

NO BOUNDARIES

2017 YEAR IN REVIEW



Changing What's Possible

About MUSC Health

MUSC Health, the clinical enterprise of the Medical University of South Carolina (MUSC), is dedicated to the pursuit of changing what's possible in health care. Nationally recognized for its innovation, patient- and family-centered care, and quality outcomes, this integrated health care system is accessible at the downtown Charleston campus and through more than 100 outreach locations, clinical affiliations with numerous health care partners, and a robust telehealth network. MUSC Health logs more than one million patient encounters annually, and its specialized care teams consistently rank among the best in the country. MUSC Health delivers transformational care shaped by world-class clinicians, health scientists, and educators who provide leading-edge care, while developing the next generation of innovative health care leaders.





**Patrick J. Cawley, M.D.,
MHM, FACHE**

CEO, MUSC Health
Vice President for
Health Affairs

Medical University of
South Carolina

Collaboration is the new competition.

MUSC Health has evolved from a local medical center into a nationally respected health sciences center. Our role now is to deliver the best care to patients, not just in the local region, but to patients anywhere and everywhere our expertise is needed.

Instead of hoarding scientific breakthroughs, we share our knowledge through leadership of nationwide clinical trials. Instead of expecting patients to come to us in Charleston, we make advanced medical care accessible to rural and underserved communities through clinics distant from our epicenter and through a robust telehealth network that is the envy of health systems across the country. Instead of co-opting patients as our own, we prefer those patients be treated by physicians close to their home.

This MUSC Health Year in Review tells stories of successful interventions in the vast geography from Puerto Rico to Las Vegas and penetrate the mysteries of structures tiny as a chromosome. Translational research accelerating application of scientific discoveries made at the Medical University of South Carolina. Bringing to market incredible devices that improve outcomes, shorten recovery and reduce pain. Closing the gaps of disparity to afford opportunity for a quality of life for all. Creating business partnerships and clinical collaborations, led by physicians, that deliver both effectiveness and efficiency.

No boundaries. That's how we change what's possible in health care.

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Cover: MUSC Health's impact is felt well outside South Carolina.

Left: Ashley River Tower, one of four hospitals in the MUSC Health System.

MUSC Health’s clinical leadership is committed to care models that improve the patient experience and achieve optimal patient outcomes. These care models are organized into 15 Integrated Centers of Clinical Excellence (ICCE) with a physician ICCE Chief overseeing the achievement of these goals.

Thomas Di Salvo, M.D., MBA

Chief – Heart & Vascular



Di Salvo the MBA likens the ICCE (Integrated Centers of Clinical Excellence) structure to a “focused factory,” a Harvard business concept calling for an organization to focus on a few manageable sets of products and get very good at them. Di Salvo the cardiologist defines that focus as a highly differentiated heart and vascular program at MUSC that could rival anything in the country. And he believes the H & V

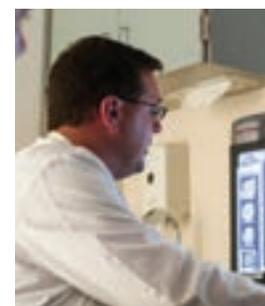
team is doing just that – offering what you can’t get anywhere else in the region. Between the veteran specialists and new strategic hires, the ICCE now includes seven (out of nine in SC) clinicians board-certified in heart transplant, the only robotic mitral valve surgery program in SC, an internationally recognized geneticist to address inherited heart diseases, the only surgeon doing ventricular tachycardia ablations, novel stentings of aneurysms, and a host of other firsts and bests. “Nothing is lost in thinking boldly,” he says.

Renowned business strategy author Peter Drucker admits that the three missions of health care – research, education and patient care – play havoc with traditional business planning. Yet Di Salvo believes that efficiency does not have to erode quality. The definition of success is not how many procedures or outpatient appointments, but the quality of the care and patient satisfaction. Although raised in a musical household, Di Salvo took up jazz drumming later in life and now plays in a combo some nights. “It requires balance of energy and control,” he says. “Improvisation means you have to listen to the other instruments.” And just as in his day job, the goal is to make the other people – the music – sound better.

Raymond D. Turner, M.D.

Chief – Neurosciences

As Chief of the Neurosciences ICCE, Raymond Turner envisions a different way to look at health care. Rather than seeing his portfolio of neurology, otolaryngology, and neurosurgery as a series of academic specialties, he sees his role as addressing disease states and developing strategies for comprehensive care, from acute care by multi-subspecialty teams to chronic management by general practitioners.



“How to best manage complex patients that span traditional departments is not the same administrative job of a department chair,” he says. However, he works closely with them, inviting them to the team so that they can collaboratively manage serious diseases for better outcomes.

Turner’s goal is to link the patient with the right doctor the first time. So, he worries about access. In his view, there are not enough specialists in metro areas, much less rural communities. He wants to get people together – neuro-specialists, of course, but also ENT specialists, pulmonologists and oncologists – to create a high-end destination program of care and bring that level of care to every physician and patient across the state. He sees telehealth as the future to solving access issues. “Imagine medical-internet cafés across the state, where patients can access our tremendous specialty expertise.”

Turner attributes his drive to being cut from the baseball team in high school. He doesn’t like to lose and proved his worth with a Division I college baseball scholarship. That feeling of wanting to be the best has not waned.

Mark A. Scheurer, M.D., M.Sc.*Chief – Children’s and Women’s Health*

Healer. Mentor. Builder. Partner. These are words that one might not expect to use when describing the role of an ICCE Chief at MUSC, yet these are the quite accurate descriptors of what that person does in this leadership role.

For Mark Scheurer, pediatric cardiologist and ICCE Chief for Children’s and Women’s Health, the day begins with an

invigorating run with a group of like-minded friends before the sun has yet to peek above the horizon. This is his moment of introspection and the time he takes to organize his thoughts about the many decisions and tasks facing him that day.

From the multiple meetings that require his thought leadership to the more personal interactions with co-workers and families, he moves swiftly to ensure that he accomplishes the most important task of the day – taking care of children and women to the best of his ability.

That might involve helping lead the design, construction and completion of the new MUSC Shawn Jenkins Children’s Hospital and Pearl Tourville Pavilion for Women, due to open in fall 2019.

It would also likely involve: delivering the highest level of care as a pediatric cardiac intensivist; collaborating with other care providers and health care leaders throughout the state to ensure equal and appropriate access to care for all children; interacting with key donors and legislators who help supply the tools necessary for pediatric health care of the future and who mold the decisions made at the local or national level; or providing guidance and mentorship to our next generation of physicians – Scheurer does so, knowing and accepting the broad range of responsibility on his shoulders without complaint.

Brenda Hoffman, M.D.*Chief – Digestive Disease, Endocrine and Metabolism*

A gifted clinician, Brenda Hoffman now finds herself in a leadership role and has developed strategies to manage her portfolio – quality, growth and access. Hoffman keeps her focus on the patient and family.

She is proud of quality metrics and national recognition: the Joint Commission Advanced Certification in Diabetes Management services, one of less than three dozen Centers of Excellence designated by the National Pancreas Foundation, and other accreditations and certifications. The Digestive Disease Center’s Division of Gastroenterology and Hepatology is recognized as a worldwide leader in gastrointestinal endoscopy.

Hoffman is motivated to grow programs in areas that include pediatrics, obstetrics and gestational onset diabetes. She envisions developing more minimally invasive procedures, laparoscopic bariatric surgery and medicine that can preclude surgery.

She is working to improve access to this quality of care through clinics closer to patients and through MUSC’s telehealth network.

Like all chiefs, she has financial responsibilities and has taken that role seriously. Such as managing funds flow between research and educational priorities and the clinical operations. She chafes at lack of reimbursement for endoscopic or minimally invasive surgical innovations. She believes educating the next generation of doctors in financial matters is essential.

The challenge can be overwhelming. Hoffman finds inner peace through exercise. Not a stroll around the park kind of peace, but six to seven days a week at a dance studio or a marine boot camp-style workout called Orangetheory: grueling 60 minute-long classes focused on high-intensity interval training, cycling through workouts on a treadmill, on a rower, and on the floor with heavy weights to develop endurance and strength.

MUSC Health Baldrige Award recognition on fast track



The Malcom Baldrige Award is a national program providing a framework for organizations to get their operating units and care team members aligned and engaged toward common goals. Relatively new in the health care industry, the goal is to achieve an integrated, safe, effective and efficient patient care delivery system.

MUSC Health achieved bronze status at the state level this year. And did so after less than two years of preparation. Baldrige is stingy with

its recognition. Only one or two health care organizations in South Carolina since 2014 have ever achieved it. Once making the state gold level, MUSC will apply for national recognition.

Six MUSC Health care team members qualified as Baldrige National Examiners in 2017. They not only help MUSC meet the rigorous standards, but also evaluate other organizations across the country in multiple industry categories.

MUSC National Examiners (L to R): Dennis Burns, Human Resources Employment and Retention Manager; Alice Boylan, M.D. ACT/ED ICCE Chief; Dan Handel, M.D., Chief Medical Officer; Danielle Scheurer, M.D., Chief Quality Officer; Patrick Macconnell, Organizational Excellence Director; Jamie McAdams, Surgical Services Innovation and Outreach Director.

Chanita Hughes-Halbert elected into the National Academy of Medicine



Dr. Chanita Hughes-Halbert is the Distinguished AT&T Endowed Chair in Cancer Equity at MUSC

Chanita A. Hughes-Halbert, Ph.D., has been elected into the National Academy of Medicine, the first woman and first African-American from South Carolina to attain that distinction. Membership in the NAM is considered one of the highest honors in the fields of health and medicine, and recognizes individuals who have demonstrated outstanding professional achievements and commitment to service.

The National Academy of Medicine is an independent organization of eminent professionals from diverse fields. Through its domestic and global initiatives, the NAM works to address critical issues in health, medicine and related policy and inspire positive action.

“I just see it as a real honor because I think it places MUSC as an institution among some of the most elite academic centers in the country,” says Hughes-Halbert, who holds the AT&T Distinguished Endowed Chair in Cancer Equity and was also appointed by President Barack Obama to the National Cancer Institute (NCI) Board of Scientific Advisors.

MUSC and SCSU team up to tackle health disparities

Marvella Ford, Ph.D., is the glue that brings two universities together in her roles as a professor in the MUSC College of Medicine’s Department of Public Health Sciences, a senior leader at the MUSC Hollings Cancer Center and the Smart-State Endowed Chair in Prostate Cancer Disparities at South Carolina State University (SCSU). She’s leading the project with Judith Salley-Guydon, Ph.D., chair of the Department of Biological and Physical Sciences at SCSU.

Ford is now leading the effort to establish the South Carolina Cancer Disparities Research Center, or SC CADRE, funded by a \$12.5 million grant from the National Cancer Institute, split between MUSC and SCSU. Goals include increasing SCSU’s ability to do cancer research, conducting cutting-edge cancer disparities research, inspiring a new generation of researchers to focus on cancer disparities and getting the general public more involved in cancer research.

The first step involves creating a biostatistics and quantitative methods shared resource at SCSU that will give SCSU a much better shot at getting funding for its cancer research. That, Ford says, benefits both SCSU and MUSC. The second step involves establishing a new biorepository at SCSU and a clinical trials office in the Regional Medical Center in Orangeburg, where 62 percent of the patients are African-American. This new biorepository is expected to be one of the most racially and ethnically diverse biorepositories in the country. The third piece of the SC CADRE grant focuses on lowering the levels of AGEs, or advanced glycation end products, in prostate cancer survivors.

“If we can drive down the level of AGEs, we can make more equitable health outcomes for blacks and whites, and it may help reduce disparity in prostate cancer survival rates,” Ford explains.



Marvella Ford (R) and Judith Salley-Guydon (L) lead the South Carolina Cancer Disparities Research Center at SCSU.

Sharing | HEALTHY COMMUNITIES

The miracle is this: the more we share, the more we have.

