University of
CINCINNATI
CANCER CENTER

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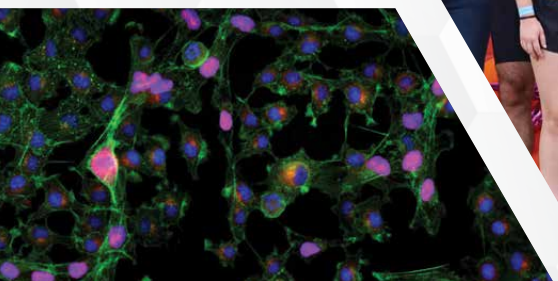
2024 REPORT TO THE COMMUNITY



At the University of Cincinnati Cancer Center, we recognize that it will take every mind and every resource we can muster to find new and better ways to prevent and treat cancer. That's why we are building support systems that facilitate collaboration between researchers, clinicians, biostatisticians, pharmacists and any other scientist who can contribute to the fight. And our efforts aren't just within our institution; we are collaborating with other cancer institutions across the country and around the world to accelerate our collective efforts.

We also are reaching outside of the scientific community and collaborating with patients, caregivers and our communities to listen to their perspectives and understand their needs so that we can build programs that actively engage our community in all areas of our work: prevention, early detection, research, treatment and survivorship.

Cancer is a formidable enemy. It's complex and ever changing, requiring us to develop new defenses. To fight this battle, we are mobilizing every resource available.

BECAUSE WE INTEND TO WIN.

10 BASIC SCIENCE RESEARCH

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A WORTHY PURSUIT

We are pursuing NCI designation for the value of the journey as much as the goal.

To our community and readers of this report,

Just four years after forming the University of Cincinnati Cancer Center, becoming an NCI-designated cancer center is within our sights. Obtaining this prestigious research designation by the National Cancer Institute will be validation of our scientific enterprise and will provide us access to additional funding to hire more researchers and conduct more investigations.

Beyond the recognition and additional funding, the value of this designation is in the journey to get there. We are using the NCI's rigorous standards to guide our program development and investments. Already, we feel we not just meet but exceed the criteria for robust and impactful programs in basic science research and clinical trials. Our powerful research infrastructure allows us to quickly assess what works and what does not work and allows us to test novel approaches. Just a few examples of the recent scientific breakthroughs developed by our researchers include:

- **Understanding the pathogenesis of leukemia, leading to novel targets and therapeutic approaches**
- **Understanding the mechanism of metastases of brain cancer**
- **Physiological and pathological roles of small GTPases in cancer**
- **Epigenetic and transcriptional gene regulation as cofactors in breast cancer metastases and therapy resistance**
- **Understanding of the contribution of environmental factors to cancer incidence and outcomes**

In the past two years alone, we have participated in more than 150 clinical trials, allowing our patients access to the newest emerging therapies. By joining the prestigious NCI Experimental Therapeutics Clinical Trials Network (ETCTN), our patients will have even greater access to more and earlier therapeutics. Currently, we are leading or participating in some of the most groundbreaking clinical trials today, including:

- **2 ETCTN trials (page 17)**
- **Pancreatic cancer vaccine (page 9)**
- **Beat AML substudy (page 23)**
- **SWOG pancreatic cancer trial (page 9)**

We also have an in-depth program for mentoring future and early career cancer researchers, and a vigorous continuing education program for our more than 250 members. In 2023, we hosted 26 cancer symposiums and seminars plus two major cancer conferences. For our young researchers, we began a Trainee Associate Membership program to provide mentoring and networking opportunities, and we funded more than $1 million in pilot projects to support nascent investigations.

Recognizing our need to improve our work in cancer prevention, education and outreach, we completed an assessment of cancer in the 10 Cincinnati-area counties where 80% of our patients live. This assessment provided us with information about what types of cancer have the highest incidence and the highest mortality in our communities. Using that information, we have begun to match it against our initiatives in outreach, prevention, research and clinical care to identify where we need to invest additional resources and recruitment (pages 24-25).

Translating our research, training programs, and cancer prevention and outreach into the highest level of patient care is the ultimate goal. Our subspecialized experts from each clinical discipline work as teams to develop and provide expert treatment in a coordinated and compassionate manner. Our exceptionally high patient satisfaction is testament to this approach.

We are grateful for the philanthropic support that has funded much of our research and has supported the development of innovative concepts. Our scientists, clinicians, trainees, support staff and community have created the ultimate team; and we are privileged to be on such an important mission to minimize the suffering and mortality associated with cancer in our community.

William L. Barrett, MD
Co-Director, University of Cincinnati Cancer Center
Professor and Chair, Radiation Oncology
Medical Director, Barrett Center for Cancer Prevention, Treatment and Research

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

2023 ACCOMPLISHMENTS

- *Increased active clinical trials by 150% since 2019*
- *Admitted to NCI Experimental Therapeutics Clinical Trials Network*
- *Conducted Catchment Area Cancer Analysis*
- *Started Trainee Associate Membership program*
- *Increased cancer-relevant grant funding by 51% to $36.9M*

TRANSFORMATIVE CANCER CARE

UNIVERSITY OF CINCINNATI CANCER CENTER › BY THE NUMBERS

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

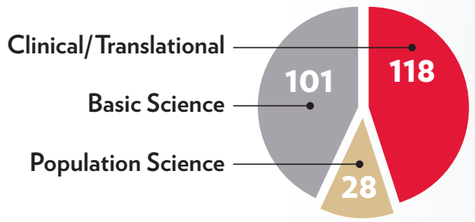
2022 PATIENT CARE

3,364 Analytic cases (patients)

40 Types of cancer treated

Cancer Center Members

247 members representing 10 UC Colleges and Cincinnati Children's



10 Multidisciplinary Disease Centers

1. Transplant & 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

2023 ADULT CLINICAL TRIALS

911 Patients participated in a clinical trial

117 Clinical trials open to accrual

27% Estimated overall clinical trial accrual rate

TOP 10 Most Common Cancer Cases (2022)

1. Breast: 394
2. Lung: 323
3. Prostate: 231
4. Lip, Oral Cavity and Pharynx: 217
5. Other Skin: 212
6. Melanoma, Skin: 212
7. Brain and Nervous System: 199
8. Colon: 142
9. Pancreas: 107
10. Liver: 90

2023 FUNDING

196 Active research grants

$36.9M Research funding

2023 Research Grants (Direct Costs)

Basic Science	Clinical/Translational	Population Science
74 awards	110 awards	12 awards
$14.8 million	$20.5 million	$1.6 million

COMMUNITY SUPPORT

$22.2 M Donated

17 CINCINNATI CHILDREN'S CENTERS & PROGRAMS

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

STRATEGIC MOVES

We're nurturing and recruiting the best and the brightest to help us build a world-class cancer center for patients today and tomorrow.

When **Michael V. Knopp, MD, PhD**, professor of radiology and endowed chair of Radiologic Sciences, talks about his work at the University of Cincinnati Cancer Center, he often drops in the phrase "Next Lives Here."

This is not only the name of the university's 10-year strategic direction, but it's a reality that drew him to join the Cancer Center in 2023. At the Cancer Center, Knopp has joined other nationally known researchers and clinicians who are building teams and knocking down barriers across institutions to bring patients the latest and most effective treatments while striving to find even better treatments for patients of the future.

Innovation in imaging, as led by Knopp, plays a pivotal role in both arenas. Today, imaging is providing precise information about tumor type and location to allow more targeted and personalized therapy delivery. Promising advancements for tomorrow include molecular imaging to allow clinicians to visualize biological processes at the cellular and subcellular levels while still in the body, and theranostics, an exciting and fast-growing discipline that uses radiotracers to find and bind to cancer cells to deliver targeted radiation.

"It's my privilege to lead an innovative team and to be in an environment where we see the opportunity to be impactful, not just by carrying on, but by bringing advancements together in ways that shape the future," Knopp says.

Bounty of Resources

When Knopp joined the Cancer Center from The Ohio State University Wexner Medical Center, he brought with him 30-plus years of experience, more than two dozen members of his research team, an ongoing affiliation with the National Cancer Institute (NCI) and experience at the German National Cancer Institute (DFKZ).

He also brought to Cincinnati the prestigious Wright Center of Innovation in Biomedical Imaging and Digital Health and his leadership role at the NCI's Imaging and Radiation Oncology Core (IROC), along with more than $2 million in NCI grant funding.

"Dr. Knopp brought infrastructure with him to the Cancer Center that would have taken us years to build," says William L. Barrett, MD, co-director of the Cancer Center.

Despite personal and professional ties to Columbus and a resume that could have taken him virtually anywhere, Knopp traded central Ohio for southern, he says, because the Cancer Center shares his urgency to impact cancer care within years, not lifetimes.

"The Cancer Center has the ambition to go forward, to grow and to expand our national visibility," Knopp says. "We're shaping cancer diagnoses and therapies that will be used in 2030."

***Michael V. Knopp, MD, PhD**, is director of and co-principal investigator for the Imaging and Radiation Oncology Core (IROC). The National Cancer Institute funds IROC to provide quality control to more than 2,200 sites across the United States, Canada and internationally that are sponsored by the NCI's National Clinical Trials Network.*

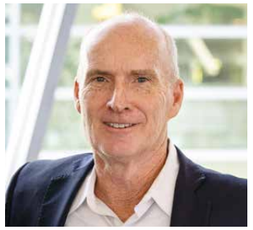
RESPECTED CANCER EXPERTS

Michael V. Knopp, MD, PhD, is the most recent high-profile cancer researcher to join the Cancer Center. He joins a team of sought-after scientists and clinicians with national and international reputations for moving the fight against cancer forward. They are doing that through their own groundbreaking work, and through connections and collaborations that link the Cancer Center to leading researchers worldwide. These leaders include:

Syed A. Ahmad, MD, co-director of the Cancer Center, chief of surgical oncology and the Hayden Family Endowed Chair for Cancer Research, is the surgical chair of the Southwest Oncology Group (SWOG) and national principal investigator of a SWOG national clinical trial to study the effectiveness of administering chemotherapy after pancreatic cancer surgery at reducing or preventing recurrence.

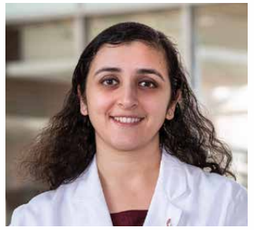
William L. Barrett, MD, co-director of the Cancer Center, professor and chair in the Department of Radiation Oncology at UC's College of Medicine, is known for his expertise in radiation oncology, his commitment to mentorship and his efforts around outreach programs, public seminars, and educational workshops aimed at empowering individuals and communities to make informed decisions about their health and well-being.

