatic cancer survivors also have more T-cells and immune cells inside their tumors that are recognized better by the immune system.

“There’s this possible link between the stool and immune response and these species in the same way that we’re seeing in melanoma. That has never been shown before, and we’re excited to explore this further,” Kharofa says.

The GIVEHOPE Foundation funded the study, which was published in March 2023 in the journal *Cancer*. PanCAN, the Pancreatic Cancer Action Network, helped locate the survivors in the study. Kharofa collaborated with Senu Apewokin, MD, a clinical/translational researcher and physician with the Cancer Center and associate professor in the UC College of Medicine. The DNA sequencing of the stool was conducted at the Microbial Genomics and Metagenomics Laboratory at Cincinnati Children’s.



Senu Apewokin, MD



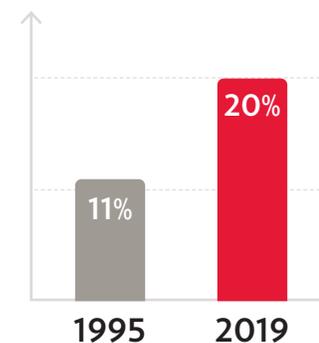
Gut Bacteria Driving Colorectal Cancer Development

Kharofa’s interest in the gut microbiome and its impact on cancer extends beyond pancreatic cancer. Noting the increase in his radiation oncology practice of younger patients with colorectal cancer, Kharofa wondered if diet — and specific species of bacteria — contribute to the increase.

“We identified a group of bacteria that metabolize sulfur enriched in young colorectal cancer patients,” Kharofa says. “One hypothesis of why we’re seeing higher rates in younger people is that they’re eating these foods at an early age, which increases the prevalence of sulfur-metabolizing bacteria leading to carcinogenic byproducts. The person may not necessarily be obese but might have a selection of bacteria in the gut through dietary patterns that indirectly elevate colorectal cancer risk.”

This study, also conducted with Apewokin, was published Sept. 3, 2022, in the journal *Cancer Medicine*.

Increase in Cases in Americans <55 years old*



45

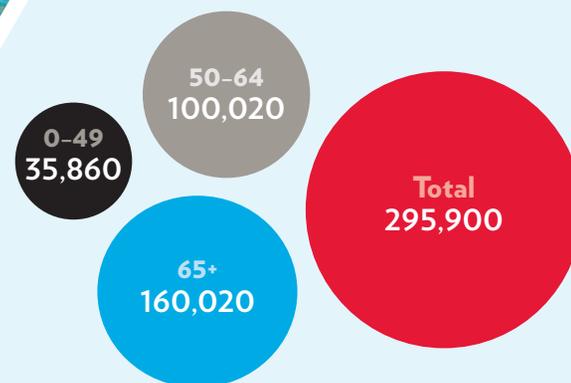
Due to the increasing number of colorectal cancer in younger Americans, the U.S. Preventive Services Task Force lowered the recommended age of starting colonoscopies to 45 years old for average-risk adults.

THE DIETARY LINK

Eating diets high in certain types of foods, including processed meats and diet soda, early in life might be contributing to an increase in sulfur-eating bacteria, leading to carcinogenic byproducts.



Estimated Number of Colorectal Cancer Cases in U.S. by Age, 2020:*



*Source: American Cancer Society



Breathing Easier

University of Cincinnati Cancer Center combines lung cancer research, advanced treatments, community education and cancer prevention efforts to try to improve smoking rates and cancer survivorship in the Midwest.

Nearly one in five adults in Ohio and Kentucky smoke, compared to the national average of 12.5%, according to the American Lung Association.

Smokers are up to 30 times more likely than nonsmokers to develop lung cancer — the deadliest of cancers — but more than 90% of patients can be cured of lung cancer if they are diagnosed early.

At the University of Cincinnati Cancer Center, a team of experts in lung cancer, including chest radiologists, interventional pulmonologists, medical oncologists, pulmonary pathologists, radiation oncologists, and thoracic surgeons along with oncology nurses and dietitians, provide personalized care coupled with innovative programs and technology. A recent study conducted at UC College of Medicine and published in the *Annals of Thoracic Surgery* found this multidisciplinary approach successfully identifies patients with early stage lung cancer while reducing unnecessary surgical interventions.



Sandra Starnes, MD

Robotic Bronchoscopy

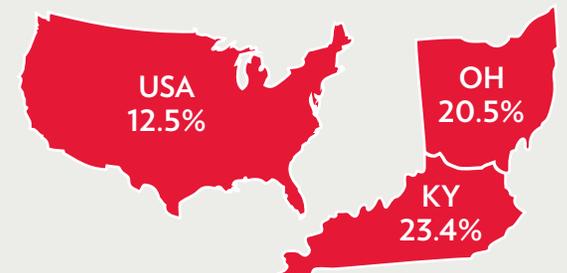
The Cancer Center's new Monarch robotic bronchoscopy helps identify lung cancer at earlier stages. The FDA-approved technology utilizes a tiny camera attached to a flexible, thin tube to view inside the lungs and biopsy tissue with up to 95% accuracy.

"With robotic bronchoscopy, we can accurately reach areas in the lung that were not possible before. Many patients with small nodules now have a more feasible option for an accurate biopsy," says Christopher Radchenko, MD, assistant professor in the UC College of Medicine.

In the past, physicians diagnosed 75% of lung cancers at stages 3 or 4 when there aren't many options for a cure, Radchenko says. Lesions of less than 1 cm were not easily or accurately biopsied.

Since UC Health began using the robotic bronchoscopy in November 2021, more than 150 patients, the most in the area, have benefited from the technology.

