UNC Lineberger Comprehensive Cancer Center

Spring 2020

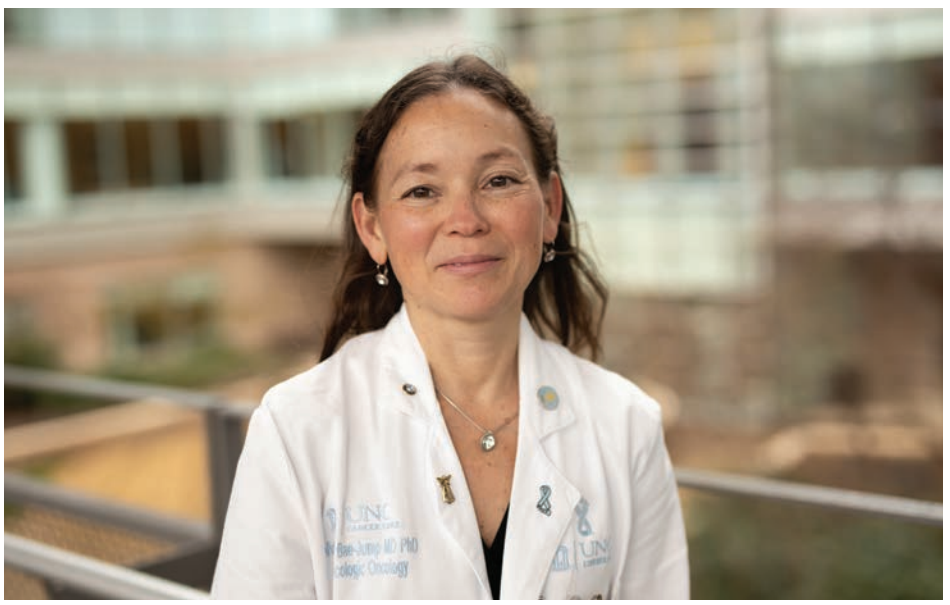
cancerlines

UNC | LINEBERGER COMPREHENSIVE CANCER CENTER

the inside lineup

UNC CANCER CARE

Study tracks endometrial cancer across North Carolina



UNC Lineberger's Victoria Bae-Jump, MD, PhD, said despite being the fourth most common cancer in women, endometrial cancer has been a long under-studied cancer.

UNC Lineberger researchers are launching a major initiative to track 1,000 women across North Carolina with endometrial cancer, cancer in the lining of the uterus, to understand why the cancer is increasing in incidence and mortality, and why the disease is more deadly for some women than others.

In the Carolina Endometrial Cancer Study, researchers will investigate factors contributing to these statistics, including patients' medical history or lifestyle. They will also evaluate the genetics of patients' tumors in order to potentially identify therapeutic strategies.

Not only do researchers want to understand why the disease is becoming more prevalent and mortality rates have increased, but also why mortality rates are higher in black women compared with white women.

"Despite being the fourth most common cancer in women, endometrial cancer has been a long under-studied cancer," said UNC Lineberger's **Victoria Bae-Jump, MD, PhD**, professor of gynecologic oncology in the UNC School of Medicine Department of Obstetrics & Gynecology. "We need to spend more time and research dollars trying to figure out this cancer."

Understanding cancer drivers

The National Cancer Institute has estimated there will be 65,620 new cases of uterine cancer diagnosed this year, representing about 4% of all new cancer cases.

And while 81% of women survive five years with this disease, endometrial cancer can be deadly once it has spread, and the statistics are trending the wrong way.

The NCI reported in the Annual Report to the Nation 2020 that between 2013 and 2017, uterine cancer mortality rates increased by an average annual rate of 2%, representing the largest increase for any cancer in women.

Researchers also found that black women have a higher risk of death from this disease, both nationally and in North Carolina.

Compared to other racial and ethnic groups, black women have a 93% higher five-year mortality rate. In North Carolina, black women have a more than two-fold risk of death.

"Endometrial cancer does harbor one of the worst disparities for African-American women," Bae-Jump said.

Already, Bae-Jump is entrenched in studies to try to identify potential new treatments

See STUDY, page 2

UNC Lineberger helps further COVID-19 virus research

The COVID-19 pandemic has impacted all aspects of our daily lives. Six-foot separations and faces covered by masks have become regular sights when we are able to venture out of our homes. Although the novel coronavirus is dictating life today, it's no surprise that people are looking for ways to give back and help in any way they can.

With health care on the frontlines of the pandemic, UNC Lineberger's faculty and staff are focused on patients and their families, while keeping themselves healthy and able to deliver quality cancer care and conduct forward-thinking research.

Donors have also made a difference in the lives of patients and health care workers. When UNC Health created the COVID-19 Response Fund to provide for emerging needs, the generosity of donors over the past few months has led to research breakthroughs, personal touches and patient benefits.

Support for science

For UNC Lineberger's **Dirk Dittmer, PhD**, director of UNC Viral Genomics Core, the pandemic is something he and his team train for in their daily work.

"There's a concern about infections among cancer patients," Dittmer said. "It's important

See COVID-19, page 7

UNC Lineberger's Dirk Dittmer, PhD.

NEWS FLASH: COMING TO THE NEXT EDITION OF CANCER LINES

- ***Carey, Serody and Basch take on new cancer center and oncology roles***

director's message

Shelton Earp, MD

I usually like to start my message with all the wonderful things going on at UNC Lineberger and the North Carolina Cancer Hospital, the cancer center's clinical home. While we're still focusing on all the great work going on, we'd also like to acknowledge that the COVID-19 pandemic has radically altered our operations model and required rapid and remarkable changes to keep our patients, their families, and our doctors, researchers, faculty and staff safe and healthy. People didn't stop having cancer; we just had to adapt to keep our patient care and provider safety top of mind.

