MUSC CATALYST news
JUNE 25, 2021 MEDICAL UNIVERSITY OF SOUTH CAROLINA VOL. 37, NO. 15

Researcher honors friend's memory, finds potential treatment for peds osteosarcoma

By Carolina Wallace

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In a cancer that has not seen new targeted therapies for over 20 years, MUSC Hollings Cancer Center researcher and oncologist Nancy Klauber-DeMore, M.D., is pioneering new discoveries.

Using a combination of personal passion and expertise, Klauber-DeMore shifted her knowledge of the pro-angiogenic protein SFRP2 in breast cancer to address the lack of treatment options for patients with aggressive metastatic osteosarcoma. The results of the combination treatment with SFRP2 and PD-1 antibodies in a preclinical model were published in Cancers.

Osteosarcoma expert William Tap, M.D., chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center said, "Osteosarcoma is an area of great unmet medical need, which unfortunately has seen few clinical advances in the last 30 years. The work of Dr. Klauber-DeMore and colleagues, which targets SFRP2, provides a spark of hope in creating novel clinical inroads against this terrible disease while providing unique insight into the application and effects of anti-

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Photo by Sarah Pack

Five-year-old Nolan Rivers watches as Kqiana Young takes a blood sample for the Moderna vaccine trial at the MUSC Children's Health R. Keith Summey Medical Pavilion in North Charleston.

'I want to protect my children' – Kids as young as 2 join vaccine trial

By Helen Adams

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When most people prepare to get their COVID-19 vaccine, they sit in a chair and roll up a sleeve. At the MUSC Children's Health R. Keith Summey Medical Pavilion, 5-year-old Nolan Rivers climbed off a bed where he'd been playing with a toy rocket and into his mother's lap.

"Nolan? Now you remember I told you you're getting that special shot so you'll be protected against COVID?" Lolanya Rivers asked gently.

"Yeah," he answered, sounding a little uncertain.

No kid wants to get a shot. But Nolan was willing because his mom wanted him to – plus, he knew it would earn him some chocolate mousse ice cream from Baskin Robbins on the way home.

"This will make you a big boy," his mother told him.

A nurse injected 50 micrograms of the Moderna vaccine into the North Charleston kindergartener's arm, half the amount an adult would get. "It's done," she said.

Nolan, who picked a Star Wars Band-Aid to protect the spot where the needle went in, is among the first children age 6 and under to get a COVID-19 vaccine. He's part of a clinical

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trial with sites across the country, including MUSC Children's Health. It's enrolling younger and younger children, building on previous research in older kids.

Nolan's mother, who works in a microbiology lab, signed him up for the trial because she thinks the science supporting COVID vaccines is solid. "I did the research on Moderna and Pfizer. I feel confident."

So does cardiologist Andrew Atz, M.D., chair of pediatrics at the Medical University of South Carolina. "I'm wicked super stoked," he said with a big smile on the day Nolan and a handful of other young vaccine trial volunteers got their first shots.

"I couldn't wait to email all the people I had meetings scheduled with today and tell them I have to cancel, because we're involved in this incredibly important study that's going to help eradicate the pandemic."

Right now, Moderna has emergency use authorization from the Food and Drug Administration to offer its COVID-19 vaccine to people 18 and up. It's asking the FDA to expand that to 12 to 17-year-olds, and ultimately hopes to offer it to people of all ages.

While the Centers for Disease Control and Prevention is monitoring reports of heart trouble in adolescents and young adults after COVID-19 vaccination, its experts say those reports are rare, and the known benefits of vaccines outweigh the unknown and potential risks.

Atz and his research team have vaccinated 15 children ages 2 to 5 so far. Each will get two shots about a month apart. The doses are half of what adults get because the children are so much smaller. Older kids were vaccinated in earlier parts of the trial.

The kids' size isn't the only thing taken into account during the study. Their emotional needs are, too. Child Life specialist Jennifer Redfern, trained to help children to cope and sometimes even thrive in medical situations, brings in toys like the rocket Nolan played with to keep the kids as happy and comfortable as possible. And their parents stay with them throughout the visit.

Alice Zwolnak does a craft while her mom talks with Dr. Andrew Atz and program coordinator Kreighton Milks about what side effects to watch for after Alice's first COVID shot.

Photo by Sarah Pack

Alice Zwolak, who will start kindergarten at Drayton Hall Elementary School next fall, settled right in during her appointment. She played with fairy toys while her mom, Pam Zwolak, sat beside her.

"My husband and I tried to get into the Novavax trial. We didn't get in, but we got a notification — I think I saw it online — about other trials. So we registered both of our children as being interested in that," Zwolak said.

"We were like, 'We're in.' No questions.' We just really decided it was something that we wanted to be part of. I want to protect my children."

Scott Appleby, father of 5-year-old vaccine volunteer Ethan, was a little more hesitant. "My wife found out about it, and she signed him up. I was worried about him getting COVID and also worried about getting the vaccine, but I figure the vaccine is much safer than COVID."

So when he got the call saying Ethan could be part of the trial, he was ready. "He was a little scared of getting the shots, but we told him we'd make it really special for him. Like ice cream for dinner or TV — he can do movies all day. That made him feel a little better. Mint chocolate chip. Right, buddy?" he said to Ethan as the Angel Oak Elementary student sat in his lap.

"My wife and I think it's important to get kids back to normal, get school back to what it used to be."

Atz thinks that's important, too. "We're getting to more vaccine resistance in adults, but the fact that we can sprinkle in kids is tremendous. I'm most excited about getting young school kids vaccinated. If we can get 100 or 200 in the local area vaccinated before the next school year, it will be amazing. Any amount is better than none."