Smoking rates in areas we serve are double the national rate, peaking at 28% in Adams County.



“With robotic bronchoscopy and initiatives like the lung cancer screening and incidental lung nodule programs, we’re able to detect nodules when they are more readily curable,” Radchenko says.

Lung Cancer Screening Program

The Cancer Center’s Lung Cancer Screening Program was the first screening program in the region.

“We’re seeing a 25-30% increase in participation year over year,” says Sandra Starnes, MD, a clinical/translational researcher, co-director of the Cancer Center’s Lung Disease Center and chief of thoracic surgery at the UC College of Medicine.

This increase is due to direct-to-patient outreach and education as well as partnerships with primary care physicians, Hoxworth Blood Center, and the Cincinnati Health Department.

The program includes three dedicated nurse navigators and a clinical coordinator who coordinate all screening and follow-up care. This approach allows earlier detection and better outcomes. Screenings are done with a low-radiation-dose CT scan that is completed in a few minutes and does not require IVs or contrast. More than 5,000 patients have participated in the program since 2011.

“While the national average for lung cancer screening is around 5.7%, we’re at about 10%, but that means there are still many eligible patients who aren’t getting screened. Individuals 50 to 80 years old who smoked in the last 15 years and have at least a 20 ‘pack year’ history are eligible for routine lung cancer screening,” Starnes says. “We’re starting to see higher rates of lung cancer in women, younger people and never-smokers. We must do a better job of reaching these populations.”

A pack year is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years smoked, with one pack year equivalent to smoking one pack of cigarettes per day for one year or two packs per day for six months. Secondhand smoke, radon, and environmental and lifestyle factors can also contribute to lung cancer.

Incidental Lung Nodule Program

The first of its kind in Ohio, the Cancer Center’s Incidental Pulmonary Nodule Program started in June 2020. It uses EON artificial intelligence (AI) technology to review every CT scan conducted at UC Health to detect any potential cancerous nodules.

“The AI detects incidentally found nodules in up to 25% of patients in our system that come in for a CT chest examination for an entirely unrelated reason, like chest pain or trauma,” says Radchenko, medical director of the Incidental Pulmonary Nodule Program.

Once nodules are identified, a dedicated team reviews the scans and determines next steps. The team has reviewed nearly 15,000 scans and has contributed to care for 5,000 patients, 500 of whom are being actively monitored. The program has led to the detection of 40 incidental cancers and conditions like cystic fibrosis and structural lung disease that would not have been found otherwise, Radchenko says.



SMOKING CESSATION PROGRAM

Telehealth turned out to be a silver lining of the COVID-19 pandemic, increasing the number of new patients enrolled in University of Cincinnati Cancer Center’s Win by Quitting Smoking Cessation Program and keeping them coming back.

- **2022 Participants: 392**
- **Percent of telehealth sessions: 80%**
- **Percent of telehealth visits kept: 82% vs. 65% of in-person visits**



University of Cincinnati Cancer Center screened 2,425 patients for lung cancer in 2022.





Engaging the Community to Improve Health

University of Cincinnati Cancer Center expands outreach efforts with new community groups and faculty resources to drive community-engaged research — the key to improving cancer outcomes in and around Cincinnati.

African Americans account for 42% of Cincinnati’s population and experience some of the area’s highest cancer death rates. Yet, they are underrepresented in cancer research — a situation that limits improvements in those statistics.

“We know that people who participate in research are more likely to have better outcomes than people who don’t,” says Melinda Butsch Kovacic, MPH, PhD, associate director for community outreach and engagement at the University of Cincinnati Cancer Center. “So, if half a population doesn’t participate in research, then they’re not getting access to the high-quality care that the research brings. And that’s what we need to change.”

The Cancer Center is working to change this scenario through community-

engaged research. This involves collaborating with people in and around Cincinnati to plan, implement and evaluate research aimed at reducing cancer incidence and mortality rates and improving early detection, survival rates and quality of life.

The keys to collaborating with the community are outreach and community groups, says Butsch Kovacic.

Everyone Should Be Doing Outreach

Butsch Kovacic says that while her team leads outreach efforts, they aren’t the only ones responsible for doing it. In fact, “every member of the Cancer Center should be doing outreach,” she says.

1. The University of Cincinnati Cancer Center was highlighted at a Coaches vs. Cancer themed basketball game. Syed Ahmad, MD, and William Barrett, MD, join the UC Bearcat to greet and congratulate cancer survivors.

2. Community members read educational stories about cancer at a Cancer Prevention and Screening Community Health Fair in the Price Hill neighborhood.

3. Participants walk in the Leukemia & Lymphoma Society’s Cincinnati Light the Night event to honor those impacted by blood cancers.

4. Ken Greis, PhD, asks a question to a speaker at the 9th annual Charge Against Cancer retreat.



1

When faculty participate in outreach efforts, they gain valuable insights into the community’s needs and challenges that they can’t get during office visits.

“As a physician, it can be difficult to really get to know your patients during office visits,” she says.

“But at community events like health fairs, it’s much more informal. You can have meaningful conversations, and people will tell you all kinds of things they might fear sharing in an office visit.”



2

Outreach Resources for Faculty

When faculty speak directly with community members, they get a better understanding of the issues around access, awareness, mistrust and fear, and can then work to remedy those.

Butsch Kovacic's team held four dialogue circles for faculty in 2022 to offer advice on how to conduct outreach in a way that benefits both patients and faculty.

Community groups are another way for faculty to learn about the concerns of various populations around Cincinnati. They also serve to educate communities about cancer research to allay fears and knock down barriers to participation.