These are trying times. Along with the rest of the world facing COVID-19, UNC Lineberger and UNC Health had to change so much, including some agonizing decisions such as reducing all but the most crucial on-site clinic visits and limiting family participation and visits with their loved ones undergoing therapy. I have been, and remain, so proud of all at UNC, particularly those involved in cancer care.

So, we are all — including you, our supporters — learning to adjust to a new normal while continuing our lives. For us, that means engaging in the forward-thinking research and top-notch cancer care we provide for patients and their families. This new reality has created a different working environment for our doctors and researchers and a changed care space for our patients.

While much has changed, our dedication and pursuit of our goals has not. We are still committed to achieving research breakthroughs, and our scientists are working just as hard as ever to make progress in the fight against cancer. Some are using our world class research infrastructure to help stem the flow of COVID-19. For obvious reasons, the National Cancer Institute's director, our own Ned Sharpless, has declared SARS-CoV-2 (the virus that causes COVID-19) a cancer emergency. This virus is affecting our ability to care for cancer patients, and cancer patients are more vulnerable to serious infection. Over the next months, you'll hear of contributions that our UNC Lineberger member's in virology, immunology and pharmacology are making in developing potential vaccines and therapies for COVID-19.

On the clinical side, our doctors and nurses are embracing telemedicine to help care for patients and answer families' questions and are relying on patients to participate in their care by providing regular and accurate reports on their symptoms. We have several videos up on the UNC Lineberger website to help patients and families understand the new normal and our commitment to their care and support.

We recently underwent our five-year evaluation of our accomplishments as an NCI-Designated Comprehensive Cancer Center. We have always been slated to be reviewed in Spring 2020; who knew there would be a pandemic!? We needed to get creative in this sphere, and UNC Lineberger hosted the first ever NCI cancer center site visit by WebEx. Instead of the normal in-person lab tours and research presentations, we welcomed 20 site visitors "virtually" from their homes to our various "sheltering at home" venues. Our digital and telehealth teams worked hard to get us ready to shine. We have an exceptional cancer center, we just had to prove it in a non-traditional way.

There's still so much progress at the center, despite the headaches caused by social distancing, and you'll read about that great work in the following pages. You'll learn about an endometrial cancer study by Vickie Bae-Jump, MD, PhD; you'll enjoy the story of a patient who underwent a grueling clinical trial knowing it may not help her but would benefit others; you'll read about Wendell (Dell) Yarbrough, MD, and how he became interested in head and neck surgery and how he went on a career odyssey that finally brought him back "home" to UNC. You'll also be inspired by the life and success of a young violinist with cancer who went on to the finals of "America's Got Talent."

Speaking of talent, it's right here at UNC Lineberger. It's in the doctors, researchers, faculty and staff at the cancer center who give their best every day, whether it's standing six feet apart in a lab, via a Zoom meeting or conference call, or even through telemedicine. No matter what obstacles are thrown our way, we're going to continue providing today's best care and tomorrow's best hope.

STUDY *continued from page 1*

for the disease, and to understand what may be contributing to rising mortality rates as well as racial disparities.

In her laboratory, Bae-Jump's working to develop mouse models of endometrial cancer using tumor tissue from patients in order to study genetic differences in the cancer of black and white women.

"If we know what the differences are, we could target those with therapy," she said.

In addition, she has sought to understand the link between endometrial cancer and obesity, which is a known risk factor for multiple cancer types. Her goal is to find ways to treat these molecular drivers linked to obesity to stop the cancerous growth.

"Obesity is a huge driver of endometrial cancer," Bae-Jump said. "My initial work looking in mouse models and gene expression profiles found that endometrial cancers that arise in the setting of obesity actually behave much more aggressively in that they grow faster, and are metabolically quite different."

An ongoing study is evaluating whether researchers can change some of the obesity-linked molecular drivers of endometrial cancer using weight loss surgery in mice.

While they've already begun working on understanding the relationship between obesity and endometrial cancer, researchers reported there's only a limited understanding of the impact of obesity and its link to the development of endometrial cancer and treatment outcomes, particularly in black women, who are more likely to meet criteria for obesity in the United States.

In addition to these factors, Bae-Jump said there are other questions that remain. Researchers in her lab are also looking at other factors that could be contributing to the disparity for black women, including the presence of other diseases such as diabetes, and a lack of information on molecular subtypes of disease.

When she reviewed existing studies that analyzed tumors to find what may be contributing to the disparity at the level of the gene or protein, she found black women were under-represented in those studies.

"When you go to the big genomic studies to find out why African-American women are doing so poorly, their cancers are under-represented," she said.

That's where the Carolina Endometrial Cancer Study, which is funded with about $1.7 million from UNC Lineberger, will come in. Researchers plan to evaluate the genetic patterns in the tumors of women who participate in the study. By investigating the molecular alterations in endometrial tumors, they intend to uncover what may be driving more aggressive behavior, or lead to worse outcomes as well as into how treatment, access to care and follow-up are all delivered.

"We are going to look at the genomic differences on a greater scale than has ever been done before," she said.

In addition, they will evaluate the microbiome – or the naturally occurring micro-organisms present – that might play a role in disease outcomes.

And ultimately, they believe their approach will uncover new ways for drug targets to improve treatment.

Making a difference in North Carolina

Growing up, Bae-Jump always wanted to be a doctor. She used to do pretend operations on her brother and had a role model of a happy doctor in her dad, a pediatrician.

She did her undergraduate studies at Duke University before attending Virginia Commonwealth University in Richmond to receive her doctoral and medical degrees. She completed her residency training and her fellowship at UNC School of Medicine.