John C. Byrd, MD, senior advisor to the Cancer Center and Gordon and Helen Hughes Taylor Endowed Chair and professor in the Department of Internal Medicine at UC's College of Medicine, is chief medical officer of the Leukemia & Lymphoma Society's national Beat AML Master Clinical Trial. He has published more than 550 scientific peer-reviewed papers.



Thomas Herzog, MD, director of the Cancer Center's Gynecological Cancer Disease Center and Paul and Carolyn Flory Professor in Gynecologic Oncology, served on the American College of Surgeons' elected Board of Governors and is President of the Gynecologic Oncology Group Foundation. He was editor-in-chief of the journal *Gynecologic Oncology Research and Practice* and serves on over 10 editorial Boards. He has over 350 peer-reviewed publications.

Daniel Starczynowski, PhD, associate director for basic science research at the Cancer Center and the Cancer and Blood Diseases Institute at Cincinnati Children's, has served as a permanent member of the NIH Molecular Oncogenesis Study Section, the Chair of the ASH Scientific Committee on Myeloid Neoplasia and a Programmatic Chair for the Department of Defense Bone Marrow Failure Program.



Vinita Takiar, MD, PhD, a clinical researcher at the Cancer Center, is a member of the NCI Head and Neck Steering Committee and NCI Metastatic-Recurrent Task Force and serves as the ASTRO Head and Neck Track Chair. Takiar also is the vice chair of research and a professor in the UC Department of Radiation Oncology.

Susanne Wells, PhD, a basic and translational science researcher at the Cancer Center and a professor in the Department of Pediatrics at UC College of Medicine and Cincinnati Children's, has until recently served as Chair of the NCI Cancer Prevention Study Section.

Trisha Wise-Draper, MD, PhD, researcher at the Cancer Center and Cincinnati Children's and co-director of the Cancer Center's Head & Neck Cancer Disease Center, serves as Chair of the NRG Oncology Head and Neck Cancer Committee PULA Working Group, senior editor for *Clinical Cancer Research* and clinical editorial board member of the *Journal of Clinical Oncology*.

BREAKING WITH TRADITION

Our researchers are shattering silos within and between institutions to accelerate pancreatic cancer breakthroughs.

Pancreatic cancer is not the most common type of cancer in the Greater Cincinnati area, but it is the deadliest. The University of Cincinnati Cancer Center is trying to change that grim statistic by connecting researchers and clinicians both inside and outside of the pancreatic cancer field.

"We understand clearly that it is going to be a team effort — oncologists, surgeons, laboratory scientists — everyone getting together," says Davendra Sohal, MD, MPH, associate director for clinical research at the Cancer Center and co-director of the Gastrointestinal Disease Center along with Jordan Kharofa, MD, a clinical/translational researcher and radiation oncologist.

The Cancer Center has earned a national reputation for its expertise in pancreatic cancer research and clinical care. It has some of the country's leading researchers whose work is supported by the most respected grant funders. It regularly initiates or participates in national clinical trials, including being the first Midwestern site to participate in the mRNA pancreatic cancer vaccine trial.

To accelerate its pancreatic cancer work, the Gastrointestinal Disease Center at the Cancer Center formed two working groups in 2023. The KRAS working group includes researchers from labs studying KRAS (an oncogene that when mutated has the potential to cause normal cells to become cancerous) in pancreatic cancer, lung cancer and colon cancer.

"We have some of the nation's KRAS experts all working on the same target," Sohal says. "We also have second-generation KRAS drugs in clinical trials."

The second working group is the pancreatic group whose goal is to unite basic science researchers with clinicians. This group has been working on a platform that will allow them to test patients who respond to treatments to find out what is particular about their cancer, and then use that information to better inform clinical care for other patients. "We can go back and forth from lab to clinic and back to lab," Sohal says.

The group also takes advantage of the Cancer Center's weekly scientific meetings, biannual conferences and communications to promote their work to members in areas not specific to pancreatic cancer — or even to cancer research — whose expertise and work might help accelerate a breakthrough. "We're trying to build connections where they might not be obvious."

Davendra Sohal, MD, MPH

TOP 3 DEADLIEST CANCERS

In the 10 counties that account for 80% of patients at the University of Cincinnati Cancer Center, pancreatic cancer has the highest mortality rate out of the 10 most common types of cancer.*

Pancreas
85.2%

Lung & Bronchus
63.2%

Colon & Rectum
37%

*Data is for 2016-2020, the most recent data available (Source: National Cancer Institute).

PANCREATIC CANCER VACCINE TRIAL

The Cancer Center is the first site in the Midwest to begin enrolling patients in a Phase II clinical trial for a vaccine to treat pancreatic cancer. The vaccine uses mRNA technology to teach the immune system to recognize and attack cancer cells. Each vaccine is tailored to the individual genetic profile of a patient's tumor. In the Phase I trial, 8 of 32 patients were completely cured, which is double the current survival rate. "This could be a game changer," says Davendra Sohal, MD, MPH.

NATIONAL TRIAL TO PREVENT RECURRENCE

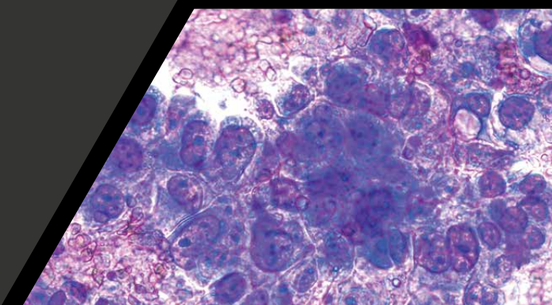
The University of Cincinnati is leading a national clinical trial to study the effectiveness of administering chemotherapy after pancreatic neuroendocrine tumor surgery in reducing or preventing recurrence. Syed Ahmad, MD, co-director of the Cancer Center, is the national principal investigator for the Southwest Oncology Group (SWOG) trial. In the trial, patients who have had surgery to remove pancreatic neuroendocrine tumors will either receive chemotherapy or a placebo. The current standard of care is surgery only, followed by observation. The trial, opened in 2023, will enroll 150 patients at SWOG sites across the country.

NCI GRANT FUNDS RESEARCH INTO PANCREATIC CANCER KRAS

The National Cancer Institute awarded a three-year, $587,000 grant to Andrew Waters, PhD, a Cancer Center researcher, to test drugs that target two KRAS mutations commonly found in pancreatic cancer. The drugs being tested are novel, unpublished formulations that will be studied both through cell lines and pre-clinical models. Waters also will study the specific mechanisms within KRAS-mutated pancreatic cancer cells that lead to resistance to targeted treatments.

STOPPING PANCREATIC CANCER METASTASIS

Pancreatic cancer is so deadly because most cases are diagnosed after cancer cells have already spread to other parts of the body. Only about 3% of patients with metastasized pancreatic cancer will survive five years after their diagnosis, according to the National Cancer Institute. Vladimir Bogdanov, PhD, a Cancer Center researcher and director of the Hemostasis Research Program, hopes to improve those odds with a new drug designed to block the growth and spread of pancreatic cancer cells. The drug, tested in pre-clinical models, is a humanized antibody that targets a molecule activating growth and spread of cancer cells.



DESIGNER TARGETS

Our researchers are engineering bacteria that can infiltrate tumors and attract cancer-killing radiation.

More than 100 years after physicians started using radiation therapy to treat cancer, they have now begun using radionuclide therapy to transport radiation through the bloodstream directly to the tumor. Like targeted chemotherapy, radionuclide therapies require a target on the cancer cell that radiation can recognize and bind to.

Nalinikanth Kotagiri, PhD

If a patient's cancer lacks that target — or mutates to get rid of it — these therapies won't work. In these cases, Nalinikanth Kotagiri, PhD, and his team are engineering bacteria with these missing receptors to serve as surrogates.

"These targeted radionuclides don't care if it's a cancer cell or bacteria that is expressing the receptor," says Kotagiri, a University of Cincinnati Cancer Center researcher and associate professor at the UC James L. Winkle College of Pharmacy.

Kotagiri's lab specializes in applying engineered bacteria to address many types of diseases, including cancer. In this case, the team was engineering Escherichia coli Nissle to bind with a low-energy radionuclide for use as a contrast agent for PET scanning. Once they saw that the bacteria could colonize a tumor and bind with that radionuclide, they swapped out that radionuclide with a virtually identical one that releases high-energy beta rays as it decays (see graphic).

E. coli Nissle is an especially good proxy because it needs a hypoxic, immunodeficient environment to grow — exactly the environment present in solid tumors. "We took advantage of this unique feature of E. coli Nissle to home and localize these tumors," Kotagiri says. And because the engineered bacteria bind with both types of radionuclides, they can be used both as a contrast agent and a therapeutic agent — a principle known as theranostics.

The study, which was conducted in pre-clinical models, was published in March 2023 in *Advanced Healthcare Materials*. To move this research to humans would require FDA approval of both the engineered bacteria and the new radionuclide. Instead, Kotagiri is looking at whether bacteria could be engineered to express human receptors for existing FDA-approved radiopharmaceuticals, which could potentially provide a quicker pathway to clinical use.

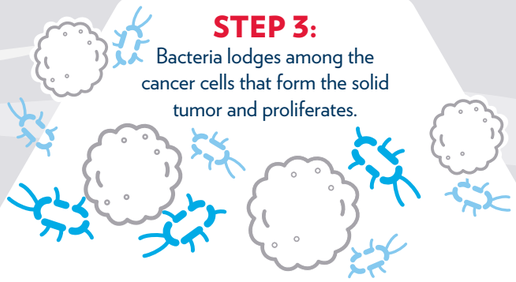
"The beauty of synthetic biology is that it has advanced to such a state that we can engineer different kinds of proteins on bacteria cells," Kotagiri says.

STEP-BY-STEP — ENGINEERED BACTERIA

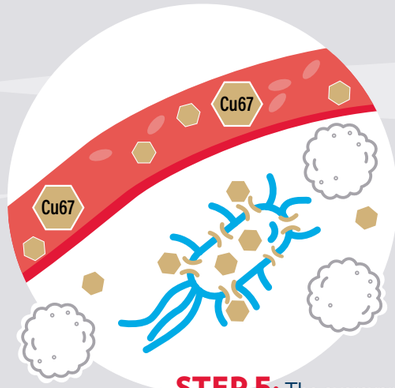
STEP 1: Create E. coli bacteria that overproduce a mechanism, called a transporter, to pull radiometals inside the membrane.