MUSC one of first national telehealth centers of excellence

“You should not die in South Carolina because of where you live,” says pediatrician Katie Cristaldi, M.D., one of two leading MUSC researchers in a landmark grant establishing MUSC as one of only two Telehealth Centers of Excellence in the nation.

On Sept. 22, Dee Ford, M.D., and Cristaldi, principal investigators on a grant submitted to the Health Resources and Service Administration, learned that their team’s bid to develop the center had been funded. The grant awarded \$600,000 the first year and up to \$2 million more over an additional two years. The COE team, which has been integrally involved with MUSC telehealth initiatives, will continue to work hand in hand with the existing MUSC Center for Telehealth as it expands the scope of its delivery of clinical care throughout the state, in addition to the guidance and resources it provides at the regional and national levels.

Telehealth is an innovative, convenient and effective way for health care providers to deliver acute, primary and specialty medical care and support to patients located in all areas of the state – even rural areas, where meeting those needs often can be nearly impossible. But now, in seconds, through the use of high-tech videoconferencing equipment, doctors miles away can be virtually at the bedside of a patient with end-stage kidney disease, in the ER with an ischemic stroke victim or at the school nurse’s office assessing a child suffering with asthma.

MUSC provides nearly a quarter million telehealth services to more than 200 sites in 27 counties at 28 hospitals, more than 100 community clinics and 50 schools, as well as alternative sites such as nursing facilities, prisons and patients’ homes.



Seventy-eight percent of sites are located in completely- or partially-medically underserved areas of the state.

**Principal investigators
Katie Cristaldi, M.D. and
Dee Ford, M.D.**

“HRSA now wants to see how telehealth can be embedded in traditional clinical practice – not an add-on,” Ford says. “They want it interwoven and integrated, and they want to see financial feasibility.” Ford explains MUSC has a lived experience of telehealth successes and failures. Most of the regional centers are not wedded to clinical operations or universities, and they are not clinical providers or IT specialists, so they don’t have that tangible experience.

The MUSC COE will fill important gaps in the national telehealth landscape, focusing on the impact of telehealth on federal and local health care spending, provider and patient engagement in telehealth, open access network evaluation and best practice dissemination. MUSC will also develop and offer at a national level teams devoted to consultation, evaluation, technical support and collaboration.

MUSC leads massive study on embolisms

The Comparative Effectiveness of Pulmonary Embolism Prevention after Hip and Knee Replacement (The PEPPER Trial)

More than one million total hip and knee replacements are performed each year in the United States. The use of blood thinners around the time of operation reduces the risk of pulmonary embolisms (PE), but increases the risk of bleeding from the raw bony surfaces that are created when the joint replacement is done.

The purpose of the study “Comparative Effectiveness of Pulmonary Embolism Prevention after Hip and Knee Replacement (PEPPER),” which is funded through a \$14 million Patient-Centered Outcomes Research Institute (PCORI) award, is to combine information about effectiveness in preventing blood clots in the lungs and legs with information about the safety of the most commonly employed blood thinners – plain aspirin, warfarin (Coumadin) and rivaroxaban (Xarelto).

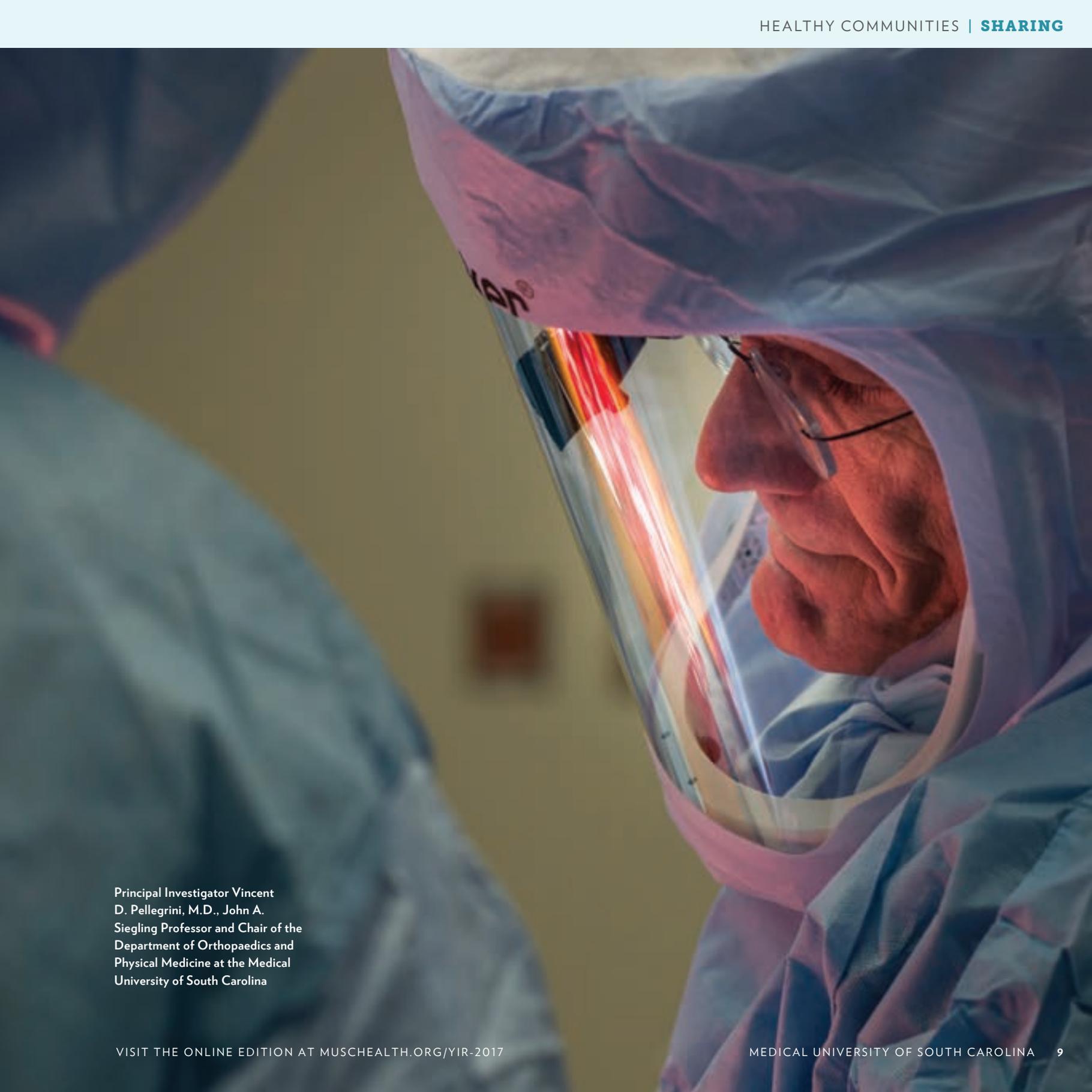
Does one automatically take universal precautions to prevent a PE and choose the most aggressive route? Or accept that excessive bleeding has its own risks for infection, additional surgery or even fatal infections? While on the surface, preventing death from a PE seems an obvious option over excessive bleeding, consider the math. Only one or two people in 1,000 are expected to die from a PE. Yet 30 to 50 patients in 1,000 administered the most potent anticoagulant to prevent PEs will have excessive bleeding, which can lead to a need for additional surgery or serious infections that require removal of the new joint replacement.

In order to generate enough data, 25,000 patients undergoing elective total hip or knee replacements will be enrolled at 25 centers across the country over a period of three-and-a-half years. The study will encompass five years, with six-month startup, six-month follow-up per patient, and six months for final data analysis. The principal investigator is MUSC’s Vincent D. Pellegrini, M.D.

Twenty-two of the 25 institutions participating have agreed to rely on a central MUSC Institutional Review Board (IRB). This is a first. Beginning in January 2018, the National Institutes of Health will mandate that multi-site studies have a singular central Institutional Review Board or IRB. This is one of the first times that such a large group of institutions have agreed to operate under one central IRB.

Typically, only a small percentage of patients sign up for clinical trials, citing natural skepticism over being a guinea pig. In this case, more than 70 percent of eligible patients have agreed to participate.

The scale of the study will help determine if – should they all be effective – one of the meds is more appropriate for certain populations. These subgroups might be defined by factors including obesity, ethnicity, smokers, genetics, comorbidities, dialysis patients or other markers.



Principal Investigator Vincent
D. Pellegrini, M.D., John A.
Siegling Professor and Chair of the
Department of Orthopaedics and
Physical Medicine at the Medical
University of South Carolina

Advances in the battle against opioid addiction

The roots of the current opioid epidemic are complex. MUSC is introducing novel models to combat the problem.

One in four to five people of all races, religions and socioeconomic classes in the U.S. has had an addiction at some point in their life.

Doctors receive little education about the intricacies of opioids and their dependence-producing capabilities or alternate ways of managing pain. Insurers often don't pay for alternative multimodal treatments of pain. Insurers, all too often, also don't pay for the treatment of addictions.

Working with the S. C. Department of Alcohol and Other Drug Abuse Services (DAODAS) to maximize the impact of the recently federally awarded 21st Century CURES funding, MUSC is spearheading the SC MAT ACCESS project, or Medication-Assisted Treatment – Academic Community Capacity Expansion for Sustainable Success.

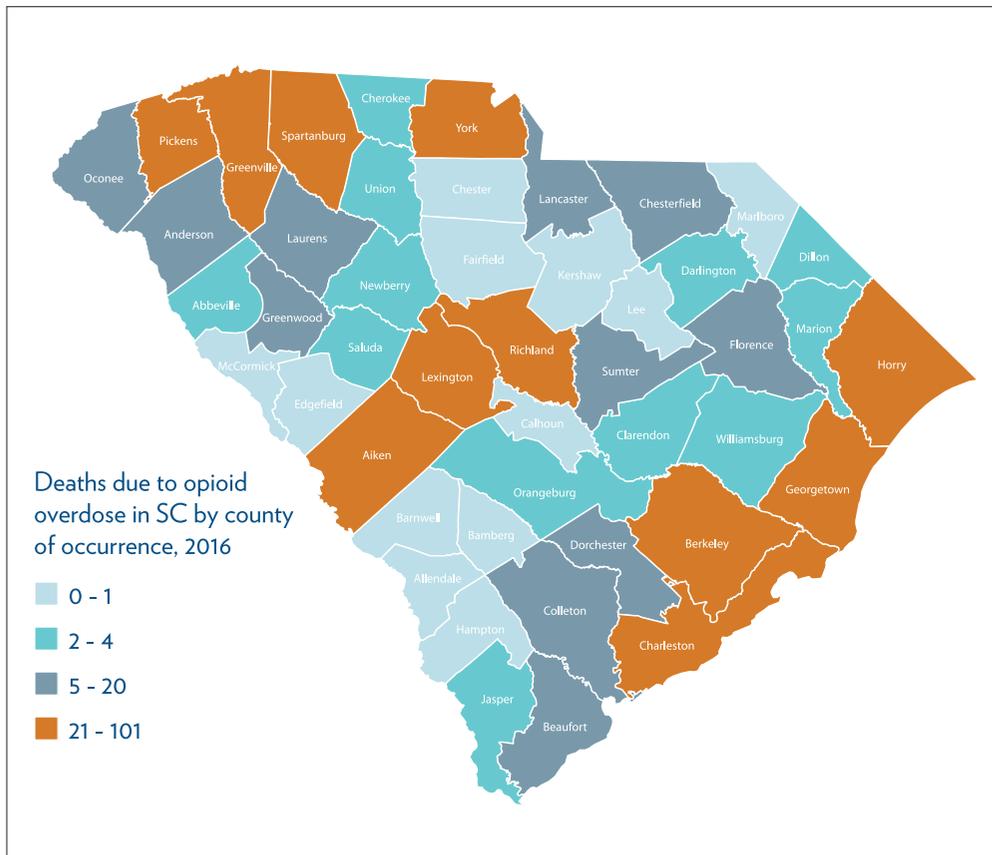
The goal of this model is to link experts at an academic 'hub' with primary care providers in nearby communities. Any doctor can contact MUSC specialists in addiction and pain management, and within 24 hours, someone will talk through a case or provide an appropriate referral.