The drive to uncover the reasons behind the disparity and potential new therapies is personal for Bae-Jump, who is both a researcher at UNC Lineberger and a gynecologic oncologist at the North Carolina Cancer Hospital. She treats women with all types of gynecologic cancers, including ovarian, cervical, vulva, vaginal and endometrial.

"Many patients with endometrial cancer have stage I disease, and they do quite well, but for women with advanced and recurrent disease, we need more therapeutic options for them," she said. "It makes me sad when I have a short list of options for women with advanced and recurrent endometrial cancer. And on top of that, there are terrible disparities. I just think it's time we spend time and money trying to figure out why, and how to make outcomes better."

She is working with a multidisciplinary team to launch the Carolina Endometrial Cancer Study, including UNC Lineberger cancer epidemiologists and co-leaders **Andy Olshan, PhD,** and **Hazel Nichols, PhD**: microbiome researcher **Temitope O. Keku, PhD;** molecular pathologist **Jason Merker, MD, PhD,** molecular pathologist **Russell Broaddus, MD, PhD,** chair of the Department of Pathology and Laboratory Medicine, and **Wendy Brewster, MD, PhD,** director of the UNC Center for Women's Health Research and professor of gynecologic oncology at the UNC School of Medicine, among others.

They're actively working to find additional grants to fund multiple projects, all with the same goal of improving the statistics for women with endometrial cancer in North Carolina, and beyond.

"We believe that we can make a real difference in a disease that's important to North Carolina," said UNC Lineberger Director **Shelton Earp, MD.** "That's a very purposeful strategic direction that we've taken."

Donor's business, philanthropy, a family affair

Manish Atma, 51, has been in the hospitality industry all his life. Growing up in Albemarle County, North Carolina, Atma learned the ins and outs of the hotel business by helping his parents run their mom and pop hotel.

"It was a family business," he said. Atma helped around the hotel, cleaning rooms, working at the front desk and the restaurant, and even cleaning the pool. So it was no surprise that Atma pursued hospitality management as a career when he went off to college.

After college, he worked for a hotel company, where he added hotel development, management and operations to his skill-set over the next five years. With that experience under his belt, Atma then managed a Hampton Inn in Albemarle County and ultimately formed Atma Hotel Group, which now manages seven properties throughout the Southeast, including North Carolina, South Carolina and Florida – a far cry from his days cleaning the pool at his parents' hotel.

But those days with his parents and the years spent building his business have created and fostered a philanthropic spirit in Atma, and his support for cancer patients and their families is unwavering. He was touched by the story of Reece Holbrook, the son of Chad Holbrook, head baseball coach at the College of Charleston and a former UNC baseball assistant coach. Reece was diagnosed with leukemia at 2 and was treated by UNC Lineberger's **Stuart Gold, MD,** the chief of pediatric hematology/oncology. While the family was still in Chapel Hill, they held the Reece Holbrook Golf Classic, and Atma Hotel Group was a sponsor. Reece is now cancer-free and will be a freshman at UNC-Chapel Hill this fall, where he'll also play baseball for the Tar Heels. Inspired by Reece's story, Atma also became a regular attendee at Roy Williams' Fast Break Against Cancer, a signature annual event that raises money to support cancer research at UNC Lineberger.

"Cancer is something that doesn't discriminate," Atma said. "It affects everyone from babies to adults, and I felt like whatever I could do to help the cancer center — because there's a lot of people in need of assistance — felt like it was a good part of our philanthropy, helping the cancer center."

Atma and his wife, Sheetal, recently created a $50,000 endowed fund to support UNC Lineberger's Comprehensive Cancer Support Program. The CCSP provides a range of patient support services, including assistance to address financial challenges patients may face when being treated for cancer. From providing gas cards to get patients to their appointments to paying utility bills or rent, the program can offer a financial lifeline when a patient needs it most.

"We want to help the people who need help and make sure they're taken care of during a time of need," Atma said. "As a community, it's our obligation to give back to the people and the state where we live. I grew up in North Carolina; this is home."

Atma, who recently joined the UNC Lineberger Board of Visitors, is also offering hotel rooms at discounted rates for cancer patients, a true blessing during the COVID-19 pandemic, since other housing options like the SECU Family House and Ronald McDonald House currently cannot provide accommodations. Atma said they're housing several bone marrow transplant patients who need to be close to the N.C. Cancer Hospital.

"Our priority is not about profits; it's about survival and helping whomever we can," Atma said.

Manish Atma

"Cancer is something that doesn't discriminate. It affects everyone from babies to adults, and I felt like whatever I could do to help the cancer center — because there's a lot of people in need of assistance — felt like it was a good part of our philanthropy, helping the cancer center."

Patient a friend to others on bladder cancer journey

Chapel Hill holds a special place in Linda Willey's heart. She grew up in the town, went to Chapel Hill High School and returns as often as she can. And while most of her memories are fond, she also has found that her hometown is a place for care and compassion, particularly for cancer patients.

Willey, in her 60s, now lives in Manteo, North Carolina, in the Outer Banks with her husband, Fletcher. Over the years, she realized the remote location of Dare County was great for those who wanted to get away from the hustle and bustle, but it also lacked services for its residents, particularly quality health care.

"No one should have to travel around the country to get cancer care; we should have it right here in North Carolina," she said.

Willey saw that struggle first-hand when a friend was diagnosed with kidney cancer in 2007 and couldn't get to a better equipped hospital for treatment. "It became my passion to get her to Chapel Hill for treatment and walk her through what it takes to go from the Outer Banks to there for treatment when you don't have the means to do it," she said.

