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Duke University
School of Medicine
The pace of scientific discovery today is unparalleled.

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Among the youngest of our peers in academic medicine, Duke is teeming with scientists and physicians—and future scientists and physicians—who are absolutely dedicated to making the world a better place.

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Just as we launched our medical school and hospital on the eve of the Great Depression,

Duke is again prepared to boldly lead. We seek to grow historic strengths in the basic sciences, invest in new models of clinical care, foster greater collaboration, and accelerate progress from discovery to grow historic strengths in the basic sciences, invest in new models of clinical care, foster greater collaboration, and accelerate progress from discovery to care.

Duke people who are leading discovery, care, and education partnership.

In these pages you will meet just a few of the people who are leading discovery, care, and education partnership.

They—and we—seek your partnership. Please join us, and together we will move Duke Forward, and deliver medicine that changes the world.

Duke University School of Medicine
Today, biomedical scientists are unlocking secrets of the human genome and molecular processes deep within cells. They are sharing information at lightning speed and using technology to see and understand like never before.

Our culture of collaboration and innovation—extending across the 10 schools of Duke University—positions the School of Medicine for extraordinary success.

THROUGH DUKE FORWARD: MEDICINE THAT CHANGES THE WORLD, we seek to grow historic strengths in the basic sciences, invest in new areas of innovation, foster greater collaboration, and accelerate progress from laboratory bench to human application. We seek philanthropic investment in endowments for faculty, fellowships, and research, and current-use funds for early-stage research, equipment, and programmatic support.
LEADING DISCOVERY

Think about making dough for dumplings. When the dough gets too thin, your fingers sense it and send that information to your brain, which gives instant feedback to your fingers, telling them to move the other way, to work a different part of the dough. “It’s a constant cycle—from touch to perception to action,” says Fan Wang, PhD, associate professor of neurobiology and cell biology. “That’s how we interact with the world.”

The human finger has four types of sensors. “How do we use four limited sensors to encode the entire world of texture and shape out there?” Wang asks.

She’s beginning to find out by mapping the circuit of thousands of neurons receiving information from each type of sensor, as well as the circuit of thousands of neurons sending information to motor neurons that control the movement of the sensors. For now, she works with mice, which have similar kinds of sensors in their whiskers.

Mapping similar circuits in humans could help scientists better understand many health problems, including chronic pain. “In many chronic pain conditions, gentle touch induces excruciating pain, and these conditions are untreatable,” says Wang. “People go through drug after drug, and after a while, the drugs don’t work.” Somewhere along the line, the brain’s wiring changed.

Wang’s work could also help scientists develop better prosthetic limbs. Motor neurons are directly connected to our muscles. When these neurons fire, our muscles move. But one motor neuron has 1,000 other neurons connected to it that give directions about when and how to fire. “If we understood the pre-motor network, we could use that knowledge to make prosthetics more responsive and move more accurately,” says Wang. She is making progress—her team has described the entire network of brain cells that are connected to specific motor neurons controlling whisker muscles in newborn mice.

REGENERATING THE AGING LUNG

Hogan’s research could lead to new drugs to treat pulmonary fibrosis, a disease that kills as many people each year as breast cancer.

“As the lung gets older, the lung gets less stretchy, and instead of having a nice little network of sacs for gas exchange, they become sort of moth-eaten,” says Brigid Hogan, PhD, George Barth Geller Professor for Research in Molecular Biology and chair of the Department of Cell Biology.

Hogan aims to find out how young lungs stay healthy and replace damaged cells. She suspected that cells in the alveoli called type 2 cells can act as stem cells and help the lung regenerate. To find out for sure, her team purified type 2 cells, then grew them in culture. Alone, the type 2 cells wouldn’t regenerate, but when Hogan added stromal cells, a type of cell that normally grows nearby, regeneration took place. She believes the stromal cells signal the type 2 cells when and how much to grow.

When the two types of cells were grown together in a culture dish, they formed structures that resemble mini alveoli. “We found if we add these stromal cells, type two cells will grow and form these little alveolospheres,” Hogan says.

Now her team can use these “alveolospheres” to screen for drugs that may be useful in regenerating alveoli tissue. They can put the type 2 and stromal cells in each of 96 wells in a culture plate, then add different drugs to each plate, to determine which drugs work best as “fertilizer.” Hogan conducts this work using mouse lung cells as well as human lung cells obtained from unused, excess donor tissue (such as when too-large donor lungs are cut to fit the recipient). When studying mice, she can genetically engineer them so that cells that begin as type 2 cells glow fluorescent red. In this way, she can trace the lineage of the new “alveolospheres,” definitively demonstrating that type 2 cells can act as stem cells—regenerating and forming new structures.

How are we wired to navigate our world?

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Alejandro Aballay, PhD, peers through the eyepieces of a microscope in a darkened lab.

“There it is,” he says. “Take a look.”

A transparent worm wriggles like a tiny snake. It looks unremarkable, and in many ways it is; it’s a soil nematode, a simple roundworm commonly found in gardens and compost heaps. But it’s impossible not to notice that the head end of this tiny worm is glowing bright green.