Butsch Kovacic's team works with Seven Hills Neighborhood Houses and an existing research advisory board of community-engaged Cancer Center members. In 2022, the Community Outreach & Engagement team began laying plans to form two new community groups specific to the Cancer Center:

- The Community Advisory Board (CAB) will be made up of community stakeholders, including representatives from organizations such as the American Cancer Society, who serve patients and promote cancer screenings. CAB will serve as a community voice to inform the research agenda at the Cancer Center.
- The Community Research Advocates Committee (CRAC) will be primarily composed of cancer survivors and family members who will learn about cancer research and research ethics and then be encouraged to advocate for research in their communities.

"The community research advocate group will bring the voice of the community back to specific researchers," Butsch Kovacic says. "So, if a researcher wants to be informed about a particular topic — for example, research design, study marketing and survey development — they can go to this group and get insights from the community."

CHARGE AGAINST CANCER TUTORING PROGRAM SEEKING VOLUNTEERS

Sometimes, making inroads into a community is really about becoming part of the community. In 2022, the University of Cincinnati Cancer Center did just this by starting the Cincinnati Charge Against Cancer Tutoring Program. Twice a week, Cancer Center faculty, staff and trainees tutor students (ages 6-13) during their after-school basketball program at North Fairmount Community Center.



Samuel Thompson, a radiation oncology research assistant, volunteers weekly.

"Each session, I am greeted by a group of young, energetic, engaged students who are ready to learn," he says. "Their passion in the face of difficult life circumstances is both humbling and encouraging."

The program is currently seeking volunteers. To learn more, contact Andrew Frankart, MD, at frankaaj@ucmail.uc.edu.





Seeing the Big Picture

Primary care clinic for cancer survivors provides expertise and approach to long-term health care that many patients can't find in traditional settings.

Cancer survivors face many types of challenges once their treatments are finished, including prolonged or permanent side effects, psychological challenges related to treatment and recovery, and impact of treatment on overall health. Many times, survivors find that traditional primary care providers aren't equipped to deal with these factors.

Bradley Wilson, a childhood leukemia cancer survivor and fourth-year medical student at the University of Cincinnati College of Medicine, found an answer to these issues at the University of Cincinnati Cancer Center's Oncology Primary Care Clinic.

"It's really important to have someone with more knowledge about things that cancer survivors

face," says Wilson. "It provides peace of mind knowing that my symptoms are being considered under the lens of my history and past treatment."

Wilson was introduced to the Oncology Primary Care Clinic by Melissa Erickson, MD, population science researcher and founder/director of the clinic. At the time, Erickson was the medical director of the Cancer Survivorship and Supportive Services Program.

"Many of the patients I saw didn't have primary care physicians," Erickson says. "Some were in their early 20s and transitioning between a pediatrician and identifying a primary care provider (PCP). Others simply felt a disconnect between their oncology and PCP needs."

Both described Wilson.

"I know firsthand what a unique risk profile cancer patients have," he says. "Having a PCP who understands that is invaluable."

The Oncology Primary Care Clinic opened in late 2019 as the first and only in the region. The clinic now operates three days a week with Erickson and Sara Kleinschmidt, MD, a palliative care physician who joined in spring 2023.

"We work closely with oncologists and the entire medical team to manage our patients' health in real time, discussing concerning symptoms that could warrant earlier scans or adjusting medications so they can undergo chemotherapy," Erickson says.



Providing Holistic Survivorship Care

The University of Cincinnati Cancer Center's Oncology Care Primary Clinic is only one component of the Cancer Center's robust survivorship program. Other components include:

- **Cincinnati Children's Cancer Survivorship Program**, started in 1987, provides specialized medical care and psychosocial support for childhood cancer survivors through adulthood. Every patient receives a risk-based evaluation that helps inform current and future healthcare providers of treatment-related health risks, symptoms to be aware of and appropriate cancer screening schedules.
- **The Cancer Wellness Clinic** provides integrative therapies, such as acupuncture, oncology massage therapy, cancer exercise and nutrition support, to help improve overall health and wellness. It also provides survivorship care to manage side effects during and after treatment.

"When patients are first diagnosed with cancer, they're often presented at a tumor board that brings together surgeons, oncologists and radiologists to come up with the best treatment plan," Erickson says. "We do a similar thing here, but during and after cancer treatment."





“There are a growing number of cancer survivors, and it’s important to put survivorship care on the radar, as it’s not always prioritized. When I started medical school, I was surprised and amazed that UC had dedicated space and clinics for cancer survivorship resources. It’s made a big difference to me as a cancer survivor as well as a future physician.”

~ Bradley Wilson



The University of Cincinnati Cancer Center’s Oncology Primary Care Clinic is currently creating a clinical registry to identify patient demographics, comorbidities and cancer treatment to determine the effectiveness of the oncology PCP model. The team also recently conducted a large needs assessment to improve what services are offered and how services are delivered.

Creativity and Medicine: The Art of Interdisciplinary Collaboration

An interactive mobile music therapy app that allows patients to listen to and create music is inspiring how medicine, creativity and cross-department collaborations intersect to advance digital health technologies.

“Our project and joining efforts have showcased the dire need for collaborations across colleges, especially when we are targeting innovation and impact in research,” says Claudia Rebola, PhD, professor and associate dean for research in the UC College of Design, Architecture, Art, and Planning.

The music app, called the Active Receptive Music for Cancer, or ARMCAN, is a collaboration between researchers led by Rebola and Soma Sengupta, MD, PhD, former associate director of the Brain Tumor Disease Center and the Harold C. Schott Endowed Brain Tumor Molecular Therapeutics Chair.



