Facing adversity, Sibley finds path to success

By Julie Greicius

At first, the symptoms were so subtle he hardly noticed them. Sometimes his foot would catch on the ground when he walked. “I would stumble a little bit,” said Eric Sibley, MD, PhD, professor of pediatric gastroenterology at the School of Medicine. “Gradually it became more pronounced, until it was an obvious limp.”

A young physician-scientist, Sibley’s focus was on the patients he cared for and the scientific discoveries he was working to achieve. Since his arrival at Stanford in 1993 as a postdoctoral scholar, he’d been investigating why the gene involved in making lactase, an enzyme responsible for lactose digestion, gets turned off in most mammals after they’re weaned. His goal was to understand the gene regulation behind this developmental phenomenon and apply what could be learned to regulating other genes in the gastrointestinal tract.

He cared for patients in the pediatric gastroenterology clinic at Lucile Packard Children’s Hospital Stanford. “The dominant theme of Eric’s practice is caring about the people who need it most,” said Dorsey Bass, MD, associate professor of pediatric gastroenterology, who shared a Friday afternoon clinic with Sibley for two decades. Some of Sibley’s patients, Bass said, were “very financially distressed and with multiple disabilities, kids with cerebral palsy and lots of complicated, difficult issues. Eric’s loyalty to them and their loyalty to him just always, well — it makes you a little proud to be human.”

Sibley couldn’t yet know how his own medical diagnosis would affect his life and career path. While his physical limitations would not change his aspirations, they increasingly opened him to his strengths as an academic mentor and role model of resilience.

A persistent shoulder injury

When he wasn’t working, Sibley enjoyed time with his wife, Carol Somersille, MD, an obstetrician-gynecologist, and their two children, Carl Somersille Sibley and Lauren Somersille Sibley, whom he credits with providing invaluable support. Sibley coached his son’s and daughter’s basketball teams. He played golf and softball, too. But after a round of golf in 1999, Sibley became aware of a shoulder injury that wouldn’t go away.

An MRI of his shoulder didn’t show much, but looking toward Sibley’s spine, the doctor noticed demyelinating lesions — evidence that the protective covering, called myelin, around his nerve fibers was damaged. It wasn’t enough for a diagnosis of multiple sclerosis — a brain and spinal cord disease in which the immune system attacks the myelin wrapping of nerve cells — but it was suspicious.

Sibley’s official diagnosis didn’t come until many years later, but when it did it was severe: primary progressive multiple sclerosis, the most aggressive form of the disease.

A career interrupted

For Sibley, the adjustment to becoming a patient — a doctor-patient using a cane, then forearm crutches and eventually a wheelchair — was challenging. “Until I developed MS, I was thinking, ‘OK, I’m going to be able to do everything,’” he said. “It was a big psychological evolution to be able to accept that, yeah, there are going to be limitations on what I can do and how people are going to perceive me. The first real hurdle was using a crutch at all.”

Strength in weakness: ‘Fragile’ DNA regions key to vertebrate evolution, according to scientists

By Krista Conger

Regions of DNA susceptible to deletion during replication may have allowed vertebrates to successfully adapt to rapidly changing environmental conditions during evolution, according to a study by researchers at the School of Medicine. The research suggests that some critical evolutionary changes are likely to have occurred in leaps and bounds through the abrupt loss of stretches of DNA, rather than through the slow accumulation and additive effects of many small mutations.

The researchers, who studied a tiny fish called the threespine stickleback, found that such “fragile” DNA regions create genetic hot spots that mutate much more rapidly and dramatically than neighboring sequences. The resulting changes can help an organism vault far ahead of its peers in the evolutionary arms race.

Although similar findings have been described in bacteria, this is one of the first studies to show that the same process has occurred in vertebrates to create dramatic changes in body structure. It also addresses a long-standing mystery in evolutionary biology.

“There is a lot of evidence that the same genes across different populations or species are often responsible for similar evolutionary changes,” said David Kingsley, PhD, professor of developmental biology. “What hasn’t been clear is how this is happening. This study describes a biochemical mechanism, down to the sequences of DNA, that can produce evolutionary change.”

Kingsley, a Howard Hughes Medical Institute investigator, is the senior author of the study, which was published Jan. 4 in Science. See FISH, page 5

Physical therapy can reduce risk, amount of long-term opioid use, new study finds

By Amy Jeter Hansen

Patients who underwent physical therapy soon after being diagnosed with pain in the shoulder, neck, low back or knee were approximately 7 to 16 percent less likely to use opioids in the subsequent months, according to a study by researchers at Stanford and Duke. See OPIOIDS, page 7

A painting of threespine sticklebacks adorns the office of David Kingsley. He studies evolutionary changes in the tiny fish.

A fragment of close-up points to vertebrate evolution, according to scientists

By Amy Jeter Hansen

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Physical therapy within three months of a musculoskeletal pain diagnosis reduced patients’ risk of long-term opioid use by about 10 percent, Stanford and Duke scientists found.
Developing radiation therapy with a brief exposure time

By Manuel Gnida

New accelerator-based technology being developed by the Department of Energy’s SLAC National Accelerator Laboratory and Stanford University aims to reduce the side effects of cancer radiation therapy by shrinking its duration from minutes to under a second.

