

Brown Cancer Center Research News

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BCC Research Newsletter

HAPPY INDEPENDENCE DAY!

A Publication of the Brown Cancer Center

Brown Cancer Center Celebrates 40th Anniversary



Leaders from UofL and UofL Health celebrate 40th anniversary of the opening of the BCC

The Brown Cancer Center celebrated 40 years of conducting groundbreaking research and providing care to hundreds of thousands of patients, with the ultimate goal of ending cancer.

“The disease of cancer used to be terminal,” explained Jason Chesney, director of BCC. “Today, most of our patients are living long lives because of the treatment we offer. It’s a dramatic change.”

The BCC first opened in 1981, four years after the Regional Cancer Center Corporation (RCCC) raised nearly \$12 million for its construction and operation. At the time, UofL Physicians took care of about 50 patients a day. Today, they care for more than 500 patients per day. The number of oncologists has grown from 7 in the early 1980s to nearly 80 now. As late as 1999, the BCC hosted four clinical trials. In 2022, there are more than 130 open clinical trials. In addition to patient care, more than 65 UofL faculty investigators conduct basic and translational research to find new and better ways to prevent, diagnose and treat cancer.

“Certainly, much has evolved in the science and technology of cancer treatment after 40 years, and I’ve enjoyed seeing the depth of talent develop in many specialties of oncology,” said Henry V. Heuser, Jr., an RCCC board member who helped lead this effort alongside several other architects

of change, including Lt. Gov. Wilson Wyatt.

The BCC offers dozens of services, including treatment for breast cancer, endocrine cancer, gastrointestinal cancer, lung cancer, bone cancer, skin cancer and more. In 2021, the BCC expanded its services to UofL Health-Medical Center Northeast and UofL Health-Mary & Elizabeth Hospital, further opening access to treatment for patients.

Forty years ago, the Louisville community came together to ensure that local cancer patients did not have to travel to get the best possible cancer treatments. In a state with some of the highest rates of cancer and cancer deaths, Kentuckiana made a considerable investment to create an academic cancer center that would lead the charge in the war on cancer and educate the next generation of oncologists and cancer researchers.

“The BCC has a remarkable legacy but, most importantly, it is positioned to dramatically shape the future,” said Tom Miller, UofL Health CEO. “Of all the cancer teams I’ve worked with across the country, this group of clinicians and researchers is the most dedicated I’ve seen. When a cure for cancer is discovered, and I believe the cure will be discovered here, it will be because of the collaborate and compassionate dedication of all those at our Brown Cancer Center.”

Since opening the doors in 1981, the BCC has been the site of significant research breakthroughs and groundbreaking treatments.

Major cancer research discoveries at the BCC include:

- Development of the first anti-cancer drugs that inhibit cancer cell metabolism
- Discovery and first in world trial of anticancer DNA aptamers (AS1411)
- Creation of the world’s largest nonprofit computer grid in Kentucky

High Schools, already used to discover more than 20 new anti-cancer drugs

- The first clinical trial of cancer metabolism, following the date of glucose at the ATOMIC level
- Discovery of a novel population of multipotent stem cells called Very Small Embryonic-Like (VSEs)
- Development of the first stem cell vaccine to prevent cancer
- Clinical trials of β -glucans as immune-stimulants in combination with therapeutic monoclonal antibodies

The BCC’s milestones in the clinical arena include:

- 1990: Creation of Kentucky’s first mobile mammography program to reach underserved communities providing access to advanced cancer screenings
- 2002: Dedication of the Molecular Imaging Research Center, housing Kentucky’s first positron emission tomography/computed tomography (PET/CT) scanner and a Nuclear Magnetic Resonance (NMR) suite that serves as a catalyst for advanced cancer research
- 2010: The Multidisciplinary Breast Cancer Program became the first in Kentucky to receive full three-year accreditation from the National Accreditation Program for Breast Centers.
- 2017: The first melanoma patient undergoes TILs procedure
- 2019: Creation of a Good Manufacturing Practices Facility and the Dunbar CAR T-Cell efforts where the patient’s white blood cells are re-engineered with a chimeric antigen reception (CAR) into the T-cells, multiplied by the millions then infused back into the patient where they bind to an antigen on the cancer cells and destroy them
- 2021: Expanded services to UofL Health-Medical Center Northeast and UofL Health-Mary & Elizabeth Hospital, further opening access to treatment for patients

On hand to celebrate this momentous event were Dawn Gee (moderator of the evening), and – among others - Mr. Greg Fischer, Mayor of Louisville, Henry V. Heuser, Jr. (BCC founding member and RCCC board member), members of the Regional Cancer Care Corporation (RCCC), Lori Stewart Gonzalez, Interim President - UofL, Tom Miller, UofL Health CEO, along with more than 250 people – clinicians, researchers, staff of the BCC, patients and supporters.