“The app is helping the rewiring and exercising areas of the brain that normally wouldn’t do it,” Sengupta says. “Dr. Rebola and her team have been instrumental in designing the app, and she is a fantastic collaborator.”

The app is designed to help improve brain fog, or chemo brain, by having patients listen to or create music. Approved neurofunction assessment tests, surveys and MRIs measure how patients’ brains are physically changing because of the app. The Brain Tumor Disease Center provided support for the preliminary study. The research team plans to publish data in 2023 and apply for further funding within the next 18-24 months.

“ARMCAN is a significant first relationship with Dr. Sengupta and really allowed us to start envisioning collaborations for other therapies,” Rebola says.

Other apps are under development, including an art therapy app that is funded by the Ian’s Friends Foundation.



Making Connections

With hundreds of independent investigations spread across three institutions, one of the University of Cincinnati Cancer Center’s greatest challenges — and greatest opportunities — is connecting researchers, clinicians and labs so they can combine efforts and achieve cancer breakthroughs faster. To do this, the Cancer Center hosts multiple types of academic gatherings and regularly communicates with its over 200 members. Cancer Center programming in 2022 included multiple formats:

Continuing Medical Education (CME) and Symposiums: Larger, professional-oriented events for cancer researchers and physicians, featuring expert presentations, research findings and best practices.

Retreats: Off-site events to share progress and insights on initial research that isn’t public yet.

Seminar Series: Twice-monthly seminars focused on cancer research and clinical care to keep members engaged and spur collaborations between retreats.

Program Meetings, Intra-Programmatic Working Groups and Transdisciplinary Working Groups: Internal meetings typically limited to Cancer Center members focused on one research program or specific topic to ignite collaboration between researchers working in the same area.

Community Education: Fairs, events, and outreach to educate the community on cancer, risk factors, and actions they can take to improve their health.



EVENT	TYPE	DATE
Community Conversations on Cancer — Cancer Survivorship: Navigating Health Challenges After Treatment	Community	2/9/22
Multidisciplinary Management of Gastrointestinal Cancers	CME	2/12/22
Cancer Screening & Prevention Community Health Fair	Community	2/19/22
Challenges in Cancer Survivorship Care	CME	4/30/22
Cancer Research Retreat	Retreat	5/7/22
Cancer Research Seminar Series (monthly, starting 5/20/22)	Seminar	5/20/22
Community Conversations on Cancer — Adopting Exercise to Combat Cancer-Related Fatigue	Community	6/22/22
Dialogue Circles: The Value of COE to Busy Basic Science, Clinical & Population Health Researchers	Seminar	7/14/22
Cancer Screening & Prevention Community Health Fair	Community	7/16/22
Updates on Hematology & Oncology	CME	7/23/22
Dialogue Circles: Critical COE Skills for the Newly Engaged	Seminar	7/28/22
Dialogue Circles: Best Practices for Giving Research Talks to Spur Outreach Discussions	Seminar	8/11/22
Dialogue Circles: Collaborative Design for Mutual Researcher-Community Benefit	Seminar	8/18/22
Charge Against Cancer: Defeating Cancer in Cincinnati Through Prevention, Education & Youth Athletics	Retreat	8/26/22
Reduce Your Risk Health Fair	Community	9/29/22
Community Conversation on Cancer — Resilience and Legacy	Community	9/29/22
Subcellular Dynamics in Cancer	Symposium	10/14/22
Breast Reconstruction Awareness Day	Community	10/19/22
Scientific Executive Committee Retreat	Retreat	11/4/22
Donald Shumrick Head & Neck Cancer Lecture	CME	11/12/22
Clinical Topics on Cancer Seminar Series (monthly, starting 12/9/22)	Seminar	12/9/22

697
People attended educational programming in 2022

Summer Experience Inspires Cancer Research Careers

Sophia Schutte thought she wanted to be a physician. But after a summer research fellowship at the University of Cincinnati Cancer Center, the Xavier University undergraduate has her sights set on a dual MD-PhD career.

“It was the perfect match for me, as cancer is something I am passionate about,” says Schutte, who has family experience with cancer.

Schutte was one of the 23 scholars selected from 400 applicants for a cancer-focused Summer Undergraduate Research Fellowship (SURF) known as the Cancer Research Scholars Program (CRSP).

“The program allows undergrads to get research experience across the cancer continuum and help them to find their career ‘homes’ in cancer research,” says Melinda Butsch Kovacic, MPH, PhD, associate director for community outreach & engagement at the Cancer Center.

“I met students from all over and built a supportive relationship with my mentor, while the educational panels and community outreach gave me new perspectives on research,” says Schutte, a junior at Xavier who is originally from Seattle.

CRSP launched in 2022 through a collaboration with members of the Cancer Center and faculty from the College of Allied Health Sciences. Funded by a five-year R25 grant from the National Cancer Institute, the program offers paid research and educational experiences for qualified summer undergraduate scholars.

For 2022, faculty opted into the Cancer Mentor Network using an online survey link or were invited to participate if a scholar’s interest matched with their research. Beginning in 2023, all mentors must be active members of the Cancer Center.

“Our faculty are excited to support undergrads and give them opportunities to experience cancer research in unique ways,” says Butsch Kovacic, who is also a professor and associate dean of research in the UC College of Allied Health Sciences.

Schutte, one of 10 CRSP scholars who have continued with research throughout the academic year, has been assisting the Privette Vinnedge Lab with breast cancer research.

“I thought I wanted to be a physician, but CRSP has made me more interested in research,” Schutte says. “Research is much more collaborative than you see. I still like the patient side of being a physician, so I’m contemplating an MD-PhD at this point.”