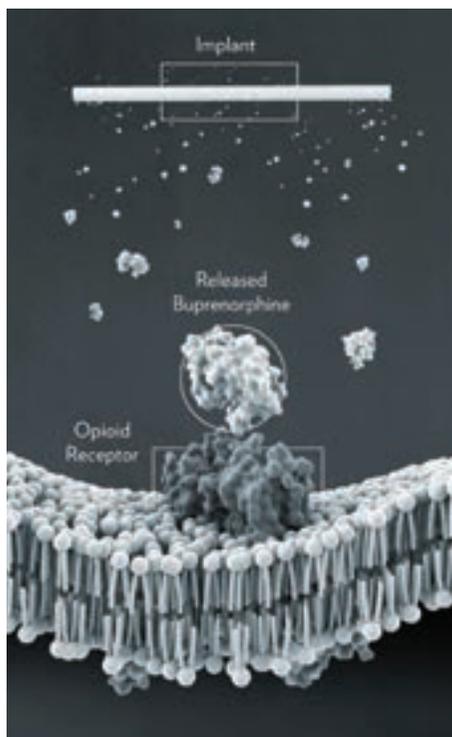
The project also will involve the creation of a network of telehealth providers throughout the state who are using medication-assisted therapy.

Methadone can only be dispensed through an opioid treatment program, of which there are only 16 in South Carolina.

Buprenorphine is now available in an implant that lasts six months and soon is expected to be available in an injectable form that will last one month.

SC physicians able to prescribe buprenorphine are all focused in urban areas. In Georgetown, there are only five physicians, and neighboring Horry County is one of the worst areas for overdoses. DAODAS has programs in most counties, but many do not offer MAT.





MUSC became the first in the state to administer Probuphine, a buprenorphine implant for the treatment of opioid dependence.

Doctors are limited to how many people they can treat. Medicaid just started to cover buprenorphine in the state, and even with that, it can take several layers of authorization to get it approved.

Kelly Barth, D.O., a psychiatrist and internal medicine doctor at MUSC Health specializing in the management of chronic pain and opioid dependence, is starting a three-week outpatient program in which pain patients receive daily physical therapy, psychotherapy and medical management – all while being weaned off their opioid pain medications.

Behind-the-scenes collaboration saves 30 lives in rural South Carolina

In 2016, Tallulah (Tullie) Fellers Holmstrom, M.D., was named chief medical officer (CMO) for the two South Carolina hospitals that make up the RCCH-MUSC Health Network: Carolina Pines Regional Medical Center in Hartsville and KershawHealth in Camden. She graduated from the MUSC College of Medicine in 1992. Holmstrom subsequently completed her internship and residency at MUSC and served as chief medical resident.



In her role as CMO, Dr. Holstrom helped to bring tele-ICU to Carolina Pines and Kershaw Health in June 2016. She says that while these hospitals were already providing high-quality care, they are making that care even better through tele-ICU. Nurses can call tele-ICU doctors at any time of the day or night, and within 60 seconds, a highly trained physician can be prescribing needed medication or directing other care.

Kershaw had 872 ICU admissions in 2016. “Based on the APACHE II score (an integer calculated at the beginning of the ICU admission to help determine the patient’s mortality risk), 30 of those patients that would likely have died in fact survived,” she says. Further, 2900 hospital days and 900 ICU days were saved, a savings of \$1.9 million.

The infusion of capital, increased resources, improved efficiencies, more robust data and analytics, and collaboration among health care providers combine to make all partners winners. More importantly, it made patients in these rural communities winners.

**Chief Medical Officer
Tallulah Holmstrom,
M.D., with patient in
KershawHealth ICU**

“We are committed to delivering the same advanced health care available at MUSC to all residents of South Carolina – and anywhere for that matter,” says Patrick Cawley, MUSC Health CEO. “That may take the form of tele-health or affiliations with other health systems like Kershaw. MUSC-trained physicians are now delivering care and managing hospitals across the state. A perfect example is our expanding relationship with Tullie Holmstrom at Kershaw.”

Which teens will abuse alcohol as adults?

Researchers hope to better pinpoint which teens would be likelier to abuse alcohol, so targeted interventions can be done.



MUSC researcher Lindsay Squeglia wants the public to know just how much alcohol and marijuana can affect children's developing brains.

MUSC researcher Lindsay Squeglia, Ph.D., assistant professor in the Department of Psychiatry and Behavioral Sciences, the lead author of a study published in the American Journal of Psychiatry, identified 34 factors that could be useful in predicting adolescent alcohol consumption. The list was compiled based on demographic, neuropsychological and neuro-imaging factors and computed using complex algorithms. These included several demographic and behavioral factors, such as being male; having a higher socioeconomic status; early dating; more externalizing behaviors, such as lying; and positive alcohol expectancies.

There were 137 participants, ages 12 to 14, who had never had alcohol. By age 18, 51 percent had initiated moderate to heavy alcohol use.

Kids who start using alcohol by age 15 are four times more likely to develop an alcohol-use disorder by adulthood. Their frontal lobe isn't fully developed; their emotional and reward centers are, so they find things very rewarding.

MUSC will be part of the long-term National Institutes of Health's Adolescent Brain Cognitive Development study, which will recruit 11,500 healthy children, ages 9 to 10, across the nation and follow them into early adulthood.



Kids who start using alcohol by age 15 are **4 times** more likely to develop an alcohol-use disorder



By age 18, had initiated moderate to heavy alcohol use

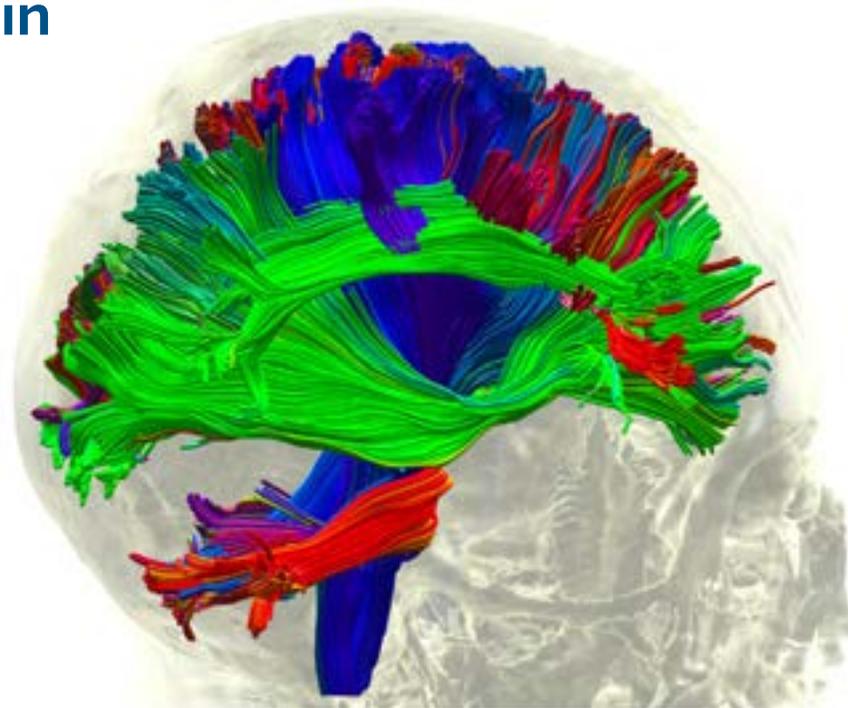
MUSC part of largest brain development study

An ambitious long-term study of brain development and child health called ABCD – Adolescent Brain Cognitive Development – is the largest study of this type in the nation. The Medical University of South Carolina is one of 21 research sites across the country helping to recruit 11,500 children ages 9 to 10. The children are followed for 10 years into early adulthood. The consortium grant will bring in an estimated \$7 million over 10 years. The study requires an initial eight-hour evaluation for the child and three hours for the parent on the first visit.

“We know that so much of what happens during adolescence predicts life achievement. We used to think brain development was done when you’re a kid. We now know that it lasts at least into the mid 20s,” says investigator Kevin Gray, M.D., a professor in the Department of Psychiatry and Behavioral Sciences.

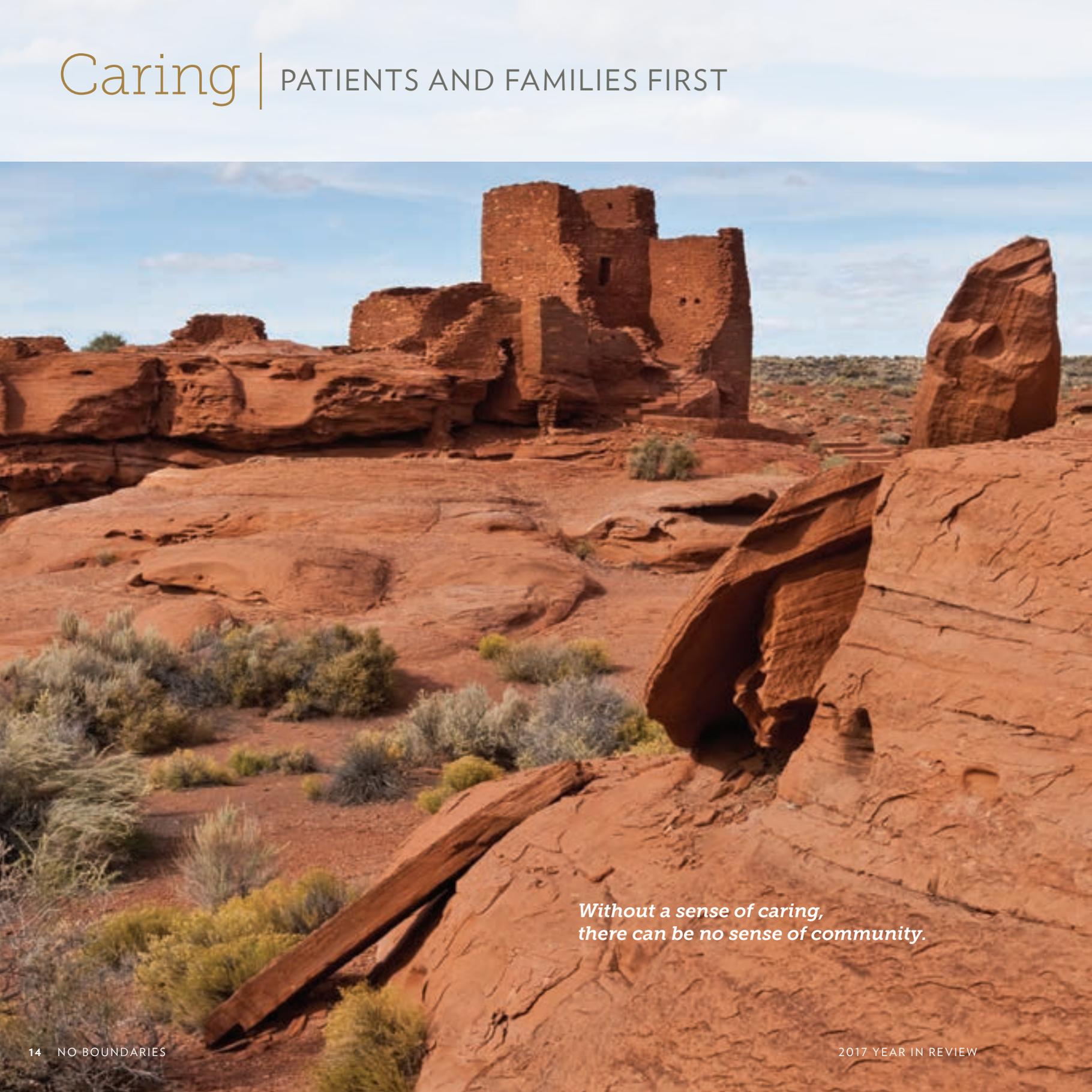
Data being collected include a medical history, genetics through a saliva sample, and environmental impacts – such as exercise and diet, socio-economic factors, mental health, substance use, extracurricular activities, cognitive testing and brain imaging.