That struggle inspired Willey to start Hands of Hope, a program that drew on her familiarity with the UNC hospitals and her desire to improve cancer care for patients in the Outer Banks. The program, which offered rides to UNC hospitals as well as other services, grew in leaps and bounds, and Willey has since passed the reins to new leaders. "It's like watching your baby grow up," she said.

Then, two years ago, her passion project was thriving, her friend had recovered from her cancer and things were going well at the insurance agency she runs with her husband, Willey learned she had cancer.

Finding blood in her urine and thinking she had a urinary tract infection, Willey went to urgent care and took a course of antibiotics, but her symptoms persisted. After a trip to Greenville to see a urologist, a scan showed a tumor on her bladder. A biopsy found the tumor was malignant, and Willey immediately knew what her next step would be.

"I said 'I need a referral to UNC.' It's our state hospital, and it's the people's hospital," she said.

Over the years, Willey's connection to Chapel Hill had only deepened, and she had relationships with doctors, researchers and staff members at UNC Lineberger and the North Carolina Cancer Hospital, the cancer center's clinical home.

"I knew that the chance to participate in clinical trials and take advantage of the research would be in Chapel Hill," she said. "I wanted to go back home for my care."

Willey was in good hands with UNC Lineberger's team of **Matthew Milowsky, MD**, and **Ray Tan, MD**. She started chemotherapy, and after four treatments, Milowsky had good news to share; her tumor had shrunk by 75%. Next, Tan surgically removed her bladder and some lymph nodes.

"He told me all about what to expect, and it was scary and as difficult as he told me it was," she said. "But I got through it. I survived the surgery."

Milowsky, the George Gabriel and Frances Gable Villere Distinguished Professor of Bladder and Genitourinary Cancer Research, told her they'd removed the cancer they could see, but there was still a chance of recurrence. As a result, her care plan included having a scan every three months. Milowsky also suggested an immunotherapy clinical trial for patients like Willey with high risk bladder cancer. The trial, designed to decrease the risk of recurrence and improve survival outcomes, would require her to be in Chapel Hill every other week for a year. Willey didn't hesitate to enroll, despite the 444-mile round trips and the possibility she could be placed on a placebo and not receive the drug, something that impressed her doctor.

Clockwise from top left: Linda Willey with her husband, Fletcher.

Linda Willey, a Chapel Hill native, wanted to return to her hometown to undergo treatment for bladder cancer.

UNC Lineberger's Matthew Milowsky, MD, Willey's doctor, suggested a clinical trial for high risk bladder cancer patients.

"Linda participated in this study understanding that she may be receiving an intravenous placebo treatment every two weeks for a year," Milowsky said. "In so doing, she clearly articulated her desire to contribute to research to develop better treatments, acknowledging that the study may not benefit her personally. It takes a lot of very special people like Linda to participate in these studies and represents the only way that we can develop better treatments for patients with bladder cancer and other malignancies."

Just as she stepped up to help when her friend had cancer, Willey was ready to do the same for other cancer patients by participating in the clinical trial.

"I realized my purpose," she said. "So much of this was to have the opportunity to try a new drug, to leave the world a little bit better than I found it. I always felt honored and blessed to be able to do it. It's the icing on the cake for me, of all the things I've done to try and be there for other people."

Willey said cancer has made her think differently about life, and she finds that she's a kinder person because of it. She recently renovated a townhouse in Chapel Hill, but due to COVID-19 travel and visitation restrictions, she's not able to stay in the home and volunteer at the N.C. Cancer Hospital like she'd planned. Instead, Willey has offered her townhome to a former playmate of her son's, a bone marrow transplant patient and his wife, to use during the duration of his treatment, a timely blessing with SECU Family House closing due to the virus.

"I will come back and volunteer at the hospital. One of the best things during the trial was connecting with other patients," she said. "I always try to meet new cancer patients, introduce myself. Being a patient is different. I want to come up and talk with others who are going through the same things I went through."

Willey's patient experience also reconnected her with several people she'd gotten to know over the years, including **Loretta Muss**, the N.C. Cancer Hospital Patient & Family Advisory Council coordinator. And as soon as she is able, Willey will join Muss' Patient and Family Advisory Council to help other cancer patients on their journeys, something she's looking forward to doing.

"I didn't know there were so many blessings with cancer, but there are. For me, I feel like I'm a better person for having gone through and experienced what I did. It's what I tell my friends; you can survive it, you can live with it, be better for it, and you can be OK."

