THE MAGAZINE OF VANDERBILT-INGRAM CANCER CENTER

Momentum

FALL
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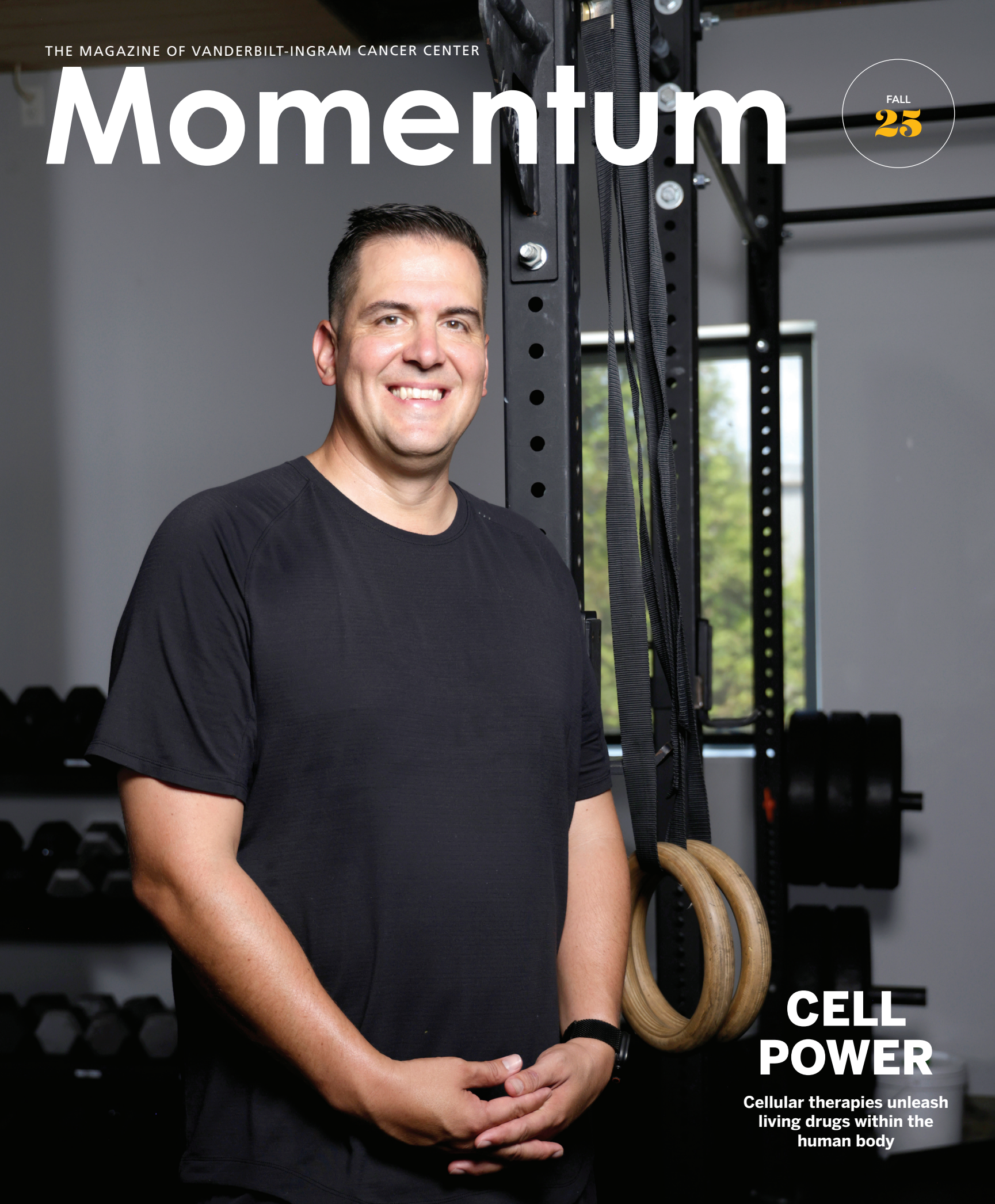

CELL POWER

Cellular therapies unleash living drugs within the human body

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On the cover:
Kyle Stephens is back enjoying life after an innovative treatment with a cellular therapy that made his immune system recognize and kill cancer cells.

Contents

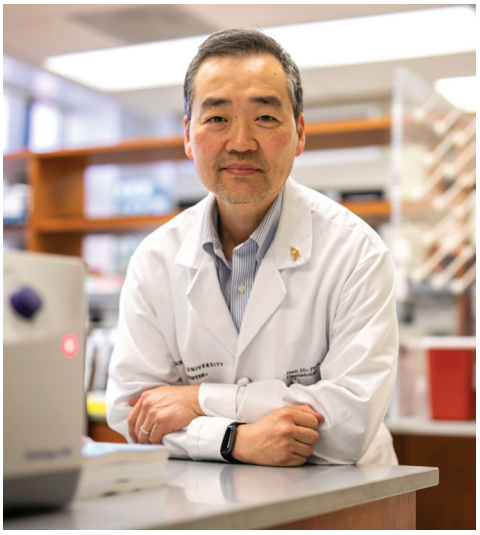
Fall 2025

Features

Departments

From the Director

BEN HO PARK, MD, PHD



Cellular therapies have emerged as a transformative catalyst in cancer care. Advancements have made them life-extending treatments for patients who had run out of options, and, for many people, they have provided durable remissions — potentially cures. Their approvals are expanding for a wider array of cancers.

What is cellular therapy? Basically, it is a living drug developed from human stem cells or immune cells. Cellular therapy can be a powerful immunotherapy when immune cells are reprogrammed to recognize and attack cancer cells with chimeric antigen receptor T cells (CAR-T). Cellular therapy can supercharge white blood cells to bombard melanoma tumors when tumor-infiltrating lymphocytes (TILs) are isolated and expanded to target the cancer cells.

Vanderbilt-Ingram Cancer Center is a leader in cellular therapies both nationally and internationally. Our hematologists and oncologists were among the first in the United States and the world to offer new advancements through clinical trials. Their expertise is sought by other researchers as they have presented their data and discoveries at international conferences. Our front-line clinicians are highly skilled and knowledgeable in taking care of our patients and implementing innovations to improve the treatment experience. Vanderbilt-Ingram has consistently had an outstanding record in stem cell transplantation outcomes and survival rates, and this has also led to our success in this relatively new area of cellular therapies as they share many commonalities. One particular area that Vanderbilt-Ingram leads in is the administration of cell therapies in the outpatient setting. Typically, patients are hospitalized for one month while they undergo treatments for cell therapies. Vanderbilt-Ingram was the first to demonstrate that cell therapies could be safely administered as an outpatient treatment, and for us, this has become our standard of care. This allows patients to have a much better experience, and can save resources for hospitals, e.g., making more inpatient beds available. It also allows for patients who live farther away to come and receive their treatments here but then go back home where they can be closely monitored using new wearable technologies. This is truly aligning with our vision of democratizing personalized health care for all.

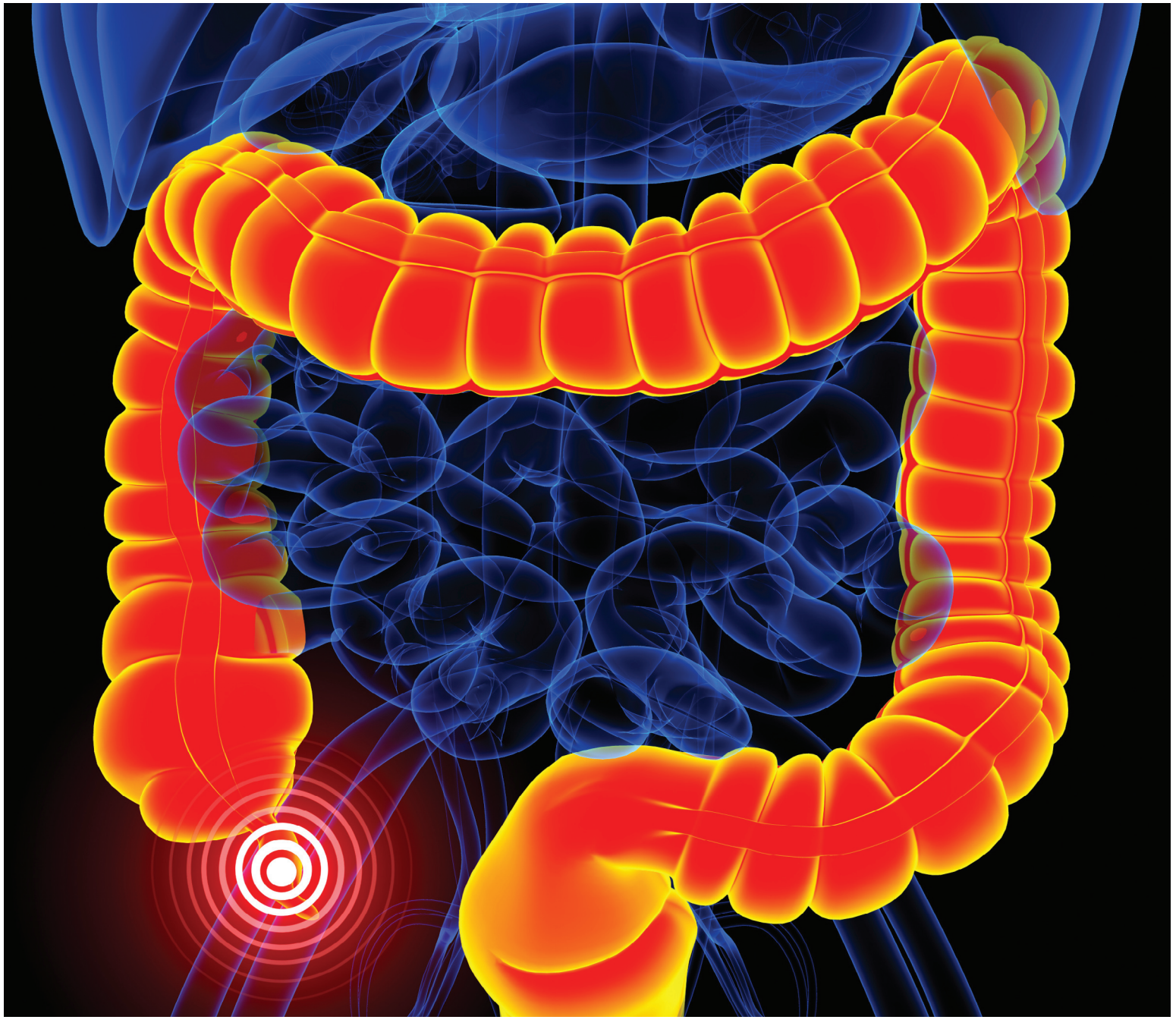
This issue of *Momentum* showcases our cellular therapy advancements. The cover story, "Cell Power," gives an overview of our cellular therapy programs and details how they have helped patients. Another story describes how our physicians have shared their expertise, enabling VA Tennessee Valley Healthcare System to be the Veterans Affairs' only certified CAR-T center. Veterans from across the nation come to Nashville to receive CAR-T treatments. There are two question-and-answer articles that explain our recently added TILs therapy as well as the role of the translational scientist in improving cellular therapies. We highlight one of the many researchers who has benefited from an Ambassadors Grant and is investigating the noninherited mutations in stem cells that can be precursors to cancer. Other features celebrate our front-line clinicians, including a nurse who has performed more than 20,000 bone marrow biopsies and a nursing team that has shown how virtual reality can make infusion appointments less stressful for our patients.