Schutte will be a student mentor for the 2023 CRSP cohort.



Sophia Schutte

In addition to research, CRSP participants engaged in three community field experiences through a collaboration with Community Outreach & Engagement and the Cancer Research Training and Education Coordination team. The field experiences targeted cancer prevention education and screening, grief, and breast cancer awareness.

“It was also really important to me to help students understand the benefits of community outreach and the connection between their clinical work, research and community engagement,” Butsch Kovacic says.



Team Approach to Efficiencies in Cancer Research

Shared resources provide highly specialized and sophisticated expertise and services across all cancer research, providing the infrastructure that is critical to moving research forward faster.

When Henry Ford was looking for a more efficient way to manufacture cars, he probably didn't imagine how the assembly line concept would impact the development of cancer treatments 100 years later. But like Ford, the University of Cincinnati Cancer Center is finding that specialization can move work forward faster. In this case, the work is not automobiles but transformative discoveries in cancer.

Following the path of National Cancer Institute (NCI) Cancer Centers nationwide, the Cancer Center — barely three years old — is developing a core of specialized services that support the work of its scientists across

the continuum of basic science, clinical and translational, and population research. In 2022, the Cancer Center reoriented the University of Cincinnati College of Medicine's biospecimen program to prioritize cancer projects and created a bioinformatics program to support cancer research.

"Unlike 15 years ago in academic research where one laboratory would try to do everything, we now have more of an industrialized process where we're putting things into the hands of those who are best suited to do that piece of work," says Ken Greis, PhD, associate director for shared resources.

Shared resources are programs that researchers have a common need for, such as normal and diseased tissue samples or advanced computational statistical analysis. Shared resources are common in academic

research programs. In fact, the Cancer Center's institutional partners — the University of Cincinnati, UC Health and Cincinnati Children's — support over 40 shared resources for their investigators. Under the Cancer Center, however,

cancer-specific shared resources will be available to cancer researchers at all three entities.

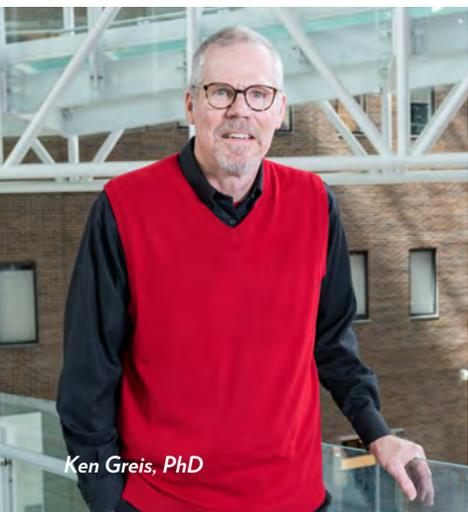
In 2022, the Cancer Center developed the Biostatistics and Informatics Shared Resource and the Biospecimen Shared Resource. "The reason we put those two in place first was because those were two of the most critical needs for our investigators," Greis says.

The Cancer Center's new Biostatistics and Informatics Shared Resource program is mandated by the NCI. Other shared resources will be selected based on the Cancer Center's core focus areas and expertise. For instance, the Cancer Center developed the Biospecimen Shared Resource first since most of its researchers need access to specimens and also because of the Cancer Center's expertise in biospecimen processing. Its expertise in peripheral blood mononuclear cells (PBMCs), for example, recently resulted in a grant to investigate how PBMC collection and storage can be optimized for best clinical use. (See sidebar article on next page.)

"You don't get those types of grants unless you are experts in an area and have the capabilities to do the research," Greis says.

The Cancer Center expects to develop one new shared resource, Radiomics, in 2023 and up to 4-6 others over the coming decade based on the needs within expanding programs. Greis and other Cancer Center leaders are surveying members, considering the Cancer Center's strategic priorities and aligning existing expertise and resources to decide which areas will be developed. Decisions also will depend on the ability to recruit personnel to complement existing expertise. Some areas that are emerging as strong contenders include:

- **Organoid Development**
- **Drug Development**
- **Cancer Metabolism**



Ken Greis, PhD

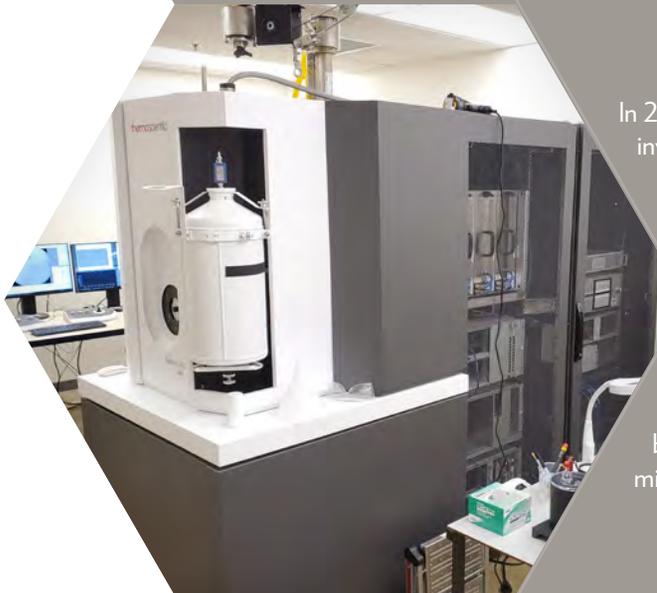
“ COLLECTIVELY, WE RIVAL ANY INSTITUTION IN REGARD TO THE SHARED RESOURCES THAT ARE AVAILABLE.”