As Mr. Heuser said: “The energy in the room was palpable and reminded me why I have remained committed to the Brown Cancer Center for the past forty years. To have former patients, family members, researchers, and clinicians all in the room together for the same reason – to celebrate the progress we have made toward ending cancer and serving our region, and to commit ourselves to the progress yet to come – was beyond inspiring!”

Excerpted from UofL Health May 23, 2022

Brad Rodu Wins Prestigious Award



Brad Rodu, D.D.S.

The 2022 Michael Russell Award was presented at the ninth annual Global Forum on Nicotine held in Warsaw, Poland, June 16-18. Brad Rodu, DDS, professor of medicine and Endowed Chair in Tobacco Harm Reduction Research at the Brown Cancer Center, was presented with this prestigious international award. Dr. Rodu was recognized for his life’s work of substantial and innovative contributions to the science and understanding of safer nicotine products and tobacco harm reduction.

The award honors the memory of UK psychiatrist and research scientist Michael Russell, who was a pioneer in the study of tobacco dependence and smoking cessation.

Kenneth Palmer Named Researcher of the Year by UofL ORI

The inaugural Research and Scholarship Awards at UofL on March 29, hosted by the Office of Research and Innovation, honored UofL faculty and staff nominated by their colleagues or self-nominated for outstanding research and scholarship accomplishments in fiscal year 2021.

At that event, in addition to the roughly 90 people who were recognized for their work, six major awards were presented.



Kenneth E. Palmer, Ph.D.

lmer, Ph.D., Professor of Pharmacology & Toxicology, Director of the Center for Predictive Medicine, the Helmsley Charitable Trust Endowed Chair in Plant-based Pharmaceutical Research, and BCC member, was named Researcher of the Year. This award was made, in part, for his work to address the global COVID-19 pandemic. For this work he was awarded an \$8.5 million grant from the U.S. Department of Defense to adapt a novel broad-spectrum antiviral as a coronavirus-fighting nasal spray.

UofL Presidential Excellence Awards

Each year the UofL recognizes the incredible work done by the faculty and staff with the annual Presidential Excellence Awards. Award winners in all categories were honored at a reception on

Monday, April 18.

We congratulate all the award winners who have brought distinction to UofL through their commitment to the cardinal principles through their passion, dynamism and innovation characteristic of a quality higher education experience.

Those members from the Brown Cancer Center honored in the area of Distinguished Faculty Awards include Jun Yan, M.D., Ph.D., and Donald M. Miller, M.D., Ph.D., for Outstanding Scholarship, Research & Creative Activity, and John P. Wise, Sr., Ph.D., as a Distinguished Teaching Professor.

UofL Researchers Share New Understanding of Origins and Types of Astroblastoma Brain Tumors



Norman Lehman, M.D., Ph.D.

A team of researchers led by a UofL experimental neuropathologist, has discovered important characteristics of certain types of brain tumors that may lead to novel options to treat them and a better understanding of how they and other brain tumors arise.

Dr. Lehman, UofL professor of pathology, biochemistry and molecular genetics, and Brown Cancer Center member (pictured above), led the study of the origins of uncommon brain tumors called astroblastomas that most often affect children and young adults.

“This research gives us a new understanding of how childhood brain tumors with origins in early embryonic development arise,” Lehman said. “It could lead to detection very early in the formation of these types of tumors, new treatments or potentially even strategies to prevent their formation.”

The research, published April 19 in *Nature Communications*,

revealed two distinct subtypes of these tumors, one that develops in early childhood, the other developing later in life.

The type of astroblastoma that occurs in young children is derived from radial glia that arise very early in the embryonic brain and are biologically related to tumors known as ependymomas. The other type of astroblastoma, typically occurring in young adults, is derived from later neural stem cells called outer radial glia and are biologically related to astrocytomas.

The research also has implications in understanding differences in tumor occurrence based on sex.

“The early-development astroblastoma tumor appears to occur exclusively in females, which may give us a better understanding of why certain types of tumors not involving the reproductive system are found more frequently in males or females,” Lehman said.

Lehman also said the tumors’ mechanisms likely involve alterations in DNA methylation that could possibly be exploited to detect tumor development early on or mitigate their development, but also are associated with other types of neural conditions.

“The altered genes that are associated with the development of these tumors are genes that also are associated with developmental neurocognitive disorders such as autism spectrum disorder, attention deficit hyperactivity disorder and schizophrenia,” he said.