> "Vanderbilt-Ingram Cancer Center is a leader in cellular therapies both nationally and internationally."

For decades, cancer doctors were limited to the "three pillars of cancer treatment": surgery, radiation and chemotherapy. While these three pillars continue to be integral to cancer care, patients now have more options, including targeted therapies, immunotherapies, and other new treatment modalities. Cellular therapies are at the axis of these advancements. They can function as both immunotherapies and targeted therapies. We're excited about what the future holds and are committed to doing all we can to expand the effectiveness of cellular therapies for more types of cancer and make them available to everyone who needs them.

THANKS!!

ADOBE STOCK



An alarming trend

Study shows sharp increase in appendix cancer for Generation X and millennials

CASES OF APPENDICEAL cancer tripled for Americans born from 1976 to 1984 and quadrupled for those born from 1981 to 1989, according to a study published June 9 in the *Annals of Internal Medicine*. The study compared chronological data in five-year intervals from the National Cancer Institute's Surveillance, Epidemiology and End Results Program, using 1941 to 1949 as the baseline. The lead author, Andreana Holowatyj, PhD, MSCI, assistant professor of Medicine at Vanderbilt University Medical Center and Vanderbilt-Ingram Cancer Center, said the findings reveal the need for increased awareness about appendiceal cancer from both clinicians and the public as well as more research to determine the reasons for the sharp spike in incidence. ■

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AT-HOME URINE TEST CAN BE ACCURATE FOR PROSTATE CANCER

Researchers at Vanderbilt University Medical Center and the University of Michigan have shown that a simple at-home urine test for prostate cancer screening is highly accurate. The exciting new results, published in *The Journal of Urology*, build upon a prior VUMC study of prostate cancer screening that required a digital rectal exam.

The results are important because this could enable at-home testing and increased access to testing for patients undergoing telehealth care or living in remote areas.

Traditional prostate cancer screening with PSA (prostate-specific antigen) testing and biopsy has been shown to lead to unnecessary procedures and overdiagnosis of low-grade cancers, according to lead author Jeffrey Tosoian, MD, MPH, assistant professor of Urology and director of Translational Cancer Research for the Department of Urology.

"The test is highly accurate for ruling out the presence of clinically significant prostate cancers — those that merit treatment — so that patients with a negative test result can confidently avoid having to undergo MRI or biopsy," Tosoian said.

"In the current study, this noninvasive urine test would have allowed patients with an elevated PSA to avoid 34%-53% of unnecessary biopsies."

MyProstateScore 2.0 (MPS2) urine test is a noninvasive test used to help identify high-grade prostate cancers that need early detection and treatment by analyzing 18 genes associated with prostate cancer. ■

Patients can ring the bell at any time

Protocol changed after family request

From his infusion chair, Matt Duckworth would clap and yell "woohoo" each time he heard another cancer patient ring the bell to mark the completion of chemotherapy treatment, even though he knew he would never get that opportunity.

On Friday, April 25 — seven months after his death — the bell pealed loudly at the Vanderbilt-Ingram Cancer Center infusion clinic as a plaque was unveiled in his honor and the announcement was made that patients receiving palliative chemotherapy would also get to ring the bell going forward.

Duckworth was in the prime of his life at age 41, working as director of Population Health Operations for Vanderbilt Health Affiliated Network and doting on his three dogs with his wife, Suzanne, when he was diagnosed in 2020 with Stage 4 gastroesophageal cancer that had metastasized to his liver. Although the chemotherapy didn't cure his cancer, the treatments did extend his life for four years.

"Matt had infusions weekly, and as we were sitting in the infusion room for hours at a time, we would hear the bell ring, and we would hear everybody clapping," said Suzanne Duckworth. "He would clap and yell, 'Woohoo!' He just emitted such a positive vibe and aura. I would sit there and think, 'He's never going to get that because he has terminal cancer.' Now, that thought might have come into his brain, but you would never know it because he never said it."

She asked Vanderbilt-Ingram about adding a plaque, and a ceremony was held in Matt's memory to mark the occasion.

Suzanne Duckworth stated, "This is for you, Matt," and rang the bell.

His mother, Betsye, stood nearby wiping away a tear. On the plaque that had just been unveiled was a poem written by his sister, Jill Comfort.

"When Suzanne shared her idea about a new plaque, I deeply appreciated what she said, how when Matt heard the bell, he felt happy for those who rang it," said Julie Bulger, manager of Patient- and Family-Centered Care. "It is rung traditionally at the end of treatment, but many patients may never have that opportunity. This thought comes from a lot of places, not only from Matt, but Suzanne articulated it so beautifully. I believe this is going to resonate with many people.

"The bell can be rung at any time. It doesn't have to be the last day of treatment. It can be rung because you're having a bad day, and you're fighting, and it's hard. Or you have achieved a different milestone. You want to ring that bell because it's going to mean something for you, and you want to feel uplifted," Bulger said. ■

Suzanne Duckworth rings the bell in honor of her husband, **Matt Duckworth.**

SUSAN URMY

DONN JONES

Celebrating 15 years of leadership

Portrait honors Jennifer Pietenpol

JENNIFER PIETENPOL, PHD, Chief Scientific and Strategy Officer and Executive Vice President for Research at Vanderbilt University Medical Center, was honored with a portrait on Jan. 14 in recognition of her 15 years of leadership as director of the Vanderbilt-Ingram Cancer Center (2007-2022). The portrait was unveiled during a celebration event at the Annette and Irwin Eskind Family Biomedical Library and Learning Center.

During her tenure, Vanderbilt-Ingram experienced remarkable growth, including a 100% increase in research funding, a more than 30% rise in newly diagnosed or first-treated cancer patients, and a 160% expansion in inpatient visits. She successfully led the center through three consecutive renewals of its National Cancer Institute Comprehensive Cancer Center designation, each time earning exceptional merit ratings.

For the past eight years, Pietenpol — who holds the Brock Family Directorship in Career Development — has led VUMC's scientific, technological and research strategy, overseeing a $940 million sponsored research portfolio that has grown 8%-10% annually. She works closely with VUMC executive and senior leaders to develop and implement high-impact strategic initiatives across the institution.

Pietenpol earned her PhD in cell biology from Vanderbilt University in 1990 and, after completing a fellowship at Johns Hopkins University, returned to Vanderbilt as a faculty member in 1994. Her research focuses on breast cancer and the p53 family signaling network. By integrating molecular genetics with bioinformatics analysis of high-dimensional genomic data, she has advanced the subtyping of triple-negative breast cancer, contributing to clinical breakthroughs for patients with this challenging disease.

A leader in national cancer research and policy, Pietenpol was a presidential appointee to the National Cancer Advisory Board for a six-year term and a member of the Blue Ribbon Panel advising former Vice President Biden's National Cancer Moonshot. She is a fellow of the American Association for the Advancement of Science and a fellow of the American Association for Cancer Research Academy. ■

VOLO FOUNDATION GRANT SUPPORTS STUDY

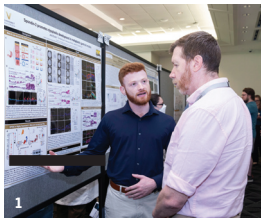
A grant from VoLo Foundation will augment federal funding for the Southern Environmental Health Study, an initiative to determine whether environmental exposures are contributing to cancer cases in the region.

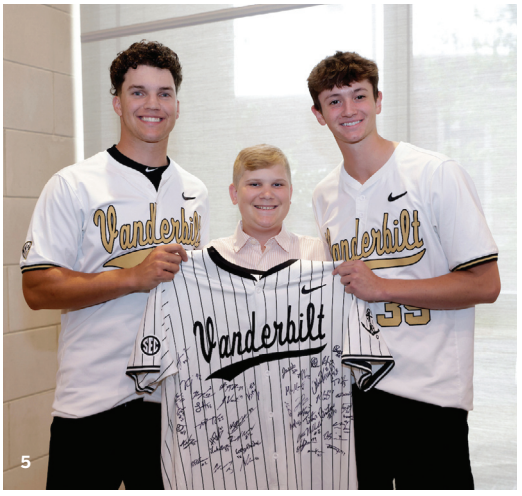
The study received its initial funding from the National Cancer Institute. A grant from VoLo Foundation — a private nonprofit organization dedicated to accelerating global impact through science-based solutions, education enhancement, and health improvement initiatives — will allow investigators to recruit additional participants and conduct methylation- and proteomics-based biological aging assays to check for biomarkers of early disease risk.

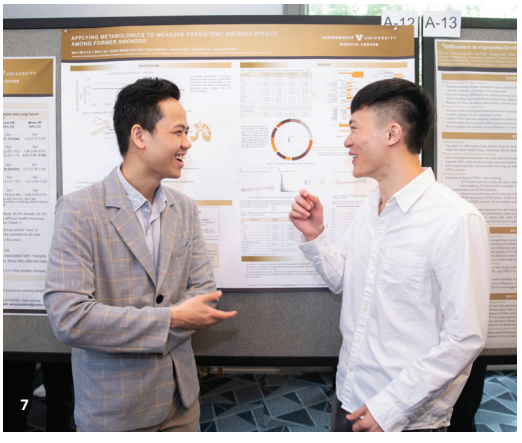
On cancer incidence and mortality maps, some of the highest rates in the country appear in the southern U.S., but whether environmental exposures are a contributing factor has not been scientifically determined. The study is a long-term cohort investigation that will follow participants for at least 10 to 20 years.

"Supporting the Southern Environmental Health Study aligns with our mission to advance data-driven solutions that can lead to healthier, more resilient communities. This research has the potential to uncover possible links between environmental exposures and chronic diseases," said David Vogel, co-founder and chief scientist of VoLo Foundation.

Vogel and his wife, Thais Lopez Vogel, formed VoLo Foundation in 2014. ■







Scientific Symposium

Event celebrates trainee achievements

The Vanderbilt-Ingram Cancer Center 26th Annual Scientific Symposium, held April 22, focused on the theme "Artificial Intelligence in Cancer Research and Clinical Care." The event also highlighted the achievements of trainees with a research poster competition and the announcements of graduate and undergraduate students of the year.

Pictured here:

1. Jared Rhodes discusses the findings of his research with Alain Gobert, PhD.

2. Xiaopeng Sun, PhD, co-graduate student of the year, speaks about his research studying blood cell markers related to immunotherapy outcomes.