Aballay, associate professor of molecular genetics and microbiology, is using these glow-in-the-dark nematodes to explore the mechanisms by which the nervous system and the immune system communicate and interact with each other. By tracing what he calls the “cross-talk” between the two systems, he is identifying potential targets for new therapies to treat human disorders, from Crohn’s disease and arthritis to many kinds of infectious diseases.

It has long been known that the nervous system and the immune system are interrelated; that is why, for example, when people are under high stress they become more susceptible to colds and other infections. But the precise mechanisms by which the nervous system and the immune system communicate are poorly known. The

nematode—*caenorhabditis elegans*—is a perfect, simple model.

“In *C. elegans* we are able to identify specific neurons that control immune pathways. We have the map that will allow us to dissect those pathways,” says Aballay.

His lab was the first to show cause and effect between genes and neurons in the nervous system and immune responses. Now he is investigating how various drugs—mainly drugs that already have FDA approval—may use the cross-talk network to activate an immune response.

“We know these drugs are safe to use on humans, we know the right dose, we know the toxicity effects,” says Aballay. “We can identify very well the targets in our model system that are important in the control of the immune system. And potentially, because these drugs have very well defined targets in humans...we could repurpose these drugs and use them to treat other conditions.”

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Alejandro Aballay

Alejandro Aballay and postdoctoral associate Argenia Doss, PhD, in his lab in the Edwin L. Jones Cancer Research Building
LEADING DISCOVERY

LEADING DISCOVERY

METABOLOMICS: TACKLING THE GROWING EPIDEMIC OF DIABETES AND OBESITY

Nearly 26 million Americans have diabetes—and if current trends continue, as many as one in three adults will have diabetes by 2050.

“It is an epidemic, especially in our region,” says Chris Newgard, PhD, director of the Sarah W. Stedman Nutrition and Metabolism Center at Duke.

Currently, family history, age, weight, and race are factors doctors use to gauge people’s risk for developing diabetes. Newgard and Debbie Muoio, PhD, associate professor at Duke’s Sarah W. Stedman Nutrition and Metabolism Center, are sharpening the focus on metabolites—the chemical intermediates generated by the body’s metabolic processes—to more precisely predict an individual’s risk of developing diabetes and other illnesses.

While genes can help determine a person’s risk for developing a disease over a lifetime, genetic variation does not predict the time at which a disease might appear. Metabolites, on the other hand, can be thought of as the end product of the interaction between genes, the environment, and behaviors such as diet and exercise. They provide a real-time assessment of the body’s chemistry and cellular activity, potentially providing more specific measures of risk.

“With metabolomics we have an opportunity to understand obesity, diabetes, and related conditions at the individual level,” says Muoio. “It can be used in novel ways to detect and understand disease, which can lead to drug discoveries and other interventions.”

Duke is investing in this potential by founding the Duke Institute for Molecular Physiology—combining the Stedman Center with the Duke Center for Human Genetics to create a collaborative basic and clinical research program focused on better methods to detect and cure obesity, diabetes, cardiovascular disease, and related metabolic disorders. Among only a handful of such programs nationwide, Newgard says it will “attack the underlying mechanisms of chronic and pandemic diseases.”

From zebrafish: reversing heart failure IS possible

Mending a broken heart—fish make it look so easy. For us, a heart attack means dead tissues, scarring, and often a lower quality of life, if we survive at all.

Tiny, striped zebrafish contain all the secrets to regenerating a limb, an injured spinal cord, and most remarkably, a damaged heart. Ken Poss, PhD, professor of cell biology, is working hard to reveal those secrets, in hopes that one day, the human heart may be taught to repair itself.

Poss led the first study to report the zebrafish’s heart regeneration phenomenon.

“In humans, the heart is one of our least regenerative tissues,” says Poss. “But you can cut off a quarter of a zebrafish’s ventricle or genetically kill up to two-thirds of all the muscle cells in the heart, and they replace those. You can even put them into end-stage heart failure…and if you give them a couple of weeks, they will regenerate the muscle and recover completely. The question is, how do they do it?”

For the past decade, Poss and his lab have employed a host of tools—from fluorescent proteins that illuminate the different structures in the heart to gene manipulations that block or enhance regeneration—to seek the answer to that question.

Most human heart regeneration studies have focused on stem cells. But zebrafish regenerate with muscle cells.

“Muscle is what you need,” says Poss. “When you have a heart attack, that’s what you lose…In fish, the heart muscle cells that are spared will divide and replenish what is lost. There’s some type of regulation there, some gene activity that keeps cardiac muscle cells competent.”

Now Poss is taking his work from the level of cell and tissue organization to the molecular level, where signals from genes and the proteins they encode instruct the body to make new tissue. He says his lab has already identified some candidate genetic signals that could be given back to the damaged human heart in some form.

“What our work with zebrafish tells you is that reversing heart failure through regeneration is possible,” says Poss. “If we figure out how to get regeneration anywhere near that level in humans, you could really improve the lives of a lot of people.”

From zebrafish: reversing heart failure IS possible
A FAST NEW TOOL TO STUDY DRUG RESISTANCE IN CANCER CELLS

Kris Wood, PhD, is an MIT-trained engineer who likes to develop tools. Wood has a PhD in chemical engineering, and he spent five years conducting postdoctoral research in cancer biology at the Whitehead Institute.