STEP 2: Inject these bacteria to seek out their desired hypoxic, immunodeficient environment created by solid tumors.

STEP 3: Bacteria lodges among the cancer cells that form the solid tumor and proliferates.



STEP 4: Inject Copper-67 radioisotope into bloodstream.



STEP 5: The overexpressed transporters in the bacteria bind with the radioisotopes and move them inside the cell.

STEP 6: The Copper-67 radioisotopes begin decaying and emitting high-energy radiation that kills surrounding cancer cells. Because the radiation extends only in a tiny radius, it kills surrounding cancer cells while reaching very few healthy cells.

***Future possibility** is to engineer the bacteria to provide 2 types of receptors. Because the bacteria are not killed by the Copper-67 emissions, they remain living if there is any remaining tumor. These bacteria could act as receptors for a 2nd type of therapy that uses a different mechanism to kill the remaining cells.*

RELATED RESEARCH

BREAKING DOWN BARRIERS

Desmoplastic solid tumors are characterized by the rapid buildup of extracellular matrix macromolecules that prevent the infiltration of immune cells and also impede the delivery of anticancer agents. Kotagiri's team engineered E. coli Nissle bacteria to carry an enzyme that breaks down these extracellular matrices. This work was published in 2021 in *Advanced Healthcare Materials*.

PAN-CANCER ONCOGENE IDENTIFIED

A University of Cincinnati Cancer Center researcher is part of a national team that has discovered a gene abnormally expressed in more than 70% of 10,000 different adult and pediatric cancer types.

The gene, Forkhead Box R2 (FOXR2), is located on the X chromosone and is normally expressed only in the testes. The team also found FOXR2 bound to specific DNA sequences, E26 transformation-specific transcription factors (ETS TFs) that control the expression of genes.

"FOXR2 and ETS TFs can interact on DNA and actually turn genes on and off, which can cause cancer," says Timothy Phoenix, PhD, a Cancer Center researcher and associate professor at the UC James L. Winkle College of Pharmacy, who co-authored the study published in *Cancer Research*.

Phoenix and his team are now working on identifying the specific proteins with which FOXR2 interacts, which they hope will allow them to identify potential therapeutic targets.

UNEXPECTED FINDINGS

Our brain tumor researchers are reaching around the world to find solutions for YAP fusion-driven cancers.

An international team of researchers affiliated with the University of Cincinnati Cancer Center wanted to understand the high mortality rate for ependymoma (EPN), the third most common type of brain tumor in children. Almost one-third of children who develop EPN die from the disease.

What they found may lead to new treatments for EPN as well as certain subtypes of skin cancer, sarcomas and breast cancer.

The research team, led by Qing Richard Lu, PhD, scientific director of The Cure Starts Now Foundation Brain Tumor Center at Cincinnati Children's, introduced YAP1 fused with other genes (YAP1 fusion proteins) identified in patients into pre-clinical models in the laboratory. They found that YAP1 fusion proteins disrupt the body's defenses against cancer in a different way than many researchers thought, driving both tumor formation and aggressive growth.

Before, researchers thought that the movement of YAP1 fusion proteins into the nucleus of cells was responsible for cancer development. However, this research found that the formation of droplet-like structures (also known as nuclear condensates) within the nucleus is key for tumor formation driven by YAP1 fusion proteins.

"Our findings suggest that it's possible to reduce the ability of YAP fusion proteins from spurring tumor growth," says Lu.

The research team discovered that inhibiting the function of a gene expression regulator called BRD4 blocks condensate formation and prolonged survival in pre-clinical models. By collaborating with researchers at other institutions, the Brain Tumor Center team accelerated the work, publishing the findings in *Nature Cell Biology* (February 2023). The team is now focused on identifying other drugs that can block formation of EPN and combinations of drugs to do this more effectively with less toxicity.

YAP Study Research Partners

- **University of Cincinnati Cancer Center**
- **Fudan University (Shanghai, China)**
- **Children's Memorial Health Institute (Warsaw, Poland)**
- **Fred Hutchinson Cancer Center (Seattle)**
- **Cleveland Clinic Foundation**

Sandra Schrenk, PhD, (left) and Elisa Boscolo, PhD

MODELING HOPE

We developed the world's first pre-clinical model for a rare type of vascular tumor that brings hope for children with KMP.

Until now, the search for effective, noninvasive treatments for Kasabach-Merritt Phenomenon (KMP) has been hampered by a lack of pre-clinical models. Caused by vascular tumors associated with a mutation in the GNAQ gene, KMP increases the risk of excessive bleeding and causes chronic pain and disfigurement. Left untreated, up to 30% of children with KMP die, usually from excessive bleeding. Surgery, the best treatment for removing the vascular tumors, is rarely performed due to the bleeding risk.

University of Cincinnati Cancer Center researchers have now developed a genetically modified pre-clinical model that mimics the formation of these vascular tumors causing KMP. And they've used this pre-clinical model to discover a potential treatment.

GNAQ is part of the MAPK signaling pathway, where abnormal activity contributes to more than 40% of cancer cases. Scientific curiosity drove Cancer Center researchers Elisa Boscolo, PhD, and Sandra Schrenk, PhD, to study the MAPK signaling pathway. They found treatment with trametinib, a MAPK inhibitor often used to treat melanoma, prevented the growth of vascular tumors, reduced bleeding and increased survival.

By reducing the bleeding risk, trametinib or other MAPK inhibitors could make surgery a viable option for many infants and children with this deadly condition. Boscolo and Schrenk are collaborating with doctors at Cincinnati Children's to explore the use of trametinib and other MAPK inhibitors to treat KMP. They also are studying other pathways that contribute to vascular tumors, with the goal of identifying an effective combination of drugs for these tumors.

The study was published in *Nature Communications* (April 2023).

> *"Our findings could lead to improved treatments for KMP and other more common vascular tumors."*
>
> Elisa Boscolo, PhD

SOLID SUPPORT

Shared resources help our investigators conduct their work faster and better.

While breakthroughs in cancer treatment are what capture headlines, what often goes unremarked is the steady pace of research and the support work needed to drive those discoveries. Shared resources are part of the infrastructure that makes a powerful impact on the ability of researchers to obtain grants and conduct studies.

In 2023, the two shared resources at the University of Cincinnati Cancer Center supported more than 70 projects and contributed to at least 10 grant proposals. The Cancer Center's Biospecimen Shared Resource, directed by Kelsey Dillehay McKillip, PhD, and Biostatistics and Informatics Shared Resource, directed by Shesh N. Rai, PhD, provide scientific services across all labs.

SHARED RESOURCES PROVIDE MULTIPLE BENEFITS:

EXPERTISE: They are directed and staffed by experts so that investigators are confident that the collaborative services offered will be of the highest quality, following established best practices in their respective fields.

EFFICIENCY: They eliminate the need for researchers to try to do it themselves or contract services from outside organizations.

COST: Because the cost of the programs is leveraged across the entire organization, the expense to individual projects is lower.

PRIORITIZATION: While shared resources often support projects outside of cancer or outside the organization, cancer investigations take priority.

One example of how an investigator leveraged shared resources has been the development of cancer model systems derived from tumor tissue that is surgically removed as part of the treatment regimen. In many cases, this tissue can be propagated in a cell culture or three-dimensional cultures known as organoids. These organoids retain many of the biological and dysfunctional properties of the tumor and thus make good laboratory models for understanding the tumor processes or to screen for drugs that may be effective for treatment.

Xiaoting Zhang, PhD, director of the Breast Cancer Research Program, and his team have partnered with Dillehay McKillip and the Biospecimen Shared Resource to collect, propagate, store and maintain multiple breast cancer organoid lines. These can be used in evaluating novel drugs to treat some of the most aggressive forms of breast cancer.

One of the greatest benefits of the shared resources is the credibility of the leaders there, says Ken Greis, PhD, associate director for shared resources at the Cancer Center. Dillehay McKillip and Rai are recognized experts in their fields who have published major studies. Both directors and their teams tailor their services to each project and write that portion of the grant.

"They add to the credibility of grant applications because they have reputations of their own in research," Greis says. "They can say they've done it before and provide supporting references."

2023 SHARED RESOURCES SUPPORT:

70
projects

10
grant proposals

Xiaoting Zhang, PhD (left), and Gregory Bick, PhD

OPENING ACCESS

Our patients now have the earliest access to some of the most exciting emerging cancer treatments.

The University of Cincinnati Cancer Center has joined an elite network of cancer research institutions that provides patients with the earliest access to the most novel and cutting-edge cancer treatments. In October 2023, the Cancer Center was accepted into the National Cancer Institute's Experimental Therapeutics Clinical Trials Network (ETCTN).

"There are two main mechanisms to do clinical trials: NCI's National Clinical Trials Network and ETCTN," says Davendra Sohal, MD, MPH, associate director for clinical research at the Cancer Center and professor of internal medicine in the UC College of Medicine. "We've been part of the first for years. The ETCTN is more exclusive with very carefully and rigorously selected institutions. Only large, established cancer centers get to be a part of it, so for us to be accepted shows that the NCI acknowledges our expertise in clinical trials."

The ETCTN is broken into nine subgroups that have specialized expertise. To become part of the ETCTN, the Cancer Center had to first apply to the University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center. UPMC's subgroup includes the University of California, Irvine, and the Montefiore Medical Center at the Albert Einstein College of Medicine.

Once UPMC completed its review and recommended the Cancer Center, the NCI then conducted an in-depth evaluation. NCI reviews an institution's clinical trials experience, facilities, staffing, laboratories, pharmacy and other support services needed to run successful trials without harming patients.

It also looks for in-house experts trained in clinical trial design such as Sohal; Syed Ahmad, MD, co-director of the Cancer Center; John Byrd, MD, senior advisor at the Cancer Center; Trisha Wise-Draper, MD, PhD, co-director of the Cancer Center's Head & Neck Cancer Disease Center; and Emily Curran, MD, medical director of the Cancer Center's clinical trials office.

"It was a very rigorous process to go through," Sohal says. "It's not a matter of just saying you can do it. We have a long track record and special training in Phase I trials. While growing our program rapidly, we have maintained quality."

In addition to being able to manage Phase I clinical trials successfully, the institution needs to have specific expertise in areas that the current members lack. The Cancer Center will contribute its expertise in GI, blood, and head and neck cancers to the UPMC subgroup. The first trials to open at the Cancer Center will focus on gastrointestinal cancers, led by Sohal; blood cancers, led by Byrd and Curran; and head and neck cancers, led by Wise-Draper.