3. Pictured left to right are Christopher Willliams, MD, PhD, associate director for Research Education at Vanderbilt-Ingram, Michael Robinson, MD, Guochong "Damon" Jia, PhD, postdoctoral scholar of the year, Katie Brown, PhD, co-chair of the Scientific Symposium, Candace Grisham, MS, PhD, co-graduate student of the year, Xiaopeng Sun, PhD, co-graduate student of the year, Jared Rhodes, co-chair of the Scientific Symposium, and Ben Ho Park, MD, PhD, director of Vanderbilt-Ingram.

4. Joshua Bauer, PhD, talks with Nourhan Aboomar about her research poster.

5. Cancer patient Easton Reeder (center) who has undergone surgery and chemotherapy for pilocytic astrocytoma — a type of brain tumor — shared about his experiences living with cancer. He received a jersey signed by the Vanderbilt Commodores baseball team, including pitchers Cody Bowker, left, and Connor Fennell.

6. Candace Grisham, MS, PhD, co-graduate student of the year, speaks about her research involving treatment challenges for tumors that develop within the membranes surrounding the brain and spinal cord.

7. Lili Liu, PhD, (right) and Huy Le Duc, PhD, chat in front of Duc's research poster.

PHOTOGRAPHS BY **DONN JONES** AND **SUSAN URMY**

Virtual Reality

Experience gives infusion clinic patients relaxing escape

STORY BY **TOM WILEMON**
PHOTO BY **ERIN O. SMITH**

Cancer patients receiving chemotherapy infusions benefited from a virtual reality experience that took them on tours of the canals of Venice, Italy; the Taj Mahal in Agra, India; and the Amazon River in Ecuador.

The distraction therapy decreased their pain and stress levels by statistically significant measures, according to a study by Vanderbilt-Ingram Cancer Center researchers published in the *Clinical Journal of Oncology Nursing*. The patients also exhibited lower heart rates, reported high satisfaction with virtual reality and experienced no feelings of cybersickness.

The responses of the patients were compared with those in a control group who engaged in the typical activities of chemotherapy patients, such as watching television, reading or talking with appointment companions.

The patients in the virtual reality arm of the study had a median heart rate of 71 compared to 75 for the control group. When asked to report pain and stress levels on a 10-point scale, patients in the virtual reality arm reported a range of 0-5 for stress compared to 0-10 for those in the control group. The overall estimated difference for stress was 1.5 points, while the difference for pain was 0.7.

"Vanderbilt University undergraduate students approached us about offering virtual reality to patients on a volunteer basis in 2018," said Cody Stansel, MSN, RN, NE-BC, administrative director of Nursing at Vanderbilt-Ingram, the study's corresponding author. "After several months it became clear that it was a huge patient satisfier. We became curious as to whether anyone had studied the impact of virtual reality on cancer patients undergoing chemotherapy and conducted a literature review. We found that there were relatively few studies, and most used outdated technology. We decided to conduct this research in order to expand the scope of knowledge of this subject and determine whether this technology could enhance the lives of our patients."

The authors noted that although the effectiveness of virtual reality has been demonstrated among diverse patient populations, few studies exist evaluating it for adult cancer patients. This was a clinical trial that the patients embraced.

"Patients were generally excited about the experience," Stansel said. "Throughout the entire study only a couple of patients declined to participate when offered a virtual reality session."

The researchers noted that improvements in virtual reality technology had rendered early research obsolete. The Vanderbilt-Ingram study evaluated 90 patients, with 45 experiencing virtual reality distraction therapy and 45 in the control group. The age range was 20-82 for patients.

The virtual reality experience lasted 12 minutes. The experience brought early learning moments for the researchers.

"Our first few participants watched a different set of videos than the majority of the cohort," Stansel said. "One of the videos took place in Africa, and there were several scenes that we determined might skew our results. For example, there was a scene that depicted an elephant sanctuary that followed the story of a baby elephant that was rescued after poachers had killed its mother. One patient responded on the affect survey that his guilt level had increased, and he commented that he felt guilty that people were poaching the elephants. Another patient noted that a scene high up in the air overlooking the African Savannah triggered their fear of heights. These incidents combined with other comments led us to file an amendment to the institutional review board and change the videos we were presenting to the patients. We ended up with some unusable data from those first few patients, but we ended up with enjoyable videos that offered patients a calm and relaxing diversion."

The research team received no funding support for the study, but the headsets were loaned from Vanderbilt University. The 90 participants in the study were recruited and evaluated from November 2021 through December 2023.

Nurses can easily incorporate virtual reality as a distraction therapy because the headsets are "widely accessible, relatively affordable and simple to use," the authors stated.

Other authors are Alexander McLeod; Shubham Gulati, MS; Catherine Ivory, PhD, NI-BC, NEA-BC; Mary Dietrich, PhD, MS; Heather Murray; Nathan Zang; Krish Shah; Hari Patel; Kristin Pegram, RN, OCN; and Wendy Howell, MSN, RN, OCN. ■

The nurse virtual reality study team included, from left, Wendy Howell, MSN, RN, OCN; Kris Pegram, RN, OCN; Cody Stansel, MSN, RN, NE-BC, OCN, CMSRN; Rachael Smith, BSN, RN, OCN; and Janet Murrian, RN, OCN. Lauren Hutchison, BSN, RN, OCN, is not pictured.

Heather Jackson, PhD, APRN, FNP-BC

The Point of Care Network has named Heather Jackson, PhD, APRN, FNP-BC, America's top nurse practitioner for pain management. Jackson treats patients at the supportive and palliative oncology clinic at Vanderbilt-Ingram Cancer Center and is an associate professor in Clinical Nursing at Vanderbilt University. The Point of Care Network, the nation's largest community of advanced practice clinicians, each year recognizes outstanding nurse practitioners and physician assistants at the apex of their medical specialties. One winner is selected for each category. The 2024 honorees were recently announced during National Nurse Practitioner Week. Jackson, who is a nationally recognized pain clinician, has served as the administrative director of Advanced Practice at Vanderbilt-Ingram since 2019.

Soraida Chavez, CCMA

Soraida Chavez, CCMA, medical assistant at the Vanderbilt Benign Hematology Clinic, knows her job description includes looking out for everyone in her community — patients and colleagues alike. Whether through her positive attitude, attention to detail or her natural ability to read what patients need, Chavez is a champion for her patients and tirelessly supports clinical staff. For her work, Chavez received a Credo Award during the January 2025 VUMC Leadership Assembly. "She makes being in clinic a joy," said one of the people who nominated her for a Credo Award. "She is motivated, completing tasks quickly and always offering to help with any additional clinic needs. She is a great communicator. She interacts with all team members effectively and respectfully and has excellent patient rapport. Many of my patients have commented on her kindness and the ease that she puts them in."

Tracey DeWire, MSN, ACNP-BC

Tracey DeWire, MSN, ACNP-BC, had a 16-year career in sales before deciding to become a nurse practitioner, a decision inspired by her best friend's cancer diagnosis. She's kept that inspiration burning in the 15 years of her second career. Her patients have benefited from the kind of compassion that typically comes only from a friend. DeWire spends extra time learning about her patients and takes notes to remember key details about their lives, so that she can meaningfully engage with them during their visits at the Vanderbilt Breast Center. Her patients know they are remembered and appreciated on a personal level. It shouldn't be a surprise that not just one patient, but four of them, nominated her for a Patient and Family Choice Award. She is the 2024 recipient of the award in the ambulatory care category, and one of six VUMC employees chosen to receive a Patient and Family Choice Award.

Molly Baldwin, BSN, RN

Molly Baldwin, BSN, RN, who works at the Vanderbilt Breast Center at One Hundred Oaks, is one of the latest DAISY Award winners at VUMC. Here's what a patient, who nominated her for the honor, said, "She made me feel like I was the only patient she had to care for. Molly went above and beyond what I could have or would have ever expected. Her genuine concern for me made all the difference, and I'm ever so grateful for her. She made coming to my follow-up appointment feel like coming to visit family! I couldn't wait to get there to meet this lovely, knowledgeable, kind lady in person! Molly very carefully and professionally removed my drainage tubes (I didn't even feel them come out), and she made sure that all my questions and concerns were addressed as well. The entire team gave me exceptional care, and I simply can't say enough good about you all! I want someone to know that Molly went above and beyond and certainly deserves to be recognized! She's making this world a better place! With all my heart, thank you!" The DAISY Award is a recognition for extraordinary nurses who exemplify compassion toward patients and families. VUMC distributes the award in partnership with The DAISY Foundation.

Kimberly Dahlman, PhD

Kimberly Dahlman, PhD, associate professor of Medicine in the Division of Hematology and Oncology, has been elected to the board of directors of the International Association of Medical Science Educators (IAMSE). Dahlman, who is the assistant director of Cancer Research Training and Education at Vanderbilt-Ingram Cancer Center, began serving her three-year term upon the closing of the association's annual conference on June 17. She serves as co-director of the third- and fourth-year undergraduate medical education curriculum at Vanderbilt University School of Medicine and as co-director of the Research Education Core of the Meharry-Vanderbilt-Tennessee State University Cancer Partnership. She is also director of the VERTICAL post-baccalaureate program, the V-EXCEL undergraduate cancer research program and the VISTO medical student research program at Vanderbilt-Ingram. Nationally, she is president of the Association of Biochemistry Educators. With more than 2,000 members, the IAMSE's mission is to advance health profession education through teacher development and to ensure that the teaching and learning of medical science continues to be firmly grounded in foundational sciences and the best practices of teaching.

ADOBE STOCK

Drug shows safety, efficacy for precancerous stomach lesions

An early-stage clinical trial, supported by the Department of Defense, has demonstrated that the targeted cancer drug trametinib shows potential as an interventional therapy to reprogram precancerous gastric lesions, potentially preventing them from becoming malignant, and that it can be administered safely. The results of the Phase 1 trial involving 15 patients, which were published recently in *Gastroenterology*, were pleasantly surprising, said James Goldenring, MD, PhD, the Paul W. Sanger Professor of Experimental Surgery and professor of Cell and Developmental Biology. The primary goal of this trial was to evaluate whether a low-dose, limited duration treatment of two weeks with trametinib would be safe for patients at risk for developing a second cancer after having undergone resection of a Stage 1 gastric cancer. The drug also showed promise that it could be the first therapeutic intervention against precancerous lesions in the stomach.

Fluorescence imaging can improve outcomes in head and neck cancer surgery
A study published June 18 in the journal *JAMA Surgery* demonstrated the benefits of using fluorescence-guided imaging to assess margins in head and neck cancer. Researchers found that leveraging data collected both during surgery (in vivo) and after the tumor's removal (ex vivo) can help guide surgeons in achieving a negative margin in cancer resection. To assist in ensuring a negative margin in a deep resection, surgeons can use fluorescence imaging techniques. Mapping tumors after resection can provide data on how close the margins are to the surface of the deep resection, and intraoperative in vivo fluorescence imaging can reveal areas of residual disease in the tumor bed. In combination, the information provided by both methods of fluorescence imaging can guide further examination and sampling to help achieve fuller resection of the deep margin.