“I knew if I was going to do important work, I needed to not only develop new technologies, I needed to understand cancer biology really well,” says Wood, assistant professor of pharmacology and cancer biology.

In his Duke lab, he develops faster technologies to catalog how cancer cells behave under many different conditions. In just six months at Duke he profiled major gene pathways that confer resistance to more than 20 different cancer drug therapies.

He uses one tool, Microscale, to turn genes on and off rapidly in cancer cells. He prints a glass slide with about 5,000 “spots” of lentiviruses, chosen because they turn particular genes on and off. He then seeds the slide with cancer cells, treats it with a cancer drug, and looks for the spots in which the cancer cells survive. Those are the cells that have resistance genes turned on.

Wood now has a list of genes that, when activated, cause a tumor to become drug resistant. Because the spots are so tiny, he can test thousands of different scenarios on a single slide.

Another tool, the Cancer Toolkit, works in much the same way, except that instead of manipulating individual genes inside cancer cells, he manipulates entire genetic pathways—cascades of genes that work together.

“There are thousands and thousands of genes in the genome, but they can be condensed basically into the signaling pathways in which they behave,” says Wood. He believes that most of the important signaling pathways in cancer have been identified. But what causes a patient to initially respond to a drug, and then develop resistance? The Cancer Toolkit enables him to ask those questions, and get meaningful answers more quickly and less expensively than ever before.

Wood has just started to test these new tools with human patient tumors. He says that Duke is one of the few places where he can obtain cancer cells and grow them long enough to conduct experiments. That’s because his basic science lab is just a five-minute walk from an operating room, where collaborating surgeons are resecting tumors.

Using genetics to understand—and one day treat—epilepsy

David Goldstein, PhD, and James McNamara, MD, run separate labs and conduct research independently, but they also collaborate in the search to understand epilepsy—one of the most common and least well understood neurological disorders.

“David’s primary focus is to identify genes that confer susceptibility to developing epilepsy in humans. My focus is to understand how a given mutant gene leads to the series of events that results in epilepsy,” says McNamara.

It is well known that genetic factors play a role in epilepsy, but until whole genome sequencing was developed and made available just a few years ago, few specifics were understood. Now, Goldstein, the Richard and Pat Johnson Distinguished University Professor in Genomics, oversees one of the largest genome sequencing facilities in the South at Duke, where researchers can analyze complete genetic data for many patients per month.

“So there is a brilliant opportunity here,” says McNamara, the Duke University School of Medicine Professor of Neurosciences. “Insights from genetics, together with genotype-phenotype analyses, leave me optimistic that we can develop preventive or disease-modifying therapies for epilepsy.”

“Right now, there are quite a few drugs you can try,” says Goldstein. “The goal is to stop the seizures, so often a clinician will just keep adding drugs, and if the patient can tolerate them without too many side effects and the seizures go away, you’ve won. So, often patients settle on combinations of therapy that may actually not be the best for them.”

With a better understanding of the genetic roots of epilepsy, Goldstein and McNamara hope to one day do much of the trial and error work of narrowing down appropriate therapies in the lab, rather than in the patient.

FAST FACTS

• 50-65 million people are living with epilepsy worldwide
• 30% of patients don’t respond to the best available drugs

David Goldstein and James McNamara

The Cancer Toolkit allows Wood to manipulate individual genes inside cancer cells.
Our country and the world face a crisis in health care, with widespread chronic disease, aging populations, economic and geographic barriers to care, and the growing complexity of care for survivors of cancer and other diseases.

The School of Medicine pioneered and continues to lead in clinical and translational research, new models of global and community health, reinventing the academic health system, and pioneering personalized medicine.

AT THE HEART OF EVERY DUKE MEDICAL INNOVATION is a passion to deliver the best care in the most compassionate manner to everyone who needs it. To succeed, we seek philanthropic investment in endowments for faculty, research fellowships, and clinical leadership education; capital for new buildings, equipment, and programs; and current-use funding for early-stage research and other priorities.
LEADING CARE

RIGOROUS CLINICAL RESEARCH LEADS TO SAFER, FASTER, LONGER-LASTING LUNG TRANSPLANTS

Scott Palmer MD’93, MHS’00, HS’93–’99, a lung transplant specialist, and Duane Davis, MD, HS’91, MBA’10, a transplant surgeon, were trying to save the life of a patient who wasn’t doing so well. The 20-year-old’s initial transplant had failed due to chronic rejection. He had a second transplant, a double-lung transplant.

“After we re-transplanted, his breathing function went up transiently for the first two or three months, then nose-dived. We thought we were going to lose him,” says Davis, professor of surgery and director of transplant services.

Then the patient began complaining of heartburn and on further testing was diagnosed with severe esophageal reflux. The doctors sent him for nissen fundoplication surgery to correct the reflux.

“Then his lung numbers went to normal, and they stayed normal...” says Davis.

The team wondered—was this happening with other patients? They started testing all patients for esophageal reflux at pre- and post-transplant. Between 50 and 75 percent of the patients had severe reflux.

That was 1997, and the standard of care when people lost lung function after transplant was to adjust medications, and the best hope was to stabilize lung function. Davis and Palmer weren’t content to just stabilize. “We were having on average a 25 percent increase in their lung function,” says Davis.