Nolan will be fully vaccinated when he starts first grade at Eagle Nest Elementary School this fall. His mother hopes that will do more than protect him from COVID-19. His example could also inspire other families.

"I know that after I got vaccinated, a lot of people reached out to me and asked about the side effects. Some said, 'Well, since you're doing this, I may consider doing it.' I think it makes a difference. There's unwillingness among some people in our community but seeing this can have a positive impact."

MUSC CATALYST news

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Editor's note: The MUSC Catalyst News is back on campus. The Office of Public Affairs and Media Relations staff has consulted with MUSC infectious disease and Safety and Quality experts and industry studies to confirm that paper products such as newsprint are safe and low-risk in surface–based transmission of the coronavirus.

Copies of the newspaper will be distributed bimonthly to racks around campus as well as via the MUSC Mailroom's zoned mailbox system on campus and at various MUSC satellite medical offices and clinics in the Tri-county and will begin distribution in MUSC's Regional Hospitals, upstate.

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Cancer *Continued from Page One*

SFRP2 therapies in cancer."

One focus of clinical research for Klauber–DeMore, a surgical oncologist and the BMW Endowed Chair in Cancer Research at MUSC, is centered around understanding how tumors hijack the development of new blood vessels, a process known as angiogenesis, to fuel their own growth. Tumors need to develop their own blood supplies to facilitate the exchange of nutrients. Blocking the angiogenesis-promoting molecules that tumors secrete has been a cancer treatment strategy for over a decade.

According to Klauber–DeMore, VEGF, the first angiogenesis factor that was targeted with an antibody, does not always slow cancer growth. "A decade ago, while I was exploring the issue of targeted VEGF treatment failing, I realized that there must be other factors promoting angiogenesis that overcame the lack of VEGF. My research in human breast cancer led me to the protein called SFRP2, which also promotes new blood vessel growth in cancers," explained Klauber–DeMore.

While breast cancer is Klauber–DeMore's specialty, both in the clinic and in the lab, personal experience and scientific discovery led to her research in pediatric osteosarcoma. In 2015, Weston Mallard, the son of close family friends, was diagnosed with osteosarcoma the week before he started eighth grade in Durham, North Carolina.

Osteosarcoma is a bone cancer that has a particularly poor prognosis once the cancer spreads to other organs. "Immunotherapy is one of the newer and more promising therapies for many cancers; however, it is not effective in osteosarcoma and effective treatments are lacking," said Klauber–DeMore.

Weston's mother, Jennifer Mallard, said it was a horrible time. "Weston was started on treatments right away. They were awful. They made him so sick. This disease really destroyed his life from the beginning."

Sadly, Weston passed away in 2017 after the cancer metastasized to his lungs. "It is easy to remember how I felt when we got to the point in the treatment where there was nothing to do. A year into the treatment, even though we had a great team of doctors at UNC, there were no promising treatment options left for him," said Mallard.

"Not being in the medical field, we did not want to jump to conclusions. But it felt like everyone was talking about adult cancers and the advancements. But no one was talking about pediatric cancer advancements," said Mallard. This painful journey and the lack of options resonated with Klauber–DeMore. Weston was one of her daughter's best friends.

During Weston's battle with osteosarcoma, Jason Yustein, M.D., Ph.D., at Baylor College of Medicine, published research showing that SFRP2 may be a therapeutic target in osteosarcoma. Klauber–DeMore contacted Yustein and started a collaboration to study the use of her novel antibody, hSFRP2 mAb, in a preclinical metastatic osteosarcoma model.

The team's research revealed the role of SFRP2 in immune cells, which are becoming an important counterpart in improving cancer treatments. The addition of the SFRP2 molecule causes an increase in two molecules, CD38 and PD-1, on T–cells. Klauber-DeMore's hSFRP2 mAb stopped the increase of CD38 and PD-1 on T–cells.

One of the paper's co–authors, Hollings Cancer Center researcher Shikhar Mehrotra, Ph.D., previously found that PD–1 immunotherapy is not effective when there are high CD38 levels on –-cells. Blocking CD38 allows PD–1 immunotherapy to work.

"A previous study showed that PD–1 immunotherapy did not work in osteosarcoma. We now know that osteosarcoma produces a lot of the SFRP2 molecule, which causes an increase of CD38 and PD-1 on the T–cells," said Klauber-DeMore.

"We found an additive beneficial effect using the hSFRP2 mAb and PD-1 — the combination blocked metastasis in our preclinical osteosarcoma model." Since SFRP2 is mainly on active T–cells and tumors, there is the hope that this combination treatment will be well tolerated and effective, she said.

Photo by Marquel Coaxum

Weston Mallard, shown here with Dr. Klauber-DeMore and her family, inspired her to begin investigating osteosarcoma treatment options.

Photo Provided

In 2017, Weston Mallard created a video, Weston's Cancer Journey – Lessons From Osteosarcoma, that shares his personal experience and insight about battling osteosarcoma.

Klauber–DeMore is working with Innova Therapeutics to get this treatment into clinical trials for osteosarcoma and, eventually, other cancers in an attempt to provide a more effective option for patients.