MUSC researcher Lindsay Squeglia’s specialty is studying teens using structural and functional neuroimaging and neuropsychological testing. Gray credits her expertise in helping MUSC become a study site. “It is a rare person who has the clinical background and imaging background and expertise with kids to pull this off,” he says, adding that MUSC also has expertise in pediatric brain imaging, mental health, addiction neurosciences and radiology. Squeglia says the research can help explore if there are biomarkers for high-risk behaviors: suicide, major medical illnesses and substance use.



1 of 21
sites in the nation

Caring | PATIENTS AND FAMILIES FIRST

A photograph of ancient stone ruins in a desert landscape. The ruins are made of reddish-brown stone and are situated on a rocky plateau. The sky is blue with some light clouds. The foreground shows a large, flat rock surface with some sparse vegetation.

*Without a sense of caring,
there can be no sense of community.*

Government calls on MUSC to address mass violence

National resource center to address victimization following mass casualties

With multiple mass casualty events in 2017 showing an increase in frequency, a team at MUSC's National Crime Victims Research & Treatment Center have their hands full in the development of a Mass Violence and Victimization Resource Center funded by an \$18 million grant it received from the Office for Victims of Crime (OVC). Dean Kilpatrick, Ph.D., center director, says the goal will not be to parachute in to save the day, but to provide long-term help and improve the quality and infrastructure of resource support. In the case of Las Vegas, an estimated 75 to 80 percent of the people affected by the mass shooting didn't live there or even in Nevada. The problem becomes how to effectively provide services across jurisdictional lines.

In addition to using resources of current faculty and staff at MUSC, the center will be partnering with 11 external groups, consulting with 26 subject matter experts and hiring 19 new staff members to manage various aspects of the grant.

MUSC will help build infrastructure and help the OVC figure out what areas need additional resources and training. MUSC may provide some direct services, but the main role is to identify gaps. These include technology and other kinds of channels and mechanisms to speed up the process of recovery and aid local states, cities and towns where this is happening. One way that will happen is through the development of high-quality, online resources and apps. Over the next three years, the mass casualty center will develop a series of resources that can be used by everyone from survivors to first responders. The center also will be working to raise stress resiliency in the general public. Kilpatrick says "it's a cumulative effect in terms of stress. It's not that you



get immune to these things, but rather more sensitized." His team will encourage the public to put such violence into the proper perspective, since they are at a greater risk from other dangers, such as motor vehicle accidents, for example. "Go on with your life, build good networks with your friends and neighbors. Social support is one of the most protective things we have," he says.

"What happens to people is depressing. They've gotten no appreciation for what they've gone through. We can't undo what happened, but we can do our parts to make things better, and we will make things better in many ways."

Memorials were set up as survivors grieve long after Las Vegas shooting. Photo by Richard Brian/AP.

MUSC psychologists take trauma expertise to Puerto Rico



The invisible victims of hurricane Maria destruction are school children. Photo by Carlos Giusti/AP.

A team of MUSC psychologists planned to train about 600 teachers in Puerto Rico in how to help students traumatized by the impact of Hurricane Maria. Psychologist Regan Stewart says after they arrived, leaders in Puerto Rico's Department of Education told them that they needed to reach not hundreds, but thousands of teachers, social workers and other people involved with children through the public education system.

Train-the-trainer became a way to quickly spread information by teaching someone how to teach other people. The MUSC team from the Department of Psychiatry and Behavioral Sciences would now do that in addition to the trauma recovery workshops it had already planned.

This important work would be funded by a 2016 grant from the Substance Abuse and Mental Health Services Administration and the National Child Traumatic Stress Network that focuses on helping children who have been exposed to traumatic situations.

MUSC psychologist Michael de Arellano, Ph.D., says it rained every day. "The bridges were getting blown out. One of the places on the west coast flooded while we were there. Within 15 to 20 minutes, there were two feet of water running through the street," he says. "I bought a water filtration system because we

couldn't drink the water in our hotel or anywhere else we went." But the MUSC team says its challenges were nothing compared to what many of the people they met were dealing with: empty grocery stores and pharmacies, damaged or ruined homes, weeks without electricity or running water and spotty or nonexistent communications.

The team of three psychologists and one intern wound up training about 800 Puerto Ricans directly, including some who are now trained to offer the MUSC team's workshop to more people. MUSC also sent a videographer to record the sessions, with an eye toward creating an online resource. They taught them what can cause trauma, how to recognize it and how to help children reduce their stress levels. The techniques they used included progressive muscle relaxation, controlled breathing and visualization.

Two of the MUSC team members are from Puerto Rico. Rosaura Orengo-Aguayo and Freddie Pastrana-Rivera had the chance to see family members for the first time since the hurricane devastated the island.

They're proud to be Puerto Rican and proud that they were able to help through their work with MUSC. Orengo-Aguayo says the trip reminded her of what matters in life. "I'm now eating all my food, drinking all my water and being very grateful for everything I have."

Effect of trauma on brain development



Seventy percent of children will experience some kind of traumatic event by the time they are 18. Fifty percent will experience some form of interpersonal trauma.

Dr. Casey Calhoun fits an EEG cap to measure response to threats.

A \$3.5 million, five-year CHARM (CHARleston Resiliency Monitoring) study funded by the National Institute of Mental Health, looks at 360 children in third, sixth and ninth grades and follows them over a two-year period. It includes a comprehensive assessment, including functional magnetic resonance imaging, EEG and questionnaires, to examine specific neural, physiological and psychological processes that contribute to long-term stress management and resiliency.

One innovative aspect is the longitudinal imaging component within a pediatric population. Researchers will have a more comprehensive understanding of areas of the developing brain related to threat-processing in children. The other distinguishing feature is merging multiple gold standards. Saliva cortisol testing and neuroimaging are combined with other common methods of assessment, such as comprehensive interviewing.

Discovering | INNOVATION

The difficulty lies not so much in developing new ideas as in escaping from old ones.

New immunotherapy gives hope to cancer patients

Young patients with leukemia may be able to get a new type of treatment known as CAR T-cell immunotherapy at MUSC Health, possibly within a year. The Food and Drug Administration recently approved the use of the “living drug” approach for kids and young adults with B-cell acute lymphoblastic leukemia (ALL) who haven’t responded to standard treatment or have had the cancer recur. In a clinical trial presented to the FDA, more than 80 percent of the children who got the treatment went into remission, according to the drug company Novartis.

T-cells, which play a key role in the immune system, are removed from the patient. They’re genetically altered to produce chimeric antigen receptors (CARs) or T-cell receptors (TCRs), which recognize and target proteins specifically linked to cancer, then returned to the patient’s body. Genetic alteration involves the use of a retrovirus or lentivirus that acts as a courier to take the messaging to the DNA of the cells.

Since CAR-T cell treatment is so personalized, it may cost patients more than \$300,000. It also comes with risks that include:

- Cytokine-release syndrome, which can cause reversible symptoms including a fever, breathing problems, delirium and seizures
- B-cell aplasia, which reduces the body’s ability to make antibodies
- Tumor lysis syndrome, which is a life-threatening condition caused by the breakdown of dying cells.

At MUSC Hollings Cancer Center, there is one of fewer than 20 clean cell facilities in the country. More immunotherapy trials and treatments are underway there than at any other institution in the state. These include:

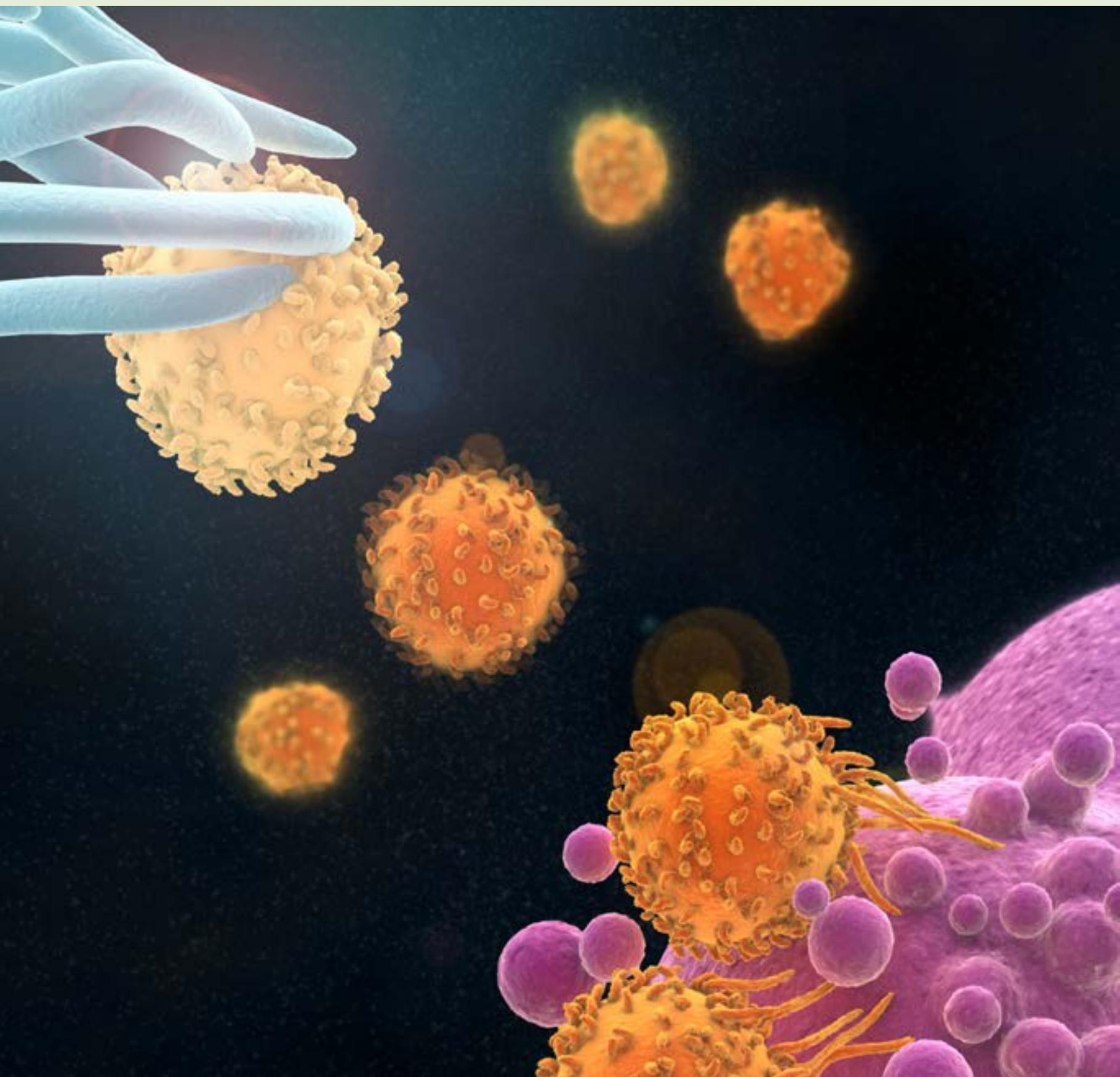
- Monoclonal antibodies (aka targeted therapy), drugs that bind to or mark cancer cells so the immune system can find them more easily
- Cytokines, proteins made by the body’s cells that help the immune system fight cancer
- Vaccines, which boost the immune system’s response to cancer cells
- Bacillus Calmette-Guerin, bacteria used to treat bladder cancer

Immunotherapy is becoming the fourth pillar of cancer treatment, joining chemotherapy, radiation and surgery. The FDA approval opens the way for more equipped hospitals to provide CTL019 and other CAR-T cell therapies. Medical centers that have the necessary clinical expertise and infrastructure in place to treat ALL and, importantly, to handle the challenging side effects of adoptive cell treatment, are now working with Novartis to be certified as CTL019 centers.