The Cancer Center expects to participate in about 25 Phase I clinical trials in 2024, with 10 of them being ETCTN trials, Sohal says.

FIRST **ETCTN** TRIALS

The University of Cincinnati Cancer Center is awaiting slots to open so that patients can be enrolled in four ETCTN Phase I clinical trials that are investigating safety and efficacy in new potential treatments for pancreatic cancer, lymphoma, GI cancer and leukemia.

The first ETCTN trial opened at the Cancer Center is an investigational treatment for non-operable pancreatic cancer. The drug blocks growth signals in cancer cells, says Davendra Sohal, MD, MPH.

"Although the trial is being led by Washington University, the drug is based on a lot of science developed here" by Daniel Starczynowski, PhD, associate director for basic science research at the Cancer Center, Sohal says. "We're fortunate that it has come full circle."

The Cancer Center also is participating in a second ETCTN trial testing whether a medicine, ASTX727, used to treat patients with chronic myelomonocytic leukemia (CMML) works better in combination with another drug, venetoclax, to decrease symptoms of bone marrow cancer. Emily Curran, MD, is the site principal investigator.

Unlike later phase clinical trials that enroll large numbers of patients to assess efficacy, Phase I clinical trials are testing safety. So only a few patients are enrolled at one time, who are watched for several months before new slots are opened, Sohal explains.

"These types of trials proceed slowly," he says. "We are waiting for slots to open up."

Emily Curran, MD

FLASH FORWARD

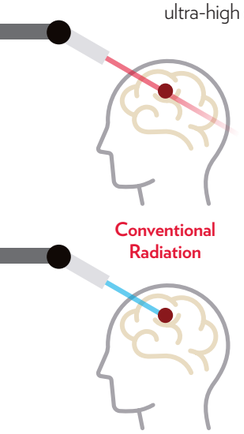
We are leading innovation into faster, less harmful radiation therapy.

The Cincinnati Children's/University of Cincinnati Medical Center Proton Therapy Center is at the forefront of cancer treatment innovation. Situated on the Liberty Campus of Cincinnati Children's, this facility was the first proton therapy center established in southwest Ohio and is one of only 45 such centers nationwide. Notably, it is the only center to:

- **House a gantry exclusively dedicated to research**
- **Conduct in-human clinical trials using FLASH proton therapy, a world-first initiative**

The center uses proton radiotherapy to treat more than 30 types of cancer in patients of all ages, while the center's basic research and clinical trials teams test new applications, like FLASH proton therapy, an investigational mode of delivering ultra-high dose rate radiation to patients in less than one second.

Preclinical research has found that the FLASH approach may result in fewer side effects than standard radiation. University of Cincinnati Cancer Center researchers are conducting a study, FAST-02, to establish the efficacy of ultra-high dose rate proton therapy in treating patients with painful bone metastases in the chest.



Unlike conventional radiation, proton therapy uses lower intensity radiation that stops once it reaches the targeted tumor. By minimizing exposure to surrounding healthy organs and tissue, proton radiotherapy potentially causes less side effects or long-term complications.

The FAST-02 study builds upon FAST-01, the breakthrough, first-ever clinical trial of FLASH proton therapy in people. FAST-01 treated patients with painful bone metastases in the arms or legs. The results of FAST-01 were published in *JAMA Oncology* in October 2022.

"These trials of an ultra-high dose rate of proton therapy are just one of our efforts to develop new and innovative cancer treatments," says John Perentesis, MD, senior advisor at the Cancer Center and research director of the Proton Therapy Center. "Our goal is to establish a foundation for future potential trials in brain tumors, sarcomas, lymphomas, lung cancer and other malignancies; and we are excited about the impact this research might have on cancer care."

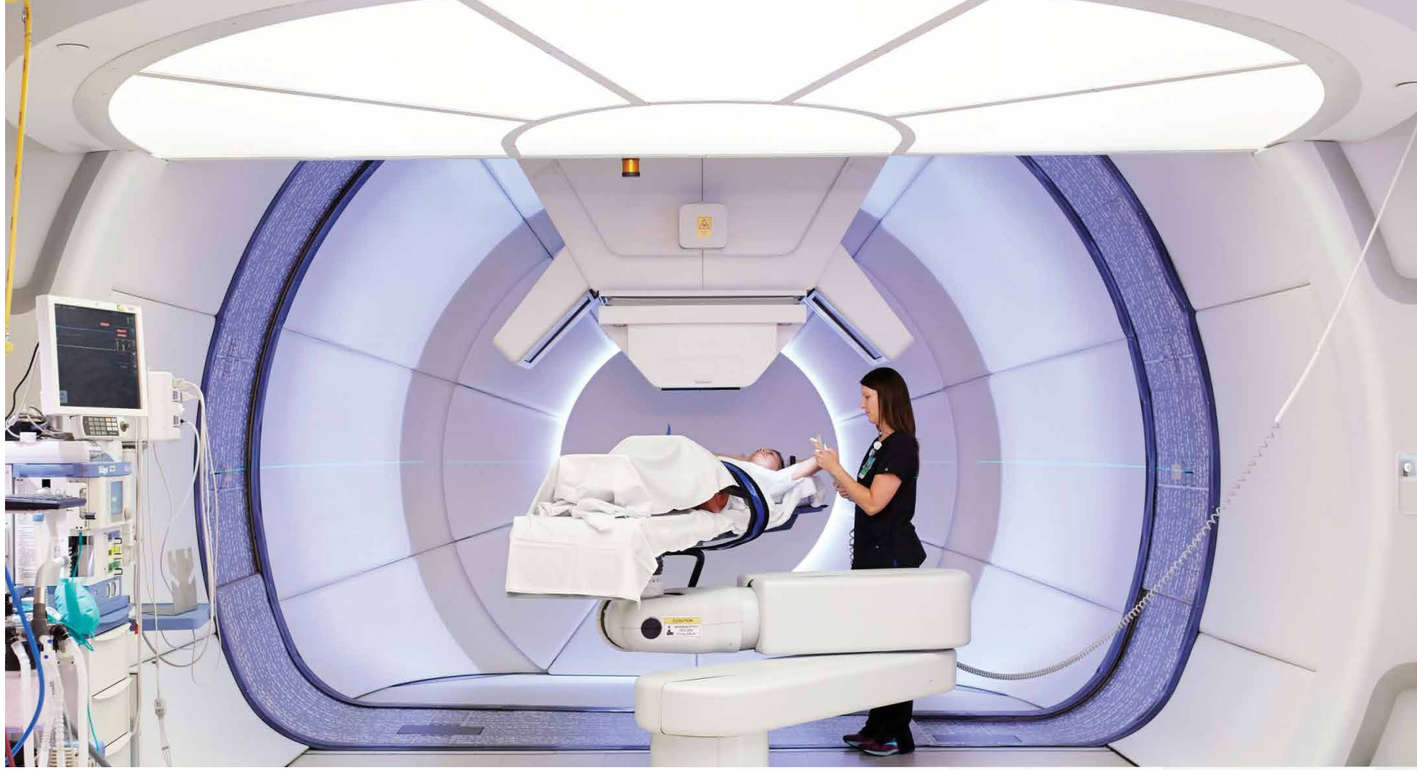
The FAST-02 study started in February 2023 and is actively enrolling patients.

"We are currently evaluating the application of FLASH in a palliative setting. However, as we grow our understanding of the safety and efficacy of FLASH for different anatomic sites, we are most excited to evaluate the effects of FLASH in curative settings, which could lead to a treatment paradigm shift for cancer patients around the world," says Emily Daugherty, MD, a clinical/translational researcher at the Cancer Center and lead co-investigator of FAST-02.

While the clinical team is focused on FAST-02, the basic science program is testing applications of FLASH that will inform future clinical trials. Cancer Center researchers recently reported that the skin-saving benefits of FLASH are reduced when delivered with multiple treatments or with multiple beams per treatment while targeting the entire treatment area, an approach that is commonly used to reduce impact on patients' healthy tissue, says Mathieu Sertorio, PhD, a member of the Cancer Center's basic science research program. Findings were published in the *International Journal of Radiation Oncology, Biology, Physics* in August 2023.

"This study suggests the number of beams and the spatial arrangement of those beams are important parameters to be considered in the design of future FLASH studies," says Sertorio, corresponding author on the paper. "Furthermore, the effect of multibeam delivery is likely different for different organs of interest."

LEARN MORE



"We have great resources here in Cincinnati. Because of the care I received, there has been no fear at all."

Courtis Fuller

A BETTER DAY TOMORROW

Courtis Fuller, an Emmy Award-winning anchor, reporter and host with Cincinnati NBC affiliate WLWT-TV, is grateful for "a better day tomorrow," his signature sign-off. He was diagnosed with a rare chordoma, a malignant tumor at the base of his skull, and underwent surgery at the University of Cincinnati Medical Center in January 2023. He then received 39 treatments of proton beam radiation at the Proton Therapy Center, which he completed in June.

CENTER OF INNOVATION

We're putting researchers, physicians and patients side by side to accelerate our work in blood cancer treatments.

Two new blood cancer centers at the University of Cincinnati Cancer Center are physical expressions of the Cancer Center's commitment to leading research and care for patients who have the most aggressive forms of leukemia and lymphoma.

The Advanced Leukemia Therapies and Research Center at Cincinnati Children's and the Blood Cancer Healing Center will unite basic science research, clinical trials and patient care in the same locations. One of the major goals of this combined investment is to accelerate collaboration between researchers and clinicians at Cincinnati Children's, UC Health and the UC College of Medicine.

"The launch of the Blood Cancer Healing Center along with the Advanced Leukemia Therapies and Research Center further galvanizes what we're trying to do to expedite innovations," says Daniel Starczynowski, PhD, associate director for basic science research at the Cancer Center and director of the Advanced Leukemia Therapies and Research Center.

The first-of-its-kind leukemia center opened in September 2023, uniting Cincinnati Children's leukemia research and clinical teams in one location. Basic science researchers access human biospecimens across the continuum of care, physician-scientists provide real-time feedback directly to the research team, and patients can participate in clinical trials for emerging therapies.

"The center helps us build on our foundation of basic science to recruit world-class acute myeloid leukemia (AML) researchers, invest in infrastructure so we can move more quickly from bench to bedside and foster more collaboration, so we're asking the right questions," Starczynowski says.