Forget me not: Novel target shows promise in treating Alzheimer's, dementias

By Matthew Greseth

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Researchers remain perplexed as to what causes dementia and how to treat and reverse the cognitive decline seen in patients. In a first–of–its–kind study, researchers at MUSC and Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School discovered that cis P–tau, a toxic, non–degradable version of a healthy brain protein, is an early marker of vascular dementia (VaD) and Alzheimer's disease (AD). Their results, published on June 2 in Science Translational Medicine, define the molecular mechanism that causes an accumulation of this toxic protein. Furthermore, they showed that a monoclonal antibody (mAb) that targets this toxic protein was able to prevent disease pathology and memory loss in AD– and VaD–like preclinical models. Additionally, this treatment was even capable of reversing cognitive impairment in an AD-like preclinical model.

"We believe our findings have not only discovered cis P–tau as a previously unrecognized major early driver of VaD and AD but also identified a highly effective and specific immunotherapy to target this common disease driver for treating and preventing AD and VaD at early stages," said Onder Albayram, Ph.D., co-lead author and assistant professor in the Division of Cardiology in the Department of Medicine at MUSC.

Aging is a normal part of life — we experience weakening of our bones and muscles, stiffening of our blood vessels and some memory lapses. But for around 50 million people worldwide, these memory lapses become progressively more severe, ultimately leading to a diagnosis of dementia.

Dementia is an umbrella term that covers AD, which accounts for 60% to 80% of cases; VaD, the second most common cause; and other less common pathologies. Currently, there are no effective treatments for AD. Interestingly, most AD cases have a vascular component, suggesting a broader relationship between cognitive function and healthy brain vasculature. A better understanding of that relationship could provide a platform to discover novel therapeutic targets.

"Our work provides evidence that cis P-tau may be a pathogenic factor that explains VaD, which is not generally linked to other dementias," added Chenxi Qiu, Ph.D., co–lead author and a postdoctoral research fellow at BIDMC, Harvard Medical School.

In a preclinical model of VaD, young mice showed signs of brain inflammation and memory loss within one month. However, treating these mice with the cis P-tau mAb prevented neural degradation and cognitive decline out to six months. In a separate preclinical model of AD, old mice showed severe cognitive impairment. Excitingly, this severe impairment was significantly reversed when mice were given the cis P–tau mAb.

"These data show that cis P–tau could be an early upstream pathogenic factor common to both diseases," said Albayram.

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Alzheimer's disease results in brain aging and the progressive loss of memory, as represented by the loss of leaves.

Translating information gained from preclinical models to humans is often difficult, but this study offers reasons to be optimistic. Accumulation of cis P-tau caused dramatic changes in the genetic architecture of affected cells in a VaD model; these changes were consistent with those seen in human AD patients. The researchers went on to show that treatment with the cis P–tau mAb reversed 85% to 90% of those changes suggesting the power of this potential therapy.

"The genomic landscape really adapts after the silencing of this toxic protein," said Albayram. "That was a big discovery."

Not only are Albayram and Qiu excited about these findings, but colleagues at MUSC are already quite enthusiastic about this work.

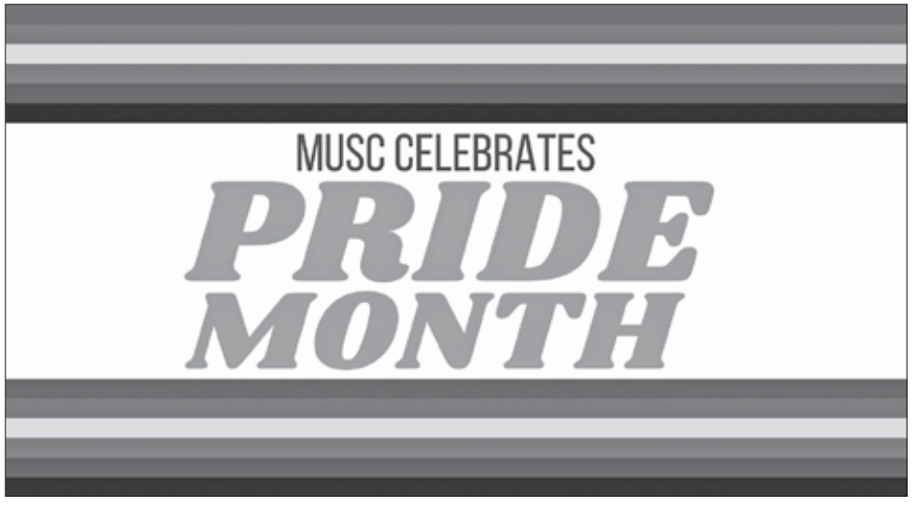
"I can go on and on about this paper," said Adviye Ergul, M.D., Ph.D., professor in the College of Medicine, Department of Pathology and Laboratory Medicine at MUSC. "They provide robust evidence that there is accumulation of a specific form of the tau protein — cis P–tau — that highlights a different tau protein pathology in VaD research."

This groundbreaking research has opened the door for new potential immunotherapies and highlighted several new areas of research that need to be explored. While the researchers delineated a pathway that leads to the accumulation of cis P-tau, the underlying linkage between vascular abnormalities and activation of the pathway needs to be identified. A better understanding of how toxic cis P–tau interacts with the healthy trans P–tau could provide further insights into the progression of AD disease.

AD and VaD might not be the only diseases affected by high levels of cis P-tau. Other brain disorders with a vascular component might also arise from this toxic protein, but further study will be required to establish such a link.

"Cis P–tau may be a common, early and pathogenic factor underlying traumatic brain injury, VaD and AD," said Qiu.

As we get older and our memory begins to lapse — misplacing our car keys or forgetting the name of a new acquaintance — we fear the possibility that these are the first signs of dementia. And while there is currently no approved treatment to reverse the physiological effects of dementia, this new research may provide hope that new therapies are around the corner.