MUSC Children’s Health is ready, according to Michelle P. Hudspeth, M.D., director of the Division of Pediatric Hematology/Oncology. “CAR-T cell therapy depends on the very infrastructure that we use every day,” says Hudspeth. “This includes bone marrow transplant coordinators, hemapheresis nurses, cryopreservation technologists, oncology physicians, critical care physicians and oncology and critical care nurses.”



Dr. Michelle Hudspeth says MUSC is poised to become the only CTL019 center in South Carolina.



Options for lung cancer patients improving

A multidisciplinary team of MUSC investigators is working at the interface of immunotherapy and genetics to develop a new treatment option for some patients with lung cancer: Tumor-infiltrating T lymphocyte—or TIL—therapy.

“Checkpoint modulators (such as PD-1 and PDL-1 inhibitors) in lung cancer have had spectacular results in a few cases and responses in about 20 percent of patients but have done little in the other 80 percent,” says John M. Wrangle, M.D., an MUSC medical oncologist who specializes in immunotherapeutic approaches to cancer, especially lung cancer.

Wrangle and his collaborators, who include cancer immunologists Mark P. Rubinstein, Ph.D., and Chrystal M. Paulos, Ph.D., thoracic surgeon Chadrick E. Denlinger, M.D., and bioinformatician Jeff Hammerbacher, are currently working on two related strategies that lie at the interface of immunotherapy and genetics. The first and most immediate goal of the team is to create a tumor-infiltrating T lymphocyte (TIL) product for lung cancer that they hope to bring to clinical trial at MUSC Hollings Cancer Center. In TIL therapy, a type of adoptive cell transfer (ACT) therapy, T cells are harvested from a patient’s tumor, expanded outside the body and reinfused into the patient to enhance the immune response against cancer.

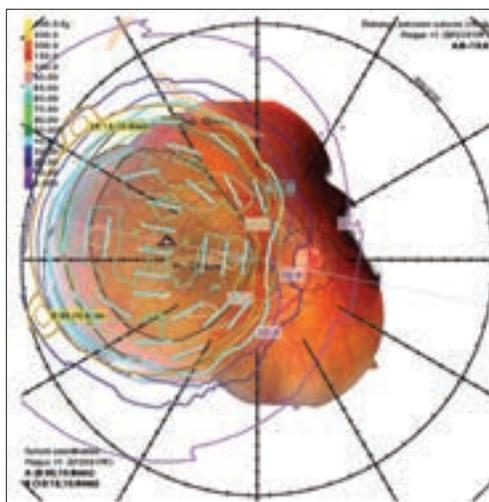
The availability of an FDA-registered clean room suite in the MUSC Center for Cellular Therapy, where cells harvested from the patient can be expanded and manipulated safely before reinfusion, makes the TIL therapy trial feasible at Hollings.

The team is working at the interface of immunotherapy and genetics to help fine tune TIL therapy and to develop personalized vaccines tailored to the neoantigenic profile of a patient’s cancer that could one day be administered in combination regimens to expand the number of people with lung cancer who benefit. Such a vaccine could consist of a mutated protein or peptide administered with an adjuvant to optimize the immune response. Next-generation genomic sequencing of both healthy and cancerous tissues has enabled identification of cancer-associated mutations known as neoantigens. Because they result from mutations that are unique to cancer cells, immunotherapies targeting them should not damage normal tissue. Cancer mutations could in fact be made recognizable — and precisely targetable — by the immune system as a result of some of those very mutations. Ironically, the mutations that define cancer and make it such a fearsome foe could become its Achilles heel.

Relying on the MUSC Center for Genomic Medicine directed by Stephen P. Ethier, Ph.D., the team is having each of the tumor samples sequenced so that neoantigens can be identified. Sophisticated machine learning and other advances in bioinformatics have enabled predictive algorithms to be developed to identify which of these neoantigens are most likely to trigger an immune response. The MUSC team is using a predictive algorithm that is being optimized by Hammerbacher to identify the neoantigens most likely to provoke an anti-cancer immune response.

Sight for Sore Eyes

Plaque brachytherapy saves vision in some patients with ocular melanoma



3-D reconstructions of the eye enable radiation dose to be tailored to the tumor.

MUSC Health ophthalmologist George N. Magrath, M.D., and radiation oncologist S. Lewis Cooper, M.D., are collaborating to make a potentially vision-saving radiotherapy available to patients with choroidal melanoma. A diagnosis of choroidal melanoma once left surgeons with no choice but to remove the eye, since in 40 percent of cases the cancer spreads to the liver and lungs and is uniformly lethal. However, the Collaborative Ocular Melanoma

Study showed that survival was no better in patients whose eye was removed than in those who underwent a form of radiotherapy known as plaque brachytherapy, which in some patients can not only spare the eye, but also save some vision.

In plaque brachytherapy, a gold disk or “plaque” studded with radioactive seeds is custom fit to the tumor and seated in the back of the eye for a specified number of days, during which the patient is hospitalized. It is effective in killing the tumor in 98 percent of cases. Although the procedure was pioneered more than three decades ago, it only became available in South Carolina last year. Patients with choroidal melanoma were once left with a harsh choice — lose an eye or travel outside the state to a center offering plaque brachytherapy.

When Magrath, an MUSC graduate, returned to take a faculty post last year after completing a fellowship at Wills Eye Hospital, he was determined to make this procedure available to patients closer to home, at MUSC’s Storm Eye Institute. The collaboration with Cooper and the radiation oncology team enabled him to bring to the Lowcountry new advances in the field that improve the chances of preserving vision.

Using 3D reconstructions of the eye, Cooper and the other radiation oncologists customize the radiation dose to the tumor and plan the deployment so as to minimize risk to the structures of the eye crucial for vision. “What Lewis (Cooper) does and what they are really

good at in radiation oncology is that they will tinker with the radiation and pull it away from the optic nerve and the critical structures of the eye,” says Magrath. “They can customize it down to fractions of a millimeter.”

The struggle to save vision continues in the two years after surgery, when radiation and the dying tumor take their toll on the macula and optic nerve. The damage done by radiation is similar to that seen in patients with diabetes, and some common diabetes medications, such as vascular epithelial growth factor (VEGF) inhibitors, are proving useful in combating radiation damage.

Radiation blocks blood flow to the retina, increases inflammation and leads to loss of different retinal cells. This causes the retina to signal for new blood vessels to grow by releasing VEGF. These new blood vessels are leaky and bleed into the eye, causing swelling and eventual scarring of the macula and the optic nerve. VEGF inhibitors help prevent the formation of these blood vessels. New postoperative laser treatments target the ischemic retina to prevent it from releasing the harmful growth factors. Corticosteroids are used to reduce the inflammation caused by the dying tumor.

“We are now able to save most of the eyes,” says Magrath. “If we can catch the tumors when they are small, we can do a really good job of saving the eye and potentially some vision.”

Novel 10-trial approach accelerates cancer breakthroughs

There are 30 researchers collaborating across academic and corporate borders to roll out 10 Stand Up to Cancer (SU2C) Catalyst clinical trial projects that combine cancer treatments from nine different pharmaceutical companies. The goal is to explore innovative approaches and accelerate cancer breakthroughs getting to patients' bedsides.

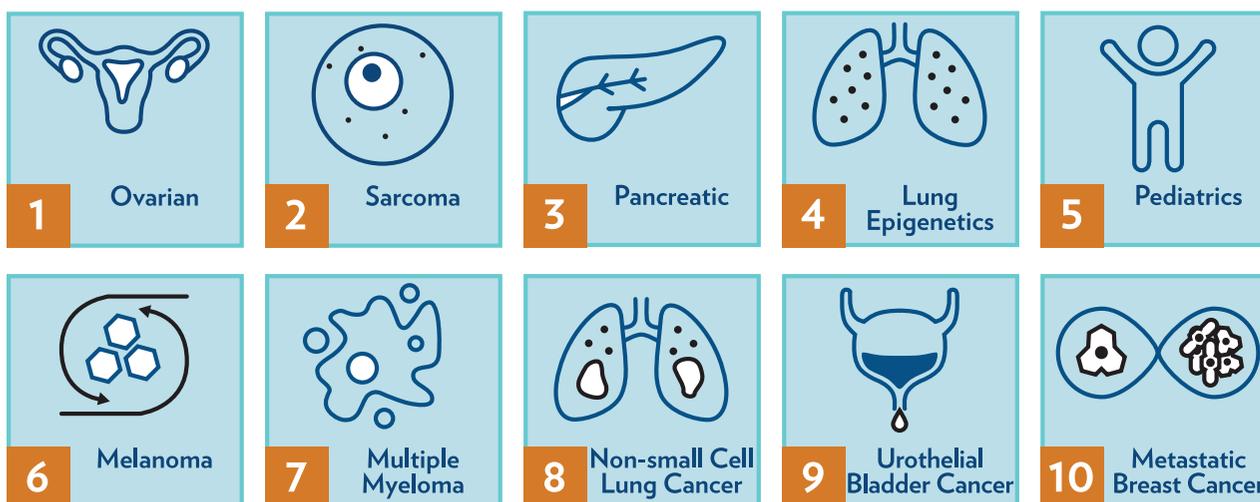
As a past member of the executive management committee for SU2C and chair of the donor-specific SU2C Catalyst steering subcommittees, Raymond N. DuBois, M.D., Ph.D., researcher and dean of the College of Medicine at the Medical University of South Carolina, has been working on this effort since its inception. The 10 inaugural clinical trials being launched will address a wide variety of

cancers, including breast, lung, melanoma, multiple myeloma, ovarian, pancreatic, hyper-mutant pediatric cancers, sarcoma and urothelial cancer. The focus of the SU2C Catalyst clinical trials is to promote novel treatments in combinations with other pharmaceutical companies' medicines, devices and therapies, as well as standard-of-care treatments.

These programs are truly innovative because they match academic and industry partners with significant support to test unique combinations of agents with cancer immunotherapeutics to help improve clinical responses and outcomes. The three companies involved, Merck, Genentech and Bristol-Myers Squibb, are allowing their drugs to be tested and combined with agents from other companies to determine their

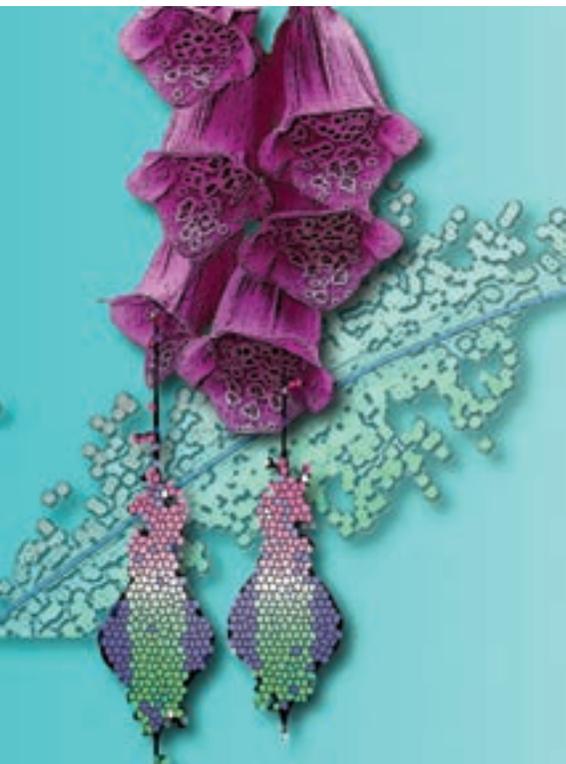
effectiveness. This will dramatically accelerate the process of getting these effective combinations approved for use in all cancer patients.