The Blood Cancer Healing Center will transform care for adult blood cancer patients. The 212,000-square-foot center, which is the newest, most comprehensive blood cancer center in the country, is designed to provide comprehensive care under one roof, ensuring patients receive continuous care around the clock. Clinical services began in July 2024, and additional spaces within the facility are scheduled to open throughout 2024 and into 2025 — including research labs for new cancer treatment discoveries and wellness areas for food as medicine and mind and movement therapies.

"Research advancements for many forms of blood cancer are giving new life to patients. You can now survive years past a blood cancer diagnosis, managing it as a chronic illness. The Blood Cancer Healing Center supports this new life for patients by bringing all the needed supportive services and pioneering research together to deliver personalized care in one therapeutic environment," says John C. Byrd, MD, a senior advisor and physician-researcher at the Cancer Center who is one of the world's leading blood cancer researchers.

Having the full continuum under one roof — or, in this case, two — promotes collaboration and accelerates research not just through formal mechanisms but also organically. Walking past an unknown lab or striking up a conversation in a hallway can spur the beginning of a collaboration that might not have happened when researchers were spread across the city. Locating patient care in the same building as research allows patient samples to be analyzed immediately in the lab and the findings taken back to the clinics — and vice versa.

"With our institutions aligned to treat aggressive diseases, we're fostering collaboration and innovation through the entire continuum of blood cancer," Starczynowski says.

> ***Collaboration is our special sauce. There are no boundaries, and we're not competitive with each other. It's really an exciting journey, and we're just getting started."***
>
> Daniel Starczynowski, PhD

Clinical Trials Start on 2 AML Therapies

The University of Cincinnati Cancer Center's new blood cancer centers ultimately mean cancer patients benefit from novel treatments sooner, as evidenced by two new drugs to treat AML that have recently been approved for clinical trials. The drugs are based on basic science research developed at the Cancer Center.

1

Partnering with Eilean Therapeutics, the Leukemia Drug Discovery Laboratory, led by John C. Byrd, MD, senior advisor at the Cancer Center, identified a compound, lomonitinib, which is a highly potent and selective pan-FLT3/IRAK4 inhibitor that targets clinically relevant FLT3 mutations (ITD, TKD), the most common AML mutations. After undergoing rigorous preclinical testing, the drug moved into human studies in under two years — a process that normally takes more than five years.

2

Kurome Therapeutics, spun out of Cincinnati Children's and based on discoveries in the Starczynowski Lab, recently received Food and Drug Administration (FDA) clearance of an investigational new drug application for KME-0584, an IRAK1/4 and pan-FLT3 inhibitor for the treatment of AML and high-risk myelodysplastic syndromes (MDS). Phase I clinical trials will begin in 2024.

"These two molecules are distinct from one another and provide the Cancer Center two shots on goal to effectively treat multiple types of blood cancers," Byrd says.

CANCER MOONSHOT HONORS

Pinder Named Among First Cancer Moonshot Scholars

Leeya Pinder, MD, MPH, a researcher at the University of Cincinnati Cancer Center and UC Health physician, was named one of the first 11 Cancer Moonshot Scholars by the National Cancer Institute and awarded a seven-year R37 grant, with initial funding of $2.75 million. Pinder's project is to develop noninvasive scalable solutions to prevent secondary cervical cancer, particularly among women living in low- and middle-income countries. Her initial study in Zambia will assess the safety and acceptability of a vaginal capsule containing protease inhibitors to treat screened women found with precancerous abnormalities who are eligible for ablative therapy. The Cancer Moonshot Scholars program is led by the Center to Reduce Cancer Health Disparities. "I focus on women's cancers, and one of the things I'm most passionate about is ending the needless suffering of cervical cancer," Pinder says.

Leeya Pinder, MD, MPH (far left)

Moonshot Project Studies Potential Treatment for Deadly Brain Tumor

Timothy Phoenix, PhD, a University of Cincinnati Cancer Center researcher and associate professor in the UC James L. Winkle College of Pharmacy, along with researchers at St. Jude Children's Research Hospital, received a nearly $4 million National Cancer Institute (NCI) grant to study how to improve immunotherapy treatments for diffuse midline gliomas (DMGs), a type of fatal pediatric brain tumor that has no current treatments. The researchers are testing whether inhibiting DNA methylation in DMG can both weaken tumors and strengthen immune cells fighting the cancer. The project is part of a new NCI Pediatric Immunotherapy Network funded by the NCI's Cancer Moonshot program to speed progress in cancer research. "Having multiple groups with unique expertise working together gives us the ability to view these topics with different perspectives and strengthens the overall science," Phoenix says.

Timothy Phoenix, PhD

2023 CLINICAL TRIAL HIGHLIGHTS

Lower-Dose Chemotherapy Regimen for AML

The Cancer Center is conducting a clinical trial to assess a lower standard dosage of a widely used treatment for acute myeloid leukemia (AML). The clinical trial is a substudy of the Beat AML Master Clinical Trial. The trial, **A Randomized Phase 2 Trial of 28 Day (Arm A) versus 14 Day (Arm B) Schedule of Venetoclax (Ven) + Azacitidine (Aza) in Newly Diagnosed Acute AML Patients ≥ 60 Years**, is designed to evaluate the efficacy of a lower dosage and treatment schedule of venetoclax plus azacitidine in newly diagnosed older AML patients. This trial will inform optimal dosing and safety information for more tailored treatments in the future, with the potential of improving treatment outcomes and survival rates for patients well beyond the local area. Only about 30% of patients with AML currently survive five years after diagnosis.

The Cancer Center is one of 16 institutions participating in the Leukemia & Lymphoma Society's Beat AML master clinical trial, the first collaborative precision medicine clinical trial in a blood cancer. The trial uses advanced genomic technology to identify each patient's cancer-driving genetic mutations, and then matches patients to the most promising, targeted treatment. John C. Byrd, MD, chair of the Department of Internal Medicine at the UC College of Medicine, is the national chief medical officer for the trial and oversees the program across all sites. Emily Curran, MD, medical director of the Clinical Trials Office, leads the trial locally.

Natural Killer Cell Therapy for Relapsed or Refractory AML

Cincinnati Children's is one of only a few centers in the nation testing a novel therapy that uses cytokine-induced memory-like natural killer (CIML-NK) cells from haploidentical donors (parent or sibling) in the treatment of AML. **Cytokine-Induced Memory-Like Natural Killer Cells (CIML-NK) for Relapsed & Refractory Acute Myeloid Leukemia** study is open to patients aged 2 to 40 with relapsed or recurrent AML regardless of whether they previously underwent a bone marrow transplant.

"To date, cellular therapy options for patients with AML have been limited by toxicity from the cellular therapy," says Principal Investigator Zahra Hudda, MD, a pediatric hematologist/oncologist with the Division of Bone Marrow Transplantation and Immune Deficiency. "NK cell therapy may be a better option for AML patients with relapsed or refractory disease since previous research shows the incidence is much lower when NK cells are utilized."

Finding more effective therapies for recurrent and refractory AML is critically important as it accounts for approximately 20% of childhood leukemia cases. "Although treatment approaches, such as intensive chemotherapy and hematopoietic stem cell transplant, have improved survival rates, the occurrence of refractory and relapsed disease remains a common scenario with poor outcomes," Hudda explains. "In addition, there are associated long-term risks and side effects despite the improvement in supportive care."

Immunotherapy Prior to Liver Transplant for HCC

Two types of treatments — immunotherapy and liver transplant — are currently used to treat hepatocellular cancer (HCC), the most common primary liver cancer and a major cause of cancer-related deaths worldwide. The Cancer Center has started a clinical trial to study the combination of the two. **Immunotherapy Prior to Liver Transplant for Hepatocellular Cancer (HCC)** will assess the safety and effectiveness of immunotherapy prior to transplantation and identify factors that may predict treatment response.

Due to factors including blood type, the severity of the condition, and the availability of donor livers in the region, patients often wait up to six months for transplants. Patients in this study will receive immunotherapy for four months during this waiting period. Because there is no standard of care for systemic treatment for patients with HCC who are awaiting a liver transplant, this trial could improve treatment options and advance our understanding of the disease, says Principal Investigator Davendra Sohal, MD, MPH, associate director of Clinical Research.

CANCER AGENTS

Our scientists are collaborating to limit environmental exposures causing cancer.

Cincinnati's industrial roots can still be seen in the health of the people who live here today. From lead in the West End to uranium in Fernald to chemicals in everyday products used by Cincinnatians, the Greater Cincinnati area is full of carcinogens that expose people to higher rates of cancer.

"There's very little appreciation of the contribution of environmental exposures to cancer. We can do something about a lot of these things in public health," says Susan Pinney, PhD, associate director of Cancer Risk, Prevention and Surveillance Research at the University of Cincinnati Cancer Center.

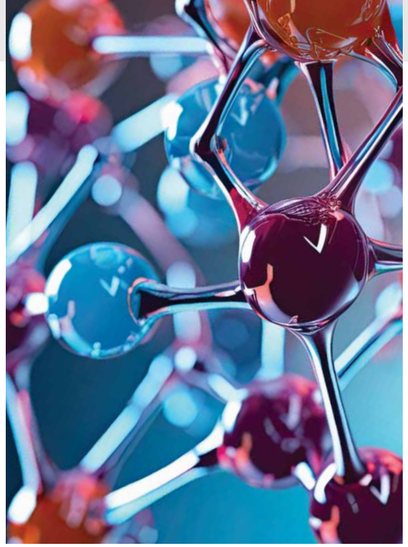
To help advance research into environmental exposures, in 2023, the Cancer Center formed a scientific research group that links basic, translational and population scientists to collaborate on measuring and combating the effects of carcinogens. Pinney, who is also the director of the UC Center for Environmental Genetics, and Chunying Du, PhD, associate professor of cancer biology at the UC College of Medicine, co-lead the group.