Meet Chase

Chase Glenn

Department; Years at MUSC *Department of Diversity, Equity and Inclusion; 2 months*

Family, pets and their names
Wife, Colleen; son, Nealy, 2-1/2; daughter, Georgia, 6 mos.; and rescue pup, Cooper

Where did you work prior to joining MUSC *I was executive director of the Alliance For Full Acceptance (AFFA), a Charleston-based LGBTQ advocacy nonprofit.*

Music currently playing in your player
Anything by Brandi Carlile

What food is a must-have in the fridge or pantry *In our house, we can't run out of Cheerios — or "Os" as they're called.*

Someone you admire and why
My dad. He's 80 years old, and his thirst for knowledge and understanding continues to inspire me. He is always asking questions and leads with listening instead of speaking. That's a great way to approach the world.

A summer recipe you like to cook
There's a warm grilled zucchini salad we absolutely love.

Pride Month finds MUSC setting new LGBTQ+ goals across the state

By Helen Adams
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Pride Month finds MUSC's first director of LGBTQ+ Health Services and Enterprise Resources making big plans in his newly created role. "There are many things we'll be taking on as we begin to establish MUSC as a center of excellence for LGBTQ health care," Chase Glenn said.

Among them:

❑ Get MUSC Health back on the Human Rights Campaign's Healthcare Equality Index. The index lists hospitals that offer the best care to lesbian, gay, bisexual, transgender and queer patients and their families.

❑ Work with the Fenway Institute's National LGBTQIA+ Health Education Center to train care team members to provide inclusive and culturally competent care for people who identify as LGBTQ+.

❑ Begin to collect data on sexual orientation and gender identity in Epic, the electronic medical records system MUSC Health uses to keep track of patient information. Glenn said that will improve the care LGBTQ+ patients receive.

❑ Find ways to make the MUSC and MUSC Health campuses more welcoming for LGBTQ+ people and their families.

❑ Make MUSC more visible at LGBTQ+ community events.

"Some of the goals that I outlined are very specific, because I feel like we need some specific metrics to be able to hit to know that we're moving forward," Glenn said.

He also wants LGBTQ+ employees to know they have support and resources. "When my email account was turned on, which I think was the day they announced my hiring, I already had probably 50 emails from employees saying, 'Wow, I'm so excited that this position even exists. I'm so encouraged by this.' Whether they identify as LGBTQ or they have a family member, or they're just generally supportive, I was so glad to hear from them."

Zaas

David Zaas, M.D., CEO of MUSC Health — Charleston Division, said it's important to make sure every employee, patient and student is treated fairly and has access to the best care. "It's a great example of clearly living our values to our team members and our community."

He hopes other health care organizations follow that example. "I'm excited that we have the commitment to move forward and really put our stake in the ground, recognizing how important health equity is. We need to be a leader — not only in Charleston, South Carolina, but nationally among academic medical centers in championing health equity for all communities, including our LGBTQ patients. It's not a political issue. It's a health issue."

Chase Glenn brings enthusiasm and experience to what he believes is the only position like his in South Carolina health care.

Photo by Sarah Pack

> *"The LGBTQ community has a higher incidence of mental health disorders, an increased risk of suicide, a greater frequency of substance abuse, just to name a few. And there are societal barriers to access as well as the social stigma that creates a reluctance to seek care."*
>
> **David Zaas, M.D.**

Glenn, former executive director of the Alliance for Full Acceptance, the state's largest LGBTQ advocacy organization, said research shows LGTBQ people have been — and are being — discriminated against. He also knows from personal experience as a transgender man.

"We know that in general, many LGBTQ folks are living at the intersection of multiple sorts of marginalized identities. They're experiencing housing insecurity and food insecurity and lack of social support. This, combined with the historical discrimination LGBTQ people have experienced in health care, can lead to folks feeling like, 'OK, I don't necessarily feel like I'm represented here. I don't know that I can count on this care.'"

Zaas said that prevents people from getting the care they need. "The LGBTQ community has a higher incidence of mental health disorders, an increased risk of suicide, a greater frequency of substance abuse, just to name a few. And there are societal barriers to access as well as the social stigma that creates a reluctance to seek care."

Glenn said the good news at MUSC is that people were already working on solving those problems before his arrival. "I'm building on what was already happening, connecting all the good things that were already in place."

Zaas called the timing of Glenn's arrival important because it comes as MUSC Health expands across South Carolina. "This isn't just a Charleston initiative. We're now a statewide health system and rapidly growing, right? So it's our ability to say, 'No, this isn't just something we're doing in Charleston. This is something that MUSC is doing to benefit our communities across the state.'"

But Glenn said it isn't just about getting a certain designation. "It is a journey that we're going to be on to raise the quality of the care that we're providing and create spaces that are inclusive and welcoming of LGBTQ folks, whether they're patients, families, employees, visitors or students."

New system gives cardiac ICU docs more data to support better decision-making

By Leslie Cantu

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Checking in on a patient in the MUSC Health cardiovascular intensive care unit recently, cardiac surgeon Sanford Zeigler, M.D., who also serves as the unit's medical director, was worried about the patient's kidney function.

A key indicator was borderline; the care team had to decide whether the patient should receive fluids or diuretics, which decrease fluid. Normally in a situation like this, the doctors would make a decision based on an on-the-spot exam of the patient and the nurses' reports.

But a few months ago, the CVICU began using a continuous data visualization system that gives doctors a minute–by–minute look at each patient's vital signs. Developed by Etiometry, a clinical decision-support software company based in Boston, the software showed the team a graph of the patient's central venous pressure reading from throughout the night. With that data in front of them, the decision of what to do was no longer borderline, Zeigler said.