Researchers at SLAC and Stanford received funding to develop two possible treatments for tumors — one using X-rays, the other using protons. The idea behind both is to blast cancer cells so quickly that organs and other tissues don’t have time to move during the exposure, much like taking a single freeze frame from a video. This reduces the chance that radiation will hit and damage healthy tissue around tumors, making radiation therapy more precise.

“Delivering the radiation dose of an entire therapy session in a flash lasting less than a second would be the ultimate way of managing the constant motion of organs and tissues, and a major advance compared with what we do today,” said Billy Loo, MD, PhD, an associate professor of radiology.

Sam Tantawi, PhD, a professor of particle physics and astrophysics and the chief scientist for the RP Accelerator Research Division in SLAC’s Technology Innovation Directorate, works with Loo on both projects. “In order to deliver high-intensity radiation efficiently enough, we design accelerator structures that are hundreds of times more powerful than today’s technology,” Tantawi said. “The funding we received will help us build those structures.”

Blasting cancer with X-rays

A project called PHASER aims to develop a flash delivery system for radiation.

In today’s medical devices, electrons fly through a tube-like accelerator structure that’s about a meter long, gaining energy from a radiofrequency field that travels through the tube at the same time and in the same direction. The energy of the electrons then gets converted into X-rays. Over the past few years, the PHASER team has developed and tested accelerator prototypes with special shapes and new ways of feeding radiofrequency fields into the tube. These components are already being used in simulations and could be the way for accelerator designs that support more power in a compact size.

“Next, we’ll build the accelerator structure and test the risks of the technology, which, in three to five years, could lead to a first actual device that can eventually be used in clinical trials,” Tantawi said.

The Department of Radiation Oncology will provide about $1 million over the next year for these efforts and launch a campaign to raise more research funding. In collaboration with the School of Medicine, the department also has established the Radiation Science Center, which focuses on precision radiation treatment. Its PHASER division, co-led by Loo and Tantawi, aims to turn the PHASER concept into a functional device.

Making proton therapy agile

In principle, protons are less harmful to healthy tissue than X-rays because they deposit their tumor-killing energy in a more confined volume inside the body. However, proton therapy requires large facilities to accelerate protons and adjust their energy. It also uses magnets weighing hundreds of tons that slowly move around a patient’s body to guide the beam to the target.

“We want to come up with innovative ways to manipulate the proton beam that will make future devices simpler, more compact and much faster,” said Emilio Nanni, PhD, a staff scientist at SLAC who leads this project with Tantawi and Loo.

That goal could soon be within reach, thanks to a recent $1.7 million grant from the DOE Office of Science Accelerator Stewardship program to develop the technology over the next three years.

“We can now move forward with designing, fabricating and testing an accelerator structure similar to the one in the PHASER project that will be capable of steering the proton beam, tuning its energy and delivering high radiation doses practically instantaneously,” Nanni said.

Quick, effective and accessible

In addition to making cancer therapy more precise, flash delivery of radiation also appears to have other benefits. “We’ve seen in mice that healthy cells suffer less damage when we apply the radiation dose very quickly, and yet the tumor-killing effect is equal to or even a little better than that of a conventional longer exposure,” Loo said. “If the result holds for humans, it would be a bit better than that of a conventional longer exposure,” Loo said. “If the result holds for humans, it would be a whole new paradigm for the field of radiation therapy.”

Another key objective of the projects is to make radiation therapy more accessible for patients worldwide.

Today, millions of patients around the world receive palliative care because they don’t have access to cancer therapy, Loo said. “We hope that our work will contribute to making the best possible treatment available to more patients in more places.”

That’s why the team is focusing on designing systems that are compact, powerful, efficient, economical, efficient to use in the clinical setting and compatible with existing infrastructure around the world, Tantawi said.

“The first broadly used medical linear accelerator design was invented and built at Stanford in the years leading up to the building of SLAC,” he said. “The next generation could be a real game changer — in medicine and in other areas, such as accelerators for X-ray lasers, particle colliders and national security.”

Peter Maxim, PhD, a former assistant professor of radiation oncology at Stanford, is a co-inventor of PHASER and made key contributions to both projects.

Members of the proton therapy include researchers at Loma Linda University and Varian Medical Systems.

Health care democratization underway, according to Health Trends Report

An explosion in data is driving increased democratization in health care, according to the second annual Health Trends Report published Dec. 13 by Stanford Medicine.

Building on last year’s findings about the emergence and changing role of data in medicine, the latest report takes a deeper look at how using and sharing data will transform research, the practice of medicine and the role patients play in their own health care.

This transformation is being driven by the growth of available data across the health care system, as well as new technologies and industry players that are taking medical knowledge from a human scale to a digital scale.

“We are on the cusp of something that’s never been possible before — the ability to truly democratize the practice of health care, spreading expertise without friction wherever it’s needed,” said Lloyd Minor, MD, dean of the School of Medicine. “Whole realms of expertise, previously siloed, are beginning to open up to more people in more places than ever before.”