Doctor leads by example from bench to bedside

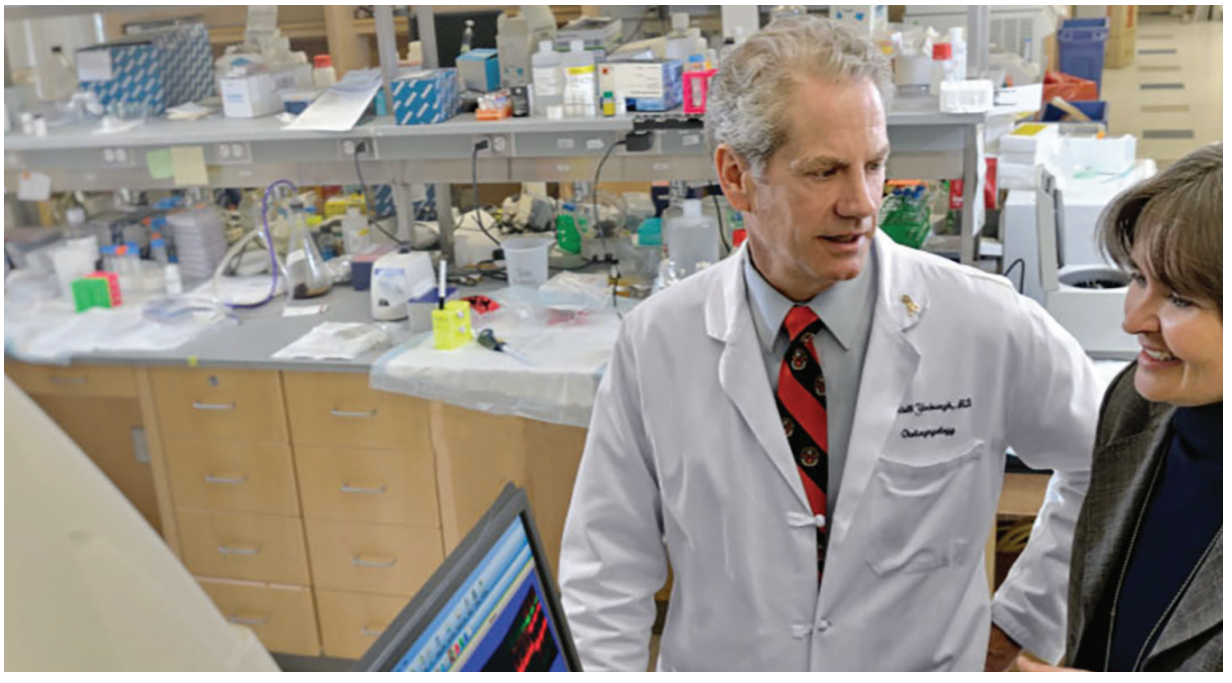
A natural curiosity and drive to discover new things led **Wendell Yarbrough, MD, MMHC, FACS**, on the path to becoming a distinguished head and neck cancer surgeon and researcher studying potential new cancer therapies.

Yarbrough is a two-time Carolina alumnus who attended the University of North Carolina at Chapel Hill as an undergraduate, and then earned his medical degree at the UNC School of Medicine.

He returned to his alma mater in 2018 as chair of the UNC Department of Otolaryngology/Head and Neck Surgery and the Thomas J. Dark Distinguished Professor of Otolaryngology/Head and Neck Surgery.

He transitioned into the role after serving as section chief of otolaryngology in the Yale University School of Medicine Department of Surgery and director of the Head and Neck Disease Center at Smilow Cancer Hospital. He was also co-director of the Virus and Other Infection-Associated Cancers Program at the Yale Cancer Center.

"I think what really keeps me going is that I love what I do — the people I work with, and the mission we serve — taking care of the people of North Carolina, and pushing the boundaries of research, all of that mixed into one," he said.



UNC Lineberger's Wendell Yarbrough, MD, MMHC, FACS, discusses lab work and research with a visitor.

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An early introduction to the lab

Growing up in Winston-Salem, Yarbrough said he was "always interested in science." He also "played pretty much every sport they had" in high school. He swam on the swim team and played baseball, football and basketball.

He said he received a few football scholarships to other colleges, but he joked he gave up his football career to attend UNC-Chapel Hill on the prestigious Morehead-Cain scholarship. He was always a Tar Heel fan growing up and joked that he "hated Duke, still do."

"Other than not being big enough, fast enough, or strong enough, I would have played football here," Yarbrough joked.

At Carolina, he worked in a molecular endocrinology lab. It was there that he first learned that a doctor could also conduct research.

"That's what set me up on that pathway," he said.

Yarbrough went to medical school at UNC, and then completed his internship in general surgery at UNC in 1990, and his residency in the Department of Otolaryngology/Head and Neck Surgery in 1994.

He was drawn to surgery early on in his medical training. "I loved the pace of it, I loved that the results were pretty immediate," he said. "Maybe I'm impatient; I don't know. It just really spoke to me."

Yarbrough's career path took him from serving as an associate professor in the UNC School of Medicine with dual appointments in the departments of Otolaryngology/Head and Neck Surgery and Biochemistry/Biophysics to Vanderbilt Ingram Cancer Center. At Vanderbilt, he rose to the position of Barry and Amy Baker Chair in Laryngeal, Head and Neck Research. During his time at Vanderbilt, he also earned a business degree.

"I like doing a lot of things," he said. After working at Yale, he returned to his alma mater.

"The caliber of the Department of Otolaryngology here and the collaborative nature of the people just made that a very easy decision for me," Yarbrough said. "The chance to come back here and be the head of this department was really an opportunity that I just couldn't pass up."

Continued focus on research

Early on in his training as a surgeon, Yarbrough said he felt an internal conflict because people told him "you can't be a surgeon and do research."

"I did surgery anyway and still continue to do research," he said.

As an undergraduate and later in medical school, Yarbrough studied genes in rabbits and rats involved in male sex development. He was part of a study that identified a genetic defect that resulted in animals that were genetically male but had female sex characteristics. The defect interfered with the rat's ability to respond to androgen hormones, which are critical for male sexual development.

"We found a mutation in the androgen receptor that causes testicular feminization," he said.

During his medical training, he worked in head and neck cancer research in a laboratory at GlaxoSmith-Kline in Research Triangle Park. Later as a fellow, he worked in a UNC lab studying a tumor suppressor protein called p16.

They found head and neck cancers with a mutation in the gene coding for the p16 protein. Without p16, the cells lacked a key braking mechanism to prevent them from moving forward toward cell division.

"Also, we found families in North Carolina that had a lot of head and neck cancer, and when we started tracking down what was going on in their families, we found that in their germline, they had defects in the p16 gene," he said.

The finding that set Yarbrough's career off was that one gene, called CDKN2a, codes for two different proteins – p16 and another called ARF – that both act as tumor suppressors.

"If you lose this one gene, you inactivate both (tumor suppressor proteins), so it's one of the most commonly defective genes in human cancer," Yarbrough said.