"That helped us make that small decision a little more easily. And if we do that multiple times every day, patient safety will be much better," Zeigler explained.

The MUSC Health CVICU is among Etiometry's first adult intensive care partners in the U.S.; the company's original focus was on pediatric cardiac patients. For adults, the data visualization portion of the software is FDA approved. That's the graph that Zeigler used to decide whether his patient needed fluids or diuretics.

"It means we can see changes in real time as they happen and compare them to what's been happening in the last hour or few days with much greater ease," he said.

Etiometry already has two Food and Drug Administration-cleared algorithms that alert doctors when pediatric patients on ventilators are either not receiving enough oxygen or not getting rid of enough carbon dioxide.

Through collaboration with MUSC, Etiometry is actively working to validate its risk algorithms for use on adult patients.

The idea is to alert doctors early that a patient is deteriorating, rather than letting a situation silently develop until "it's become so obvious you couldn't miss it, and the patient's in danger," Zeigler said. "It's an early warning system in a lot of ways."

Some of this information can be found in the electronic medical record. But EMRs are designed more for recordkeeping than bedside decision-making or prediction. They don't offer a continuous detailed record of the patient's physical state but only show those moments in time when someone entered the information into the patient's chart.

"You think, 'Oh the EMR is going to be this treasure trove of data' — and it is — but when you get down to the individual patient and making a decision in the moment, it's not the best source," said Henry Szymanski, Etiometry's senior director of marketing.

Even without the risk-analysis algorithm, the Etiometry software has made a difference for the CVICU, Zeigler said.

"It unlocks the data that otherwise the only way you could get it was to sit at the bedside all night and look at it yourself," Zeigler said. "It makes life much easier for everybody to be able to see all this data and not be chasing our tails trying to find it. We can actually just look at it and start thinking, rather than spend all that effort trying to collate everything."

Doctors can review the data at the patient's bedside or from their offices, giving them the opportunity to check on patients while completing paperwork.

Etiometry and MUSC Health are working on an agreement to implement the system within the operating room so that doctors in the CVICU will be able to see their patients' vital sign histories from when they were in surgery as well as their time in the ICU.

The company's ultimate goal is to provide doctors with an uninterrupted, moment–to–moment account of a patient's journey through the hospital, from the operating room to intensive care to a general care floor and finally, discharge.

Photos by Sarah Pack

Dr. Sanford Zeigler, medical director of the cardiovascular intensive care unit, says a new program provides data that otherwise would be available only by sitting by the patient's bedside and charting every minute's change.

Zeigler reviews a patient's data with nurse Hannah Brown.

Quarterly 'I am an MUSC Innovator' awards recognized

Staff Report

The Office of Innovation is proud to recognize the following teams as the June 2021 recipients of the "I am an MUSC Innovator" awards. These teams were contestants during our Shark Tank competition held on April 29.

Michelle Spiegel, M.D., Carolyn Bell, Amanda Davis, Annie Simpson, Lindsay Smith, Janet Byrne, Achsah Philip, Greg Hall and Andrew Goodwin, M.D., conceived a project titled "Work Smarter, Not Harder: Innovative Re-Design of Computerized Provider Order Entry (CPOE) to Drive Evidence-Based Fluid Prescribing." This project aims to redesign the process of adult IV fluid ordering within the CPOE system and incorporates a decision support system that assists providers with patient-specific and evidence-based IV fluid prescribing at the point of care.

Rebecca Nickell, Brittany Jones, Pharm.D., Joli Fermo, Sahar Torabi, Carolyn Bondarenka and Aulbrey Drisaldi began work on their project "Home Hemoglobin A1c Monitors for Patients with Diabetes Mellitus." The goal of this project is to increase the number of patients that have A-1 monitoring completed timelier, with an in-home point-of-care HbA1c monitor as an alternative to getting them during office visits.

Heather McGhee, Melissa Montiel, Phayvanh Pecha, Julia Black, Kimberly McClure, Eric Barbarite, Diane Andrews, Heather Bonilha and Krishna Patel are pursuing the development of "The Craniofacial Care Team App" to provide valuable access to the most up–to–date, evidenced–based resources for the care, management and treatment of the nearly 300 patients with craniofacial anomalies seen each year by multiple specialists at MUSC locations.

The team of **Cindy Kramer, David, Mahvi, M.D., Michelle Hudspeth, M.D., and Courtney McNeil,** along with the Hollings Cancer Center's Bone and Marrow Transplant (BMT) and Oncology Navigation programs, is creating a virtual, centralized digital library for patients and their families to access multi–specialty oncology–specific care called "Clicks for Cancer Care: BMT and Oncology Navigation Programs."

Photo by Anne Thompson

MUSC innovators who participated in the 2021 MUSC Shark Tank competition are recognized.

Andrew Novak, Sarah Screws and Kasey Jordan are working on "Changing Your Reality." This project leads to the creation of a modular, customizable virtual reality product, which will be customizable to their clients' needs and specifications.

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Allison Wood, Layne Cave, Michelle Vandermaas, Morgan Ford and Betsy McMillan have combined their skills to launch the project "Scars on the Inside: Preventing Pediatric Medical Traumatic Stress (PMTS) through Institutional Emotional Safety (ES) Initiatives." This project aims to implement institutional emotional safety initiatives through intensive training of designated staff champions to become experts in ES methodology and the subsequent implementation of mandatory education for both clinical and nonclinical pediatric staff.