- Ken Greis, PhD



While these shared resources are being developed specifically for cancer research, Cancer Center investigators also have access to shared resources across the partner institutions. Some of the major ones used by cancer investigators include: flow cytometry, confocal microscopy, NMR-based metabolomics, proteomics and mass spectrometry, preclinical animal imaging, pluripotent stem cells, single cell sequencing, and a humanized mouse resource core.

“Collectively, we rival any institution in regard to the shared resources that are available,” Greis says. “And the subsidies by the institutions keep the cost relatively low for investigators, compared to what it would cost if they were to go outside and try to do some of these things.”



In 2022, the UC College of Medicine invested in a JobsOhio grant to purchase and establish cryogenic electron microscopy (Cryo-EM). UC then leveraged that state funding to successfully compete for a \$2 million National Institutes of Health (NIH) grant for additional instrumentation to recruit faculty with programs in structural biology who have already been successful at attracting more than \$3 million in NIH research funding.



Can Blood Be a Predictor of Therapeutic Response?

Biospecimen Shared Resource recognized for its expertise with NCI U01 grant.

The University of Cincinnati Cancer Center has received a National Cancer Institute U01 grant to investigate how to collect, process, and store peripheral blood mononuclear cells (PBMCs) in a way that maintains their cytotoxic activity to predict and monitor clinical response to immunotherapy. If this can be achieved, it would have profound implications on clinical trials and ultimately on patient care, its investigators say.

“If we’re successful, then in the future, all we would have to do is to take a peripheral blood sample, send it for a cytotoxic assay, and you’d be able to determine earlier if we’re going to get a treatment response,” says Trisha Wise-Draper, MD, PhD, clinical/translational researcher and co-director of the Cancer Center’s Head & Neck Disease Center.

The \$1.1 million, five-year grant has several components that must be completed to reach that endpoint, says Kelsey Dillehay McKillip, PhD, director of the Cancer Center’s Biospecimen Shared Resource. The first step is identifying the optimal specimen collection, processing and storage conditions. “We’re assessing a variety of preanalytical variables to determine the best way to handle these cells to ensure that when we take them out of the freezer, they’re going to recapitulate the function of the cells at the time they were collected from the patient,” Dillehay McKillip says.

The overall focus is to investigate a promising liquid biopsy approach that can be widely utilized based on immune profiling of PBMCs. Evidence suggests that such a liquid immune profile-based signature (LIPS) may, for example, predict both overall and progression-free survival in patients with metastatic cancer on immune checkpoint inhibitors (ICIs). However, use of LIPS is limited in widespread use due to the necessity of immediate processing and analysis, and the lack of availability of centers with sophisticated multicolor flow cytometers and/or expertise in analysis, Dillehay McKillip says. She adds that current PBMC processing limitations for biomarker analysis remain, and this proposal aims to directly confront these primary challenges.

The team is currently in the first stages of the project, studying how various seemingly minute factors affect function, including various types of anticoagulants, collection tubes, collection to processing times, even the volume in which specimens are stored. “We’re trying to minimize the potential for preanalytical bias so that the goal of a reproducible ‘liquid biopsy’ that can be used to guide treatment and predict outcomes can be achieved,” Dillehay McKillip says.



*Kelsey Dillehay
McKillip, PhD*





Biostatistics and Informatics Core Opens

Shared resource at Cancer Center brings specialized expertise to support researchers' publication and grant applications.

The University of Cincinnati Cancer Center opened its new Biostatistics and Informatics Shared Resource in 2022, with the recruitment of Shesh N. Rai, PhD, a fellow of the American Statistical Association, as the core director. The shared resource provides expertise and support to advance research across the Cancer Center's basic, clinical and population research.

Before joining the Cancer Center, Rai served as director of the Biostatistics Shared Facility at the University of Louisville JG Brown Cancer Center. While there, he led work to support numerous grants in varied areas, including cancer immunology and immunotherapy, functional microbiomics, diabetes and obesity research, and environmental exposure of superfund sites for cardiometabolic disease. "I came to the Cancer Center for the opportunity to assist in building a top-notch facility and obtaining NCI designation," says Rai, who is also director of the Cancer Data Science Center at the UC College of Medicine Department of Environment and Public Health Sciences.



Shesh N. Rai, PhD

In addition to Rai, four biostatisticians were recruited to staff the program, and the Cancer Center expects to add to that team. The team has special expertise in preclinical and clinical studies, survival analysis, mixed effects (hierarchical) models, sample survey, bioinformatics and health informatics. Since starting in October 2022, the team has assisted in designing clinical studies and providing analyses for preclinical and clinical studies in multiple labs studying leukemia, glioblastoma multiforme, head and neck, anal, pancreatic, and oral cavity cancers, as well as clinical trials on cognitive improvement in long-term cancer survivors, a population-based study on uranium exposure and lung cancer, and two hypothesis-driven studies based on the National Cancer Institute database data.

"Biostatistics is absolutely critical for any of the clinical trials and the research associated with a cancer center," says Ken Greis, PhD, associate director for shared resources. "This was an area where our investigators didn't have routine access to these capabilities and were sometimes forced to do it on their own. Now they will have direct access to dedicated biostatistics and bioinformatics professionals to support their research projects, which will lead to greater levels of data to support grants and publications."



Getting Off the Ground

Pilot grants are what fund truly innovative research until it can produce proven results.

Trisha Wise-Draper, MD, PhD, co-director of the Head & Neck Disease Center at the University of Cincinnati Cancer Center, is grateful every day for the \$25,000 grant she received from the Brandon C. Gromada Head & Neck Cancer Foundation in 2020 that allowed her and her team to study the cytotoxic response in head and neck cancer. Without it, her research might never have gotten off the ground.