The Environmental Carcinogenesis Working Group meets monthly to provide feedback on current research projects, develop ideas for new research and establish new research collaborations. Feedback on the specific aims section of grant applications, study design, subject recruitment, statistical analysis and biospecimen acquisition are especially important, Pinney says, due to the unique challenges of research into environmental exposures and cancer:

- **Long periods between environmental exposure and cancer diagnoses**
- **Lack of banked biospecimens for a control group**
- **The cost of conducting lengthy studies with thousands of participants**

"I've been pleased by how much people are willing to share about their developing research studies," she says. Members are currently researching a number of specific carcinogens, including:

- **PFAS (per- and polyfluoroalkyl substances) (principal investigator: Du, PhD)**
- **Radon (principal investigators: Angelico Mendy, PhD, MD, and Pinney, PhD)**
- **Copper (principal investigators: Maria Czyzyk-Krzeska, MD, PhD, and Jarek Meller, PhD)**
- **Flame retardants (principal investigator: Susan Kasper, PhD)**



Studying the Link Between Uranium and Breast Cancer

A uranium processing facility built in a rural community 18 miles northwest of Cincinnati in 1951 during the Cold War exposed thousands of residents to uranium metal toxicity. Susan Pinney, PhD, and colleagues at the UC Department of Environmental & Public Health Sciences studied the results of that exposure in nearly 10,000 Fernald residents between 1990 and 2008. Building on that work, Pinney is now researching the link between breast cancer and exposure to uranium. She used feedback from the working group in writing a National Institutes of Health grant proposal, now under review, to study alterations in metabolism with uranium exposure and genetic susceptibility.

PFAS Linked to Delayed Puberty

Girls may experience delayed puberty when exposed to PFAS, a group of synthetic chemicals found in thousands of consumer products, from nonstick cookware to cleaning products, according to a recently published study conducted by researchers at the University of Cincinnati Cancer Center.

The study found an average delay of puberty onset by five or six months among girls with PFAS exposure. However, some experienced even longer delays, which raises concerns about their health risks, says Susan Pinney, PhD, the study leader.

"Puberty is a window of susceptibility," Pinney says. "Environmental exposures during puberty, not just to PFAS, but anything, have more of a potential for a long-term health effect. What these have done is extended the window of susceptibility, and it makes them more vulnerable for a longer period of time."

The delay of puberty in girls can lead to negative long-term health outcomes, including a higher incidence of breast cancer, renal disease and thyroid disease.

"Scientists are frustrated with the slowness of movement to change regulatory guidelines," Pinney says. "Not only do we need to publish our research findings, but also do our best to inform the general population and the health care community."

The study was published in *Environmental Health Perspectives*.

The Fernald Preserve, a nature preserve created following the $4.4 billion cleanup of the heavily contaminated site.

PFAS Are Found in Everyday Products Including:

- NONSTICK COOKWARE
- PERSONAL CARE PRODUCTS
- FIREFIGHTING FOAMS
- FAST FOOD PACKAGING
- STAIN-RESISTANT PRODUCTS
- COSMETICS
- PAINT
- CLEANING PRODUCTS

LIFELONG JOURNEY

We're building programs and conducting research to support life after cancer.

A journey through a cancer diagnosis and life beyond treatment have galvanized a Cincinnati woman and her physician to help other patients understand how life permanently changes after cancer — and to provide services to help cancer patients and survivors cope with those changes.

"It's taught me that I'm truly not alone," breast cancer survivor Sharen King told ABC affiliate WCPO 9 News in Cincinnati.

King was diagnosed with breast cancer and treated at UC Health in 2020. But her visits didn't stop when her treatment was complete. Today, she drives other patients to the University of Cincinnati Cancer Center and participates in the Cancer Center's survivorship program. The program is run by Alique Topalian, PhD, MPH, Cancer Center researcher, and Beth Shaughnessy, MD, PhD, Cancer Center member and division director of survivorship in the UC College of Medicine. Both are cancer survivors themselves, and Shaughnessy was King's surgeon.

"You've suddenly lost the life you had," Shaughnessy says about a cancer diagnosis. After treatment ends, she says, "everyone expects you to be back to normal — but your survivorship is a new normal, which may not resemble the old one as much."

The Cancer Center's Survivorship & Supportive Services program helps patients during and after cancer treatment to help manage the side effects of treatment as well as the social, emotional and personal changes that can happen as a result of cancer. The service is open to patients at any health system and provides a gamut of programs.

"Survivorship matters because the treatment and its side effects impact your baseline physiology and mental attitude going forward," Shaughnessy says. "This type of care helps regain as much as you can back so you can optimize your quality of life."

Lifelong Care for Childhood Cancer Survivors

Thanks to modern cancer treatments, more children survive cancer than ever before. But the treatments that save their lives may cause other medical conditions or health complications, sometimes during or soon after treatment but sometimes years later.

Started in 1987, the Cincinnati Children's Cancer Survivorship Center provides support throughout a patient's life, starting from the day they are diagnosed. It is one of only a handful of programs in the country that doesn't have an age limit.

At the Cancer Survivorship Center, every person follows a personalized survivorship care plan tailored to their type of cancer, treatments and age when they were diagnosed and treated. These plans help patients and their caregivers know the chances of developing health issues related to treatment, how and when to screen for those issues, and how to treat them if they occur.

Improving Cognitive Care

The University of Cincinnati Cancer Center understands that cancer patients face a variety of issues during treatment. And while a patient's physical health is crucial, their cognitive health is just as important.

"Cancer treatment affects a number of different systems," says Rhonna Shatz, DO, Cancer Center member, Bob and Sandy Heimann Endowed Chair in Research and Education in Alzheimer's Disease, and director of the Division of Behavioral Neurology at UC Health. "Often, the elephant in the room is the effect [of cancer treatment] on cognition. It's been called 'chemo brain,' but it's so much more than that."

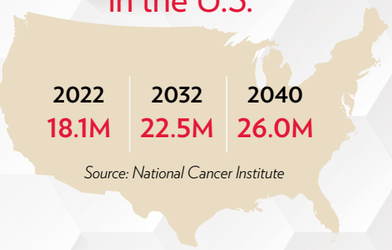
Shatz and her team address these brain changes head-on at UC Health's Cognitive Cancer Clinic, where patients receive monitoring and treatment for neurological changes that happen as a result of cancer treatment. The team is using a new AI-enabled cognitive screening tool called CognICA to help assess those changes.

"It's an extremely sensitive way of identifying disruptions in brain networks," Shatz says. "With it, you get an idea if the patients are falling into an at-risk or impaired area. Then, those patients can meet with one of our survivorship physicians or nurse practitioners to do a preventive health plan with sleep, exercise and nutrition."

The clinic also is using a resource called NIH Toolbox that integrates into the patient's electronic medical record and tracks the results of the cognitive screenings alongside the patient's diagnosis and treatments. Both tools are helping to streamline the diagnostic process, giving medical professionals more time to focus on patient care.

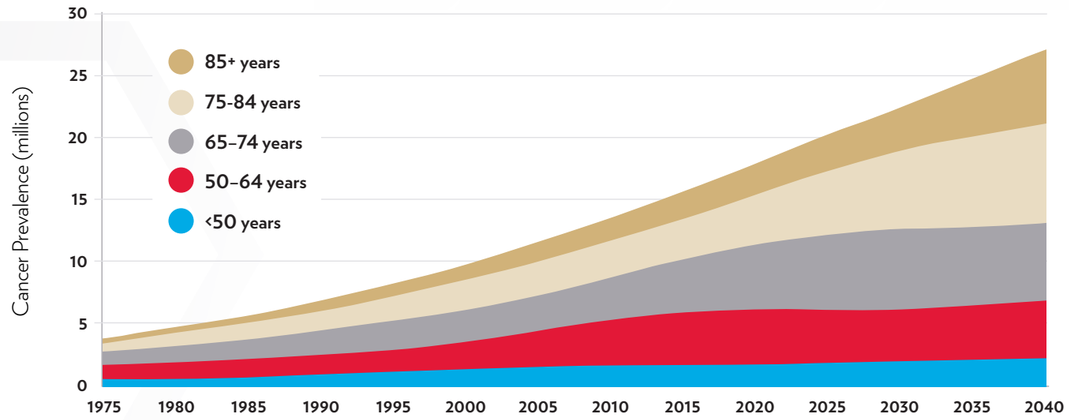
"We want the time with patients to be focused on them and not so much on the information gathering," Shatz says. "We are thinking about how to use technology in different ways to make our work as patient-focused as possible."

Cancer Survivors in the U.S.



Source: National Cancer Institute

Cancer Prevalance and Projections in U.S. Population from 1975-2040



Source: National Cancer Institute

CLOSE CONNECTIONS

We're going into our communities and letting them tell us how to beat cancer.

The University of Cincinnati Cancer Center has completed an in-depth analysis of cancer across the 10 counties where the majority of its patients live, a region known as its catchment area (see map at right). The Cancer Center hopes to use the findings to tailor prevention, cancer screening and research to improve the cancer health of the region.

"Understanding which cancers impact our population the most can help us set priorities so that the work we're doing is in alignment with what the community needs," says Melinda Butsch Kovacic, MPH, PhD, associate director for community outreach and engagement at the Cancer Center.

Community partners play a critical role in the goal to prevent cancer and to increase the number of cancers found early through screenings.

"Our community partners are critical to the success of our efforts. Having engaged cultural insiders is better," Butsch Kovacic says. "When community members observe and talk to neighbors, they have ownership in the initiative and begin to trust us. When we work with the community to improve prevention and screening efforts, uptake is better."