The researchers are most interested in accelerating the progress in those areas that have the most promise and will have the biggest impact on the clinical front. Competition for funding is extremely high, and individual principal investigators only bring projects forward that are highly innovative and on the verge of a major breakthrough. For example, the lung epigenetics team combines two epigenetic drugs that reshape DNA with an immune-based therapy for patients with advanced non-small cell lung cancer (NSCLC).



The 10 areas that SU2C researchers will focus on.

A multi-level drug screen in liver-like cells shows promise for treating hypercholesterolemia



Mother nature may offer a way to help patients with high LDL cholesterol.

Cardiac glycosides found in the leaves of the foxglove plant potentially could reduce LDL cholesterol differently than statins. Stephen Duncan, Ph.D., Chair of the Department of Regenerative Medicine, says the glycosides were identified through a stem cell screen for compounds that could be used off-label for the treatment of high cholesterol. “The nice thing about finding new uses for drugs already on the

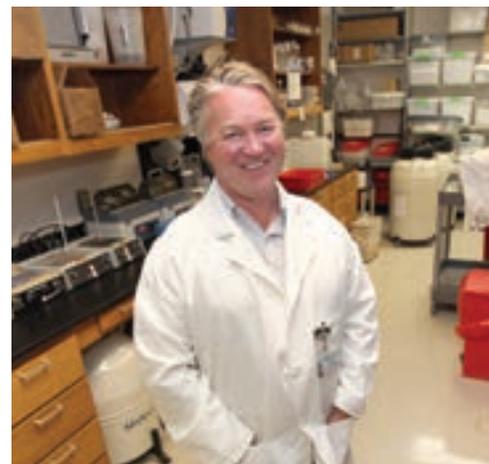
market is that they can be used relatively quickly in patients, because most of the needed safety trials have already been completed.”

Not everyone with high LDL cholesterol responds to statins. Statins increase levels of a cell surface receptor that removes LDL cholesterol from the bloodstream. However, statins do not work in patients with familial hypercholesterolemia (FH) who have a rare mutation in that receptor. It is an inherited disorder that leads to aggressive and premature cardiovascular disease. FH patients have very high cholesterol and can die of cardiovascular disease by their forties. The existing drugs for FH can cause fatty liver disease, and the best treatment is a liver transplant.

Duncan and his graduate student Max Cayo, who is finishing his medical degree at the Medical College of Wisconsin, developed a drug screen to identify an alternative to statins. Apolipoprotein B (apoB) is a molecule that liver cells use to make LDL. Drugs that decreased apoB could potentially lower cholesterol independently of the LDL receptor in FH patients and also in patients with other forms of high cholesterol. FH was a perfect model for testing alternatives to statins. Yet the rarity of FH meant these liver cells were scarce. Duncan’s group made induced pluripotent stem cells out of skin fibroblasts taken from a single patient with FH that provided a renewable source of liver-like

cells that retained the mutation. The group tested these liver-like cells with the SPECTRUM library, a collection of 2,300 pharmaceuticals, many of which had reached clinical trials. Surprisingly, all nine cardiac glycosides in the collection, some widely prescribed for heart failure, reduced apoB in liver-like cells from the patient with FH. Next, the team combed through the medical records of more than 5,000 patients, who also had LDL cholesterol records. Similar drops in LDL levels were observed in patients prescribed cardiac glycosides for heart failure.

This study provides the first evidence that cardiac glycosides could potentially reduce LDL cholesterol independently of the LDL receptor by reducing apoB.



Dr. Stephen A. Duncan holds the SmartState Chair of Regenerative Medicine at MUSC

Gift of the Magi may be a treatment for cancer

Cancer surgeon and researcher Nancy DeMore, M.D., is leading a clinical trial using frankincense to try to treat breast and colon cancer at the Medical University of South Carolina. The study was inspired by a research specialist in DeMore's lab. Ingrid Bonilla had researched frankincense as a treatment on breast cancer cells as an undergraduate student at Charleston Southern University.

DeMore, who has done extensive research on new treatments for breast cancer, says boswellic acid, the extract from Indian frankincense, may help patients by reducing inflammation. The chemical structure of boswellic acid is similar to other anti-inflammatory drugs such as ibuprofen. DeMore and Bonilla wrote the current clinical trial with data from clinical trials of the extract in Europe. DeMore says their study is a "window of opportunity" trial that takes advantage of the window of time between the initial diagnosis of breast or colon cancer and surgery to remove the cancer. "The tumor from the biopsy that was taken to make the diagnosis of cancer before treatment will be compared to the tumor taken at surgery after treatment," DeMore says. "This will allow us to assess whether taking boswellia changes the biology of the tumor."

Frankincense would not be the only plant-based treatment for illness. For example, digoxin, from the foxglove plant, is used to

treat cardiac arrhythmias. DeMore says "a lot of herbs and alternative therapies haven't been studied scientifically, so it's really important to know, in a well-designed clinical trial, if these natural products work." DeMore started her research into natural products with curcumin in the 1990s. Extracted from turmeric, curcumin inhibits blood vessel growth in tumors. She then set out to test medicinal uses of other natural products. The MUSC Hollings Cancer Center is funding the trial for 40 breast cancer and 20 colon cancer patients over the next one to two years. "I would just encourage patients to really be open to clinical trials. They're the only way to make new discoveries and to move the field forward."

While the preclinical evidence for boswellic acid seems promising, it's important not to replace standard treatment with natural therapies that haven't been studied well. Therapies that aren't based on clinical trial results could have unexpected side effects, or even harmful effects. Over-the-counter frankincense may not contain the dosage or quality of the extract being tested in this study.

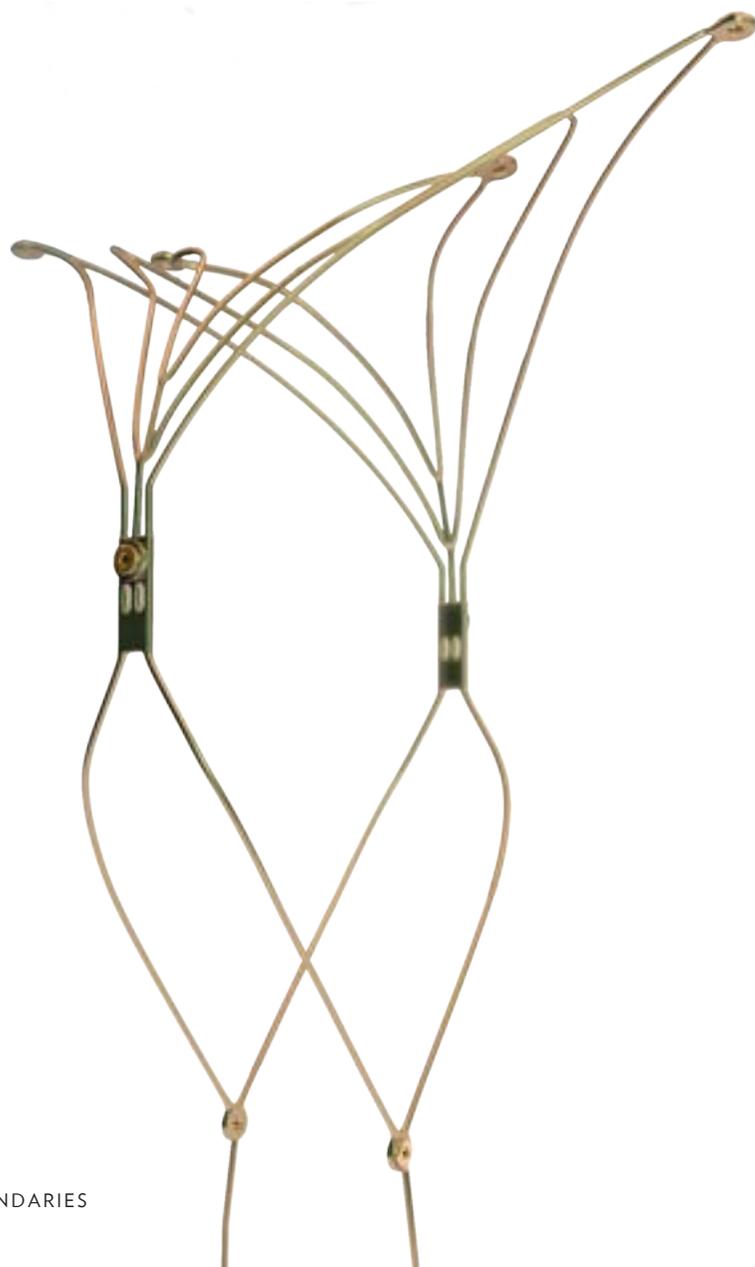
Above right: Research Specialist Ingrid Bonilla

Right: Boswellic acid, the extract from Indian frankincense, is similar to other anti-inflammatory drugs.



MUSC developing fresh surgical approaches to stroke

In 2017, MUSC's Comprehensive Stroke Center clinicians continued to refine and reinvent stroke care, from initial patient evaluation to surgical intervention.



Stroke is an emergency that requires immediate intervention. Yet most hospitals are not equipped to deal with complex strokes. Ultimately, valuable time could be saved if complex patients could be identified by emergency personnel in the field and transported directly to a comprehensive stroke center for treatment. A new device developed by CerebroTech Medical Systems, Inc., was tested on the first 45 patients in a pilot study at the MUSC Comprehensive Stroke Center. The CMS-5000 is a portable visor that detects changes in patients' blood flow to identify those with large vessel occlusions who must be transported to a comprehensive stroke center. Neurointerventional surgeon Aquilla S. Turk, D.O., professor in the MUSC Department of Neurosurgery, oversaw the pilot study and is participating in data analysis for the larger multi-site clinical trial, called VITAL (NCT03148340). In that trial, clinicians were able to correctly identify patients with large-vessel occlusions up to 92 percent of the time. The company hopes to test the CMS-5000 with emergency personnel in the field in 2018.

To care for complex patients, comprehensive stroke centers must be staffed with clinicians skilled in advanced procedures for acute ischemic stroke and repair of vessels in cases

MUSC surgeons evaluated the Pulserider device for reconstructing broad-necked bifurcation aneurysms.

of hemorrhagic stroke. The COMPASS trial (NCT02466893) for acute ischemic stroke compared thrombectomy using a direct aspiration first pass technique (ADAPT) and standard stent retrieval as first approaches to removing clots. The trial was led by Turk in collaboration with the Icahn School of Medicine at Mount Sinai and the University of Buffalo, and MUSC neurointerventional surgeons Raymond M. Turner, M.D., Mohammad I. Chaudry, M.D., Alejandro M. Spiotta, M.D., and Jonathan Lena, M.D., served as procedural experts. Early data showed that, in patients who received ADAPT alone, arteries were recanalized twice as fast and good outcomes were achieved more often compared to patients who required additional treatment. The trial wrapped up in summer of 2017 and full results will be presented in a featured talk at the International Stroke Conference in February of 2018.