“It’s clear that we have work to do in terms of making this incredible amount of data easier to access, share and protect,” he added. “But I am certain that we are advancing toward a future of care that is more predictive, preventive and personalized.”

Findings

The report reflects a comprehensive review and analysis of existing health care research and publicly available data on the current and emerging trends facing the health care sector, combined with insights from Stanford faculty and external health care experts.

The report identifies three main pillars influencing the democratization of health care: intelligent computing, sharing and data security.

Intelligent computing: Artificial intelligence and data analytics are rapidly improving as tools to manufacture insights from health data at scale. This is likely to result in health care that is more precise and efficient, drawing cost out of the system and eliminating bottlenecks for providers and patients alike. With the size of the AI health market expected to reach $36.6 billion by 2021, AI’s impact on the medical field will have significant near- and long-term effects. However, as the health care industry embraces the potential of AI, it must take certain practical and ethical steps to ensure its safety. Intelligent computing has the potential to make health care more personalized, accessible and efficient, but only if the industry is prepared to take on the challenges that come with it.

Sharing: Information sharing must be improved. See TRENDS, page 3
By Samantha Beal

These days it’s hard to find someone who doesn’t use digital health technology. Most of us go online to make appointments, access our medical records, look at test results and exchange notes with our doctor’s office. Many of us take advantage of remote virtual appointments and use devices to track health data that can give providers a broader picture of our well-being.

Digital health technology is also helping Stanford Children’s Health offer patients and their families better access to Stanford Medicine pediatric experts. This year, Stanford Children’s plans to more than double its number of telehealth appointments — from 1,100 visits in 2018 to 2,500 visits in 2019. Currently, telehealth visits are offered to patients for follow-up appointments. Some of those are clinic-to-clinic visits, in which a nurse practitioner at a primary care office connects with a physician at a specialty clinic.

During a clinic-to-clinic visit, a nurse practitioner at the remote clinic examines the child while a high-resolution camera and microphone let the physician at the specialty clinic see and hear exactly what the nurse practitioner does.

Vandana Mittal, director of digital health services at Stanford Children’s Health, said these clinic-to-clinic telehealth visits are used for an array of appointments, from diagnosing eye problems in premature infants to performing video electroencephalograms for neurology. Because the Stanford Children’s Health network spans from Santa Rosa to Salinas, these virtual visits help families fit appointments into their schedules.

“Through virtual visits, we are not only saving families time traveling to appointments and taking their kids out of school and work, we are also maximizing our providers’ ability to see more patients, fill in last-minute cancellations and accommodate urgent requests,” Mittal said.

Enabling more realistic evaluation

Patients also benefit from clinic-to-home telehealth visits. Through the Stanford Children’s Health MyChart patient portal, patients and families can connect with their physicians remotely using their own devices, such as phones and tablets. Mittal said such virtual visits are popular among teen behavioral health patients who go away to college but want to maintain a close relationship with their mental health provider at Stanford. Providers at the developmental-behavioral clinic are using these visits to observe patients in their natural play environments, at home or even on the playground, enabling a more realistic evaluation of the child’s condition.

In addition, Stanford Children’s Health offers clinic-to-school visits, in which physicians can connect remotely with a patient in a school nurse’s office. For instance, a physician caring for a child with Type 1 diabetes can communicate directly with the school nurse and the patient’s parent through a telehealth visit at the nurse’s office, minimizing the need for the parents and the child to travel to the doctor’s office and enabling the doctor and the school nurse to interact. Accord- ing to Mittal, this approach is working well among patients with diabetes who may live far away from the hospital, but require ongoing support and blood glucose monitoring.

Telehealth is also being used within Packard Children’s Hospital. From inpatient units, on-call doctors are evaluating patients in the emergency department via telehealth before they are admitted; in some cases, specialists are able to advise ED care teams on the most appropriate transfer methods for patients. This approach cuts down on provider walking time and limits the time families spend waiting for care consultations.

“Although virtual telehealth visits are not a blanket solution for everyone or every visit, they are instrumental in helping patients and families who require more care or live away from their specialists, without sacrificing that vital connection,” Mittal said. “Thanks to advances in medicine and science, we are able to care for more children with chronic or serious conditions than ever before, and digital health allows more flexibility and greater access to the best care available.”

Digital second opinions

In November, Stanford Children’s Health launched a new service in conjunction with Stanford Health Care that offers digital second opinion consultations from Stanford physicians. Patients don’t have to visit the hospitals or clinics for this service. (See story, this page)

Mittal noted that Stanford Children’s Health’s multipronged digital health approach — including telehealth, remote care monitoring and patient portal access — will continue to empower families and patients to manage their health care and enable providers to make better-informed care decisions.

Families can connect with Stanford Children’s Health specialists from their pediatricians’ office, minimizing the need to travel long distances and take time from work and school.

Through the Stanford Children’s Health MyChart patient portal, patients and families can visit with their physicians remotely using their own devices, such as mobile phones and tablet computers.