The team has established a new model of transplant care at Duke, and now they hope to conduct a randomized clinical trial to prove their theory definitively for dissemination to transplant doctors and patients everywhere.

Other Duke transplant research has shown definitively that early and extended medication to prevent a virus called cytomegalovirus, the most common opportunistic infection seen in patients post-lung transplant, dramatically reduced CMV infection rates. Doctors know that CMV infection is a major risk factor for transplant failure and death, thanks to a database developed at Duke by Palmer.

“Because we document our case studies in such a rigorous manner and share it, other transplant centers can benefit from it, and it changes the standard of care nationwide,” says Palmer, scientific director of the Duke Lung Transplant Program.

3.6 months
National average wait-list time

12 days
Wait-list time at Duke

84%
One-year survival rate nationally

89%
One-year survival rate at Duke

1,200
Transplants have been performed at Duke since 1992

Duane Davis and Scott Palmer

Duke’s Lung Transplant Program is the largest in the world, and it offers transplants to older patients and more complex cases.
With a buoyancy in her step reflective of someone much younger, 76-year-old Jeanine Rhymes walked into the examining room, sat on the cushioned table, and with a wide, confident smile, told her surgeon, “I just feel so good. It’s like I have a whole new life.”

Just six months earlier, the simple task of eating brought fierce pain knifing through her upper body. “Every time I ate it was like having a heart attack,” says the grandmother of eight. “The pain would radiate up into my chest all the way to my jaw.”

Rhymes suffered from a para-esophageal hernia, characterized by part of her stomach being in the chest cavity, a condition that is becoming increasingly common. It had steadily worsened over a nearly four-year period to the point “that I don’t think I could have lasted much longer,” Rhymes says. She had lost 22 pounds, was malnourished, extremely weak, and frail.

The only fix was a complicated, hours-long surgery.

Rhymes benefited from a new Duke program that pairs high-risk older patients with a team of surgeons, geriatricians, anesthetists, nurses, and social workers before, during, and after surgery to optimize care and improve outcomes.

“Surgery in an older patient who is frail and has multiple co-morbidities presents a unique challenge,” says Rhymes’ surgeon, Associate Professor of Surgery Sandhya Lagoo-Deenadayalan, MD, HS’00–’02.

She says seniors can withstand the stress of surgery, but it’s more difficult to withstand the stress of complications. Frailty and other syndromes of aging can affect outcomes after surgery.

“Geriatricians have a more comprehensive understanding of these conditions, and as a team, they help us to do everything that can be done to prepare patients for surgery, to be vigilant in recognizing possible complications and initiating appropriate treatment,” she says.

For Rhymes, increased strength and better nutrition were paramount to giving her the best chance for a successful surgery and recovery, so Lagoo-Deenadayalan and Mitchell T. Heflin, MD, HS’94–’97, director of the Duke Geriatric Evaluation and Treatment Program, prescribed a program of physical activity and suggested a diet rich in protein and calories.

Statistics show that people over age 65 with chronic illness or other factors of aging have more complications during and after surgery.

> FAST FACTS
• Duke’s Center for the Study of Aging and Human Development is the oldest in the country.
• Duke’s Geriatric Evaluation and Treatment Program is a national model.
• More than one-third of in-patient surgeries are performed on adults age 65+.

Doug Tyler, MD, HS’92, opens his laptop and scrolls through photograph after photograph of a patient’s leg, which is peppered with dozens of what look like small moles. Each little spot is actually a melanoma tumor, says Tyler, professor of surgery and chief of the Division of Surgical Oncology—“and for every one you can see, there’s one you can’t see.”

Tyler, who directs the Melanoma Program at the Duke Cancer Institute, runs the nation’s largest regional therapy center for the treatment of skin cancer. He develops novel treatments to battle these stubborn cancers, including innovative approaches that direct drugs to the most seriously affected regions while minimizing the deleterious effects of whole-body chemotherapy. Using catheters, he can channel drugs directly to the stricken limb and then use a carefully applied tourniquet to keep the treatment concentrated for precise periods.

“When you give whole-body chemotherapy, it suppresses immune response,” Tyler says. “By giving chemotherapy regionally, we can give 20 times the normal dose of a therapeutic agent, making it more effective, and the benefit is that we don’t suppress the immune system.”

Tyler’s passion for both clinical care and scientific research stems from his days as a surgical resident under longtime former chair David C. Sabiston, MD, who began the practice of having surgical residents do two years of research amid their clinical work. Duke remains one of the few academic surgery departments with such a rigorous research requirement, which is a critical component in the development not only of great surgeons, but of academic leaders who will advance the field and lead new discoveries.
Lawrence Breakley, a 62-year-old man from Danville, Va., has end-stage renal disease that requires him to visit a clinic three times a week for a treatment called hemodialysis, which filters excess waste and fluid from his blood.

In that, he is one among many; more than 350,000 Americans receive hemodialysis for renal disease.

But in one remarkable respect, Breakley stands alone. On June 5, 2013, a Duke University Hospital surgical team led by vascular surgeon Jeffrey Lawson, MD, PhD, implanted a bioengineered blood vessel into Breakley’s arm. The procedure was the first of its kind in the United States, and it represents a new horizon in medicine, one in which many sorts of replacement tissues and organs may one day be grown in the lab and successfully transplanted into patients.