Lower health literacy increases mortality risk for cancer patients
Cancer patients who scored lower on health literacy screening experienced higher all-cause mortality, according to a study published March 15 in the journal *Cancer*. The study followed Vanderbilt-Ingram Cancer Center patients for a median of 3.1 years who had taken the Brief Health Literacy Screen. Patients who had high health literacy on the screening lived 9.4 months longer compared to those with low health literacy (score of nine or lower). The 9,603 patients in the retrospective cohort study were diagnosed with either prostate, lung, breast, renal, colorectal, brain, head and neck, bladder, pancreatic, liver, sarcoma or gastric cancer.

Low blood cell counts drive cancer in explosive blood disorder
One person in 10 over the age of 70 will experience an explosive, clonal growth of abnormal blood cells, called clonal hematopoiesis of indeterminate potential, or CHIP, that increases the risk of blood cancer and death from cardiovascular, lung and liver disease. The risk of blood cancer differs significantly, however, depending upon whether patients with CHIP also develop cytopenia (low blood cell count). An analysis of genetic sequencing data from more than 34,000 people over a 17-year period by researchers at Vanderbilt University Medical Center has found that persistent cytopenia appears to be a critical step in the progression of CHIP to blood cancer. For patients with CHIP who developed cytopenia, the risk of progression to blood cancer was 10 times higher than it was for patients without cytopenia — a 1-in-200 chance per year versus 1 in 2,000, the researchers report in the June 2025 issue of *The Lancet* journal, *eClinicalMedicine*.

Presurgery consults using 3D models improve shared decision-making and reduce anxiety
A study published June 3 in *JAMA Network Open* determined that presurgery consults with 3D models made patients feel they played a bigger role in decision-making and that their anxiety levels decreased. The patients were scheduled for partial or complete colon and/or rectal resections for colorectal cancer, diverticulitis or inflammatory disease. Fifty-one patients participated in the study, with 28 receiving consultations using the 3D models and 23 receiving conventional consultations. The patients in the 3D arm of the study reported a significantly higher involvement in shared decision-making and significantly reduced anxiety levels compared to the other patients.

Q|A

Personalized cellular immunotherapy

Vanderbilt-Ingram launches tumor-infiltrating lymphocyte therapy for advanced melanoma

PHOTOGRAPH BY **ERIN O. SMITH**

Douglas Johnson, MD, MSCI, professor of Medicine, is clinical director for melanoma and associate director for Translational Research at Vanderbilt-Ingram. He holds the Susan and Luke Simons Directorship.

Q What is tumor-infiltrating lymphocyte therapy?

A It's a therapy where a patient's tumor is removed, and white blood cells in the tumor — tumor-infiltrating lymphocytes, or TILs — are isolated, "supercharged" and given back to the patient so they can hopefully eliminate the tumor. It's a little bit like CAR-T therapy, but in CAR-T therapy the white blood cells are engineered to specifically target the cancer, and with TILs there's no genetic engineering. TILs are already in the tumor, recognizing and targeting something in the tumor; the idea is to boost their number and activity.

Q How many TIL therapies are there, and what kind of cancer can be treated with TIL therapy?

A There is just one approved TIL therapy — lifileucel; it's a first-in-class treatment. Right now, it's only approved for advanced melanoma. It's the first approved cellular therapy for a solid tumor.

Q Which patients with melanoma are eligible for lifileucel?

A Patients with metastatic melanoma who have already been treated with other available therapies, including immunotherapies and targeted therapies for a particular mutation, are eligible. The patients go through a battery of tests to make sure their heart, lung and kidney function are all in good shape. And they must have a tumor that can be safely removed by a surgeon, and that's at least two-thirds of an inch in size.

Q What happens during TIL therapy?

A After the tumor is surgically removed, it gets sent to a company that isolates the TILs and treats them with growth factors to expand and "supercharge" them. That takes three to four weeks. When the TILs are ready, we give the patient high-dose chemotherapy similar to a stem cell transplant or CAR-T therapy. Then the patient is admitted to the hospital to receive the TILs followed by three days of high-dose interleukin-2, a growth factor. If everything's OK after that, they can leave the hospital. In most places, patients are hospitalized from the start of chemotherapy up to about 30 days after treatment. We minimize time in the hospital by monitoring patients daily in the clinic and giving them wearables to track heart rate and other vitals. This is a real strength of Vanderbilt-Ingram Cancer Center.

Q What are the side effects of TIL therapy?

A The TILs themselves have basically no side effects. The side effects come from chemotherapy, which can cause low blood counts, GI toxicities and hair loss. The high-dose interleukin-2 is also a very potent drug that causes low blood pressure and fever and can strain the liver and kidneys. We monitor patients very closely while they're getting those treatments.

Q How effective is TIL therapy?

A About a third of patients are responding to treatment, which is not as high as we'd like. But when patients do respond, the response is very often durable, and patients are effectively being cured. It's a complicated and toxic treatment, but when it works, it can be absolutely transformative.

Q What's next for TIL therapy?

A Theoretically, this is the kind of treatment that can be used for any kind of cancer. Clinical trials of TILs for lung and cervical cancer are the furthest along. There are also efforts to get TILs from biopsies or from blood and to modify the TILs so the high-dose interleukin-2 isn't required. I think the current version of TIL therapy is version 1.0, and I think we're going to have many different versions over time. There's a potential future where a majority of solid tumor patients are able to get these therapies and have them be curative in a percentage of patients. ■

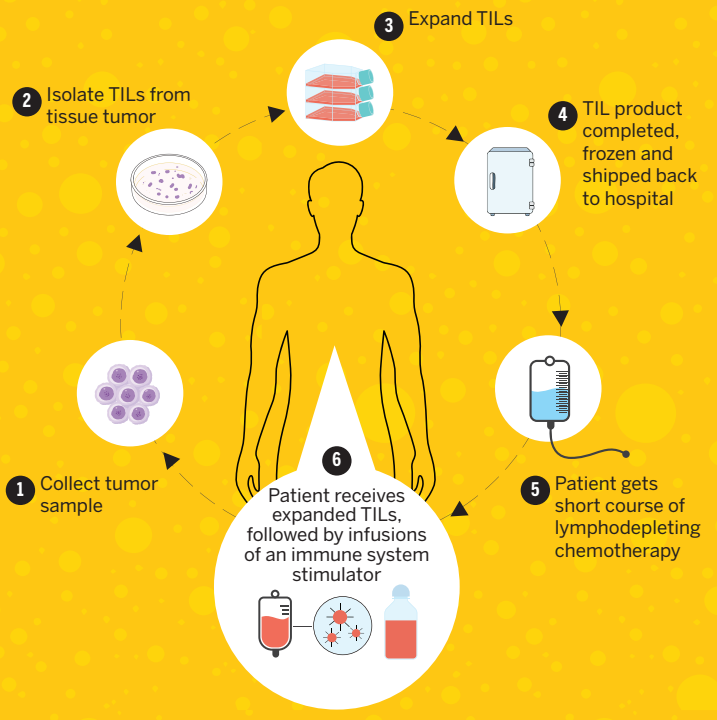
"When patients do respond, the response is very often durable, and patients are effectively being cured."

— DOUGLAS JOHNSON, MD, MSCI

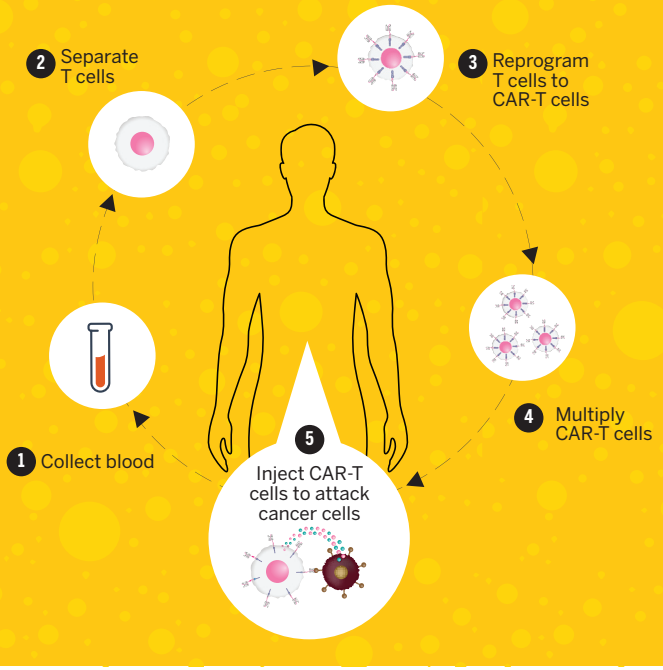
TYPES OF CELLULAR THERAPIES

There are many types of cellular therapy. Vanderbilt-Ingram has one of the nation's best stem cell transplant centers based upon procedure volume and patient outcomes. The center was the first in Tennessee to offer CAR-T (chimeric antigen receptor T cell) therapy, which reengineers a patient's immune cells to recognize and attack cancer. Another cellular therapy Vanderbilt-Ingram recently added is TIL (tumor-infiltrating lymphocyte) therapy for advanced melanoma. TIL became the first cellular therapy approved by the Food and Drug Administrations for solid tumors in February 2024.

Tumor-Infiltrating Lymphocyte (TIL) Therapy



CAR-T Therapy



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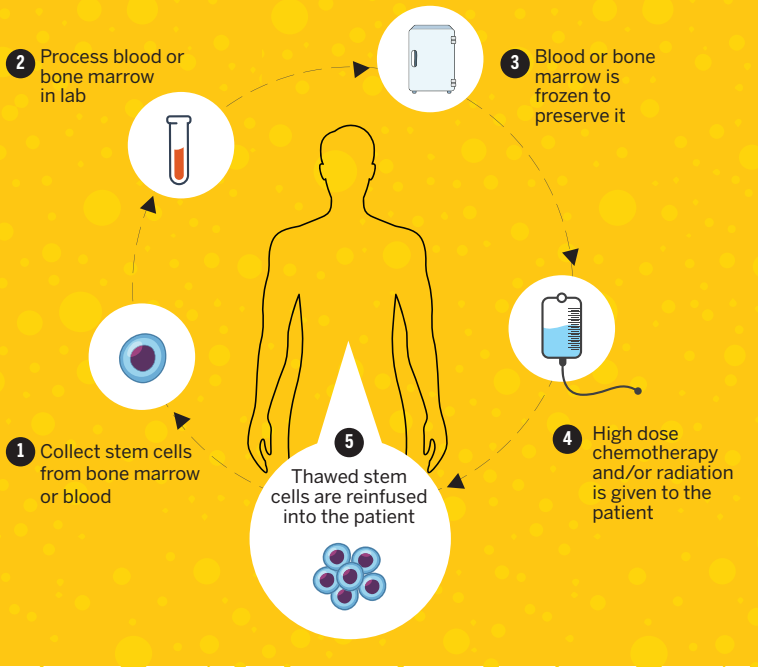
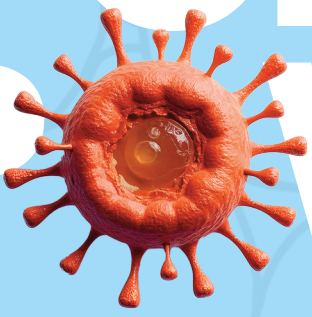


Kyle Stephens

CELL POWER



Cellular therapies unleash living drugs within the human body

Kyle Stephens thought his days were numbered. His cancer had recurred after intensive chemotherapy, and he feared that he would not be around for his three young children or his wife.