COMMUNITY PRIORITIES

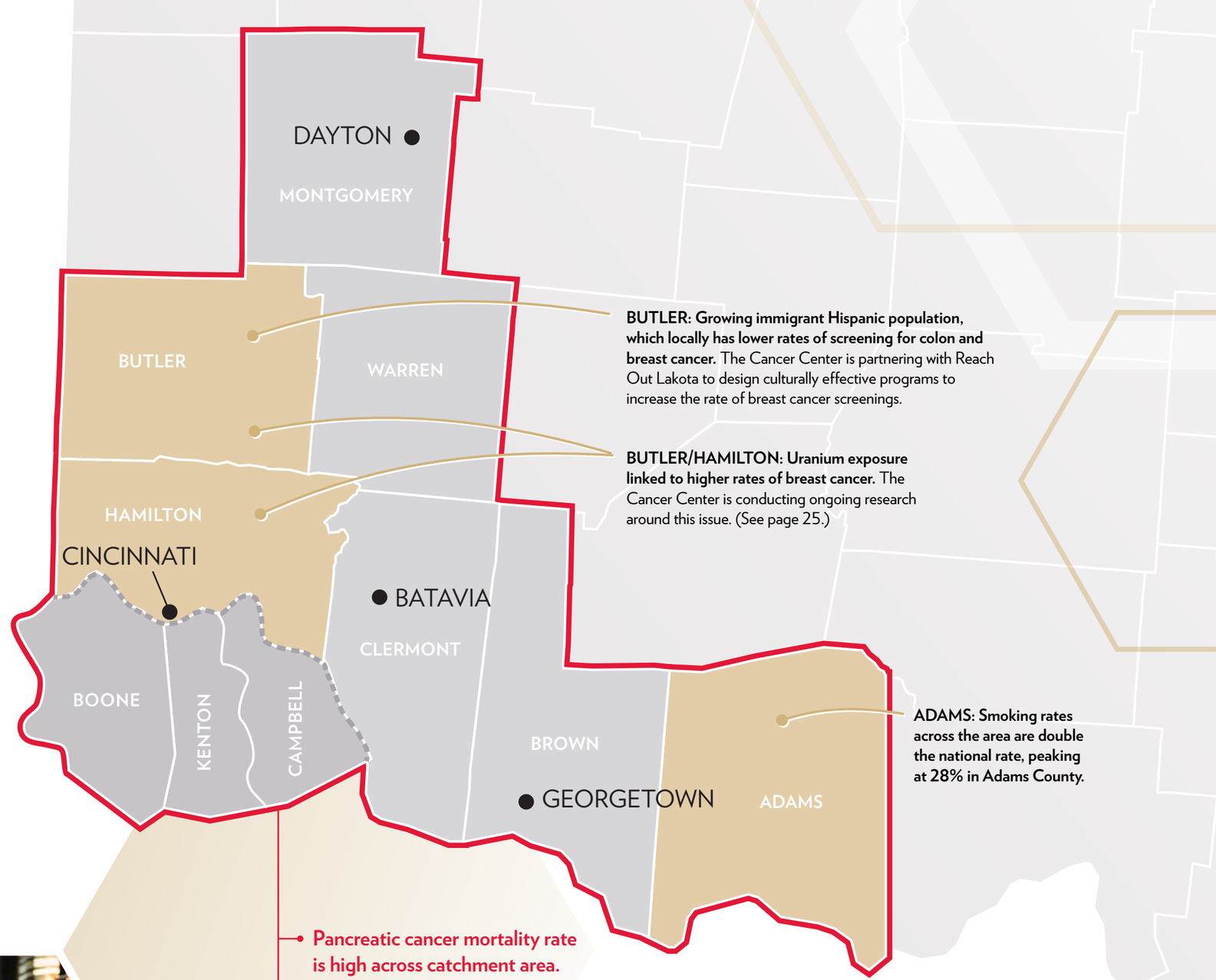
The Cancer Center selected cancer types and community initiatives based on the community assessment and input from its new Community Advisory Board.

CANCER FOCUS:

- Lung
- Prostate
- Breast
- Colorectal
- Blood
- Head and Neck

RISK FACTORS/POPULATION FOCUS:

- Cancer screening in urban minorities and underserved communities
- Smoking/vaping use
- Environmental exposures
- Obesity



BUTLER: Growing immigrant Hispanic population, which locally has lower rates of screening for colon and breast cancer. The Cancer Center is partnering with Reach Out Lakota to design culturally effective programs to increase the rate of breast cancer screenings.

BUTLER/HAMILTON: Uranium exposure linked to higher rates of breast cancer. The Cancer Center is conducting ongoing research around this issue. (See page 25.)

ADAMS: Smoking rates across the area are double the national rate, peaking at 28% in Adams County.

Pancreatic cancer mortality rate is high across catchment area.
University of Cincinnati Cancer Center is a national leader in pancreatic cancer research, with multiple clinical trials and basic science research projects. (See pages 8-9.)

Non-hodgkin lymphoma and leukemia have higher incidence rate in the region compared to Ohio and the nation.
Cincinnati Children's opened a new blood cancer center in 2023, and an adult blood cancer center opened at University of Cincinnati Cancer Center in 2024. (See pages 20-21.)

Prostate cancer is the third most common cancer in the catchment area.
UC Health offers ongoing prostate health testing at local health fairs, and the Cancer Center is expanding its focus in this area.

NURTURING TALENT

We are mentoring tomorrow's researchers to ensure we never stop making cancer breakthroughs.

Cancer research trainees receive guidance and support from their mentors but often find themselves siloed from their peers, which can inhibit networking and lead to feeling isolated during formative years. That's why, in fall 2023, the University of Cincinnati Cancer Center established the Trainee Associate Membership (TAM) program, creating a community of cancer research trainees that encourages and supports one another.

Facilitated by the Cancer Research Training and Education Coordination (CRTEC) team, TAM not only provides opportunity for trainees to meet and network but also encourages exploration by offering access to exclusive pilot grant award programs and other membership benefits.

"It's quite a unique program," says Susan Waltz, PhD, associate director of CRTEC. "Most of the funding in institutions, especially in pilot programs, goes to the principal investigators. These grants are actually given to the trainees so that they'll be able to supplement their research projects or travel to a scientific meeting to present their research. Our trainees will also be recognized for their contributions to high-quality cancer research."

In the first three months following its launch, 50 trainees became TAM members. Waltz expects the number to rise when the grant programs begin in 2024.

"The TAM program provides valuable resources for trainees such as pilot and travel awards, while also providing opportunities for professional development. With access to these resources, I am confident that TAM membership will enhance both my graduate education and development into an effective cancer researcher."

Levi Fox, PhD candidate, cancer and cell biology

Susan Waltz, PhD (right), works in the lab with TAM member Levi Fox.

CHARGE AGAINST CANCER

We are working to harness AI to improve cancer care and make faster discoveries.

As much of the world worries about how artificial intelligence (AI) will be used at its worst, University of Cincinnati Cancer Center members are eager to learn how to use AI at its best. That was the focus of the Cancer Center's 10th annual Charge Against Cancer conference, "Leveraging Artificial Intelligence and Data Sciences to Conquer Cancer."

More than 100 Cancer Center members attended lectures from local and national speakers on topics such as leveraging data in health care, advancing precision medicine using AI and AI-enabled imaging.

Working groups competed to develop AI-related research projects.

"Artificial intelligence has far-reaching implications for cancer research and clinical care," says Thomas Herzog, MD, director of the Cancer Center's Gynecological Cancer Disease Center and co-host of the event, providing a few examples:

- **Treatment planning:** AI can assess care options so physicians can best counsel and select therapies from a comprehensive menu of acceptable treatments with weighting based on the literature.
- **Clinical trials:** AI can quickly assess a patient's eligibility for a trial and identify the closest sites where the trial is open to facilitate accessibility for patients.
- **Research breakthroughs:** AI provides the opportunity to scan enormous genomic and proteomic databases to identify novel targets. If these databases grow sufficiently, important discoveries, even in rare cancers, will be possible.

Using AI to Identify Pancreatic Cancer Earlier

An exciting feature of Charge Against Cancer is a competition that breaks attendees into working groups to develop a project idea related to the conference topic. Each team pitches their ideas, and the winning team is determined through a voting process and awarded $75,000 to transform their idea into a reality.

The 2023 winning project, named Get PAIRED (Pancreatic AI Repository for Early Detection), will use AI to analyze patients from two to three Cincinnati-area hospitals to identify early predictors of pancreatic cancer, explains Brett M. Harnett, MS-IS, principal investigator of the winning team's project. "The idea is to implement artificial intelligence in a way that enhances human insight and allows early intervention to be considered," Harnett says.

RECOGNIZING POTENTIAL

The American Cancer Society is funding our early stage researchers.

In 2023, the American Cancer Society (ACS) awarded the University of Cincinnati Cancer Center an Institutional Research Grant (IRG) to support recently recruited early stage researchers. Cancer Center member David Plas, PhD, is the primary investigator for the grant, with members Maria Czyzyk-Krzeska, MD, PhD, and Kathryn Wikenheiser-Brokamp, MD, PhD, serving as co-principal investigators. Plas attributes the win to the partnership between UC, UC Health and Cincinnati Children's.

"That partnership has allowed us to create a robust cancer research community worthy of being recognized by this prestigious grant," he says. The grant is "a really substantial validation of the strides that we've made as a Cancer Center in a relatively short period of time. Most IRG recipients are NCI-designated centers, which means we're joining a group of peer institutions that have substantial cancer-focused research activity."

David Plas, PhD (third from right) with 2024 IRG grant recipients and Dr. Syed Ahmad, MD, Cancer Center co-director (far right).

The ACS awards IRGs to academic institutions with a record of outstanding cancer research and a pool of experienced researchers who can mentor junior faculty.

"By supporting institutions with seed funding for newly independent investigators to initiate cancer research projects, these institutions can utilize the preliminary results to successfully compete for national research grants," says Natasha Coleman, MPH, vice president of community impact, American Cancer Society. "We are confident that this institutional research grant, under the mentorship of our longtime collaborators and established leaders at the University of Cincinnati Cancer Center, will launch new researchers who can further our understanding of cancer and its treatment."

The ACS grant totals $360,000 over three years, with the Cancer Center matching that to provide up to $80,000 each to nine early stage investigators.

"The amount of work an early stage investigator can do with this award is substantial," Plas says. "It will completely fund a person in a laboratory and enable them to do some of the really high-end, large-scale types of experiments that become the foundation for whole research projects."

2024 ACS IRG Grant Recipients

Ali Kord, MD, MPH, MHA
Diagnostic Imaging of Low-Dose Y-90 Microspheres: A Prospective, Single-Arm, Preliminary Study

Linde Miles, PhD
Interrogation of Non-Canonical BRAF Mutations in AML

Ramesh Nayak, PhD
Chromatin Regulator SATB2 Controls Epigenetic Landscape, B Cell Precursor Reprogramming and Progression of Ph+ and Ph-like B-ALL

Mentoring Early Stage Researchers

As demonstrated by the American Cancer Society IRG grant, the University of Cincinnati Cancer Center has a robust mentorship program for early stage researchers.

Pier Paolo Scaglioni, MD

"Mentorship is the holy grail of academic medicine," says Pier Paolo Scaglioni, MD, associate director for translational research at the Cancer Center and professor and division chief of hematology-oncology in the Department of Internal Medicine in the UC College of Medicine. "A mentor is someone successful in their own field, but this is not enough. A mentor should be invested in your success, be accessible, have an open mind and respect your opinion."

A career in academic medicine is like a walk in the woods, where walking in a straight path will often not lead you where you need to go, Scaglioni says.

"If you did that, you may find a river or a valley that you cannot cross. A great mentor helps you navigate the many opportunities that exist to get to the place where you want to be," he says.

Scaglioni shared more about mentorships on the Medicine Mentors podcast. Scan the code to listen.