“We hope this sets the groundwork for how these things can be grown, how they can incorporate into the host, and how they avoid being rejected immunologically,” says Lawson, who helped develop the technology. “We start with this, and one day we may be able to engineer a liver or a kidney or an eye.”

The surgery to implant the new blood vessel in Breakley’s arm took just two hours, but it represented the culmination of more than a decade’s worth of work and research. Lawson and Laura Niklason, MD, PhD, a former faculty member at Duke who is now at Yale, teamed up in the late 1990s to begin the long task of developing a process for creating bioengineered blood vessels.

The need was, and is, immense; every year hundreds of thousands of patients require replacement of blood vessels for heart bypass surgery, grafts for hemodialysis treatments, and other vascular surgical procedures. Currently, most such treatments use either synthetic blood vessels or vessels taken from elsewhere in the patient’s own body. Both those options involve complications: synthetic vessels are prone to clotting and rejection by the patient’s body, and harvesting a patient’s veins carries the risk of infection, weak or damaged vessels, and other problems.

Lawson and Niklason, working at Duke and a spinoff biotechnology company called Humacyte, bumped up against numerous setbacks, but they learned from each obstacle. Ultimately they came up with a process for using a tube-shaped biodegradable mesh as a scaffolding and seeding it with smooth muscle cells. The cells grow in a special medium of amino acids, vitamins, and other nutrients, filling in the gaps in the mesh and taking on the scaffold’s shape. A nutrient solution is continually pumped through the growing vessel, mimicking the rhythm of a heartbeat. The mesh gradually dissolves, and the vein is finally rinsed in a special solution that washes away its cellular properties, leaving behind a flexible tube made of collagen that, when implanted, will not trigger an immune response.

“At the end of the process, we have a non-living, immunologically silent graft that can be stored on the shelf and used in patients whenever they need it,” says Niklason. “Unlike other synthetic replacements made of Teflon or Dacron, which tend to be stiff, our blood vessels mechanically match the arteries and veins they are being sewn to.”

“Unlike other synthetic replacements made of Teflon or Dacron, which tend to be stiff, our blood vessels mechanically match the arteries and veins they are being sewn to.”

Laura Niklason

Jeffrey Lawson
Long QT Syndrome, a frightening and potentially fatal condition in which the heartbeat suddenly becomes rapid and irregular, has a strong genetic component; parents with the specific gene mutations that cause it can pass it to their children. These families, and families with a variety of other inherited heart conditions, could benefit from genetic testing to assess risk and possible preventive treatments. But genetics and genetic testing are complex issues, more complicated than most family physicians and general cardiologists have the time or expertise to fully discuss. That’s where cardiologist Svati Shah, MD, MHS, and the Duke Adult Cardiovascular Genetics Clinic come in. Shah, the founder and medical director, established the clinic, the only one of its kind in the Southeast, in order to give multidisciplinary genetics care and information to patients who have or suspect they have a genetic cardiovascular disease.

If testing is warranted, the clinic arranges for it and helps patients negotiate with their insurance companies. The rotation of seven physicians assesses patients and provides specialized clinical care.

“Iain Sanderson is bringing Duke Medicine into the future with informatics.”

Iain Sanderson is bringing Duke Medicine into the future with informatics.

“We won’t have to ask five times what your allergies are. It will be a significant improvement in safety.”

Iain Sanderson

Bringing genetics into clinical heart care

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Robert Butler, DPT, PhD, was coaching soccer players in the U.S. Youth Soccer Olympic Development Program when he became frustrated. He could see that some of the athletes needed to improve certain skills, but he had no systematic way to test and improve their movement.

“Even with all my education, I couldn’t efficiently take my team through a movement assessment regimen and come up with anything to personalize their movement training,” he says.

Now, as an assistant professor in the Doctor of Physical Therapy Program at Duke, he is developing and applying new standardized assessment methods that can be performed anywhere, with little specialized equipment. At the Michael W. Krzyzewski Human Performance Lab (the K-Lab) he uses a series of tools called the Functional Movement Screen and the Y Balance Test, which tests how people move—squat, sit-and-reach, and push-up, under their own body weight. He and colleagues from another university recently published a study showing that in 183 college athletes, an algorithm—a formula combining an FMS score, the Y Balance score, injury history, and other measures—could predict risk of non-contact injury.

“Butler’s team also uses simple tests to systematically measure whether or not an injured athlete is ready to return to activity. ‘Right now, there aren’t standardized guides for when to return someone to activity or sports after an ACL tear, for example,’ he says. In athletes who have an ACL injury, 50 percent will have early knee osteoarthritis in 10 years. Butler’s goal is to help standardize measurement both before and after physical therapy, so athletes can be returned to activity at the optimal time and avoid further injury.
In 2007, a man came to Duke for treatment of what appeared to be a tumor growing on his inner thigh. Doctors scanned his body for evidence of cancer and found suspicious nodes in his lungs. After removing the growth from his leg, they discovered he did not have cancer. Instead, the lesions had been caused by an infection. Somehow, the man had become infected with a fungus gone wild. It was time to call in the specialists.