He was in his early 40s in 2022 when he was diagnosed with Stage 4 non-Hodgkin lymphoma that had spread throughout his abdominal cavity. Chemotherapy had put it into remission, but follow-up scans in 2024 showed that the cancer had come back. A year after undergoing therapy with a cellular therapy called CAR-T, the cancer is now gone, and Stephens is running half-marathons and hiking mountains.

STORY BY **TOM WILEMON** • PHOTOGRAPH BY **DONN JONES**

Stephens had never heard of CAR-T, which is shorthand for chimeric antigen receptor T-cell therapy, until his oncologist at Vanderbilt-Ingram Cancer Center, Nishitha Reddy, MBBS, MSCI, professor of Medicine, recommended the immunotherapy that reengineered his immune cells to recognize and attack the cancer cells. Many patients have achieved durable remission with CAR-T, and Stephens is the 200th patient at Vanderbilt-Ingram treated with it.

Vanderbilt-Ingram has for decades been a leader in cellular therapies and continues to be at the vanguard in this field of oncology, which entails transforming human blood cells into either healing therapies with stem cell transplants or cancer eradicators with immunotherapies like CAR-T. The array of cellular therapies is expanding, and Vanderbilt-Ingram is pioneering these treatment advancements for patients in Tennessee and beyond.

"All in all, the CAR-T is a lot easier than the chemotherapy," Stephens said. "The rounds of chemotherapy really wear you out. With the CAR-T, it was a one-time deal."

CAR-T is a form of immunotherapy where a patient's T cells, which are part of the immune system, are harvested, reengineered in a laboratory to recognize and attack cancer cells, and then infused back into the patient's body. The Food and Drug Administration has approved seven CAR-T therapies, which are made from a patient's own T cells, for lymphomas, leukemias and multiple myeloma. Other clinical trials are underway to potentially expand their approvals, and Vanderbilt-Ingram is offering them to patients who meet the medical protocols. Vanderbilt-Ingram was the first center in Tennessee to administer CAR-T to patients, and it treats more patients with this immunotherapy than any other provider in the state.

Stephens' doctor, Olalekan Oluwole, MBBS, MPH, associate professor of Medicine, is one of a team of physicians at Vanderbilt-Ingram specializing in CAR-T and other cellular therapies. He has been an investigator on numerous clinical trials that have led to treatment approvals by the FDA, including two trials for which he presented data on patient outcomes at the European Hematology Association meeting in June 2025 in Milan.

He and colleagues have established Vanderbilt-Ingram as an international leader in cellular therapies.

The first CAR-T approval by the FDA occurred in 2017, and the therapy has proven to be a durable treatment for patients who respond. Vanderbilt-Ingram was offering CAR-T to patients even before the approval through clinical trials.

The first Tennesseans treated were four very ill lymphoma patients who had run out of treatment options. All four of the patients had a clinical response to the treatment, and three were cured, Oluwole said.

"The fact that we can now say that many who responded to CAR-T therapy are cured of their lymphoma is truly remarkable," Oluwole said.

Ongoing clinical trials are testing whether it can be used for solid tumors in addition to blood cancers. Other research seeks to identify which patients will respond to the therapy and develop strategies to enable responses in more patients. Several initiatives are underway by pharmaceutical companies working with Vanderbilt-Ingram and other top cancer centers in the U.S. to develop "off-the-shelf" CAR-T, where T cells would be reengineered from donors instead of patients, which would expedite the manufacture of the immunotherapy and make it readily available, allowing patients to start treatment sooner.

Bhagirathbhai Dholaria, MBBS, associate professor of Medicine, presented interim results from one off-the-shelf CAR-T clinical trial in September 2024 at the 21st International Myeloma Society Annual Meeting in Rio de Janeiro. He described the results as "remarkable" in the ongoing clinical trial for patients with relapsed or refractory multiple myeloma who had run out of treatment options.

CAR-T is one of many breakthroughs that the cellular therapy program has made over several decades to

DONN JONES

Stephens' doctor, **Olalekan Oluwole, MBBS, MPH**, associate professor of Medicine, is one of a team of physicians at Vanderbilt-Ingram specializing in CAR-T and other cellular therapies.

Translational scientists aim to improve cellular therapies

Vanderbilt-Ingram Cancer Center is committed to doing more than treating patients with the latest advancements in cellular therapies. Its physician-scientists are focused on expanding their use for more types of cancer and improving response rates among patients.

Andrew Jallouk, MD, PhD, assistant professor of Medicine, is a translational scientist committed to hastening the progression of laboratory discoveries into better treatments for cancer patients. After finishing an undergraduate degree in biomedical engineering and chemistry from Vanderbilt University, he then obtained a dual MD/PhD degree from Washington University in St. Louis followed by a clinical fellowship at MD Anderson Cancer Center in Houston, where he conducted clinical and laboratory research on the use of engineered cellular therapies for lymphoma. He was recruited to Vanderbilt-Ingram in 2023.

Q: Can you describe the role of a translational scientist in the medical realm?

A: Historically, there have been clinical investigators that run clinical trials, and there have been physician-scientists who work in the lab. That's been great, but what this field needs are people who can speak both languages and really bring the two together. That's what we are trying to do.

Q: What's the next step for the advancement of cellular therapies?

A: With cellular therapies, we take the immune cells out of the patient, reprogram them and then put them back in. What's really unique about this is the manufacturing step. If the treatment doesn't work for some patients or is not working as well as we would like, we can figure out what's going on there and then make tweaks during the manufacturing process to improve the therapies. What fascinates me about this technology is the bench-to-bedside (science lab progression to clinical use) and back to bench perspective. We're putting these cellular therapies into patients, and we can see what's happening — what is going well and what is not going well; what are the toxicities and how can we avoid these toxicities. We have a lot of ability to then feed that information back into the lab, optimize our manufacturing, optimize our patient selection and really try to make things better.

Q: What you've described is CAR-T therapy or chimeric antigen receptor T cell therapy. Isn't that primarily for blood cancers?

A: There are no CAR-T cells approved for any solid tumors right now. There are other therapies called TIL therapies or TCR therapies. One of those, TIL, has just been approved for melanoma, and there's a TCR therapy that's been approved for synovial sarcoma. They all fall within the realm of immune therapies, where you're using cells to fight cancer. The issue with that historically has been that solid tumors have a hostile tumor microenvironment, so it's been hard to develop immunotherapies that overcome that.

Q: How much does your training as a biomedical engineer play into what you do?

A: I think it helps in terms of speaking both languages. I have a lot of great scientific training and give a lot of credit to my mentors, both in undergraduate and graduate school and throughout my training. The engineering background has really made it easy to pick up the concept of cellular engineering and the technologies that are associated with that. The PhD work that I did gave me a lot of experience and insight into various laboratory techniques, so it's made it easier to keep doing what I'm doing on the laboratory end even when I have responsibilities on the clinical end as well.

extend the lives of cancer patients. In 2007, Darrell Tyler of Knoxville, Tennessee, was diagnosed with chronic myelogenous leukemia. By the time he was diagnosed, the cancer had progressed to the point that his elevated white blood cell count, a hallmark of the disease, had skyrocketed. His Vanderbilt-Ingram physician estimated that he had about three to six weeks to live, but the doctor offered him hope with a new drug, which would not be a cure but could stabilize his white blood cell levels.

The drug worked. The next step was a stem cell transplant, which would require finding a matching donor. A stem cell transplant is a potentially lifesaving procedure for blood cancers, but patients must endure a conditioning regimen with chemotherapy that depletes their bone marrow of normal and diseased cells to make room for healthy transplant cells — a process that results in myelosuppression and poses infection risks. There's also the potential for other complications, including graft-versus-host disease, which occurs when donor T cells begin attacking the recipient's healthy tissue. Sometimes finding a matching donor is a patient's biggest obstacle to overcoming cancer. Matches are made according to human leukocyte antigens (HLA), cell surface proteins the immune system uses to determine which cells belong in a patient's body and which ones don't. Typically, a

Vanderbilt-affiliated cellular therapy programs reaccredited

The cellular therapy programs at Vanderbilt-Ingram Cancer Center, Monroe Carell Jr. Children's Hospital at Vanderbilt, and the VA Tennessee Valley Healthcare System have received reaccreditation from the Foundation for the Accreditation of Cellular Therapy (FACT).

Founded in 1995, FACT establishes standards for high-quality medical and laboratory practice in cellular therapies. FACT is a nonprofit corporation co-founded by the International Society for Cell and Gene Therapy and the American Society for Transplantation and Cellular Therapy for the purposes of voluntary inspection and accreditation in the field of cellular therapy.

"FACT is an internationally recognized accrediting body for hospitals that offer stem cell transplant and cellular therapy, and recognition by FACT indicates that the accredited institution has met the most rigorous standard in every aspect of cellular therapy," said Adetola Kassim, MBBS, MS, professor of Medicine and clinical director of the Adult Stem Cell Transplant Program. "This covers the entire spectrum of stem cell therapy from clinical care to donor management, cell collection, processing, storage, transplant, administration and cell release."

The Vanderbilt and VA Tennessee Valley Healthcare System programs received accreditation notification April 14 after on-site inspections in October 2024. The accreditation is effective for three years.

close relative can be a donor, but not in Tyler's case. He was matched with someone in Switzerland but then disappointed when that donor didn't pan out.

Tyler had one option left — stem cells that had been saved from a newborn baby's umbilical cord that might match his HLA type. He wound up being one of the first patients at Vanderbilt to receive a cord stem cell transplant. It worked. In the years since, he's continued to run his farming equipment business, share his story of how his faith got him through his illness and enjoy time with grandchildren. He continues to be monitored by Adetola Kassim, MBBS, MS, professor of Medicine and clinical director of the Adult Stem Cell Transplant Program. Having lost a stepdaughter and a brother to cancer, Tyler knows how lucky he is. He recently donated funding to Vanderbilt-Ingram for stem cell research in honor of them.

Another Vanderbilt-Ingram blood cancer patient, Bhagya Samudrala, who has homes in Detroit and Nashville, also faced the uncertainty of finding a match. Her brother, who lives in India, was a perfect match. Her family and caregivers navigated the logistics of getting a bone marrow transplant from him. She and her family did a testimonial video encouraging more people to sign up for the National Marrow Donor Program (NMDP). When a patient doesn't have a family member who is a match, the NMDP assists with a database of 42 million potential donors, but more people with varied ethnic backgrounds are needed. Matching donors are more likely to be of similar ethnic backgrounds because HLA genes are inherited. Donor registries aren't diverse enough to ensure every patient finds a fully matched donor.