Leah Plumblee, M.D., Satish Nadig, M.D., D.Phil., and Carl Atkinson, Ph.D. have titled their project "Printed Vessel Perfusion Chamber." The goal is to develop a 3D printed vessel perfusion chamber to facilitate the testing of endothelial targeted therapeutics, determine binding dynamics and allow testing novel therapeutics on human tissue that can be used in a humanized mouse model.

Full FDA approval, baked goods and other things you should know about the COVID-19 vaccine

By Bryce Donovan
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Beer. Doughnuts. Lotteries.

There is no way that in 2019 you would have believed those words would be related to a vaccine. And yet, here we are. In the never-ending battle against vaccine hesitancy, states and employers are getting increasingly more creative (or desperate, depending on your viewpoint) in how they are looking to entice the roughly 55% of Americans who have yet to be vaccinated against COVID-19.

Maryland, New Jersey, Ohio, California — states all across the country seem to be offering incentives. Even Krispy Kreme is getting in on the action. And recently, West Virginia announced it would be offering rewards ranging from cash to trucks to guns.

Danielle Scheurer, M.D., MUSC Health System chief quality officer, who oversees all things vaccine for the hospital system, is impressed by the creativity people have been showing.

"It's so interesting to see what people respond to," she said. "I think in the end, you just have to figure out people's currency."

Photo by Najla Cam on Unsplash

Krispy Kreme thinks it's pretty sweet if you get vaccinated.

With the vaccine landscape still in a state of flux, we are periodically checking in with Scheurer to ask her the most pertinent questions that are hanging in the balance.

What you need to know about the COVID-19 vaccine – Part 7

Danielle Scheurer, M.D., MUSC Health System's chief quality officer, weighs in on issues related to COVID-19 and vaccinations.

Q. What is the most popular or effective way MUSC is providing vaccines right now?
A. It's about half appointments, half walk–ups right now. Because of that, we've tried to completely decentralize. We're moving away from the large sites and are more focused on giving people the opportunity to get vaccinated in more places. So right now, we offer the vaccine at virtually all MUSC locations. Meaning that if it's an MUSC building, the odds are you can get a vaccine there, without an appointment.

Q. How many people are we vaccinating a day right now?
A. Somewhere around 1,000 a day if you combine all locations. The pace has really slowed down.

Q. President Biden wants 70% of Americans to be fully vaccinated by the July 4 holiday weekend. Do you think that's possible for South Carolina?
A. If I had to guess, I'd say we'll be about six months late for that deadline.

Q. So what kind of person isn't getting vaccinated at this point? Is it anti-vaccine folks or is it still those who think it's inconvenient?
A. I don't think it's a convenience thing anymore. There are ample opportunities to get vaccinated out there right now. It's still a lot of younger folks in the 18 to 35 range who seem to think they don't need it. On the bright side, the racial gap is closing. High-profile community and government leaders being vocal about how important it is to get vaccinated has a lot to do with that. And that's happening both locally and nationally.

Q. Simple question: What do people who missed their second dose do?
A. They should still get in there and get their second dose. It doesn't even matter if it's been months since the first dose; you still go get it. The body still knows what to do.

Q. Any idea if or when a booster might be necessary and available?
A. We're still in the "wait and see" phase. The manufacturers are saying yes, but they have obvious reasons why they feel that way. The science is still unknown.

Q. There was a story in the NY Times talking about people who had COVID and got vaccinated — that they might not ever need a potential booster for the rest of their lives. First off, how do we know that and second, does that in a roundabout way indicate that natural immunity trumps vaccinated immunity?
A. I saw that too. To the first part, I think they had a large enough sample size and by looking at serum titers (blood tests that measure whether or not you are immune to a disease) in those who both got COVID and had the vaccine, they saw a ton of antibodies there. And to the second part of your question, if you look at what the risk of reinfection is amongst those who got COVID and those who got vaccinated, and it's about the same. Where it's tricky is some people mistakenly thought they got COVID and really didn't. So it's really just a matter of being better safe than sorry. We're over a year into trial data, and we know these vaccines are crazy safe. And they're effective.

Q. Do you think full FDA approval of these vaccines will help with vaccine hesitancy?
A. I don't think so. For the most part, that isn't the reason people aren't getting vaccinated. So directly speaking, I would be surprised if it sways a lot of people. That said, both OSHA (Occupational Safety and Health Administration) and the EEOC (Equal Employment Opportunity Commission) have said it is legal to mandate the vaccine. Now add in full FDA approval — which I suspect is coming in the next couple of weeks — and those employers who were on the fence might feel emboldened to make it mandatory. It'll be super interesting to see how the employer thing shakes out. That might be the turning point to getting us to 70%.

Q. When do we think children under the age of 12 will be able to be vaccinated?
A. Last I heard they were thinking the end of summer. That seems pretty likely to me.

Q. This is basic and probably obvious to many by now, but just to be clear, what is safe for a vaccinated person to do in our state right now?
A. I've tried to go along with the CDC. So if I'm outside, I don't wear a mask, but if I'm

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Research project aims to make CAR-T-cell therapy safer, more effective

Staff Report

A new project led by researchers at MUSC Hollings Cancer Center could significantly decrease the side effects associated with CAR–T–cell therapy and make the treatment available to more patients who could benefit.

Led by Hollings hematologist and oncologist Brian Hess, M.D., and Shikhar Mehrotra, Ph.D., co-leader of Hollings' Cancer Immunology Program, the project involves manufacturing a "purified" version of the CAR–T–cells that are currently used to treat patients with certain types of lymphoma and leukemia to reduce the side effects associated with treatment and potentially make the treatment more effective. The therapy will be given to patients as part of a clinical trial, including lymphoma and leukemia patients who don't currently have approval from the Food and Drug Administration (FDA) to receive CAR-T.