John Perfect, MD, directs Duke’s Mycology Research Unit. He has been treating people for fungal infections since 1978. In most cases, the immune system isn’t working properly—some have HIV, others are organ transplant patients, many are cancer patients, a few use inhaled steroids to treat asthma. But this otherwise healthy patient was different. Despite starting antifungal treatment, the fungus traveled to his brain, and he began having seizures.

“Even today, with the best treatment we have, about 20 percent of people will die from fungal infection,” says Perfect.

After switching his medication and several months of treatment, this patient did gradually improve and is now apparently cured or able to live with his infection.

Still, a mystery remained. What type of fungus caused the infection, and where had the man contracted it? Perfect turned to his longtime collaborator, Joseph Heitman, MD, PhD, director of the Center for Microbial Pathogenesis.

Heitman and his colleagues read the organism’s DNA sequence, which revealed it to be a variety of Cryptococcus never before seen on the east coast of the United States. The organism is typically found only in Australia, where it lives on eucalyptus trees. The man had never been to Australia. But he had been to California several weeks before falling ill. Why would the Australian fungus suddenly be showing up in California?

The researchers suspect the landscaping trade, which imports thousands of plant specimens each year, including eucalyptus.

“Fungal infections are on the rise worldwide,” says Heitman. Global travel and commerce are introducing fungi that used to live in isolated areas to new locations.

Doctors are still relying on amphotericine, a drug identified in the 1950s to treat serious fungal infections. It has severe and potentially lethal side effects. “Some of the house staff call it ‘ampho-terrible,’” says Perfect.

To fill the gap between current medicines and the growing number of fungal infections, Heitman’s group has begun partnering with companies to develop and test a new generation of antifungal agents. Currently, they are testing small molecule inhibitors of a protein, calcineurin, which Heitman’s group identified as essential for the growth of Cryptococcus under the high temperatures found in the human body.

“Once fungi form a biofilm, they become extremely drug-resistant, making them very difficult to treat.”

Joseph Heitman

Clinician and basic scientist collaborate to solve mystery of “a fungus among us”
Innovating curricula to mold leaders for the future has long been the culture in the School of Medicine. Today we are integrating the best of our educational tradition with a new focus on team-based learning, simulation, exposure to basic and clinical research, and real world global and community health settings.

WE ARE EDUCATING STUDENTS TODAY WHO WILL BE LEADERS in a rapidly changing world of health and medicine. To succeed, we seek endowments for faculty, fellowships, and financial aid, and current-use funds for curriculum advances and medical education technology.
When Tracey Spencer enrolled in Duke University School of Medicine’s Class of 2013, supporting a patient’s leg in the delivery room was not the first clinical care image that popped to mind. “I held my patient’s leg for an hour while she pushed,” says Spencer. “It was my first time seeing a baby delivered. The patient was so comfortable with me and really considered me to be a big part of her care team.”

Spencer is part of a new program for second-year Duke medical students called the Primary Care Leadership Track. It places students in mostly outpatient settings, such as primary care, community, and obstetrics-gynecology clinics. Students spend nine months in outpatient clinic training, and they also have the unprecedented opportunity to rotate through the emergency department. They spend three months working in the hospital.

They are required to compile their own panel of patients, a group of individuals whom they follow through the health care system, including making referrals to specialists and serving as patient advocates. “I don’t think even fourth-years or residents get the same continuity with their patients as we do,” says Christopher Danford, MD, also a member of the Class of 2013. “All of us have had a patient we’ve been close to die or get a new diagnosis of cancer. And on the other hand, we’ve been able to deliver babies. That’s a very emotionally charged experience.”

During the third year, the students complete a research project in collaboration with the Duke Center for Community Research. Projects focus on a community or population health issue facing Durham residents. “This is the year where students will really see the health care system through the patient’s eyes,” says Barbara Sheline, MD, MPH, program co-director and assistant dean for primary care.

“It’s been most interesting to see the transition of care as a patient goes from different practice to practice. I’ve realized that many patients have trouble getting to and from appointments, and I’ve seen them struggle to make their co-pays,” says Cassandra Kisby, another 2013 class member. “I know our classmates don’t see that, because they are transferring from service to service rather than rotating with the patient.”

Cassandra Kisby did not expect to deliver a baby as a medical student.

Chris Danford listens to a patient’s heart with preceptor Bruce Peyser, MD.
Kaf Dzirasa, PhD’07, MD’09, planned to put his undergraduate engineering degree and an MD to work in the new field of brain-machine interfaces, working in the lab of Miguel Nicolelis to develop robotic prostheses that patients can manipulate with their thoughts.

That changed on his first day of psychiatry rotation, when he met a middle-aged veteran suffering from schizophrenia. The man believed the government had implanted a chip in his head, causing him to suffer intense headaches.

“He was ‘pretty much constantly homicidal,’” says Dzirasa. “I left that day with a scientific curiosity...If we were able to figure out how to wire robotic body parts to the brain and get them working, how was it that no one could tell what was actually wrong with this guy?”

Dzirasa shifted his focus to exploring mental illness. He chose a demanding but rewarding route: Duke’s MD/PhD dual degree program, one of the oldest in the nation, combining the clinical curriculum of medical school with the research focus of basic science graduate work.