Trends

continued from page 2

at a foundational level to allow data to flow freely between various participants in the system, including health care providers, patients, technology providers and insurers. While the health care industry still faces challenges with data sharing, there are exciting advances being made through collaborations between traditional health care players and new market entrants.

Data security: A more open data environment underscores the importance of the security, privacy and safety of patient information. Ensuring patient data is protected will continue to be a priority as the importance of the security, privacy and safety of patient information.

The medical records are collected on behalf of the patient, if the records are in the United States, patients and families who require more care or live away from their specialists, without sacrificing that vital connection,” Mittal said. “Thanks to advances in medicine and science, we are able to care for more children with chronic or serious conditions than ever before, and digital health allows more flexibility and greater access to the best care available.”

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Online second opinion program launched at Stanford Medicine

Stanford Health Care and Stanford Children’s Health have launched a new online program that provides patients with a second opinion about their diagnosis or treatment plan. A Stanford Medicine specialist develops the second opinion based on a patient’s summary of medical history, including their diagnosis, as well as all relevant medical records.

The medical records are collected on behalf of the patient, if the records are in the United States.

The specialist sends a written second opinion to the patient and his or her doctor, usually within two weeks. The cost for the second opinion service is $700 and is available to patients in almost every location. (Most health plans do not cover online second opinions.)

To get access to the service, adult patients can create an account on the Stanford Medicine Online Second Opinion website at https://stanfordhealthcare.org/second-opinion/overview.html.

For patients 17 or younger, parents may create an account at the Stanford Children’s Health Online Second Opinion website at http://secondopinion.stanfordchildrens.org.

Online second opinions for children are available for a limited number of specialties and conditions, including otolaryngology, orthopedics and epilepsy. For parents of pediatric patients who are being considered for neurosurgery, heart transplantation, heart failure treatments or cardiothoracic surgery, a medical record review service provides evaluation of eligibility for surgery. This service is complimentary to patients who already have a diagnosis in the participating specialty, may require surgery and are considering options.
new technology for monitoring blood flow. The development of this technology was driven by a need for non-invasive, wireless monitoring of blood flow, which is crucial for understanding the health and function of blood vessels. The researchers at Stanford University have designed a battery-free, biodegradable blood flow sensor that can be used to monitor blood flow without the need for wires or external power sources.

The sensor is a wireless version of technology that chemical engineer Zhenan Bao has been developing to give prostheses a delicate sense of touch. This one has a history,” said Bao, PhD, the K. K. Lee Professor and the paper’s other senior author. “We were always interested in how we can utilize these kinds of sensors in medical applications, but it took a while to find the right fit.”

The researchers had to modify their existing sensor’s materials to make it sensitive to pulsing blood but rigid enough to hold its shape. They also had to move the antenna to a location where it would be secure, not affected by the pulsating motion of the capsin they could be placed around an artery.

It was a very exciting project and required many rounds of experiments and redesigns,” said postdoctoral scholar Levent Beker, PhD, a lead author of the paper. “I’ve always been interested in medical and implant applications, and this could open up a lot of opportunities for monitoring or telemedicine for many surgical operations.”

Making connections

The idea of an artery sensor began to take shape when Clementine Boutry, then a postdoctoral scholar in the Bao lab, reached out to Ana-Lisa Chang, a postdoctoral scholar in the Fox lab, and connected those groups — along with the lab of James Chang, a professor of surgery in the Department of Surgery (the Bao lab’s paper other lead author).

Once they set their sights on the biodegradable blood flow monitor, the collaboration won a 2017 Post-docs at the Interface seed grant from Stanford ChEM-H, which supports postdoctoral research collaborations exploring potentially transformative new ideas.

“We both value our postdoctoral researchers but did not anticipate the true value this meeting would have for a long-term productive partnership,” Fox said.

The researchers are now finding the best way to affix the sensors to the vessels and refining their sensitivity. They are also looking forward to what other ideas will come as interest grows in this interdisciplinary field.

“We use sensors to allow a patient to discover problems early on is becoming a trend for precision health,” Bao said. “It will require people from engineering, from medical school and people to really work together, and the problems they can address are very exciting.”

Bao is a member of Stanford Bio-X, a senior fellow at the Precourt Institute for Energy, a fellow at Stanford ChEM-H, an affiliate of the Stanford Woods Institute for the Environment and a member of the Wu Tsai Neurosciences Institute at Stanford. Fox is a member of Stanford Bio-X. Fox is a fellow at Stanford ChEM-H.

Other Stanford co-authors are Christopher Vassos, Huilin Tian, Allison Hinsley, Kay Takahashi, Bangter, Simiao Niu, Junheng Li, Jean Clairelive, Zhen Wang.

This work was funded by the Swiss National Science Foundation, the European Commission, Stanford ChEM-H and the National Science Foundation.

Researchers develop flows that help bacteria feed on biofilms

By Taylor Kubota

Under threat of being scrubbed away with disinfectant, individual bacteria can improve their odds of survival by join- ing together to form colonies, called biofilms. What Arnold Mathijssen, PhD, wanted to understand was how station ary biofilms find food once they’ve de voured nearby nutrients.