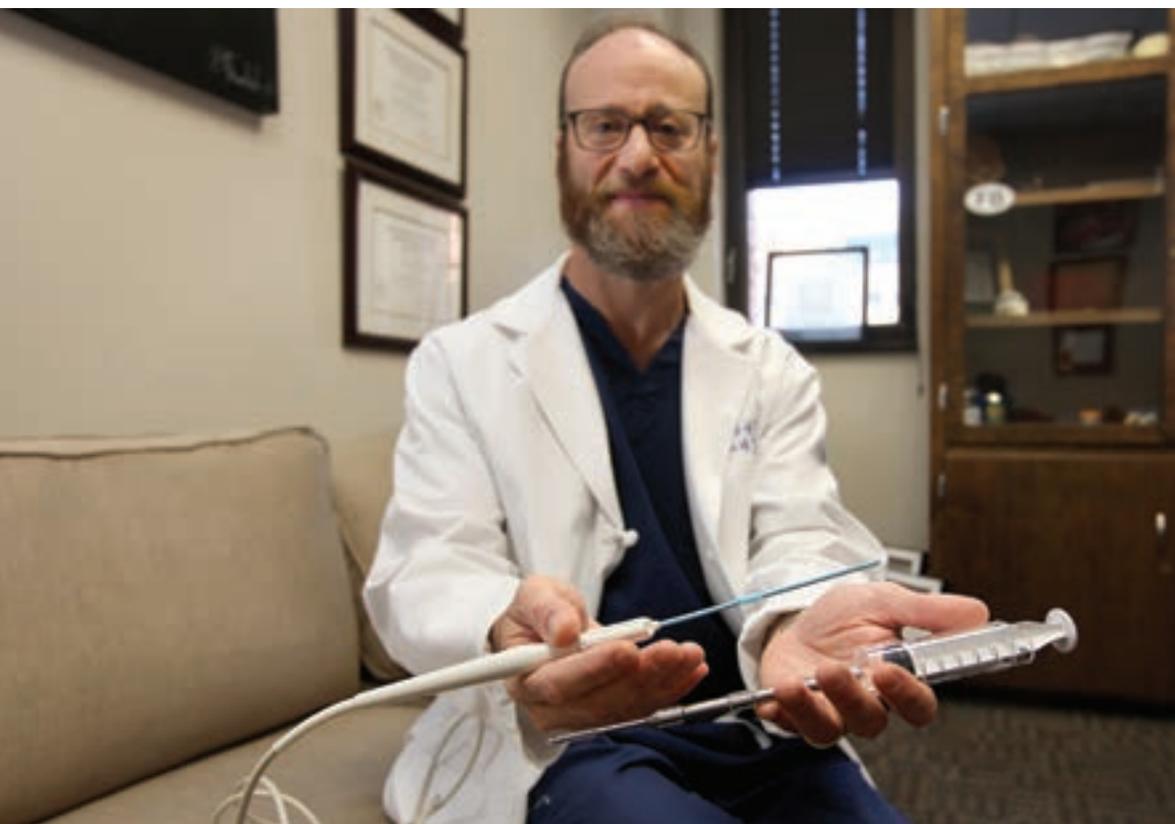
Turner, Spiotta and Lena were also among the first in the world to treat patients using two new devices for the surgical treatment of hemorrhagic stroke. The Artemis™ Neuro Evacuation Device (Penumbra, Inc., Alameda, CA) was approved by the FDA on August 14, 2017, for evacuation of deep intracranial hematomas, which can occur as a result of hemorrhagic stroke. Similar to the BrainPath device (NICO Corp., Indianapolis, IN) evaluated in the ENRICH (NCT02880878) trial, the Artemis provides a more complete, quicker evacuation of a hematoma during minimally invasive

surgery. MUSC Health neurosurgeons deploy both devices in patients with life-threatening hematomas not controlled by medication. While traditional treatment requires a wait-and-see approach of close evaluation and blood pressure control, the devices represent a paradigm shift in treating hemorrhagic stroke, proving that it can be managed surgically in certain cases.

Turner, Spiotta and Lena were among the first in the world to treat patients using two new devices for surgical treatment of hemorrhagic stroke.

To prevent brain aneurysms from rupturing and causing hemorrhagic stroke, they must be repaired surgically when they reach certain measures of size or fragility. MUSC just completed the ANSWER trial (NCT02312856), which evaluated the new Pulserider® Aneurysm Neck Reconstruction device (Pulsar Vascular) for reconstructing broad-necked bifurcation aneurysms. In the July 1, 2017 issue of *Neurosurgery*, Spiotta, Turk and Turner reported that the new device was safe and offered probable stroke prevention benefit for patients with this type of aneurysm. The Pulserider was approved by the FDA on June 19, 2017.

MUSC neurosurgeon proves necessity is the mother of invention



Bruce Frankel, M.D., holds a smart Instrument that allows for the attachment of multiple surgical tools used in brain and spinal surgery that can be visualized by a tiny ultrasound built into the handle (R) and a device used to perform vertebroplasty, as well as to cement screws into spines affected by osteoporosis or metastasis (L).

Whether Bruce Frankel is placing screws in a spine, forging 160 layers of steel into a Bowie knife or creating a way to see beneath a tumor, his brand of curiosity doesn't end with simply wondering how something might work better. He, like many inventors, has been compelled from boyhood to fix problems by creating unique solutions. He has 12 patents and 10 licenses to show for it. His first medical invention

was a cement tap. When he was a young surgeon, he had a patient in Memphis with a fracture in a bone that was very osteoarthritic. He realized the screws he was going to insert into it weren't going to stay put.

"This is terrible,' I thought to myself. She's going to get up, and the screws are going to rip out of her back," he says.

"I would take a needle and inject the cement in the bone, but the bone was like Swiss cheese – it would squirt backward along the needle and out another hole. So, I thought, 'Why don't I make a disposable tap that would prevent backflow of cement that could be followed by screw placement?'"

It's not just how something can be done better that he grapples with but also how to improve on something that's inferior or possibly even

dangerous. Such was the case when he devised a way to use a hand-held ultrasound-containing instrument to see within and around a tumor. "I was doing surgery and couldn't see blood vessels behind the tumor no matter what I used, and that posed serious risks." The device was unique enough that it is used in a number of different surgical applications. For that invention, he received two patents, with others still pending.

Not long after, he recognized there was still a need for a safer way to locate pilot holes in bone prior to performing a pedicle screw implantation. He crafted a small ultrasound device with a probe attached to the tip that could be used to detect even the smallest bone breaches prior to the screw being inserted with the potential to greatly decrease the risk of injuring spinal nerves traveling millimeters away.

Earlier this year, Frankel received notice that the FDA had approved another device he invented, a curved titanium rod he invented for use in minimally invasive lumbar spinal fusion surgeries where degenerative spinal conditions, fractures, dislocations or tumors are present. Frankel noticed during his surgical procedures, when he would tighten the construct down, the curvature of the rod would cause the top part of the tall screws he was inserting to touch or overlap. When the screws are not placed properly, it puts stress on the components. After the procedure, that could lead to loosening or other complications. But because of the device's wave shape, several concave dips in the rod allow screws to stay put and not touch when tightened.

While he's fortunate to have been granted so many patents, licenses and relicenses, he also says he's had lots of failures. That just keeps him going back to the drawing board. And not for the prestige, but for the people who benefit from his work.

Concussions identified in the blink of an eye



A concussion detection aid developed at the Medical University of South Carolina may help with field sobriety testing and detect diseases such as Parkinson's, Huntington's and schizophrenia. All of those conditions can cause changes in the way a person blinks.

The Zucker Institute for Applied Neurosciences (ZIAN) at MUSC recently partnered with BLINKtbi, Inc. to test and bring a Blink Reflexometer to market. Co-inventor and ZIAN CEO Mark Semler says because a blink is an involuntary reflex, it's a good way for a trainer trying to make a call on the sidelines to check neurological function. The Blink Reflexometer has the potential to better identify concussions and help the more than 400,000 children and teenagers who suffer sports-related concussions each year.

BLINKtbi co-founder and COO Ryan Fiorini says ZIAN made the licensing process much

easier than usual for a university-related device. "ZIAN has cracked the code on efficient licensing and being a technical partner for building medical products."

Over the past few years, the device was tested on trial participants at MUSC and athletes at The Citadel. The ZIAN team hopes the Food and Drug Administration will approve the device within two years.



A prototype of the Blink device tracks eyelid movement to indicate possible concussion.

A Robotic Revolution



MUSC offers robotically assisted procedures in many areas. While the duodenal switch surgery has been done previously, mitral valve repair and DIEP flap surgery were offered in 2017. “These are procedures offered by very few centers in the country, and certainly we are the only center in the state doing these procedures,” says MUSC Health cardiothoracic surgeon Marc R. Katz, M.D.

The da Vinci SI System available at MUSC Health provides high-definition 3D visualization of the valve and has wristed robotic arms that are capable of greater dexterity than human hands. “The robot does what the surgeon’s hands do,” says Katz. “It translates the normal motions of the surgeon’s hands in through tiny incisions.”

Mitral Valve repair instead of replacement

Katz has more than 15 years of experience with the da Vinci robotic system. He had the third robot in the U.S., was an investigator on the clinical trials that led to its approval and has been engaged in each of its developmental iterations. He is now able to repair leaking mitral valves before patients have heart failure. He is the first to offer robotic mitral valve surgery, the least invasive of all mitral valve repair techniques, to patients in South Carolina. In appropriately selected patients, and when performed at high-volume centers such as the MUSC Health Heart and Vascular Center by surgeons experienced in the technique, robotic mitral valve repairs achieve results at least as good as those attained by other minimally invasive techniques or via open surgery, but with less pain, a shorter hospital stay, a quicker recovery and a more rapid resumption of normal activities.

“Patients return to work when they feel like it after robotic repair,” explains Katz. “For most, that’s within a week or two instead of the eight to 12 weeks required after open heart surgery.”

For robotic mitral valve surgery, the surgeon makes several small ports — approximately half an inch long — into which the robot's arms are docked and a small camera is inserted. "The scope is sitting right next to the valve and so the valve looks like it is ten feet tall," says Katz. "Due to that better visualization of the valve, we can achieve excellent mitral valve results."

Over 90 percent of degenerative mitral valves are suitable for repair.

As the mitral valve degenerates, the seal becomes leaky, leading to backflow of blood into the atrium. Backflow may reduce both the supply of oxygenated blood to the body's organs, causing shortness of breath and other symptoms, and result in a backup of fluid in the pulmonary vessels, which can lead to pulmonary hypertension. The resulting stresses on the heart can cause congestive heart failure.

In the past, the mitral valve was replaced with a prosthetic and surgery was reserved largely for those who had already developed congestive heart failure. Over 90 percent of degenerative mitral valves are suitable for repair, and better short- and long-term results are achieved with repair than with replacement. Unlike replacement, repair does not require long-term anti-coagulation.

MUSC Health surgeons also use innovative robotic surgery in breast reconstruction

Chitharanjan Pullattrana, M.D., and plastic surgeon Kevin Delaney, M.D., have joined forces to do robotically assisted

breast reconstruction in what is one of the first procedures of its kind in the nation. Delaney proposed an innovative idea to try a less invasive way to harvest the DIEP, or deep inferior epigastric artery perforator flap. The DIEP flap is a technique in which skin, vessels and tissue are taken from the stomach to recreate the breast following a mastectomy.

In this procedure, fat and skin tissue from above the patient's belly muscles has already been harvested. Delaney works above and Pullattrana works below the abdominal muscle, hooking the blood vessels needed to support a transplant of tissue to the patient's breast. Plastic surgeon Jason Ulm has already prepared the breast site to receive the flap while Delaney and his team do the abdominal incisions. In addition to the robotics surgical unit, the surgeons used a fluorescence imaging system that allows them to visualize microvascular blood flow and perfusion in tissue as they operate.

This procedure allowed for a small cut in the abdomen about the size of a quarter, versus the former method, which would have meant an eight-inch cut into her muscle and fascia. The patient who is among the first in the nation to have the procedure done robotically said she is fine because she trusted her doctors and was able to go home after only three days.

Laparoscopy should be the bedrock of surgeons' training, and the great majority of the cases that are done in general — GI, surgical oncology — can be done well laparoscopically, Pullattrana says. "In tight spaces and when the patient is obese, the robot enables us to do these challenging procedures in a minimally invasive fashion with less fatigue and greater dexterity for the surgeon, both of which help the patient."

Trials at the MUSC Hollings Cancer Center, an NCI-Designated Cancer Center, run the gamut from Phase 1 trials to translation



Carolyn D. Britten,
M.D., associate director
of clinical investigations

Spingosine kinase inhibitor for patients with liver cancer

Led by Carolyn D. Britten, M.D., associate director for clinical investigations at the MUSC Hollings Cancer Center, a phase 1 trial of a first-in-kind sphingosine kinase (SK) 2 inhibitor showed it to be safe and well tolerated by patients with solid tumors.