“During the third year at Duke, you’re not going to be a lab tech,” he says. “This is building your career.”

“I learned a lot about seeing a research project through and how much manpower it takes before something like this can be launched,” says Sharma.

Duke’s medical school curriculum is unlike any in the country: With an emphasis on intellectual curiosity, scientific study, and an understanding of the relationship between research and advances in care, our curriculum provides early exposure to both research and clinical care. Students cover all the basic sciences in year one and see patients a year earlier than most medical students. They dedicate their third year to a scholarly research project—often publishing findings in peer-reviewed journals—and return to clinical classrooms in year four.

Daniel Laskowitz, MD’91, HS’95–’97, Sharma’s faculty mentor, says the two worked closely on the study, but emphasizes that the project was Sharma’s.

Daniel Laskowitz and Richa Sharma

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Simulation was first developed by the military to train soldiers. Your training is in orthopedics, but you’re in a Combat Support hospital serving an indigenous population, and you’re the closest thing on hand to an anesthesiologist. So you examine the man, evaluate his vital signs, decide what drugs and doses to administer, and begin the sedation procedure.

The patient’s airway is constricting! What do you do?

Jeff Taekman, MD, says digital technology, much of it borrowed from video games, is rapidly changing the way students learn. Virtual environments allow students scattered anywhere in the world to control virtual versions of themselves and interact with other team members and virtual patients (called “avatars”) to learn in ways that are vastly more efficient than older teaching models.

First developed by the military to train service members, games-based learning comes in many forms and is almost infinitely adaptable. The virtual environments are remarkably detailed; they can recreate any actual room in the hospital, every patient has a unique physiology, and every piece of medical equipment can be operated and monitored by the participants. Every exercise is recorded so that instructors, participants, and others can re-watch it and discuss it.

Virtual learning will never entirely supplant hands-on learning, but Taekman says it is playing an increasingly important role in teaching the next generation of physicians and nurses.

“There are psychomotor skills you have to do directly, but virtual scenarios allow students to practice all sorts of cognitive and diagnostic skills, like deciding what drugs to use, what doses to use, what equipment should be used, what order things should be done in,” says Taekman, director of the Human Simulation and Patient Safety Center. “What is going to be most efficient is having them do a lot of learning in interactive scenarios, and when they’ve reached a certain level of competence, that’s when you bring them together to do the things you can’t do in a virtual environment.”

The patient’s airway is constricting! What do you do?

Suddenly, the oxygen monitor indicates the patient’s airway is constricting. His face flushes and begins to swell, and his blood pressure plummets—signs of potentially fatal anaphylaxis. Quick, what do you do?

Fortunately for you—the medical student faced with this pulse-quenching situation—the patient in front of you is not flesh and blood but digital bits and pixels. The exercise is one of the many virtual scenarios prepared by the Human Simulation and Patient Safety Center at Duke, among the nation’s leaders in using simulation technology and games-based learning as educational tools for health care.

The patient’s airway is constricting! What do you do?

Physician assistants in high demand

Since becoming chief physician assistant for Wake Emergency Physicians in Raleigh in 2009, Miguel A. Pineiro, MHS’04, PA’04, has seen the number of physician assistants (PAs) he oversees double—from 20 to 40. This growth shows the high demand for emergency care and the increased importance of mid-level practitioners in medicine.

The PAs in Pineiro’s group provide emergency medical services at seven emergency departments. Because of the fast-paced, high-stress, and often unpredictable environment, most EDs look for PAs with previous emergency medicine experience. Pineiro says finding PAs—even recent graduates—with this type of experience is hard to come by.

“In emergency medicine, PAs are called upon to not ‘miss the bad stuff,’” Pineiro says, adding that PAs face critical questions such as: When is a headache just a headache, and when is it meningitis or a cerebral aneurysm? Or, when is chest pain cardiac in nature, and when is it just a musculoskeletal issue?

Still, Pineiro felt confident when he hired three recent graduates of Duke’s PA program, which was the first of its kind when created in 1965. While none of them had much ED experience, he says they had no problem hitting the ground running, a fact he attributes to Duke’s number one ranked program.

A 2004 graduate of the program himself, Pineiro says he had no reason to doubt his hiring choices. “It’s sink or swim in emergency medicine,” he says. “I know Duke PA graduates are highly motivated and come ready to excel. They all have worked out fantastically.”

Today he feels right at home practicing in the ED. He says the hustle and bustle is in line with his “restless attitude.” However, it’s not the adrenaline-pumping trauma cases that get him most excited. Instead, he loves talking with patients and discovering what’s wrong. He says simple, attentive conversations can reveal a lot about a patient’s condition, a lesson he teaches the students and new PAs he mentors.

“If you talk to people, even in casual conversation, you will learn more about their health, spirituality, and what drives them,” he says. “We’re trying to take care of the whole person.”

The patient’s airway is constricting! What do you do?
Aedes mosquitoes can cause big problems for people in sub-Saharan Africa.

The aggressive daytime biters transmit a virus called Chikungunya (CHIKV), for which there is no specific treatment or cure. Although not usually fatal, the virus causes sudden high fever and severe joint pain and can lead to serious complications among infants, the elderly, and chronic disease sufferers.