Contributors to the work included Brian Williams and Akshikumar Mistry, both assistant professors in the UofL Department of Neurological Surgery and neurosurgeons with UofL Health, UofL biochemistry and molecular genetics graduate student Müge Sak and former UofL pathology resident Khaled Alkhateeb. Dr. Mistry is also a member of the BCC.

“We have very few treatments for brain tumors,” Mistry said. “If we can get to the bottom of this very rare brain tumor in terms of its biological origins or its biological behavior, then that knowledge could be applied to some of the

other aggressive brain cancers. The question is, how does this sort of research apply to other tumors that are not well understood, and can we gain insight into those other tumors to hopefully figure out how they’re behaving?”

Other important contributors included developmental biologist Nathalie Spassky of the Institut de Biologie de l’École Normale Supérieure in Paris and Kenneth Aldape of the National Cancer Institute Center for Cancer Research.

Astroblastomas exhibit radial glia stem cell lineages and differential expression of imprinted and X-inactivation escape genes

[Norman L. Lehman](#), [Nathalie Spassky](#), [Müge Sak](#), [Amy Webb](#), [Cory T. Zumbar](#), [Aisulu Usualieva](#), [Khaled J. Alkhateeb](#), [Joseph P. McElroy](#), [Kirsteen H. Maclean](#), [Paolo Fadda](#), [Tom Liu](#), [Vineela Gangalapudi](#), [Jamie Carver](#), [Zied Abdullaev](#), [Cynthia Timmers](#), [John R. Parker](#), [Christopher R. Pierson](#), [Bret C. Mobley](#), [Murat Gokden](#), [Eyas M. Hattab](#), [Timothy Parrett](#), [Ralph X. Cooke](#), [Trang D. Lehman](#), [Stefan Costinean](#), [Anil Parwani](#), [Brian J. Williams](#), [Randy L. Jensen](#), [Kenneth Aldape](#) & [Akshikumar M. Mistry](#)

Nature Communications volume 13, Article number: 2083 (2022)

UofL-BCC Small Business Awarded Research-match Funding from Commonwealth of Kentucky

Seven Kentucky companies will split \$900,000 in grants as part of the Small Business Innovation Research and Small Business Technology Transfer Matching Funds, a commonwealth Program that is nationally recognized. The grants awarded are intended to further the state’s technology industry. These funds will match, in part, \$8.71 million in federal grants that the 7 businesses will receive. One of the seven companies in this prestigious group is 3P Biotechnologies, whose founder and President is Dr. Ramesh Gupta, Professor of Pharmacology & Toxicology and member of the Brown Cancer Center at UofL.

“Innovative companies are growing at an impressive rate in Kentucky, and we must ensure that continues by investing in the resources, people and companies that are tackling the problems of tomorrow,” said Kentucky Governor Andy Beshear. “Our SBIR-STTR Matching Funds Program provides

Kentucky companies with an incredible opportunity to turn their game-changing ideas into cutting-edge products, while also creating quality jobs in some of our country’s most high-paying fields. To continue the economic momentum we are currently experiencing, we must invest in our future. Congratulations to this latest round of awardees. I am extremely excited to see your future success in the commonwealth.”

The main technology development by 3P Biotechnologies is a method of using exosomes derived from cow’s milk to deliver drug treatments for inflammatory diseases. The company’s technology development creates a way to isolate clinical-grade exosomes from the milk in large volumes, impacting both industry use and academic research. This match funding is for work to be done on an R41 NIH grant awarded with a start-date of June 1, 2022.

Gibbs Foundation Grants UofL \$1.5 million to Expand Cancer Immunotherapy Clinical Trials

More individuals will have access to new treatments for cancer at the UofL Health-Brown Cancer Center thanks to a new gift supporting immunotherapy clinical trials.

The Gibbs Foundation Inc. is giving \$1.5 million to the UofL over three years to fund additional research staff and faculty time dedicated to clinical trials, increasing capacity for trial participants in the tumor infiltrating lymphocytes program, or TILs.

“We are so very grateful to the Gibbs Foundation for this gift. By allowing the Brown Cancer Center to expand this clinical trial and treat more patients with this innovative therapy, it provides hope for more families who are battling cancer and advances these therapies, potentially benefitting even more cancer patients and families,” said Lori Gonzalez, interim UofL president.

In clinical trials at the BCC, therapy known as tumor infiltrating lymphocytes, or TILs, has been shown to be effective in treating advanced melanoma patients, for whom the median survival is only 8

months. TILs treatment involves removing one of a patient's own tumors, preserving, activating and expanding immune cells from the tumor, then administering these immune cells into the patient. As a result of its success in melanoma patients, BCC is expanding the TILs program to test the therapy for the treatment of other cancers.