Leading an international team of re searchers in creating simulations of how fluids move, Mathijssen, a postdoctoral scholar in bioengineering at Stanford, found that individual bacteria and biofilms can generate currents strong enough to draw in distant nutrients.

In their work, published Dec. 11 in Physical Review Letters, the researchers were able to find predictable patterns of how fluids move based on the general shapes of biofilms, insights that could find applications in many fields.

“They are a very strong universality in the physical properties of microhydro dynamics,” said Mathijssen, who works in the lab of Muna Prakash, PhD, associate professor of bioengineering. “We’ve talked about bacteria, but we could replace the word ‘organism’ with ‘micro robot’ and the physics would be exactly the same.”

Starting simple

When bacteria move, they disturb the liquids that surround them. The researchers explored the strength of that disturbance in a single bacterium that moves in a way similar to many pathogenic species, including those that cause gastritis and cholera. They found that as this bacterium swims forward, it creates a tiny but stable current in the surrounding liquid with fluid moving backward toward its head and toward its tail.

In a vortex pattern, the bacteria move in concentric circles and produce a flow that brings nutrients down to the biofilm’s center and then pushes the fluid out the sides. In an aster pattern, the bacteria move toward a central point, creating a flow that moves from the edge of the biofilm until it rises back up, over the center.

“We can have really powerful thing about this is you can add these patterns up,” Mathijssen said. “Rather than having to know the full strength of each bacterium, you only need to know the basic patterns that make up the colony, and then it’s very easy to derive the overall transport flow.”

Seeing what’s hidden

The researchers were able to combine vortex and aster patterns within a single biofilm to determine how the bacteria would push, pull and withstand the fluids around them. As a final test, the researchers took calculations representing the complex, consistent role of pulling in nutrients. This occurred regardless of the orientation of each bacterium, so long as the colony was thicker in some areas than others, which causes fluid to move from high points to low points. Simulations of more orderly bacteria resulted in even stronger circulation.

Within organized biofilms, the researchers found two common patterns of movement: vortices and asters. In a vortex pattern, the bacteria move in concentric circles and produce a flow that brings nutrients down to the biofilm’s center and then pushes the fluid out the sides. In an aster pattern, the bacteria move toward a central point, creating a flow that moves from the edge of the biofilm until it rises back up, over the center.

“This work started with simple curiosity about the invisible flow of fluids around bacteria. But what the researchers discovered could be quite practical, guiding ways of cutting off an infectious biofilm’s source of food, for example. What’s also been cool is when you take into account a bacterium’s shapes and movement, the research also could apply to inanimate objects like synthetic drug delivery mechanisms or micro-robots.”

“This started off as a relatively fundamental problem but turned out to be more relevant for biomedical applications than we would have predicted,” Mathijssen said. “That’s what excites me: When you start from curiosity, drive us in a very different direction than where we started, and what we found has a lot of potential.”

Researchers affiliated with the University of Chile, the University of Chile, Pennsylvania State University and the University of Wuppertal also contributed to the work.

The study was funded by the Human Frontier Science Program, the Ministry of Economy, Development and Tourism in Chile and the German Research Foundation.

Stanford’s Department of Biengineering, which is jointly managed by the School of Medicine and School of Engineering, also supported the research.
Packard Children’s broadcast studio brings fun and a way to connect

By Samantha Beal

The countdown begins: 3, 2, and 1. “Hey guys, it’s Mat and Brianna, and we are live in Sophier’s Place studio right now.” Brianna Chambers and Mat Vido, studio coordinators in the Sophier’s Place Broadcast Studio in Lucile Packard Children’s Hospital Stanford, are streaming through the hospital’s closed-circuit television system Get Well TV. Their show, Radio Talk Show (despite the name, patients can watch as well as listen), was the studio’s first live broadcast after months of preparation and planning. It launched in October.

The bubbly duo sound much like the personalities on radio stations and podcasts. They chat about how they spent their weekends, how much they love The Incredibles 2, national cupcake day, the perfect pizza toppings and other important topics — like the difference between French dips and Fun Dip. The half-hour show, which airs one to two times weekly, is punctuated with music and calls from patients, listening or watching from their rooms, who answer questions posed by the hosts, such as whether it’s appropriate to start playing holiday music before Thanksgiving.

Social and creative outlet

For patients like 10-year-old Morgan Passalacqua, the studio can be a fun distraction. “The shows and programs really lift her spirits,” said her mother, Stacey Passalacqua. “She was going through some tough procedures, and it always put a smile on her face.”

Stacey said that “show time” was a bright spot for her daughter and everyone on the unit, including the nurses and staff.

“Children in the hospital often experience extreme periods of isolation when they are unable to interact with their peers as they would normally at school or in their communities,” Chambers said. “Sophie’s Place offers this social and creative outlet that allows connection and play through technology.”

Sara Devaney, the Sophier’s Place studio manager, said such connections are important in giving young patients a sense of community while they are in the hospital. During their stay at Packard Children’s, the youngsters can tune in and see kids who are also receiving care for illnesses and injuries.