Yarbrough's research interests shifted to head and neck cancers associated with the human papillomavirus, or HPV. His research evaluated the molecular characteristics of HPV-linked head and neck cancers — work that has led to clinical trials for potential new treatments.

"By understanding the molecular characteristics, we have found some Achilles' heels of these tumors," he said. "Being able to take what I do in the lab, and have it come out in the clinic is terribly exciting."

Yarbrough said the effort to understand molecular characteristics of these cancers could help physicians tailor treatment for individual patients.

"It's exciting that we might be able to take these markers, look at patients' tumors before we treat them, and know which ones we need to treat less or more aggressively," he said.

Across his career, he's witnessed an "explosion" in scientific understanding of head and neck cancer.

Yarbrough said he's "never been more hopeful for cancer patients."

"The progress I see on clinical research and translational research is moving at a pace that is unbelievable," he said, with new drugs approved for head and neck cancer, and innovative clinical trials underway.

His wife, Glen, is a book editor who "puts up with a lot" and who "keeps me from being a total nerd," Yarbrough said. They recently adopted a dog, and have two sons, Miller and Gray.

research briefs

B-cell signals prevent treatment efficacy

Researchers identified the culprit that keeps cancer-killing immune cells from reaching pancreatic cancer tumors.

In a study in Cancer Immunology Research, scientists led by UNC Lineberger's **Yuliya Pylayeva-Gupta, PhD,** implicated B-cells, a type of immune cell, in the releasing of signals to keep T-cells from reaching pancreatic tumors to kill tumor cells.

Pylayeva-Gupta

From preclinical studies of pancreatic ductal adenocarcinoma in mice, researchers identified B-cells as the source of interleukin-35, or IL-35. Pylayeva-Gupta's lab found in previous studies that IL-35 is a broadly immunosuppressive signal for T-cells in pancreatic cancer models.

"We find that IL-35 produced by B-cells acts directly on cytotoxic T-cells and prevents their activation and migration to target the tumor cells," Pylayeva-Gupta said.

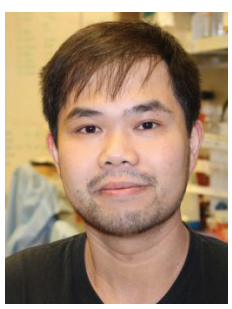
The study also reveals details on how IL-35 could be helping to suppress T-cell activity against tumors by initiating the action of STAT3, which is a transcription factor. Specifically, STAT3, once activated by IL-35, contributes to the T-cells' decreased migration and activation.

Researchers improve immune cell survival

Tumors can create a hostile environment for cancer-fighting immune cells. In a new study, UNC Lineberger researchers have developed a method for engineering immune cells to improve their survival and proliferation, even within a hostile tumor.

Researchers led by UNC Lineberger's **Gianpietro Dotti, MD,** report in the journal Nature Biotechnology, they have created a method for providing a stimulatory signal to super-charge cancer-hunting immune cells, called chimeric antigen receptor T-cells, (CAR-T) that have been genetically engineered to hunt and kill specific cancers. Their preclinical finding offers an alternative method to amplifying the modified T-cells while avoiding activating other immune cells that could cause off-target side effects.

Dotti



Xu

"Our study was trying to see if we could find an alternative strategy so that we could still provide the T-cells with proliferation signals, but also when and where we want them to proliferate, causing less of a global effect in terms of the cells' activities," said **Yang Xu, PhD,** postdoctoral research associate at UNC Lineberger and the study's senior author.

'Biological flashlight' controls cell function

UNC Lineberger researchers can illuminate cells from within using an embedded "biological flashlight," and then use the light to control the cell's function.

In a proof-of-concept study published in the journal ACS Synthetic Biology, researchers describe an advance in "optogenetics," a field in which scientists use light to control cells with light-sensitive proteins.

"Our technology revolves around the light itself – it's no longer external; instead, it's now generated within any cell wherever we put it," said UNC Lineberger's **Antonio Amelio, PhD,** assistant professor in the UNC Adams School of Dentistry. "We then used the technology to control existing optogenetic tools."

This technology works by using light to trigger proteins that are activated by light at certain wavelengths. Since then, Amelio said researchers have developed different tools to control living cells in the laboratory, and this has led to discoveries important to neurobiology, cancer biology, molecular biology and other fields.

Amelio

A challenge for this field, however, is the exterior light source used to control cells can damage living cells, the researchers said.

Parag-Sharma

"The problem, for the most part, has been that when you bring cells into play, and you're using really bright light from sources like lasers, then they can cause light-induced damage and kill cells over time. However, if your cells can self-illuminate, then there is minimal damage or phototoxicity, as we demonstrated in our study, "said **Kshitij Parag-Sharma**, the study's first author and a graduate student in the UNC School of Medicine Department of Cell Biology and Physiology.

Drug shows improved immune function

An early-stage clinical study investigating a method of boosting the body's defenses against two blood cancers found the drug pomalidomide could be safely added to conventional treatments, and help improve immune function.

UNC Lineberger researcher **Joshua Zeidner, MD**, led a phase I clinical trial evaluating the impact of adding pomalidomide to chemotherapy treatments for acute myeloid leukemia and myelodysplastic syndromes, or MDS. The results were published in the journal Leukemia.

They launched the study to try to reverse immune-suppressive factors that allow cancerous cells to escape the body's defenses.

Zeidner

The study involved 43 patients who were newly diagnosed with non-favorable risk acute myeloid leukemia or high-risk MDS in order to study both the safety of their strategy and the potential clinical benefits.

Researchers found in previous studies that cancer-killing immune cells are exhausted, and overpowered by the growth of other cells that suppress immune function after chemotherapy.