TILs patients face a long wait time due to the complex and time-consuming nature of the therapy and demands on clinical research staff. The gift from the Gibbs Foundation will allow UofL to hire additional nurses and coordinators and dedicate more of the oncologists' research time to support TILs, a complex inpatient procedure. The gift is expected to result in the treatment of at least 25 additional patients.

"The Gibbs Foundation Board of Directors has been dramatically impressed with the success of the Brown Cancer Center's immunotherapy work conceived and spearheaded by Dr. Jason Chesney. We look forward to continuing the vision of our founder George Gibbs in helping to facilitate this great effort," said Ivan J. Schell, Gibbs Foundation board member. "The Gibbs Foundation supports the BCC and its dedicated team of physicians as they gain ground in the search for a cure for all cancers."

Cancer remains one of the most difficult and deadly challenges in health care, killing more than 600,000 people each year in the U.S. and nearly 10 million people worldwide. Kentuckians are affected at a higher rate than residents of any other state. The BCC serves more than 26,000 cancer patients every year and has the largest early-phase cancer trials program in the region. The BCC is a global leader in the clinical testing of new immunotherapies, treatments that activate the body's immune system to fight cancer and is an early adopter of these treatments.

"My goal is to help make cancer something that people one day study in history classes instead of medical schools, and I truly believe

we are getting closer to that day," said Jason Chesney, chief of the UofL Division of Medical Oncology & Hematology and director of the Brown Cancer Center. "This gift allows us to increase the number of patients and advance this lifesaving technology."



UofL Hospital breaks ground on \$144 million Tower Expansion

UofL Health broke ground June 6 on a new 7-story tower to anchor a \$144 million expansion and upgrade to UofL Health-UofL Hospital. The project will increase the downtown Louisville hospital's operating capacity and facilitate a phased modernization to include all private beds throughout the remainder of the hospital.

When complete, UofL Hospital will offer more than 360 beds, each in a private room, 20 operating rooms, plus a new 24-bed observation unit. Alongside the increased clinical space, the expansion will include an enhanced visitor experience with a new lobby and waiting area, along with updates to the gift shop and coffee shop.

The hospital expansion also will lead to an expansion of the UofL Health team, with approximately 325 new jobs being created. Positions will include nurses, plus clinical and non-clinical support.

"By expanding UofL Hospital to meet today's medical needs, we are also investing to grow the physicians, nurses and other allied health professionals of tomorrow," said Lori Gonzalez, UofL interim president. "Together, with UofL Health, our blended mission of healing, teaching and research is building a stronger health care workforce and healthier future for Kentucky."

UofL Hospital is the primary teaching and research hospital for UofL Health, affiliated with the UofL. Its Level 1 Trauma Center, one of only two adult trauma centers in the state, includes a comprehensive burn unit and admits more than 3,500 patients each year. The hospital is home to Kentucky's first Comprehensive Stroke Center and includes UofL

Health-Brown Cancer Center. The BCC specializes in treating cancers of the nervous system, breast, gastrointestinal and reproductive systems, head and neck, lungs and skin.

According to the ASHE, an association devoted to professionals who design, build, maintain and operate hospitals and other health care facilities, there are nearly 1,700 individual teaching hospitals in the United States. Of these, roughly 300 are considered major teaching hospitals, including UofL Health.

"Academic medical centers offer significant advantages, especially in complex cases," said Jason Smith, UofL Health chief medical officer. "The treatments of tomorrow are available today at UofL Health with the collective wisdom of expert researchers and clinicians. The new tower allows us to make that care available to more patients."

The hospital is licensed to operate up to 404 beds, but the existing facility limited operating capacity to 340 over the past several years. The combined impact of the additional beds and the observation unit creates room for nearly 50 more patients and reduces wait times as patients transition between different levels of care. The seven-story tower expansion also will include the infrastructure to accommodate two more floors for future growth.

The investments at UofL Hospital are part of an overall commitment to increase access to care in the region, particularly in federally medically underserved areas (MUAs). Over the past 2 years, UofL Health has opened 5 Urgent Care *Plus* locations, added 2 new locations for the BCC and recruited more than 140 new physicians. Two of the urgent care facilities, a cancer center location and more than 100 physicians are specifically located to serve people living in MUAs.

More than 1.5 million patients seek care through UofL Health each year.

The tower is expected to open to the first patients in early 2024.

Excerpted from UofL Today by Jill Scoggins,
June 7, 2022