Vanderbilt's cellular therapy program originated in 1979 when its first patient received a stem cell transplant from a donor. The Vanderbilt-Ingram Stem Cell Transplant Program now ranks among the best in the nation for survival rates among comparative programs, according to the annual report for the Center for International Blood and Marrow Transplant Research.

The program continues to innovate as other cellular treatments emerge, such as tumor-infiltrating lymphocyte (TIL) therapy for melanoma and T-cell receptor (TCR) therapy for soft tissue sarcoma. Vanderbilt-Ingram has 10 physicians who provide cellular therapies and is investing in research, having recently recruited a translational scientist to focus on hastening laboratory discoveries to treatment improvements.

Stephens, who lives in the Old Hickory neighborhood of Nashville, said he's grateful to be near a cancer center with an internationally respected cellular therapy program.

Bhagya Samudrala considers herself lucky to have received a stem cell transplant and advocates for people to sign up as donors through the National Marrow Donor Program. Scan the QR code above to learn more about joining the registry.

DONN JONES

Kyle Stephens has recently rejoined CrossFit, completed a half-marathon and hiked the Half Dome in Yosemite with his family.

"The hard part about this experience has been going through it with my wife and three kids, who are 10, 8 and 4," he said. "They've had to go through all this as well. My wife took me to all my appointments and was by my side all the time. I am thankful for her and just having family. I am fortunate to have a good support system. When I had talked to other folks and told them my cancer had come back, the reaction in their eyes was 'Oh, my God, the cancer came back. This guy is cooked.' When I see people now, they'll ask, 'How are you?' and tell me they've been thinking about me.

"Since completing the treatment and going into remission, I've gone back to CrossFit, completed a half-marathon and just hiked the iconic Half Dome in Yosemite. It's interesting to see people's reactions now, and I hope my experience can provide hope to anyone in a similar situation." ■

Children benefit in multiple ways from cellular therapy advancements

Cancers that were once almost always fatal for children are now curable because of advancements in cellular therapies that Vanderbilt-Ingram Cancer Center pediatric oncologists and hematologists have introduced to Tennessee.

The advancements have included improvements for HLA (human leukocyte antigen) matching with stem cell donors, better medicines for infection prevention, new therapies for graft-versus-host disease (GVHD) and CAR-T therapies.

"We were one of the first sites in the state to be able to use CAR-T to treat our patients, and that's really been a big game changer for some of our patients who had relapsed or refractory leukemia that would have otherwise been fatal," said Carrie Kitko, MD, Ingram Professor of Pediatric Oncology and medical director of the Pediatric Stem Cell Transplantation Program.

The program has established itself as a leading innovator in preventing and treating GVHD, which occurs when donor immune cells begin attacking the stem cell recipient's healthy tissue. Vanderbilt-Ingram is part of an international consortium called MAGIC that has developed risk-stratified treatments according to both GVHD symptoms at presentation and biomarkers, or certain proteins in their blood, to predict patients who are more or less likely to respond to treatments for GVHD.

"We have had several clinical trials to potentially improve outcomes for patients with GVHD. If you're a low-risk patient, we've been able to offer trials where we avoid steroids, which are normally what we use to treat our GVHD patients, but steroids have lots of side effects that can be quite unpleasant," Kitko said.

"You can identify those low-risk patients that don't need steroids, and you can use a less toxic therapy. And then for the high-risk patients, if we know that they're unlikely to respond to steroids, why wait for them to fail on steroids. We have been able to offer some of these studies to both pediatric as well as adult patients."

Kitko is the senior author of a study published in 2024 in *The New England Journal of Medicine* that led to the Food and Drug Administration approving a new drug for recurrent or refractory chronic GVHD. Patients who were given the drug, axatilimab, had an overall response rate of 74%.

"Now, patients have access to more drugs to treat chronic GVHD, which is really a very morbid condition for many of our patients," she said. "Moderate to severe chronic GVHD really impacts their quality of life and their ability to do normal day-to-day activities."

HIDDEN WOUNDS

Veterans with blood cancers receive treatment at the VA's only certified CAR-T center

STORY BY **DANNY BONVISSUTO** • PHOTOGRAPH BY **DONN JONES**

In 2016, Johnnie Lee Weaver visited his general practitioner in Paducah, Kentucky, seeking relief for a sore shoulder. When his X-rays came back, he was referred to an oncologist. "That's when the red flags went up," he said.

After additional testing, Weaver was diagnosed with multiple myeloma, a blood cancer in which plasma cells in the bone marrow become cancer cells. He was sent to Vanderbilt University Medical Center to determine the type and returned later for a stem cell transplant. Over the past nine years, he has undergone three changes in regimens. When the last one stopped working, Weaver, now 79, was evaluated for and met the criteria to receive chimeric antigen receptor T (CAR-T) cell therapy at VA Tennessee Valley Healthcare System's Nashville VA Medical Center — Veterans Affairs' only certified CAR-T center.

A wound you can't see

When he was 21 years old, Weaver enlisted in the United States Army after completing the ROTC program at Murray State University. After completing basic training, he spent two years in Germany and was subsequently deployed to Southeast Asia when the Vietnam War began. He served in various roles, including rifle company commander, division operations officer, and adviser, after his division returned to the United States and he stayed in Vietnam.

"I didn't realize it at the time, but that's where I was exposed to Agent Orange," he said of the chemical herbicide used to clear vegetation that has been linked to many health conditions. "It shows up several years later and is what caused me to have multiple myeloma."

Weaver counts fatigue and exhaustion as the most debilitating symptoms of his disease, plus the symptoms he carries over from his original stem cell transplant, including chemotherapy-induced neuropathy and pain that "permeates" his body.

"My situation is the same as someone who was wounded and 100% disabled in Vietnam," said Weaver, who retired as a captain. "This is a wound you can't see, but it's a wound that inalterably changes my life."

The VUMC-Nashville VA connection

Because VUMC is in the Nashville VA's backyard, and the organizations share medical personnel, there has always been a natural collaboration between the two.

The first stem cell transplant at the Nashville VA was performed in 1995. Over the past 30 years, veterans have received either autologous (using the patient's stem cells) or allogeneic (using donor stem cells) transplants to treat lymphomas, myelomas and leukemias.

In 2016, when Weaver was diagnosed with multiple myeloma, Vanderbilt-Ingram Cancer Center became the first cancer center in Tennessee to provide CAR-T cell therapy as part of a clinical trial, and, a year later, became one of a few cancer centers in the United States authorized to deliver the new immunotherapy.

"CAR-T cell therapy uses a patient's own T cells. T cells are immune cells which are then reengineered to learn how to treat the underlying disease. Currently, we use CAR-T to treat some lymphomas, leukemias and multiple myeloma that have not responded to other treatments," said Salyka Sengsayadeth, MD, medical director of the Stem Cell Transplant and Cellular Therapy program at the Nashville VA Medical Center. "We collect their T cells, and they're sent to a manufacturer that reengineers the cells to attack the lymphoma, myeloma or leukemia cells.

Then we infuse those reengineered CAR-T cells back into the patient to treat their disease. This is the cutting edge of medicine treatment, and where we think the future of cancer treatment is headed."

In late 2019, VA Tennessee Valley Healthcare System performed its first CAR-T infusion at its Nashville VA Medical Center — the first CAR-T treatment to take place at a VA hospital.

Covering the cost of CAR-T

CAR-T treatment involves an integrated multidisciplinary team and advanced laboratory software. A 2018 donation from The Journey Home Project — a foundation created by the late country music legend Charlie Daniels and music industry executive David Corlew that helps veterans transition from service to civilian life — funded software, monitoring and other administrative costs associated with CAR-T treatment.

"I have a tremendous amount of respect for what Vanderbilt does, both personally and professionally through The Journey Home Project," Corlew said. "We were happy to help make this treatment possible for veterans and look forward to continuing to support this fundamental cause."

Support comes in many forms: Every veteran who meets the criteria for CAR-T treatment receives it at no cost at the Nashville VA. Their travel and lodging for multiple visits are fully covered as well, which is vital because veterans come to Nashville from all over the country for this treatment. And the referral process and time to treatment are often much quicker for veterans than civilians.

"Patients have to be referred by their local oncologist or hematologist. Thanks to telemedicine, of which the VA was a pioneer, we can evaluate patients quickly," Sengsayadeth said. "If we get a referral for a patient from Texas and see they need CAR-T cell therapy, we usually evaluate them within the first week, sometimes within days, because everything is integrated within the VA. This speeds everything along, including the time to collect T cells and the time to treatment, which is critical for patients where time is of the essence. We work hard to get patients here as quickly as possible, especially since we're the only VA in the country that performs this treatment."

"CAR-T cell therapy uses a patient's own T cells. T cells are immune cells which are then reengineered to learn how to treat the underlying disease."
– Salyka Sengsayadeth, MD

Another factor in the speed with which veterans get their CAR-T cell therapy is due to the lack of a financial clearance process. Adetola Kassim, MBBS, MS, director of the Vanderbilt-Ingram Cancer Center Stem Cell Transplant and Cellular Therapy Program, sees it firsthand every day.

"I work on both sides of the aisle. On the commercial side, these are expensive therapies and a lot of hoops to jump through based on various insurance plans," Kassim said. "But at VA, once it's approved, almost every veteran who needs it can get it. It's impressive. I've seen situations on the commercial side where some insurance companies put you through the wringer before approving you. But at VA, once the transplant group agrees the veteran can benefit, it's smooth sailing after that."

The value of hope

Without having to worry about mounting costs, insurance issues and managing travel for himself and his wife, he can focus on the matter at hand, which is

JOE HOWELL

ERIN O. SMITH

Adetola Kassim, MBBS, (left) director of the Adult Stem Cell Transplant Program at Vanderbilt-Ingram Cancer Center

Salyka Sengsayadeth, MD, (right) medical director of the Stem Cell Transplant and Cellular Therapy Program at the Nashville VA Medical Center

dealing with the effects of treatment and testing and staying alive as long as possible.

Because each person and blood cancer is different, there's no framework for how long CAR-T therapy extends life, only that it buys more time.

"When you're told that you have cancer, and it's an incurable but manageable cancer, you're trying to figure out, what does all that mean? I'm still working on that," Weaver said. "But one of the things it does when you get started with the treatments, and a lot of times the treatments are very unpleasant, is that they give a person hope — and that's one of the things we don't recognize or talk about enough.

"The medical staff at VA and Vanderbilt are really fantastic. They've been so good to me, kind, thoughtful and reassuring. Whether it's the doctors or any of the other nurses, they've all been so kind and generous with their time and seem to sincerely care about what's going on."

During the infusion and treatment phase, Weaver spent several days in the hospital for observation and returned almost daily for blood tests (anywhere from four to 34 vials), results and injections to boost his white or red blood cell count. If his numbers indicate progress, he'll undergo a bone marrow biopsy, which involves injecting a syringe through his pelvis and into the bone to sample the bone marrow. When he's not needed at the hospital, he rests.