Holm Earns Sole ThyCa Award

The Thyroid Cancer Survivors' Association (ThyCa) awarded its only 2023 research grant to Tammy Holm, MD, PhD, a basic science researcher at the University of Cincinnati Cancer Center. Holm is using the funding to deepen the understanding of thyroid tumor biology to both clarify the mechanism of disease and identify rational, effective therapeutic targets. The award is given to members of the American Association of Endocrine Surgeons (AAES).

"I am so grateful to ThyCa and the AAES for providing such amazing and consistent support of thyroid cancer research," Holm says. "As a junior faculty member, this grant is essential to my work because it not only provides immediate funding to investigate our aims, but it also serves to buttress future endeavors for federal funding and expansion of our research."

Dr. Tammy Holm

MILLION-DOLLAR MILESTONE

Cincinnati cyclists ride each year to raise money for cancer research.

Ride Cincinnati scored a personal best in 2023, raising $1.3 million for cancer research. This was the first time since its inception in 2007 that the ride broke the $1 million mark.

Each year, cyclists of all abilities ride to raise money for research and care at the University of Cincinnati Cancer Center. Funds from Ride Cincinnati support the Pilot Project Award Program, which funds early stage research projects until investigators are able to secure large-scale funding from the federal government or cancer research organizations. Ride Cincinnati is one of 10 local organizations that help support the program, which funds more than a dozen projects annually.

"As a researcher at the Cancer Center, I feel very fortunate to have funding opportunities made possible by Ride Cincinnati for pilot projects," says Jordan Kharofa, MD, a clinical/translational researcher, co-director of the Gastrointestinal Disease Center at the Cancer Center and rider in the annual event. "These funds directly impact our ability to generate early stage research projects and clinical trials that would otherwise not be possible."

"The Cancer Center offers pilot funding to our members so they can test novel hypotheses, refine their methodologies and gain valuable data that paves the way for groundbreaking discoveries," says Tammy Mentzel, MPH, associate director for administration at the Cancer Center. "The insights uncovered through pilot projects help our investigators secure larger grants that propel impactful research forward, leading to novel approaches and new clinical interventions that impact the health of our community."

Research made possible by Ride Cincinnati has included targeting the genes responsible for aggressive tumor growth in breast cancer and identifying what mutations are most likely to block therapies from being effective in fighting cancer.

"The work of our researchers is so crucial; it's what helps drive the best patient care possible," says William Barrett, MD, co-director of the Cancer Center. "Through Ride Cincinnati, the community has really embraced the challenge of making Cincinnati a destination for cancer care."

Between the first ride in 2007 and 2022, Ride Cincinnati has donated more than $5 million to the Cancer Center's Pilot Project Award Program, funding more than 70 pilot studies that enabled researchers to secure an additional $17 million in critical follow-on grants from the National Cancer Institute and other funding sources.

MAKING PILOT RESEARCH POSSIBLE

The Cancer Center's Pilot Project Award Program is funded by the support of 10 local organizations:

Bergman Family Research Fund

Brandon C. Gromada Head and Neck Cancer Research Pilot Grant

BSI Engineering Pancreatic Cancer Research Grant

GIVEHOPE Pancreatic Cancer Research Grant

Jeff and Gail Forlenza Fund

Lyle and Gretchen Shaw Cancer Research Fund

Marlene Harris-Ride Cincinnati Cancer Pilot Program

Mischell Family Prostate Cancer Research Pilot Grant

Steven Goldman Memorial Pancreatic Cancer Research Grant

William Wong Family Cancer Research Fund

PROMISING RESEARCH

The University of Cincinnati Cancer Center's Pilot Project Award Program awarded $1 million in 2023 to fund 19 projects. These three projects represent some of the novel investigations that would not otherwise be possible without pilot funding.

Vinita Takiar, MD, PhD
Member, Clinical/Translational Research Program
Project: **Targeting PLK1 Signaling in Head and Neck Cancer Treatment**

Takiar is studying a protein called PLK1 and its implication in cancer cell division. Her lab will investigate the role of this protein in cancer progression and ways to manipulate it with drugs and radiation therapy.

Brian Turpin, DO
Member, Clinical/Translational Research Program
Project: **Comparing Cystatin C-Derived Kidney Functional Reserve (KFR) Between Adolescent and Young Adult Solid Tumor Survivors and Healthy Sex- and Weight-Matched Controls**

Children who receive chemotherapy for the treatment of a solid tumor are at increased risk of chronic kidney disease. Turpin is studying a promising measure of kidney function (Cystatin C-Derived KFR) that could be used to detect kidney disease earlier when it is most treatable or even preventable.

Meifeng Xu, MD, PhD
Department of Pathology and Laboratory Medicine
Project: **Exosomes in Neurofibroma**

Xu is researching how inflammatory macrophage cells in plexiform neurofibromas (PNFs) are activated and how to block the intercellular communication, potentially identifying a new therapeutic target.

SELECTED RESEARCH GRANTS

The University of Cincinnati Cancer Center researchers were funded by more than 196 active grants totaling more than $36.9 million in 2023. Following are some highlights of those grants.

	Lead PI	Title	Sponsor*
CINCINNATI CHILDREN'S	Fukun Guo, PhD; Yi Zheng, PhD	Rational targeting of Cdc42 to benefit immunotherapy	NCI
	Nicolas Nassar, PhD	Novel RAC pathway inhibitors for the treatment of metastatic RAS/MAPK activated leukemia	DoD
	Daniel Starczynowski, PhD	Dissecting innate immune signaling in pre-leukemia evolution	NCI
	Laura Walkup, PhD	Early detection of pulmonary complications of hematopoietic stem-cell transplantation in children using hyperpolarized xenon MRI	NHLBI
	Timothy Chlon, PhD	Decoding the paradox of DDX41-mutant MDS	NHLBI
	Soona Shin, PhD	Pathogenic role of Foxl1+ hepatic progenitor cells in fibrotic liver disease	NCI
	Soona Shin, PhD	The role of DNAJB1-PKAc-β-catenin axis in fibrolamellar HCC	NCI
	Leighton Grimes, PhD	Towards an inclusive genomic risk classification for acute myeloid leukemia (AML)	NCI
	Takahisa Nakamura, PhD	RNA silencing machinery in extracellular vesicle-mediated immunometabolic regulation	NIDDK
	Mohammad Azam, PhD	Target the DUSP1 in JAK2-dependent myeloproliferative neoplasm (MPN) for curative treatment	NCI
UNIVERSITY OF CINCINNATI	Leeya Pinder, MD, MPH	Repurposed antiretroviral therapies to eliminate cervical cancer (POLESA trial)	NCI
	Amanda Wasylishen, PhD	Histone chaperones and cell state regulation	NIDDK
	Maria Czyzyk-Krzeska, MD, PhD	Metabolic effects of copper in renal cancer	NCI
	Jun-lin Guan, PhD	Intersection of autophagy and vesicle trafficking in HER2+ breast cancer	NCI
	Chenran Wang, MD, PhD	Roles of glial autophagy in breast cancer brain metastasis	NCI
	Timothy Phoenix, PhD	Targeting tumor and T cell DNA methylomes to improve CAR T cell therapies for diffuse midline glioma	NCI/SJ
	Michael Knopp, MD, PhD	Prospective randomized Phase II trial of pazopanib (NSC #737754, IND 75648) versus placebo in patients with progressive carcinoid tumors	NCI/ACTOF
	Jane J Yu, PhD	Polo-like kinase 1 and sphingosine-1-phosphate circuitry enhances TSC-mutant cell survival	NIDDK
	Davendra Sohal, MD, MPH	Experimental Therapeutics Clinical Trials Network (ETCTN) supplement	NCI/UP
	Michael Knopp, MD, PhD	Randomized Phase II trial of 177Lu-DOTATATE versus everolimus in somatostatin receptor positive bronchial neuroendocrine tumors	NCI/ACTOF

*Sponsors (in order listed): National Cancer Institute (NCI); U.S. Department of Defense (DoD); National Heart, Lung, and Blood Institute (NHLBI); National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); National Cancer Institute/St. Jude Children's Research Hospital (NCI/SJ); National Cancer Institute/Alliance for Clinical Trials in Oncology Foundation (NCI/ACTOF); National Cancer Institute/University of Pittsburgh (NCI/UP)

UNIVERSITY OF CINCINNATI CANCER CENTER IN THE NEWS

DDN EXPLORING DRUG DISCOVERY AND DEVELOPMENT

Silence in healthy cells makes FOXR2 a potential cancer target

physicsworld

Engineered bacteria attract cancer-killing radioisotopes into tumors

MEDPAGETODAY®

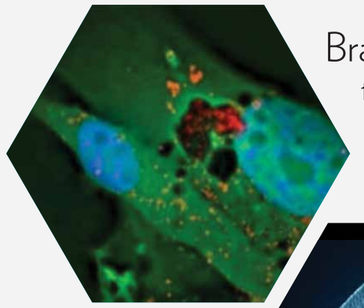
ADC Plus Low-Intensity Chemo Promising in Older Patients With B-Cell ALL

Healio

Sleep, diet, and exercise key to preserving cognitive function during cancer survivorship

SINCLAIR BROADCAST GROUP

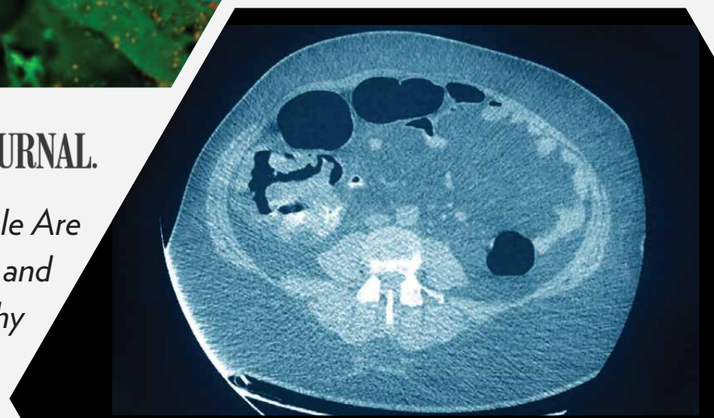
Local 12: UC's Pinder named Cancer Moonshot Scholar



Brain tumor vaccine trains immune system to fight glioblastomas

THE WALL STREET JOURNAL.

More Younger People Are Getting Colorectal Cancers, and Doctors Don't Know Why



SELECTED PUBLICATIONS

382 Total Publications

148 Cancer Center Member First or Last Author

In 2023, University of Cincinnati Cancer Center researchers published 382 studies in peer-reviewed journals, including 148 with Cancer Center members as first or last author.

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