“I would not have been able to support my trainees and generate the data I needed early on without the pilot program,” Wise-Draper says. “The Gromada grant was instrumental to generating pilot data that we used in both grant applications as well as some of our industry-funded trials. The data allowed us to submit for a larger grant so we could focus on the activation of Natural Killer cells that may be important for immunotherapy-based treatment.”



**Trisha Wise-Draper,
MD, PhD**

Pilot research — small-scale studies researchers use to make discoveries and test their methods prior to launching a full-scale research project — are as important for solidifying study designs and sample sizes as they are securing funding. Successful pilot research is generally required before federal government, national nonprofit and industry organizations will consider investing the kinds of money it takes to conduct large-scale studies. But pilot studies require funding, too. That’s where pilot grants come in.

“Our Pilot Project Award Program enables researchers to explore areas that lead to cutting-edge discoveries and novel approaches that will further our understanding of cancer, enhance the care we provide and improve cancer-related outcomes in the community,” says Katie

Fulton, MPH, the Cancer Center’s administrator for grants, pilots and program development.

Pilot grants are also instrumental in helping early stage investigators who are at the beginning of their independent research careers and have not yet received their first significant research grant. Pilot grant funding is what allows these researchers to vet their ideas and gain experience in order to attract additional sources of funding.



*69 Pilot Projects
Funded*



GIVEHOPE grant funds research into bacteria linked to pancreatic cancer survival. Read more on page 20.

Brandon C. Gromada



5 Pilot Projects Funded



16 Pilot Projects Funded



The Organizations Making It Possible

Several organizations have been hugely supportive to Cancer Center researchers through the Pilot Project Award Program in recent years. Here are just a few:

The Brandon C. Gromada Head & Neck Cancer Foundation was founded in 2012 by Dr. Joseph and Karen Gromada the day after their oldest son, Brandon, died of poorly differentiated squamous cell cancer. Since, the foundation has contributed more than \$325,000 to head and neck cancer research. In March 2023, Dr. Joseph Gromada passed after his own battle with head and neck cancer.

“Our ultimate vision is to end head and neck cancer,” Karen Gromada says. “Research is the only way to do that.”

GIVEHOPE and BSI Engineering partnered when the organizations’ founders bonded after learning they both had experienced personal losses due to pancreatic cancer. Since, the partnership has donated more than \$1 million to help advance pancreatic cancer research at the Cancer Center. The funds have been awarded to investigators studying causes, disease pathways and treatments of pancreatic cancer, and have been a key pipeline for early stage research leading to national funding and clinical trials.

Ride Cincinnati was established in 2007 by the Harris family who lost their wife and mother to cancer. Their objective was to become the “leading grassroots organization funding cancer research and care in Greater Cincinnati.” Today, the nonprofit specifically raises money to support clinical trials and provide seed funding for novel ideas, primarily through its annual two-day cycling event, held each September. In 2022, Ride Cincinnati donated nearly \$1 million to the University of Cincinnati Cancer Center Pilot Project Award Program.



SELECTED RESEARCH GRANTS

The University of Cincinnati Cancer Center researchers were funded by more than 140 active grants totaling more than \$24 million in 2022. Following are some highlights of those grants.

	Lead PI	Title	Sponsor*
CINCINNATI CHILDREN'S	Christopher E. Dandoy, MD, MSc	Reduction of bloodstream infections from oral organisms in pediatric stem cell transplant: A randomized, multicenter, double-blind, placebo-controlled study evaluating twice daily oral xylitol	NIDCR
	Yaping Liu, PhD	Inferring 1D and 3D epigenomes by cell-free DNA fragmentation patterns	NHGRI
	Daniel Lucas, PhD	Hematopoietic stem cell engraftment in the injured niche	NHLBI
	E. Melinda Mahabee-Gittens, MD, PhD	Prevalence and clinical correlates of thirdhand smoke exposure in a pediatric patient population	NIEHS
	Meghan E. McGrady, PhD	A pilot feasibility trial of a tailored intervention to improve adherence in adolescents and young adults with cancer	NCI
	Linde A. Miles, PhD	Dissecting the role of clonal evolution in NPM1-mutant AML	NCI
	Jose A. Cancelas Perez, MD, PhD	Mechanism of a novel approach for platelet cold storage	NHLBI
	Daniel Starczynowski, PhD Iannis Aifantis, PhD (New York University)	Dissecting innate immune signaling in pre-leukemia evolution	NCI
Ronald R. Waclaw, PhD	Genetic approaches to address oligodendrocyte progenitor cell diversity	NINDS	
UNIVERSITY OF CINCINNATI	Laura Conforti, PhD	Liposome-based mRNA cancer immunotherapy targeting ion channels	NCI
	Pankaj Desai, PhD	Translational studies to facilitate rational therapeutic combinations of letrozole for the treatment of glioblastoma	NINDS
	Zhongyun Dong, MD, PhD	Proliferating cell nuclear antigen in regulation of androgen receptor signaling in castration-resistant prostate cancer cells	NCI
	Krushna Patra, PhD	Investigating the molecular mechanisms of growth in GNAS mutant pancreatic cancer	NCI
	Atsuo Sasaki, PhD	Mechanistic role of phosphatidylinositol 5-phosphate 4-kinase beta in GTP-dependent lysosomal acidification for stress-resilient cell growth and metabolism	NIGMS
	Pier Paolo Scaglioni, MD	Fatty acid metabolism regulates ferroptosis in mutant KRAS lung cancer	NCI
	Trisha Wise-Draper, MD, PhD Kelsey Dillehay McKillip, PhD	Optimization of peripheral blood mononuclear cell (PBMC) processing for robust downstream functional immune cell analysis and correlation with therapeutic efficacy	NCI
	Bingfang Yan, PhD, DVM	Circular RNA regulators of common drug-eliminating genes	NICHHD
	Xiaoting Zhang, PhD	Role of MED1 in HER2-mediated tumorigenesis	NCI