"When I have a good day, I try to do as much as I can," he said. "When I'm not having a good day, I try to rest up and recoup as well as I can to have another good day. I'm always moving back and forth between good days and bad days."

Since 2019, Nashville VA has performed almost 100 CAR-T cell therapies on veterans — and Weaver is grateful to be one of them.

"I've been exposed, let's say to the possibility of death quite a few times, and it's something I think, I hope, that I've reconciled with," Weaver said, reflecting on his time in Vietnam and his current battle. "I see myself as a spiritual being in this body; I understand there's a beginning and end for this body; and I try to do the next best thing while I'm in it and live with that. Mortality doesn't frighten me — at least it hasn't to this point. I have a wife, four children and 10 grandchildren, and want to try to be with them as much as I can — and be with them so that they remember me in a very positive way, despite being ill." ■

VA's first bloodless stem cell transplant leads to veteran's cancer remission

Earlier this year, VA Tennessee Valley Healthcare System (TVHS) performed the first-ever bloodless autologous stem cell transplant in the VA system.

Keith Cody, a Marine Corps Veteran, walked out of TVHS in remission and caught a flight home to California, something he thought would not be possible.

"I already feel much better. They've told me that I still need more time to get my energy back, but I do feel much better already," Cody said.

As Cody's cancer progressed while he was in California, he underwent extensive chemotherapy and suffered from its side effects. With this, he decided to ask more about bloodless transplants that could improve his quality of life.

Stem cell transplants treat blood cancers like leukemia, lymphoma, multiple myeloma and germ cell cancers. The patient's own stem cells are collected during chemotherapy when bone marrow releases them into the peripheral blood. These cells are then concentrated and transplanted to replace the diseased bone marrow.

Typically, stem cell transplants can cause a significant drop in blood count due to the impact on the bone marrow, which produces blood cells. This often requires blood or platelet transfusions as part of replacement therapy.

However, Cody opted for a bloodless transplant due to personal reasons.

Bhagirathbhai Dholaria, MBBS, associate professor of Medicine in the Division of Hematology and Oncology at Vanderbilt University Medical Center, had previously performed the procedure at Vanderbilt. Taking this knowledge, he trained the TVHS team to follow similar protocols after receiving Cody's request.

"[For the bloodless autologous stem cell transplant], we don't give any red cell transfusions, platelet transfusions or any plasma product. And we use a set intervention before patients come to Nashville to optimize their blood count, such as iron infusion," said Dholaria, TVHS hematology attending physician.

After opening its stem cell processing lab, TVHS became the only VA in the nation with a comprehensive stem cell transplant program, including apheresis, processing and infusion labs housed internally. Following the Seattle VA Medical Center, TVHS is the second VA to start a stem cell transplant program.

In addition, no VA facility has ever performed a bloodless transplant until now. With Cody becoming the first patient in April 2025, there was measurable success.

"Number one, did it achieve myeloma control? Because that's the whole reason we are doing this procedure. And in this case, Mr. Cody is in a complete remission, one month after stem cell transplantation," Dholaria said.

Even though this was the first VA procedure, the process was very easy and comforting, according to Cody.

"After talking with him (Dholaria) ... the level of confidence that they had in this procedure was kind of what made it a little easier for me to decide to make the journey and come here ... the way they conveyed it to me, I felt confident in the care I was going to get," Cody said.

TVHS is also the only VA that performs CAR-T cell therapy, a type of immunotherapy used to treat certain types of blood cancers like lymphoma and leukemia. This therapy allows the immune system to target and attack cancer cells, and TVHS receives referrals from all over the country, including Puerto Rico.

– by Abby Woodruff

Seeds for Science

VICC AMBASSADOR GRANTS HAVE WORLDWIDE IMPACT

When Alexander Bick, MD, PhD, associate professor of Medicine, came to Vanderbilt University Medical Center in 2020, he was an early-career physician-scientist with big plans for human genomics research using novel genetic sequencing technologies.

Like many of his peers, he was eager to probe questions and unlock answers around how and when gene mutations occur, factors that contribute to these changes, and how this knowledge could then be used to prevent diseases such as cancer and to develop better treatments.

Today, Bick is the head of the Division of Genetic Medicine and Clinical Pharmacology. His investigations are advancing the understanding of somatic (noninherited) mutations in blood stem cells that can trigger an explosive growth of abnormal cells called clonal hematopoiesis of indeterminate potential, or CHIP.

Bick and his colleagues have demonstrated that this abnormal growth of cells is virtually absent in adults under 40 but is found in more than 10% of adults over 70 and confers a tenfold increased risk of blood cancers, a twofold increased risk of heart attack and a 1.5-fold increased risk of death.

Bick is now internationally recognized for his groundbreaking research, and his lab's gene sequencing expertise is sought out by other researchers to support their investigations.

STORY BY **JILL CLENDENING** • ILLUSTRATION BY **ADOBE STOCK**

"There are groups all over the world who come to us and ask us to help them with their sequencing," he said. "The sequencing we've developed is now being run on about 100,000 people's blood samples every year. We've scaled it up, and now this is a tool that's helping not just us, but blood cancer research around the globe."

Bick joined VUMC from Massachusetts General Hospital and the Broad Institute of MIT and Harvard. In 2021, he was named the first VUMC Discovery Scholar in Health and Medicine, funded in part by the Brock Family Directorship in Career Development Endowment to support the recruitment and development of talented early-career, basic scientists.

"When I came to Vanderbilt, I discovered we actually have a time machine here," Bick said. "That time machine is a program called BioVU in which all patients seen at VUMC are invited to contribute their blood left over from testing to this repository."

Bick's ability to unlock the potential of BioVU's 350,000-plus samples for his investigations was expedited in 2022 when he received a $50,000 Vanderbilt-Ingram Cancer Center (VICC) Ambassador Grant. These grants support high-risk, high-reward basic and clinical research at Vanderbilt-Ingram and act as "seed" funding.

Seed or discovery grants fill in funding gaps faced by researchers, especially early in their careers. These grants are catalysts for discovery, allowing scientists to test hypotheses, gather preliminary data and refine their research designs. The resulting findings often lead to securing sizable research funding from national resources for further investigations. The Vanderbilt-Ingram Ambassadors award approximately two grants of $50,000 annually.

For Bick and his colleagues, the VICC Ambassador Grant allowed them to develop a new gene sequencing tool, which they then tested on a few hundred BioVU samples.

"What the Ambassador Grant let us do for the first time was to prove that we could go back in time, and we could measure mutations in people's blood from when they were healthy," Bick said. "Then we can measure mutations in their blood later in time, either when they're starting to show signs of blood abnormalities or ultimately when they develop cancer."

BioVU includes de-identified electronic health records linked to the samples, so Bick also began looking at the medications individuals who developed blood cancers were prescribed for other conditions, such as ibuprofen for joint pain or biologic medications for autoimmune diseases. He wanted to trace their impact on the trajectory of the cancer.

"We were fortunate after our initial studies to then get a much larger investment of around $6 million from the National Institutes of Health to do this with samples from thousands of individuals, and that's what we've done," he said. "It's amazing to see how a small investment at a really critical time in my career as a new investigator really changed the arc of what we've done and what we're going to do."

Bick and his colleagues have since produced more than 125 scientific publications and secured more than $25 million in external research funding to further unwind the genetic drivers of blood and other cancers and diseases. And his Ambassador Grant, like many others, has resulted in extending tendrils of research innovation to the laboratories of investigators throughout the world. Which means the program is doing exactly what it is intended to do.

The Vanderbilt-Ingram Ambassadors program is a volunteer group of young professionals that raises money to award grants for high-risk, high-reward cancer research to promising investigators. The group has raised more than $1.5 million for grant awards through personal contributions, events and peer-to-peer fundraising efforts.

Early-stage research supported by the Ambassadors has led to hundreds of publications and more than $45 million in funding from the National Cancer Institute and other external resources.

With the support of the Vanderbilt-Ingram Board

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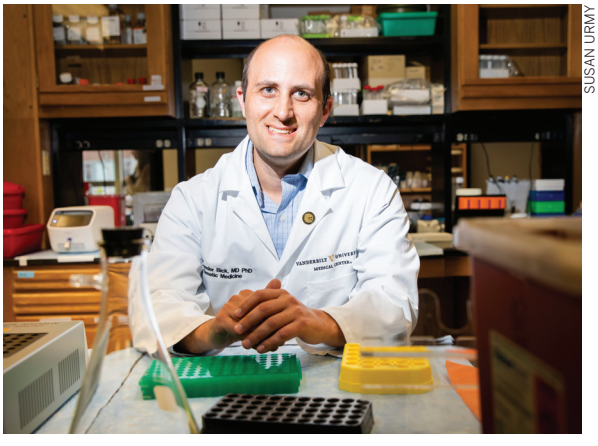
SUSAN URMY

Scott Hiebert, PhD, professor emeritus of Biochemistry (left), served as faculty champion since the founding of the Vanderbilt-Ingram Ambassadors.

Alexander Bick, MD, PhD, associate professor of Medicine, developed a new gene sequencing tool with the help of the VICC Ambassador Grant.

125

Bick and his colleagues have produced more than **125** scientific publications

$25M

Bick and his colleagues secured more than **$25 million** in external research funding

$1.5M

The Ambassadors program has raised more than **$1.5 million** for grant awards through personal contributions, events and peer-to-peer fundraising efforts

of Advisors, and its chair, Orrin H. Ingram II, the VICC Ambassadors program was co-founded in 2009 by Emily Blake (E.B.) Jackson and her husband, Todd Jackson. Todd Jackson had been diagnosed with a brain tumor, and the couple wanted to engage other young professionals in the fight against cancer. The group awarded its first grants in 2010. Todd Jackson was subsequently treated in 2013 for a glioblastoma. He died in 2014.

The Vanderbilt-Ingram Ambassadors worked closely with Vanderbilt-Ingram Director Ben Park, MD, PhD, the Benjamin F. Byrd Jr. Professor of Oncology, and faculty champion Scott Hiebert, PhD, professor emeritus of Biochemistry. Park and Hiebert selected the researchers who present their grant proposals for consideration each year.

Hiebert, who has served as faculty champion since the founding of the Vanderbilt-Ingram Ambassadors, retired Aug. 1. The Scott W. Hiebert, PhD, Ambassador Award has been established in his honor. An award recipient will be selected based on research proposals submitted by investigators at Vanderbilt-Ingram. Douglas Johnson, MD, MSCI, professor of Medicine, holder of the Susan and Luke Simons Directorship and associate director for Translational Research at Vanderbilt-Ingram, and David Cortez, PhD, chair of the Department of Biochemistry, the Richard N. Armstrong, PhD, Professor of Innovation in Biochemistry, and associate director of Basic Research at Vanderbilt-Ingram, have been named to share this role.