“We had one little girl share her cancer diagnosis and remove her princess tiara to show the audience her bald head,” Vido said. “Other children watched the bravery of the girl, and took the courage to step to participate on air after previously feeling too self-conscious.”

Live and recorded shows

In addition to the live talk show, the studio offers daily live and recorded TV shows, including the popular shows and “kids’ choice” programs, in which youngsters can help select what they will see that day based on the week’s shows. Patients can also come into the studio to participate on air or call in from their hospital rooms to interact with the studio team and other patients.

The hospital’s child-life studio team is committed to finding ways to connect with all patients, ranging from toddlers to teens, as well as their siblings in ways that are meaningful for each.

“We strive to provide opportunities for all ages here in the hospital,” Vido said. “We have game shows based on Snazzy Street or Disney trivia that speak to our youngest patients, and we create opportunities that are just for teens, like our radio talk show segments where patients can call in to share their thoughts or ideas on a given subject. Teens have also joined as co-hosts for some of our TV segments.”

The team notes that even though the studio produces “mass media,” the experience of watching or listening to the shows, or participating in them, can be quite personal and fulfilling for patients. They recalled one boy who came to the studio daily before it had officially opened to film his own projects. He had been in the hospital for many months, and the studio was

Matt Vido and Brianna Chambers hosted a live show that patients can watch in person or from their hospital rooms. The show is part of the programming created in Sophie’s Place Studio at Packard Children’s.

Fish

continued from page 1

student Lauren Ploch said that the key dinucleotide repeat associated with many different young stickleback populations shows significant differences in body structure. Marine sticklebacks, for example, have a hind fin with a large spine projecting down from their pelvic structure. In contrast, dozens of freshwater populations show that hind fin is missing in its freshwater brethren to increase the rate of chromosome breaks and deletions of stretches of DNA. When Xie and her collaborators then tested similar DNA sequences in mammalian cells, they observed that the key dinucleotide repeat sequence often led to the deletion of sections of DNA more than 100 nucleotides long. The increase in the rate of chromosome breakage observed by Xie, coupled with the likelihood that this damage causes deletions of entire sections of DNA, may have been a key factor in allowing the prominent hind fin skeletal trait to emerge over and over again in many different young stickleback populations.

Elevated mutation rates may play a similar role when advantageous traits arise in other organisms, the scientists believe.

“Many vertebrates, including early humans, are dealing with a small population size and relatively long generation times,” Kingsley said. “There aren’t that many generations available in which to evolve new, potentially advantageous traits. Under these conditions, it may be particularly important for mutations to occur at elevated rates, and to have sweeping effects.”

When the researchers investigated known instances of adaptive changes in humans, they found that about half were due to mutations that also arise at elevated rates compared with more typical DNA letter changes.

“One thing that’s interesting is that ‘arrival of the fittest,’ or the relative speed with which a potentially favorable mutation arises, can sometimes be as important as ‘survival of the fittest,’” Kingsley said. “The mutation process itself has an important effect on the outcome, and the relative speed with which a mutation affects the fitness of the organism to bring about major changes in vertebrate evolution.”

Other Stanford authors are former graduate student Abbey Thompson, PhD, and graduate student Julia Wuchse-Benedict. Researchers from the University of Texas-Austin, the University of Victoria, the University of Nottingham, the University of British Columbia and the University of California-Berkeley also contributed to the study.

The research was supported by the National Institutes of Health, the National Science Foundation, a Stanford CEEG Graduate Fellowship and the Howard Hughes Medical Institute.

Stanford’s Department of Developmental Biology also supported the work.
**Nutrition in 2017.**

American Society for Pediatric Gastroenterology, Hepatology and Sibley received the Distinguished Service Award from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition in 2017.

"All those things were lining up, and if I had been able to continue at that pace healthwise, I was on a trajectory to continue as a leader in those different societies," Sibley said. "So that became a bit of a frustration, to have everything lining up perfectly, but then have the realization that I can't keep traveling to these national leadership meetings. It's just too hard on the body.

Lynee Olds, a research associate in the Sibley lab, recalled learning of his diagnosis around 2010. "Eric came to the lab to tell me he'd been diagnosed some time before but had not made it public," Olds said. "My private reaction was profound sadness that this was happening to such a good man." Olds focused on making accommodations in the lab so that Sibley could continue working. "I wanted him to know that this was his lab, and whatever it took to make it possible for him to be physically in it would be done," she said.

Support from his colleagues helped Sibley focus on moving forward. "As his disability evolved, some of the procedures that he wasn't able to do I took on for him to some degree," Bass said. "Maybe the most remarkable thing is: It didn't really seem to change who Eric was. He addressed his disability, like, OK, how are we going to work around this? How can I keep going?"

### Minority in medicine

Sibley's illness puts him among the 2 to 10 percent of practicing physicians with a disability, according to 2005 study in the American Journal of Physical Medicine & Rehabilitation. Yet, as an African-American, Sibley was already well aware of what it was to work as a minority in medicine. Only 4 percent of full-time medical school faculty identify as black or African-American, according to the Association of American Medical Colleges. Sibley attributes his perseverance in the discipline to his mentors who had paved the way.