*Sponsors (in order listed): National Institute of Dental and Craniofacial Research (NIDCR); National Human Genome Research Institute (NHGRI); National Heart, Lung, and Blood Institute (NHLBI); National Institute of Environmental Health Sciences (NIEHS); National Cancer Institute (NCI); National Institute of Neurological Disorders and Stroke (NINDS); National Institute of General Medical Sciences (NIGMS); National Institute of Child Health and Human Development (NICHD)

SELECTED CLINICAL TRIALS

In 2022, the University of Cincinnati Cancer Center had hundreds of clinical trials open to accrual (patient enrollment). Here, we feature four clinical trials currently open to enrollment.

A Phase I open label followed by a Phase II randomized, controlled study to assess the efficacy and safety of ABTL0812 in combination with FOLFIRINOX for first-line treatment of metastatic pancreatic cancer. This national trial investigates whether a drug that targets a small molecule known as AKT, which has been found to play a role in helping cancer cells survive and form tumors, might work to stop metastatic pancreatic cancer. The drug has shown promise in treating lung and uterine cancer. The study is being conducted at 23 institutions. The Cancer Center enrolled six new patients for a total of 13 enrolled patients since the trial opened in May 2021. (PI: Davendra Sohal, MD, MPH)



Cytokine-induced memory-like natural killer cells (CIML-NK) for relapsed and refractory acute myeloid leukemia. To date, cellular therapy options for patients with AML have been limited by toxicity from the cellular therapy. NK cell therapy may be a better option for AML patients. Prior research studies suggest that the incidence of these complications is much lower when NK cells are used. T cells and NK cells are both lymphocytes but have one critical difference when it comes to using them for cancer-fighting purposes. In order to recognize and kill cancer cells, T cells must



be “taught” by previous exposure or genetically modified to recognize cancer cells. In contrast, NK cells can recognize cells that are not “self” and kill them on the first interaction. Cincinnati Children’s is one of only a few centers in the nation to test a novel therapy that uses cytokine-induced memory-like natural killer (CIML-NK) cells from haploidentical donors in the treatment of acute myeloid leukemia (AML). This study is open to patients ages 18 to 40 with relapsed or recurrent AML who have not undergone bone marrow transplantation. (PI: Michele Wang, MD)

UCCC-HN-21-02: Phase II study to evaluate amivantamab in recurrent and metastatic adenoid cystic carcinoma. ACC is a rare cancer of salivary glands and other glandular tissue. It is slow-growing and is usually treated with surgery and radiation. However, this type of cancer tends to have a high rate of recurrence and metastatic spread, which develops over several years. Investigators are looking to see if amivantamab, a bispecific EGFR and MET inhibitor will be efficacious in ACC. The Cancer Center enrolled three of the 18 participants in this trial, which opened August 2022. (PI: Trisha Wise-Draper, MD, PhD)



S2104: A Phase II randomized trial of postoperative adjuvant capecitabine and temozolomide versus observation in high-risk pancreatic neuroendocrine tumors. This trial focuses on patients with pancreatic neuroendocrine tumors. The current standard of care for these patients is surgery only, followed by observation, but a subset of patients are at high risk for their cancer to return. In the trial, patients who have had pancreatic neuroendocrine tumors surgically removed will be randomized to two study arms. Select patients will either receive the two chemotherapy drugs or a placebo. The study opened in 2022 at UC and aims to enroll 150 patients at sites throughout the country. (PI: Syed Ahmad, MD)

SELECTED PUBLICATIONS

In 2022, University of Cincinnati Cancer Center researchers published numerous studies in peer-reviewed journals.

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IN THE NEWS

The University of Cincinnati Cancer Center is regularly featured in regional, national and even international news stories. Here are a few prominent stories:

1. *MSN* and *People.com*: Ohio man who beat cancer for the third time walks full marathon through hospital while receiving treatment
2. *Medical News Today*: Lung cancer treatment: Specific gene mutation may be a key
3. *Yahoo News*: FDA-approved electricity cap could help treat brain tumors, cancer
4. *Yahoo News* and the *Cincinnati Enquirer*: Your doctor's prescription for a healthy 2022: Stop delaying health care
5. *Yahoo Finance*: Varian receives investigational device exemption (IDE) for FLASH technology clinical trial, FAST-02
6. *Yahoo News*: UC Cancer Center research aims to bring more treatment options to patients
7. *Cure*: Future directions in CLL treatment
8. *Physics World*: First trial in humans reveals promise of FLASH proton therapy
9. *Cincinnati Enquirer*: Ohio expanded breast cancer screen coverage. Will the nation follow?
10. *Medical Xpress*: Researchers identify new target for treatment of aggressive childhood brain tumors

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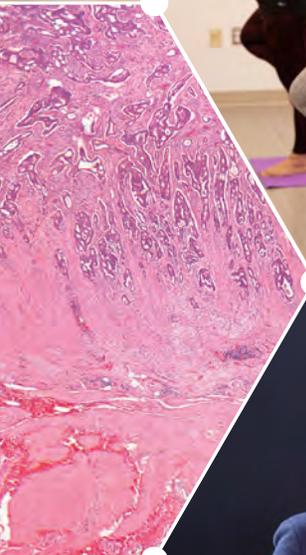
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