The project is supported in part by a new $50,000 grant from LOWVELO, Hollings' annual community event that rallies everyone together to raise money for lifesaving cancer research. The CAR-T-cell program is one of the first programs to benefit from the fund.

"The grant we've received from LOWVELO is a really great start to help us to get this project off the ground and to help us to treat our first patient," Hess said.

CAR–T–cell therapy works by collecting a patient's T–cells, genetically modifying these cells to identify specific targets (CD19) on cancer cells and then infusing them back into patients to fight their disease.

CD19 directed CAR–T-cell therapy is currently approved for B–cell acute lymphoblastic leukemia (B–ALL) patients age 25 or younger and adult patients with specific subtypes of CD19 expressing non–Hodgkin lymphoma. The clinical trial at Hollings will be open to adult patients with B–ALL up to any age and certain patients with CD19 expressing non–Hodgkin lymphoma both who are and are not currently eligible to receive the FDA–approved products.

As part of this trial, researchers at Hollings are collaborating with Loyola University Chicago researchers to build on their existing technology by utilizing a specific cytokine (protein) IL–12 in the manufacturing process of the CAR–T–cell product. In September 2018, Loyola and Loyola Medicine received a $250,000 grant from the Leukemia Research Foundation to develop purer, less toxic CAR–T–cells to treat leukemia and lymphoma.

Mehrotra, who also is the scientific director of MUSC's FACT–accredited Clean Cell Therapy Unit, said the MUSC project for developing CD19 CAR-T was initiated through a collaboration with Michael Nishimura, Ph.D., at Loyola, who worked with the researchers to generate CD19 CAR–T–cells at MUSC's clean–cell facility.

"Our clinical partnership with Brian will not only help to treat patients, but we are excited to gain more understanding of the complex biology of patient responses as we track these adoptively transferred CAR–engineered T-cells. This will be an important advance for Hollings, where we strive to bring cutting-edge treatment for cancer patients," Mehrotra said. "As they say, 'It takes a village.' The different basic science and clinical expertises that we have developed over many years at Hollings are all coming together to implement new strategies for cancer care. It is a great testimony to a big team effort and institutional leadership and vision."

Hess agreed and hopes the treatment will not only improve patients' outcomes but their quality of life during treatment. "This new approach will hopefully improve the toxicity profile related to CAR–T–cell infusion as well as make the CAR–T–cells more effective in fighting the lymphoma or leukemia," he said. "We also hope that this trial improves the availability of this dynamic therapy to patients throughout South Carolina."

Dr. Brian Hess is leading the clinical portion of the trial to test a purified version of CAR-T-cells.

Photo by Emma Vought

A shot at a cure

Patients often are referred for CAR-T-cell therapy when they have relapsed multiple times and have few or any standard therapy options left available to them. While there are associated risks, CAR-T-cell therapy provides hope to these patients.

"CAR-T-cell therapy has been able to provide durable remissions and hopefully a cure to patients who otherwise have an extremely poor prognosis," said Hess. "FDA–approved CAR–T–cell therapy, as well as this upcoming trial, helps in the hope of offering cures to patients who otherwise would have very poor outcomes."

Hollings first introduced CAR-T-cell therapy to South Carolina in 2019, and it is the only center in the state with both an adult and a pediatric CAR–T–cell program. In 2020, the therapy was used to treat 14 patients. In 2021, Hollings' physicians expect to treat between 40 and 50 patients, with continued growth on the horizon, thanks to new approvals to use the therapy in additional cancer types.

Nationwide, CAR–T–cells therapy currently is being tested as a possible treatment for blood, brain, breast, gastrointestinal, lung, ovarian, pancreatic and skin cancers. On March 5, it was approved by the FDA for a common type of lymphoma called follicular lymphoma, and on March 27, it was approved for multiple myeloma.

Hess said Hollings is fortunate to have access to a clean–cell facility that is necessary to manufacture these cells and the benefit of a multidisciplinary team to oversee a program of this scope.

"A patient's journey from evaluation for CAR–T, to infusion of cells, to the post CAR–T therapy care requires multidisciplinary expertise throughout Hollings, including cellular therapy coordinators, apheresis/cryopreservation nurses, clinic nurses, nurse practitioners, pharmacists, quality coordinators, physicians, etc., all of whom specialize in cellular therapy. We also rely on the expertise of other departments outside of Hollings, such as a partnership with the emergency department and the medical intensive care unit, which help to manage side effects of CAR–T."

By doing this work at Hollings and taking advantage of the center's multidisciplinary team of researchers, Hess hopes to learn more about the science behind CAR–T–cell therapy to determine how to make it safer, more effective and applicable to additional cancer types, including solid tumors.

"Just like we need physicians to see patients and administer CAR–T–cell therapy, we need researchers to be able to manufacture the best possible CAR–T–cell product. They are a vital partner in making this clinical trial available to patients," said Hess. "They're also the team with whom we will collaborate to perform the science related to this study to advance the field and inform future studies."

See **Therapy** *on page 11*

Innovative gateway platform supports campus innovators

Enterprisewide, everyone at MUSC is encouraged to solve problems creatively, and now, there is an easy tool to help them to advance their innovative ideas and projects to the next level – the MUSC Innovation Gateway. This unique tool serves as a key support mechanism that feeds and elevates the culture of innovation at MUSC.