AYA patients see increased survival rates

The five-year survival rate for adolescents and young adults with cancer has significantly improved from 1975 to 2005 in the United States overall, but this was not the case for all cancers, according to a report in the Journal of the National Cancer Institute.

Nichols

"We are making improvements in survival for adolescents and young adults with cancer over time, but adolescents and young adults are a heterogeneous group, and we have to make sure that overall improvements don't hide the fact that there are specific cancer types that haven't had equivalent advances, and we need to do more," said UNC Lineberger's **Hazel B. Nichols, PhD,** the study's senior author.

The researchers identified substantial improvements in five-year mortality rates for adolescents and young adults (AYA) diagnosed with leukemia, non-Hodgkin lymphoma, Hodgkin lymphoma, central nervous system tumors, melanoma and other skin cancers, breast cancer or kidney cancer.

Honors and Awards

Honors

*The University Committee on Teaching Awards has selected **Adrienne Cox, PhD,** as a recipient of the Mentor Award for Lifetime Achievement.*

*The Lung Cancer Initiative of North Carolina (LCI) has awarded The Vicky Amidon Innovation in Lung Cancer Research Award to **Hongwei Du, PhD,** a postdoctoral fellow.*

*The Triangle Business Journal named **Stuart Gold, MD,** as one of its 2020 Health Care Heroes.*

***Sunil Kumar, PhD,** postdoctoral associate, was elected as a member of The Royal Society of Biology.*

***Emily Ray, MD, MPH,** was awarded a Young Investigator Award by the Conquer Cancer Foundation of the American Society of Clinical Oncology, in conjunction with the Breast Cancer Research Foundation.*

***Aziz Sancar, MD, PhD,** has been named the 2019 recipient of the Hyman L. Battle Distinguished Cancer Research Award.*

Awards

*The Prostate Cancer Foundation has awarded $225,000 across three years to **Catherine C. Coombs, MD,** to study whether genetic mutations that accumulate in the blood over time are linked to worse outcomes for prostate cancer.*

The Breast Cancer Alliance has awarded **Pengda Liu, PhD,** *a 2020 Young Investigator Grant. The two-year award of $125,000 will support work to investigate a specific therapeutic target in basal-like breast cancer.*

Kirsten Nyrop, PhD, *received a $50,000 award from the Integrated Approach to Breast Health Equity Competitive Grant Program, a collaboration between the American Cancer Society and Pfizer.*

COVID-19 fund aids patients, families, health care workers

With the onset of COVID-19, **Loretta Muss**, the N.C. Cancer Hospital Patient & Family Advisory Council coordinator, worried about the toll fighting the virus would take on the hospital's doctors, nurses and staff. That concern was shared by patients, as well as members of the Patient and Family Advisory Council. It was fortunate coincidence that a consortium of restaurants in Carrboro, North Carolina reached out to Muss' husband, Hy, the Mary Jones Hudson Distinguished Professor of Geriatric Oncology and director of geriatric oncology at the hospital, and said they were interested in helping, so she asked if they could do a meal for the hospital's workers on limited funds.

Initially, Muss received funds from the Patient & Family Advisory Council, and, thanks to the efforts of some of the N.C. Cancer Hospital's student lay navigators, UNC-Chapel Hill's Interfraternity Council and Panhellenic Association also donated money, as did some local churches and the Muss' neighbors. The COVID-19 Response Fund will continue to fund the effort once the other sources have been exhausted.

With these resources at her disposal, Muss was able to go from her initial thought of providing 50 dinners to serving more than 200 lunches to health care workers in the N.C. Cancer Hospital once a week. She said it's the best way to help the coworkers she's missing on a daily basis and to help keep the local economy solid.

"This is love," she said. "I know so many of the staff; I work with them, establish relationships with them, and my husband works with them. These are very scary times. We feel like they're going to be spoiled once a week, and we're going to continue to do this until [COVID-19] is in our rearview mirrors," she said.

Loretta Muss

Cindy Rogers

Muss is also a talented baker and has been making desserts to go with the meals during her time at home. In addition to bringing her checks, friends and neighbors have been gifting Muss with bags of King Arthur flour, her preferred brand for baking.

"I will find 25 pounds of flour on my doorstep because people want to help, and they want to help those on the frontlines," she said.

Addressing personal patient needs

Cindy Rogers, JD, UNC Lineberger's Patient Assistance coordinator, has found COVID-19 is making the lives of many cancer patients and their families even more challenging. Rogers helps patients and their families address financial burdens they may experience while undergoing treatment, and she said COVID-19 has created additional barriers and hardships for vulnerable, low-income populations.

"With so many of our families experiencing loss of income, the demand for assistance with basic needs such as rent or mortgage, utilities, car repair and transportation are high," Rogers said. "With children home from school, there is an increased need for food at home. With the closing of SECU Family House and Ronald McDonald Houses, we've had increased demand for lodging."

COVID-19 has also changed the way Rogers interacts with patients and the distribution of benefits that come from UNC Lineberger fundraising for patient support and the CCSP.

"Because of the need for social distancing, gas cards are being mailed to patients, rather than given in person. I am meeting patients by telephone to assess eligibility and need. Finally, to accommodate increased needs, the annual spending limit per patient has been increased," Rogers said.

Rogers is keeping track of patients facing problems related to COVID-19 and plans to use COVID-19 Response funds to help provide those patients the support they need as she learns of their issues. She said she is also hoping to work with the Patient and Family Resource Council to use funds for a food or grocery card gift program in the future.

COVID-19 *continued from page 1*

that we're prepared. That's why the UNC Lineberger building was the right place to do it. We not only study viruses that cause cancer directly but also viruses that affect overall cancer treatment mortality."