Sibley's father, William Sibley, MD, practiced family medicine in South Los Angeles, not far from the family's home in the View Park-Baldwin Hills neighborhood. "View Park-Baldwin Hills was one of the few neighborhoods in the area that were not white," Sibley said. "And the African-American professionals and entertainers could purchase homes with less reality discrimination," Sibley said. "That's why music was so overrepresented there."

### Making his mark at Stanford

Sibley completed his pediatrics residency at Harbor-UCLA Medical Center in 1993. His scientific pursuits ultimately drew him to a postdoctoral fellowship in pediatric gastroenterology at Stanford. Gary Gray, MD, professor of gastroenterology, was investigating intestinal lactase persistence in humans. In 2004, he began to explore regulation of the lactase gene. "Besides being a trained pediatrician, Dr. Sibley had a PhD in molecular biology, an area that was crucial for our research," said Gray, now a professor emeritus. Gray's lab included technicians, a research associate and postdoctoral scholars. Sibley immediately displayed exceptional leadership skills. "He's just a spectacular human being — a humble, mature, quiet leader whom everyone was highly fond of," Gray said.

### Changing the pace

By 2011, Sibley needed more than crunches to keep going. He began using a wheelchair, and had an automatic door installed in his office at the School of Medicine. Around the same time, he was appointed an academic advising dean.

"With about 475 students in the medical school at any one time, Sibley — one of four academic advising deans — supports between 110 to 120 students. "It ends up being possibly hundreds of one-on-one or group meetings with students over the course of the year, which is remarkable given that he's also doing research, interacting with other leaders in the school and in the community," said Neil Gesundheit, MD, MPH, professor of endocrinology and senior associate dean for medical education.

Sibley has a unique flair for supporting medical students, not only in routine academic, research and career guidance, but also when things aren't going well. "Sometimes students who are struggling in school begin to isolate themselves. We call it cocooning," Gesundheit said. "A student who is self-isolated because of not meeting a deadline starts to compound the problem by being ashamed that they haven't met the deadline. This makes matters worse."

Sibley has a way of reaching out to those students sympathetically and putting them at ease, Gesundheit said. "He'll say, 'I know it's hard for you to communicate back with me and maybe you've got something that's happened, but let's just start over and get things moving in a positive direction.' He's excellent at that, at really disarming a student and helping them address those kinds of issues.

"Students who are the most vulnerable — those with physical or mental health challenges — Sibley found he could be the most helpful. 'That's one area where my own health has made it a little bit easier for students to approach for the support they need,'" he said.

Gesundheit agreed. "He's vulnerable, and he's saying to you: If you're vulnerable, I can understand that and help you."

### Minority in science

In the spring of 2018, Maïté Van Hentenryck, a first-year medical student, and her roommate Claire Rhee launched a group for medical students with disabilities and chronic illnesses. A blood infection when Van Hentenryck was a baby left her in the hospital for many reasons, including the opportunity to interact with cardiothoracic surgeon Levi Watkins Jr., MD, who had been the first black student to attend and integrate Vanderbilt Medical School, and who went on to be the first successful implant a automatic heart defibrillator in a human patient. At Hopkins, Sibley began to develop his research interests in gastrointestinal physiology. His doctoral thesis focused on insulin gene regulation.

Gesundheit agreed. "He's vulnerable, and he's saying to you: If you're vulnerable, I can understand that and help you."

"I reached out to Dr. Sibley to see if he'd like to be the group adviser," Van Hentenryck said. "And he and his research and clinical practice, he said, 'I think he's got a tremendous resource for us,'" Van Hentenryck said. Gesundheit had excelled in biomedical research, clinical care and education, but as a mentor and role model he provided something distinctive. See SIBLEY, page 7
Sibley could identify with students in ways that few other faculty could, and proved that there was a place for them in the highest ranks of medicine.

Mentoring the next generation

Sibley’s efforts as an advisor and mentor at Stanford soon earned him national responsibilities, as well. In 2016, he was named the inaugural chair of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition’s Mentoring Program for Investigative Junior Faculty. The program pairs assistant professors of pediatric gastroenterology with senior mentors at another institution to facilitate long-term mentorship affiliations. “In my communications with the leaders in the society, it is evident that Eric is deeply respected and admired — not just for his research, but also for his citizenship, generosity, teaching and mentoring,” said Mary Leonard, MD, professor and chair of pediatrics.

Sibley has also been active in the department’s efforts to build a supportive and inclusive environment for all faculty. He has advocated for the importance of mentorship and has helped cultivate a culture of collaboration and inclusivity within the department.

Opioids

continued from page 6

to a new story by researchers at Stanford and Duke.

For patients with shoulder, back or knee pain who did use opioids, early physical therapy was associated with a 5 to 10 percent reduction in how much of the drug they used, the study found. Amid national concern about the overuse of opioids and encouragement from the Centers for Disease Control and Prevention and other groups to deploy alternatives when possible, the findings provide evidence that physical therapy can be a useful, nonpharmaceutical logic approach for managing severe musculoskeletal pain.