“Sphingolipid metabolism has been widely studied in cancer models, but translation of these basic science results to the clinic is limited,” says Britten. “The phase 1 trial was unique because it provided the first data on sphingolipid profiles in patients treated with an SK inhibitor.”

Britten is also the principal investigator of the phase 2 trial of YELIVA® (RedHill, Tel Aviv, Israel) as a second-line monotherapy in patients with advanced hepatocellular

carcinoma (HCC) who have experienced tumor progression despite treatment with currently available FDA-approved therapies. The most common primary malignant cancer of the liver, HCC has one of the highest mortality rates. The phase 2 trial is now recruiting patients at Hollings, with an initial goal of enrolling 12 patients. If a response is seen in these patients, additional patients will be recruited, with a target enrollment of 39.

Sphingolipids are known to be involved in the growth of solid tumor cancers. Sphingosine-1 phosphate (S1P), a pro-cancer, pro-inflammatory lipid signaling molecule formed when sphingosine picks up a phosphate group from SK1 or SK2 enzymes, has been shown to promote the proliferation of cancer cells and treatment resistance. By blocking the activity of SK2, the inhibitor helps prevent the formation of S1P.

The study is being funded by a grant from the National Cancer Institute (NCI) awarded in 2016 to Hollings with additional support from pharma manufacturer RedHill.

The effect of AGE on cancer. No not that kind of age.

Advanced glycation end products (AGEs) are reactive metabolites produced by glycation. They accumulate in the body as the result of poor diet, including processed foods and char-grilled meats.

MUSC researcher David Turner, Ph.D., is working with colleagues on two clinical trials exploring the role of AGEs in breast and prostate cancers. The breast cancer trial, led by Carolyn Britten, M.D., is seeing whether AGE levels can be reduced in women with metastatic breast cancer.

In the pilot trial, women receiving endocrine therapy for metastatic estrogen receptor negative breast cancer will take metformin and oligomeric proanthocyanidin complex (OPC) for 12 weeks. Turner says the trial will determine if the medication regimen will lower AGE levels. It also will see if high AGE levels are associated with increases in body mass index or insulin resistance, which also can predict poor outcomes for breast cancer patients.

The prostate cancer clinical trial, led by Michael Lilly, M.D., is a continuation from a pilot trial with 13 patients that found AGE levels came down in nine patients when they took the antioxidant OPC. These AGE and reactive oxygen species are very much intertwined.

Turner says the new trial is exploring if metformin and OPC have an effect on the AGE levels in the blood in prostate cancer patients. “This is the first time AGEs have been looked at in clinical trials in cancer. That’s a real push forward,” he says. “AGEs have been related to cardiovascular disease, diabetes, Alzheimer’s and Parkinson’s, but when it comes to cancer, there’s been very little out there.”

Frontiers in neuroblastoma treatment

Beat Childhood Cancer (BCC), a national clinical trials consortium, is sponsoring two multicenter phase 2 trials on advanced treatments for high-risk neuroblastoma. MUSC Hollings Cancer Center will serve as a site for both trials, each led by Jacqueline M. Kravaka, D.O., a pediatric hematologist-oncologist.

Neuroblastoma is the most common cancer in infants. The survival rate for the 40 percent of patients who are high-risk



is less than 50 percent.

The PEDS-PLAN trial is the first to incorporate precision medicine into upfront therapy for newly diagnosed high-risk neuroblastoma. This study uses a novel, molecular-guided therapy protocol in which each patient’s tumor and blood samples generate a genomic report that identifies genetic mutations and altered molecular pathways. An algorithm identifies known drugs that target these features.

“Most personalized medicine studies only look for one specific genetic mutation. So, these studies find a match for only 25 percent of cases,” explains Kravaka. “By including RNA sequencing and bioinformatics, we’ve come up with a precision medicine plan that includes six possible drugs.”

Jacqueline Kravaka, M.D., with patient enrolled in the first upfront pediatric precision medicine trial in neuroblastoma

Educating | INNOVATIVE LEARNING

*Not all classrooms
have four walls.*

MUSC collaborates on operating room design

The typical OR in most hospitals is a cramped, square white room with a patient bed in the middle of the space. Many doctors and nurses feel that ORs are outdated and restrictive, and in light of today's state-of-the-art hospitals and cutting-edge technologies, should be modernized.

In a groundbreaking project, co-investigators Scott T. Reeves, M.D., chair of the Department of Anesthesia and Perioperative Medicine at MUSC, and Anjali Joseph, Ph.D., the Spartanburg Regional Health System Endowed Chair in Architecture and director of the Center for Health Facilities Design, working with Clemson University, have made great strides taking the health care industry's standard operating room suite and incorporating modern architectural principles to create a focused, comprehensive design that is efficient and enhances the patient care experience.

Both have been working collaboratively with a team of researchers, engineers and clinical specialists with a four-year \$4 million grant funded in 2015 by the Agency for Healthcare Research and Quality.

Reeves and Joseph are examining how to maximize space in the OR to improve accessibility to equipment and the patient, implementing changes like rearranging the typical placement of the patient bed and analyzing traffic flow in the room.

The project covers three specific areas of research designed to improve patient care and efficiency in a future OR design:

- unmasking of anesthesia-related alarms
- communications traffic flow and door openings
- decreasing risk of surgical site infections to patients; and
- an integrated OR suite design.



With the project now in its third year, Joseph, Reeves and the team are building a full-scale mock operating room in the Clemson Design Center located in the Charleston Cigar Factory to expand the cardboard mock design created in 2016.

The mock OR will be created based on: research of past literature on OR functionality; observation of best practices in updated, modernized ORs; and input from South Carolina nurses, doctors and anesthesiologists on how the new OR should function.

Clemson University Architecture and Health students envision an operating room that is safe, efficient, flexible as well as patient- and staff-centered.

Work-family balance can tip wrong way for young doctors

Study looks at why women run greater risk for depression during medical internship year and later in their careers



Dr. Connie Guille knows what it's like to juggle family and medicine. Here, she holds a picture of her two daughters.

According to a study published in *JAMA Internal Medicine*, both women and men experience more depression during their internship year, yet female medical interns are more likely to suffer from symptoms of gender difference. Connie Guille, M.D., an associate professor in the Department of Psychiatry and Behavioral Sciences at MUSC, and Srijan Sen, M.D., Ph.D., an associate professor at the University of Michigan, began the Intern Health Study in 2007 during their residency training at Yale University. They first noted the extent of stress during their internship year and how it affected their colleagues, one of whom attempted suicide. Since that time, they've looked at rates of depression, as well as interventions to prevent it, in a pool of interns that is now up to 15,000.

The most recent study involved more than 3,000 medical interns during the 2015-2016 academic year, recruited across all specialties from 44 medical institutions. It was funded by the National Institute of Mental Health, National Institute on Drug Abuse and National Center for Advancing Translational Sciences.

"Medical internships were designed 50 years ago when interns were predominantly men, and they mostly had families who would take care of life outside of work. Women now make up half of this workforce, and the work environment is completely different," Guille says. "If you were in the hospital as an intern 50 years ago, over

the course of a month, you had five or 10 new patients. We have five or 10 new patients in a day now. Yet the model and tradition of internship year has not changed."

That predisposition to depression, combined with long work hours, sleep deprivation and stressors inherent to caring for patients who are suffering and dying, may further increase this risk. This work-family conflict can lead to the loss of women from upper-level jobs in medicine. Fifty percent of graduating medical students are women, but the representation of women decreases precipitously as physicians progress up the academic ladder from full-time faculty (38 percent) to full professor (21 percent), department chair (15 percent) and dean (16 percent).

Guille noted that seeking treatment for depression is still taboo, especially in the medical field. "Physicians are concerned that people would question their capabilities and there might be repercussions in terms of licensure later."

Expanding on the effort to find effective interventions for the prevention of depression in medical trainees, Guille and Sen just received a \$300,000 grant from the American Foundation for Suicide Prevention to investigate the use of mobile technology – such as the MoodGym app, a cognitive behavioral therapy tool she found in a previous study – to prevent suicidal ideation and depression.

MUSC MyQuest a national model for continuing education

MUSC's MyQuest was the 2016–17 bronze winner of the Brandon Hall Group Excellence Award for Best Launch of a Corporate Learning University, an international award that spans all industries.

Servicing more than 19,000 employees and students, MyQuest provides more than just annual mandatory education. Last year, “non-mandatory” education increased 74 percent with learners launching more than 117,000 learning events in addition to their annual requirements. With approximately 285 catalogs, MUSC is utilizing MyQuest to drive key organizational strategies, such as telehealth and innovation. MUSC's lifelong learners can also explore topics of personal interest, such as computer technology skills or wellness. MyQuest houses content created both internally and externally and provides mobile and tablet applications for learners on the go.

MUSC Learning, an external version of MyQuest for non-MUSC learners, offers fee-based classes and programs, including certification training within the MUSC Community Training Center.

Albany Cromer, MUSC Health manager of Learning Technologies in the Learning Office, accepting the 2016-2017 Brandon Hall Excellence Award for Best Launch of a Corporate Learning University



Residents' reporting key to safety improvement

The American Association for Physician Leadership chose the Medical University of South Carolina as the sole 2017 Leape Ahead Award Winner. The award recognizes organizations that have exhibited innovation in the creation of education or training programs to advance physician leadership and improve health care for medical students or residents.

MUSC Health's chief quality officer, Danielle Scheurer, M.D., developed a resident incentive program that rewards trainees for meeting goals aligned with institutional quality goals. She also created a position for the Medical Director of GME Quality and Safety to push the envelope in all six of the Accreditation Council for Graduate Medical Education clinical learning environment review focus areas.

In this role, Elizabeth Mack, M.D., has actively tackled the three common barriers to the reporting of serious safety events and near misses: time, lack of feedback and fear of retaliation. MUSC added a hotline, in addition to the online reporting system, to improve real-time reporting. Quarterly reviews involving leadership, faculty, nurse management and safety officers detail issues raised by residents and their mitigation. MUSC Health has successfully adopted a “Culture of Safety” policy and a “Just Culture” that fosters a non-punitive environment in which all employees can feel safe reporting errors and near misses.

As a result, culture of safety scores continue to improve.



(L to R) Sarah Yale, M.D., MUSC resident physician, Elizabeth Mack, M.D., medical director of GME quality and safety, and MUSC Health CEO Patrick Cawley, M.D.

Students transform clinic for Spanish speakers

Medical student Javier Laguillo speaks his patients' language on Spanish Night at the MUSC CARES Medical Clinic in more ways than one. "I was six when my family moved from Puerto Rico to Denver," he says. "It was a pretty drastic transition." So he knows something about what the patients who come to the monthly Spanish Night at the clinic are facing.

The CARES Clinic is a nonprofit group that offers free basic health care, including blood pressure checks, diabetes care, flu tests and immunizations. Medical, pharmacy and physician assistant students from MUSC volunteer there along with licensed doctors three evenings a week.

Once a month, the clinic is staffed with students who speak Spanish and a certified Spanish interpreter to care for patients who speak only Spanish. Laguillo helped make that happen. He sees it as a continuation of the way he grew up. His mother and father, both community medicine doctors, worked to help low-income populations.

CARES clinic student director of operations Celeste Jilich applauds Laguillo's drive to go beyond what's expected of an already busy doctor-in-training. She also sees Spanish Night as important for MUSC. "Spanish Night is an invaluable opportunity to provide comprehensive and culturally competent health care to our patients, regardless of national origin, first language, socioeconomic status, race or ethnicity."



Medical students talk before seeing patients at the CARES Clinic. All either come from families that speak Spanish or have spent enough time in Spanish-speaking countries to be fluent.



Spanish-speaking students Elizabeth Ogunrinde, Javier Laguillo, Michelle Ascanio and Carlos Sanchez volunteer at a nonprofit clinic in Mount Pleasant, SC.

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