With support from the COVID-19 Response Fund, Dittmer's lab has been upgraded to biosafety level 2 plus, which allows for a protected, secure and safe space to work with COVID-19 samples. Dittmer said they've created a high containment infrastructure with pharmaceutical grade freezers and upgraded centrifuges designed to deal with airborne viruses. His team also has undergone training to work in such a space.

Together with **Melissa Miller, PhD,** director of UNC Medical Center Microbiology and Molecular Microbiology Laboratories, Dittmer and his team are running coronavirus tests, and they are determining the viral sequence in the clinical samples taken from UNC Health patients who test positive for the virus, something they couldn't do in a normal lab setting.

"We do that as a backup for the clinical labs and to support research studies at UNC," Dittmer said. "It's part of a wider quality control effort at UNC. By looking more in depth, we can assure you that the current tests really work well, and they do."

Dittmer is going a step further, as well, sequencing the RNA in the viral samples, and contributing the findings to a worldwide database of SARS-CoV-2, such as NIH's Genbank and the Global Initiative on Sharing All Influenza Database (GISAID). This database has allowed countries around the world to determine where the virus came from and how it's affecting patients.

Though focused on what the team can do to help COVID-19 patients now, Dittmer is also looking to the future, using the sequencing data to help prepare for the second wave of coronavirus and for any new viruses on the horizon.

"We are sequencing people who are at UNC hospitals with respiratory symptoms and sequencing every piece of nucleic acid in the swab and asking what are the bacteria, what are the viruses, what's new there?" he said. "It will allow us to find the next new virus if it's out there."

Dittmer said clinical trials will continue for the next two years at least, so they can gather more data to stay on top of the next possible outbreak. Using the same technology scientists currently use to analyze cancer biopsies, they will take a more thorough look at respiratory secretion samples and compare the results with information already in the database.

"Clinical tests test for only eight known viruses," Dittmer said. "We would look for the other 100 plus viruses that are out there, and see if there's anything remotely similar, whether it's a respiratory coronavirus or an influenza strain."

As Dittmer continues to gather data on N.C. COVID-19 cases, he and his team are preparing for what might come next with the virus.

"The more you know, the better you can design the vaccines and drugs," Dittmer said. "And we would also notice if there's a major change happening. That's what we're preparing for. We will get a second wave, and we will be able to compare those viruses to the first wave and see how they've changed."

Dittmer said UNC Lineberger is an ideal place to conduct this research, and credits a steady stream of resources to the team's continued success, including bioinformatics data gathered during sequencing and the continued emphasis and support for basic science research.

"The reason we can do all this is because for the past five years we've been doing basic virus and cancer research," he said. "The reason we can go so quickly is that the people who work on this have been doing this for a long time and are highly trained. Even five years ago, we didn't know we would need those skills."

COVID-19 Response

Our doctors and staff are keeping patients and families in the loop on the North Carolina Cancer Hospital's response to COVID-19. Check out the following videos for more information.

- ***Keeping UNC Cancer Care patients safe during the COVID-19 crisis:***
  go.unc.edu/cancer-care-COVID-19
- ***Support for cancer patients and their caregivers during the COVID-19 pandemic:***
  go.unc.edu/cancer-patient-support-COVID-19
- ***Mantener a los pacientes de UNC Cancer Care seguros durante la crisis de COVID-19:***
  go.unc.edu/b3BSa

calendar of events

July

11th CarrieOn Golf Tournament, Raleigh

September

5th Victory Ride to Cure Cancer, Raleigh

13th Golfing for the Gals, Browns Summit

For more information about these events and other UNC Lineberger news, visit www.unclineberger.org, or follow us on

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***Above**: Tyler Butler-Figueroa performs for UNC Lineberger's Stuart Gold, MD, and the crowd at the Lineberger Club event.*
***Right**: From left to right: Kristi Geib, CPNP, Shelley Earp, MD, UNC Lineberger director, Rameses, Tyler Butler-Figueroa, Kisua Butler-Figueroa, Adam Butler-Figueroa and Gold.*

Lineberger Club event features AGT finalist Tyler Butler-Figueroa

Leukemia is not something anyone would wish for, but for Tyler Butler-Figueroa, his cancer opened up doors for him he never thought would be possible. Tyler, now 11, competed and was a finalist on "America's Got Talent," something he and his family never expected when he was first diagnosed.

Tyler was four years old when he was diagnosed with leukemia. Under the care of Stuart Gold, MD, chief of pediatric hematology oncology at the North Carolina Cancer Hospital, the clinical home of UNC Lineberger, Tyler started chemotherapy. His treatment lasted nearly five years, but today, Tyler shows no sign of disease and is thriving as a young, talented violinist.

Tyler recently spoke at the annual Lineberger Club dinner and basketball event, crediting Gold and his team for taking care of him and his family during his cancer journey.

"UNC has been there for my family every step of the way," Tyler said. To help lift spirits, Tyler would often perform in the clinic for other young patients who were going through the same ups and downs he experienced during treatment.

Following his remarks at the dinner, Tyler performed for the crowd with a rendition of Callum Cott's "You are the Reason," playing while walking among the tables. A true showman, Tyler played the last notes of the song kneeling in front of Gold as a tribute to the care he received at UNC Lineberger.

"I am a perfect example of what your generosity does," Tyler said. "Dr. Gold and his team are part of the reason I'm still standing."

Annual golf tournament celebrates 22 years of support, raises $16,000

The Polar Challenge golf tournament was held in March. Proceeds from this annual event benefit Dina's Dynasty Ovarian Cancer Fund, which supports ovarian cancer research at UNC Lineberger.

The tournament was held at the Chapel Hill Country Club. This year, the event raised $16,000.