“We asked ourselves, ‘How can we address the pain that people are having, while not encouraging the use of needing opioids?’” said Eric Sun, MD, PhD, assistant professor of anesthesiology, perioperative and pain medicine at Stanford. “And what our study found is that if you can get these patients on physical therapy sooner, or more rapidly, that reduces the probability that they’ll be using opioids in the longer term.”

The study, from an analysis of private health insurance claims, was published Dec. 14 in JAMA Network Open. Sun is the lead author. Sten Hoegh, PhD, professor of orthopaedic surgery at Duke, is the senior author.

The study screened out patients who had participated in opioid prescriptions within three months of their initial diagnosis and were given at least one opioid prescription within 90 days. The final sample consisted of 88,985 participants.

Fewer opioid prescriptions

After adjusting for co-morbidities, such as diabetes and hypertension, Sun and his colleagues found that the odds of patients filling an opioid prescription decreased by 10.3 percent less for patients with knee pain; 9.7 percent less for shoulder pain; and 5.1 percent less for back pain in the period three months to a year after their diagnosis. There was no significant reduction for neck pain.

Physical therapy within three months of diagnosis also was associated with a decreased likelihood that patients with two of the conditions would chronically use opioids. Sun and his colleagues found that physical therapy, a component of physical therapy, reduced pain and improves function for some musculoskeletal conditions. Other studies have shown that patients with past prescriptions for opioid medication are at increased risk for overdose and misuse.

Less need for pain relief

“Eric Sibley has shown an indomitable spirit both personally and professionally,” said Lloyd Minor, MD, dean of the School of Medicine. “Science can be unpredictable and at times discouraging, but even so, he has become a nationally recognized mentor. I am so proud to see him land a top faculty position.”

For Sibley, prevailing through adversity had a lot to do with those who’d cleared the path ahead of him, like Eric. At the time, there were times later in my career when there was no one like me in a role ahead of me, no one to advise or mentor me, he said. “It’s important to me to be that for Sibley, as he helped him through the ranks to the highest level of career as a postdoctoral scholar to a tenured faculty member.”

Even as he has become a nationally recognized mentor, he still remains in touch with those who’d cleared the path ahead of him, like Eric. The study also measured the quantity of opioids by converting prescribed amounts to oral morphine milligram equivalents. They found, “after adjusting for confounding factors, that patients who had undergone early physical therapy used 10.3 percent less opioid medication for knee pain; 9.7 percent less for shoulder pain; and 5.1 percent less for back pain in the period three months to a year after their diagnosis. There was no significant reduction for neck pain.

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Surgeon creates tools for assessing hands-on clinical skills

By Stephanie Bruzzese

When describing the inspiration for her life’s work, Carla Pugh, MD, PhD, recalled her time as a medical student and surgical resident. “Before I could operate on a tumor, I needed to know how densely it was attached. A CT scan couldn’t tell me — the only way I’d know was through my hands,” said Pugh. “I realized I would truly learn how to diagnose with my hands just by watching my instructors, and I wanted to find a better way.”

Today, Pugh is an international expert in the science of touch. She has created sensor technologies to quantitatively measure hands-on skills. She has combined those tools with educational concepts together, they help medical students and residents learn to more effectively use touch when treating their patients.

After completing her surgical residency at Howard University, Pugh enrolled as a doctoral student in the Stanford Graduate School of Education, where she began to explore optimal training methods in the medical environment and to develop the sophisticated sensor, video and motion-tracking technologies that would be key to capturing haptic — or touch-sensing — information.

“It really all started at Stanford 17 years ago,” said Pugh, who received a PhD in education in 2003 and now holds three patents on the use of sensor and data-acquisition technology to measure and characterize hands-on clinical skills.

Since returning in December 2017 — to take a dual role at Stanford Medicine as professor of general surgery and director of the Technology Enabled Clinical Imagination Center — Pugh has created collaborations across campus and beyond that are bringing the new field of touch technology and training to the next level.

On the technology side, for example, the Pugh lab has partnered with the Israel Institute of Technology to develop a fabric force-sensor bra that captures clinical data during a breast examination. Pugh is also exploring the creation of new touch-sensing tools with Stanford faculty members Allison Okamura, PhD, professor of mechanical engineering and an expert in haptics as well as virtual environments and simulators, and Zhenan Bao, PhD, professor of chemical engineering and of materials science engineering, who builds stretchable, flexible sensors.

Pugh is working with colleagues in the Graduate School of Education, including Dean Daniel Schwartz, PhD, and Karin Forsell, PhD, on the training half of the equation.

“In terms of the best approach to training students to use haptic data,” she explained, “we need to know: How much of this should be learned while using your hands in context, or on a computer? Does this learning objective require a haptic display, or virtual reality? How much data can you collect during the process of care, right in front of the patient, and get real-time feedback that goes directly to a database?”

Pugh and her colleagues plan to engage industrial and systems engineers, social scientists and other experts in answering these critical questions about using the growing quantity of haptic data in training.

“Nationwide, trainees are telling us they want this information,” said Pugh. “There’s a lot more work to be done — but the audience is ready.”

People