"The VICC Ambassadors are truly the next generation of philanthropists who are committed to turning the tide against cancer through awarding grants to promising young researchers at Vanderbilt-Ingram Cancer Center," said Hiebert. "These grants allow the pursuit of discoveries in basic and clinical science to further our understanding of disease processes.

"For Vanderbilt physicians and scientists, this funding not only yields early results, it also helps develop the ideas that then grow to large federally funded projects and collaborative investigations which ultimately result in transformative breakthroughs in care and prevention."

Tiffany Holland, a business development officer at Ascend Federal Credit Union, chairs the Vanderbilt-Ingram Ambassadors, a community service role that is especially close to her heart.

"My family unfortunately has a history of cancer," she shared. "I lost my dad to colon cancer when I was 18. My mom had breast cancer twice. Three of the four of my grandparents passed away from some type of cancer. Sadly, I feel like everyone has had cancer touch them in some way, so it resonates with everyone.

"I was invited to the VICC Ambassadors' breakfast in November 2019 and loved it. By January, I knew I wanted to be a part of this group. I'm not in the medical field, so this is my way of trying to do something. There has been an amazing expanse of work funded with this 'seed for research,' and I'm just so grateful that these researchers are able to receive this support."

Holland said listening to researchers talk about proposed investigations as the Ambassadors select the projects for funding and then later as they share their results is exciting and rewarding, and she invites others to engage with the Vanderbilt-Ingram Ambassadors.

"It's inspiring to hear what these researchers can do and everything that has come from their investigations," she said. "We want them to know that we 100% are behind them and want them to be successful in their research. It's so important for us to be a stepping stone for the investigators.

"We would love to get more people involved with the Ambassadors. The more investigators we can fund, the more we can help fight cancer with the knowledge gained by this science."

For Bick, his investigations centered on BioVU continue to grow as his lab analyzes additional commonly used medicines taken by millions to determine their impact on the development and progression of blood cancers.

"As we keep working through some of these top medicines, we're testing them out, not just in the computer but at the lab bench and in animal models," Bick said. "I think over the next three years we'll go full circle back to patients and run clinical trials here at Vanderbilt-Ingram to test whether these common medicines can really change the trajectory of pre-blood cancer." ■

The Scott W. Hiebert, PhD, Ambassador Award has been created following his retirement. To donate visit: give.vanderbilthealth.org/hiebert

Breaking records

"Biopsy Queen" reaches milestone number of procedures

STORY BY **TOM WILEMON**
PHOTO BY **DONN JONES**

Krista Kuhnert-Gainer, ACNP, once underwent a bone marrow biopsy so she could answer, 'yes,' whenever a patient asked if she ever had one.

With that kind of dedication, it's no small wonder that the nurse practitioner at Vanderbilt-Ingram Cancer Center has performed more than 20,000 bone marrow biopsies since 1996. Her colleagues, many of whom she's trained, threw a celebration in her honor and proclaimed her the "Biopsy Queen."

Kuhnert-Gainer is an expert at making patients feel comfortable when they undergo the procedure.

"We have, over time, developed a great system," she said. "We have a wonderful team that plays music. We also perform back massages and hopefully make the patients comfortable. We listen and make the patient feel that everything is all about them. I try to distract them for a few minutes by talking with them about the things that are important to them."

A few patients had pointedly asked if she ever had a bone marrow biopsy herself, so Kuhnert-Gainer volunteered when the opportunity arose during a training program so she could answer affirmatively.

Over the course of her professional career, she's taught dozens of other nurses as well as physicians how to do bone marrow biopsies.

"The fellows used to come down to the stem cell clinic and hang out, and I would show them how to do the biopsies," she said. "Several of the doctors that I have worked with over the years, I trained as fellows."

She was hired by the late Steve Wolff, MD, the founder and first director of the Vanderbilt transplant program, and John Greer, MD, who retired in 2018. They were wonderful mentors and friends, she said.

"Both of them were fantastic physicians with long careers at Vanderbilt," she said. "I loved working with them, and they taught me so much. John Greer even walked me down the aisle in 2000 when I got married."

She's kept in touch with many of the patients who received bone marrow transplants, and she continues to make new friends with the cancer patients she sees daily.

As of August 2025, the total number of bone marrow biopsies she has performed totaled 22,330. In March 2026, she will celebrate her 30th anniversary as a Vanderbilt University Medical Center employee.

A Second Opinion

Cancer patient seeks treatment validation at Vanderbilt-Ingram Cancer Center

STORY BY **WILLIAM DOUGLAS**
PHOTOGRAPHS BY **PAUL NURNBERG**

In the summer of 2021, I was diagnosed with Stage 4 renal cell carcinoma. Needless to say, my world was turned upside down. Cancer is such a devastating disease, and no one wants to be a part of that club. No preplanning for this one. Yet, there I was, handed this diagnosis with no plan in hand.

"What's next?" I thought. While the radiologist was giving me some direction on my recent discovery, I totally passed out! "This couldn't be happening, could it? Look at me, I'm a healthy, physically fit, soon to be retired happy-go-lucky male." Ironically, in all of this, I just received my very first Social Security deposit earlier that morning. Good luck seeing my next one!

Two weeks later, I was undergoing a serious operation to remove my right kidney and 11 centimeter tumor when the unimaginable happened. Parts of the tumor broke apart during the resection. A loose thrombus from the large tumor traveled up my inferior vena cava and into my heart, which stopped my blood flow for up to 10 minutes. That generally means instant death! Obviously, I didn't "expire," as I am here writing this dialogue for you. However, there are many excruciating details of how I ultimately survived that surgery and lived to talk about it. That particular incident and my cancer journey that followed are quite a story. In fact, I authored a bestselling book describing that operation and what really happened in those 10 "lifeless" minutes.

The book recounts that major event along with the six months that followed. It was quite a ride enduring the cancer emotions for both me and my wife along with the continual cancer treatments. My therapy following the operation involved a regimen of pembrolizumab infusions, which is an immunotherapy, along with a daily intake of Inlyta pills, a targeted therapy that inhibits the growth of cancer cells.

After following this schedule for the two years that was prescribed, it was decision time. I had great success with the mix of these two drugs in fighting my cancer, although I encountered many side effects along the way. I was determined to stay the course no matter what the consequences were. Now at this crossroad, I had many options to consider. Keep the medication intake the way it was? Reduce the number of medications? Or a combination of many other variables? After giving this much thought, I asked my oncologist at the Medical University of South Carolina, Dr. Theodore Gourdin, about getting another opinion. Dr. Gourdin was gracious regarding my question and suggested two other oncologists who specialized in kidney cancers. One of the doctors he mentioned was Dr. Brian Rini at Vanderbilt-Ingram Cancer Center in Nashville. I researched Dr. Rini online and felt like he was my guy. After all, he had authored the treatment study that I'd been on for the past two years.

Hollings Cancer Center at the Medical University of South Carolina contacted Vanderbilt-Ingram and introduced me to them in order to get the ball rolling. I followed their introduction with a call to set up an appointment. I was impressed from the moment the receptionist answered the phone. She was very welcoming, and after some discussion she switched me over to Dr. Rini's navigator who was already familiar with my case. She scheduled an appointment for a Thursday at 10 a.m. That was only 48 hours from the time I was speaking to her.

I would need to step it up as the cancer center was over 500 miles away involving an eight-hour-plus drive. We would have to leave early Wednesday morning to arrive in Nashville at a reasonable hour. Considering that MUSC and VUMC used the same software company, (Epic Systems Corp.), I was able to merge the two systems so Dr. Rini would have immediate access to all my medical records. It was amazing how all of this came together in short order.

My wife, Linda, and I, along with our standard poodle, Gianni, loaded up our SUV Wednesday morning and headed toward Nashville. Ingram Content Group, the company that would print my book on cancer is located in La Vergne, Tennessee, southeast of Nashville. Considering it was along the way, I thought it would be beneficial to stop and see the facility that would ultimately publish my book when it came out. This trip was kind of full circle for me, being that the cancer center that I was heading to was named in honor of the family who made a large contribution to Vanderbilt University Medical Center for the cancer center. This was all very surreal to me in a good way.

We arrived in Nashville on Wednesday evening and checked into a hotel near the Vanderbilt campus. After unpacking, we drove

around the college campus and noted the beauty of it all. We found the cancer center and parked our car in the convenient parking garage adjacent to the large glass building. I had Linda take my picture next to the Vanderbilt-Ingram Cancer Center sign located in front. We noticed that they had complimentary valet parking. We thought that was a nice offering, but we would forgo that service the next morning. After finding a good barbecue restaurant that evening, we went to bed with great anticipation for my appointment the next morning.

We woke up early and took Gianni for a nice stroll in the downtown area. Nashville is a very friendly town that displays country music everywhere you look. The downtown atmosphere was relaxing and a joy to walk through. After our short dog walk, we got Gianni situated in our motel room and headed to our appointment with Dr. Rini.

When we walked into the lobby of the cancer center, I immediately noticed the piano situated against the paneled wall of the room. It was a shiny black piano that had a calming appearance to it. It all made sense being we were in Nashville.

The flooring was carpeted, with comfortable seating scattered throughout the spacious room. I took note of the coffeepot on the self-service bar that I thought was a nice touch. It was obvious that Vanderbilt went to great lengths to make its cancer patients feel comfortable while visiting their oncologists. We checked in with the nice lady at the front desk, who entered my information into their system, then we took a seat in the lobby. It was approximately 10 minutes to 10 a.m. when Dr. Rini's nurse called my name. "That didn't take long," I thought. We followed her to the exam room, where she asked a few questions and said that Dr. Rini would be in shortly.

At precisely 10 a.m., Dr. Rini entered the room. He didn't have a medical chart, laptop computer or anything such as this with him. He was sharply dressed; however, he wasn't wearing the usual white coat that most doctors wear. This created a much more relaxing atmosphere. We shook hands; he introduced himself; and we all took a seat.

He looked me in the eye and said, "I have studied your case and know it very well. Your situation is very unique, and I'm glad you're doing so well after a rocky start to your journey." We jumped into some particulars regarding my nebulous cancer outlook. I was very impressed that he didn't have to refer to any notes on the topics we discussed. After a 30-minute conversation, we jointly came to a satisfactory conclusion as to how I needed to proceed going forward. As we exited the exam room, Dr. Rini said he would keep up with my progress and to never hesitate to reach out to him if I felt the need to do so. I felt comfort in knowing that.

As I exited the Frances Williams Preston Building, I turned around, took a good look and thought, I know I came to the right place, at the right time, and saw the right doctor. This is probably the most satisfied feeling I've had since my cancer diagnosis. To have the validation from this wonderful cancer facility along with the work that my magnificent cancer center in Charleston has already accomplished, I couldn't be in a better place. I'm very fortunate to have been treated by two outstanding National Cancer Institute-designated Cancer Centers, and my success in fighting this terrible disease will be a reflection of that. ■

William and Linda Douglas take a stroll on the beach with their standard poodle, Gianni.

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