The portal, created by the Office of Innovation in collaboration with Information Solutions and the MUSC Foundation for Research Development, serves as a one–stop connection tool to all things innovative in the MUSC system. Users can submit innovative ideas and be automatically connected to teams and resources in the MUSC innovation community.

According to Jesse Goodwin, Ph.D., MUSC chief innovation officer, the portal is an easy, user–friendly tool and a valuable way to understand and navigate MUSC's robust, but complex, innovation ecosystem. Goodwin is excited to launch it, as MUSC's innovation effort welcomes ideas of all types from individuals at all of MUSC's divisions across the system, she explained. "No longer does an individual with an idea need to know the name of a specific team or department that is equipped to help. The Innovation Gateway does that for them. And, the portal's online accessibility is helpful as MUSC expands its innovation culture across all of its campuses.

Since its launch in March, MUSC innovators have used the portal to submit ideas ranging from the development of new software or algorithms to medical devices and care pathways. The Gateway serves as a convenient path for submitting a record of invention (ROI) to the MUSC Foundation for Research Development, according to Goodwin. MUSC receives as many as 150 ROIs annually for ideas related to research outcomes, research materials and drug/therapeutic development.

Another key feature available on the Innovation Gateway is a link to funding opportunities. As innovation is not always free, MUSC provides several funding opportunities and resources to help to advance ideas with high potential for impact, said Goodwin. "Many of the ideas have the potential for intellectual property. As such, it's important to bring awareness to both funding and IP resources that MUSC offers, without requiring people to navigate multiple websites for information that's important to an idea's success. It's our equivalent to the 'easy button' for innovators," she said. Soon, the Gateway will feature categories related to intellectual property and other such resources.

Under the OneMUSC strategic plan, MUSC is amplifying its focus on and support of activities related to innovation, including the annual Innovation Week celebration, which gathers creative minds on campus to present and showcase ingenious ideas in health care through poster presentations and collaborative Shark Tank competition events — activities that continue to feed a vigorous culture of innovation at MUSC.

For information, visit the MUSC Innovation Gateway at https://musc.service-now.com/idea.

Therapy *Continued from Page Ten*

Mehrotra sees this as the beginning of an array of promising trials. Generally, most patients' T–cells are collected and sent off to commercial labs for genetic engineering. This new in–house approach involving the creation of purer CAR–T–cells could help patients to avoid serious side effects and lower the cost of treatment, making it available for more cancer patients.

"These are exciting times for cellular therapies and engineering autologous T–cells with CARs to recognize tumor antigen puts us at the forefront of treating cancers," said Mehrotra. "We are excited to partner with Brian and to be able to treat patients in the next six to eight months with the first in-house generated CAR–T therapy. I am sure that once we get off the ground, similar strategies can be used for targeting other cancers."

Innovator *Continued from Page Eight*

Jennie H. Kwon, Morgan Hill, Steven W. Kubalak and T. Konrad Rajab, M.D., are proposing a novel approach to heart transplantation with their "Partial Heart Transplantation: A New Operation for Children Requiring Valve Replacement" project. The plan would be to deliver a growing heart valve replacement with the ability to self-repair and avoid thrombogenesis. This involves transplantation of the heart valve only, which will grow with the recipient child, similar to a conventional heart transplant or a Ross pulmonary autograph.

M. Andrew Rowley, Royal M. Pipaliya, Mallory J. Raymond, M.D., Mitchell J. Isaac, M.D., and Ted A. Meyer, M.D., Ph.D. are working on the project "Measuring Otologic Surgical Performance with Computer Vision (OTOVision)." The goal would be to use an artificial intelligence framework to objectively measure surgical performance in a database of otologic surgical video clips and provide trainees with quick, objective analytics of videos in near real-time to drive improvement**.**

The I am an MUSC Innovator campaign is designed to raise awareness of the many forms that innovation can take, to inspire others and to recognize publicly the individuals and teams that are making impacts.

Each quarter, the campaign showcases innovative educators, researchers, care team members and service team members enterprisewide who have been nominated for their innovation impact.

Nomination process

Nominations are solicited by and submitted to the chief innovation officer and evaluated based on the merits of the innovation, including potential impact and unique factors that contributed to the innovation. Nominations are solicited on a quarterly basis but may be submitted for consideration at any time. Fill out and submit a nominatio.

Award criteria

To be eligible for the I am an MUSC Innovator campaign, the individual must be:

- Employed by MUSC or attend MUSC as a student.
- Recognized within the organization for the creation of an idea, product or process which can solve a problem or create a new opportunity.
- Recognized as collaborative, respectful, adaptive to change and committed to quality care.

The individuals or teams that are finalists in the Shak Tank Competition during Innovation Week are also recognized. Up to 6 individuals/teams are selected each cycle. Recipients receive lanyards and crystal trophies. Notice of their awards are also published in The Catalyst News and various department newsletters and on the MUSC Innovation website.

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inside I do. It's just best to err on the side of wearing a mask. Some people have complicated family dynamics, and by doing so, they're safeguarding them a little further.

Q. Last question, where do we stand on a clinic for long–hauler COVID patients (those who still have lingering symptoms, such as loss of smell or taste)?

A. Our primary care team is putting together a clinic focused solely on them. Unfortunately right now, because there is still so much unknown about the long-term effects of this virus, it's more focused on symptom management. But besides helping those with long-term complications, it will also help to screen out or identify people who might be suffering from something totally different than the effects of COVID.

***Have a question you'd like answered? Email it to donovanb@musc.edu with the subject line "Vaccine Q."*