Julian Hertz became fascinated with the virus while on an NIH Fogarty International Clinical Scholarship-sponsored year in Moshi, Tanzania. After working with Duke faculty mentors at partner institution Kilimanjaro Christian Medical Centre and Medical University College, Hertz received two Duke scholarships, the Eugene A. Stead Jr. Clinical Research Scholarship and a Duke Global Health Institute Research Scholarship, that allowed him to stay another year.

He helped to show that CHIKV is a significant but unrecognized cause of fever-related illness in the region, and that it is commonly misdiagnosed as malaria. He also observed the first-ever case series of patients who were co-infected with HIV and CHIKV.

“My time in Tanzania opened my eyes to the ways in which clinical research can help address major global health challenges,” says Hertz.

Despite his youth, Hertz is a veteran of serving the underserved. He spent time between undergraduate studies at Princeton and medical school running a rural health clinic in Haiti. He sent his medical school application to Duke from Haiti. He also has done a clinical rotation at a hospital emergency room in Lagos, Nigeria, where he was shocked at the senseless deaths due to lack of resources in such a large, teeming city.

Hertz, who graduated in 2013, will soon begin a residency in emergency medicine at Vanderbilt University Medical Center. He hopes to get back to Haiti or Tanzania, but says, “I’ll go wherever my career takes me. Emergency medicine is an undeveloped field in global health.”
DUKE-NUS PIONEERS TEAM-BASED LEARNING

Throughout the Team-Based Learning Center, teams of six or seven students ponder the medical record of a fictitious patient, Mrs. R. They discuss and debate issues surrounding hypertension, heart rhythm, medication, and more in an effort to reach a collective conclusion about what ails her. A cacophony of animated conversations fills the room. Laptop computers glow as students back up the studying they did before class with on-the-spot research.

Student 1: “So you think those little bumps are P-waves?”
Student 2: “Yes.”
Student 1: “I think they are actually T-waves.”

Student 1: “I think you’re really straining to find those P-waves.”
Student 3: “I agree. The rhythm is between 90 and 100, so I think we could be looking at A-fib.”
Student 4: “Do we all agree that the answer is letter A—A-fib?”
Student 2: “I don’t know. I just feel like there are P-waves. But, I’m willing to go with the rest of the group.”

The team holds up a cardboard letter A.
Student 1: “Hey, if we’re wrong, it’s totally my fault.”

Team-based learning has been a staple of business schools for decades, and it’s gaining traction at medical schools as health care moves toward team-based approaches to caring for patients. Duke medical faculty pioneered the innovative model of medical education at sister school, Duke-National University of Singapore Graduate Medical School (Duke-NUS). Now, the American Association of Medical Colleges (AAMC) has recognized Duke-NUS for its success in being one of the first schools of medicine to successfully apply team-based learning throughout the basic science curriculum.

The AAMC reports that in less time, Duke-NUS students achieved comparable scores to U.S. medical students on standardized tests of basic science knowledge. By the end of their second year, Duke-NUS students scored significantly higher than the U.S. students.

Back in Durham, Duke University School of Medicine has put the concepts developed in Singapore into practice—a portion of the first-year basic science instruction is covered via team-based learning.

“Team-based learning results in a deeper understanding and greater retention of the material,” says Colleen Grochowski, PhD, associate dean for curricular affairs. “Collaboration is the future of health care delivery.”
As part of Duke Medicine’s historic $1.2 billion campaign, Duke University School of Medicine seeks $970 million to fund Medicine that Changes the World. We need your help to succeed. We seek philanthropic investment across three key areas. Will you lead with us?

**LEADING DISCOVERY**

We seek to grow our historic strengths in the basic sciences, invest in new areas of innovation, foster greater collaboration, and accelerate progress from laboratory bench to human application.

**Goal**
- Endowments for faculty, fellowships, and research
- Current-use funds for early stage research, equipment, and programs

Our campaign goal includes gifts to the Medical Annual Fund; gifts to establish endowed funds for research, fellowships, faculty support, and financial aid; gifts of capital support for new buildings, equipment and programs; and gifts of current-use funding that can be immediately applied to research, technology, and education.

**LEADING CLINICAL CARE**

We seek to improve the delivery of care for complex and chronic diseases, to improve the health of people in communities large and small, and to ensure that the best care is available to all who need it.

**Goal**
- Endowments for faculty, research fellowships, and clinical leadership education
- Capital for new buildings, equipment, and programs
- Current-use funds for early stage research

**LEADING EDUCATION**

We seek to develop future leaders in health care with team-based learning, independent study, cross and interdisciplinary education, simulation, patient and family experiences, management training, and global and community health experiences.

**Goal**
- Endowments for faculty, fellowships, and financial aid
- Current-use funds for curriculum advances and medical education technology
- Learning spaces

![Artistic rendering of an immune cell shows the petal-like sheets on its surface.](Source: Courtesy of Donald Blis and Selam Gebremarian, National Institutes of Health)
The Mary Duke Biddle Trent Semans Center for Health Education opened in January 2013. Thanks to a historic gift from The Duke Endowment and generous gifts from alumni and friends, it was funded almost entirely by philanthropy. Naming opportunities are still available, and funding is also needed for curriculum advances and medical education technology.
Medicine that Changes the World