A latticework of iridescent color and light

New sculpture in Li Ka Shing Center to be dedicated to former dean Philip Pizzo

By Rosanne Spector

How do you portray space?

One possible answer now hangs from the ceiling of the Li Ka Shing Center for Learning and Knowledge. The new sculpture, artist Alyson Shotz’s vision of the skeletal structure of emptiness, was commissioned by the School of Medicine to honor former dean Philip Pizzo, MD. It will be dedicated May 21.

Sailing above the Yang and Yamazaki Lobby on the second floor of the center, the glimmering, undulating lattice appears lightweight and ephemeral — like a scaffold made of dragonfly wings. In reality, it weighs more than 3,000 pounds. The 56-foot-long sculpture, titled Three Fold, is actually made of curved aluminum slats covered on both sides with dichroic-acrylic-coated plastic. Though the acrylic is clear, it both reflects and refracts, resulting in a spectrum of iridescent colors that change with the angle and quality of the ambient light.

“It is of course an honor to be associated with the work of Alyson Shotz, and it is humbling to have her work dedicated to my contributions as dean,” Pizzo said. “I am also deeply humbled by the generosity of the many faculty and of the Li Ka Shing Foundation for their contributions that allowed the commission and creation of this incredible work for Stanford Medicine.

“Art, science and medicine are interconnected in so many important ways. The extraordinary work of Alyson Shotz takes these connections to a deeper level since it is based on scientific precision and principles of physics, chemistry and engineering.”

The concept of the sculpture was inspired by a CAT scan, Shotz said. “I was very interested to learn that CAT scans image by sections, using a penetrating wave. This seems quite relevant, as my work represents an imaging of space, and the wave illuminating the shape in this case, is color: the varying wavelengths of light that the viewer will see reflecting off the sculpture,” she wrote in her proposal.

The result is an artwork that will become a destination for anyone interested in contemporary art, said Cantor Arts Center curator Hi-See SCULPTURE, page 4

State’s African clawed frogs harbor deadly amphibian pathogen, researchers find

By Ruthann Richter

In a new study, School of Medicine researchers provide the first evidence that African clawed frogs in California harbor a deadly fungal infection that is decimating amphibian populations across the world.

Among 23 samples tested, the researchers identified three frogs, including one found in Golden Gate Park in San Francisco, that were carriers of the pathogen that has led to the decline or extinction of some 200 amphibian species worldwide. The research was conducted on archived samples from the herpetology collection at the California Academy of Sciences in San Francisco.

“Our goal was to document historically how far back this fungus might have existed in California. Until this study, there were no reports to substantiate that Xenopus laevis (African clawed frogs) in California were infected with this fungus,” said Sherril Green, PhD, DVM, professor and chair of pathology, is the senior author of the study with postdoctoral scholar Diana Hartgevans, PhD, Gerald Crabtree, MD, professor of developmental biology and of pathology, is the senior author of the study, which was published online May 5 in Nature Genetics.

“The broad reach of the effect of mutations in the complex, called BAF, rivals that of another well-known tumor suppressor called p53. It also further a growing notion that these so-called chromatin-regulatory complexes may function as much more than mere cellular housekeepers.

“Although we knew that this complex was likely to play a role in preventing cancer, we didn’t realize how extensive it would be,” said postdoctoral scholar Cigall Kadoch, PhD. “It’s often been thought that these complexes play supportive, maintenance-like roles in the cell. But this is really changing now.”

Researchers at the School of Medicine have identified a group of proteins that are mutated in about one-fifth of all human cancers. The finding suggests that the proteins, which are members of a protein complex that affects how DNA is packaged in cells, work to suppress the development of tumors in many types of tissues.

“Chromatin-regulatory complexes work to keep DNA tightly condensed, while also granting temporary access to certain portions for replication or to allow the expression of genes necessary for the growth or function of the cell,” Kadoch shares lead authorship of the study with postdoctoral scholar Diana Hartgevans, PhD, Gerald Crabtree, MD, professor of developmental biology and of pathology, is the senior author of the study, which was published online May 5 in Nature Genetics.

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Members of Crabtree’s laboratory have been interested in BAF complexes and their function for many years. Recently, they reported in the journal Nature that switching subunits within these complexes can convert human fibroblasts to neurons, which points to their instructive role in development and, possibly, cancer.

“Somehow these chromatin-regulatory complexes manage to compress nearly 2 yards of DNA into a nucleus about one one-thousandth the size of a pinhead,” said
Blocking protein expression delays onset of paralysis in mice with a form of multiple sclerosis, study finds

By Krista Conger

Blocking the expression of just one protein in the brain delays the onset of paralysis in mice with a form of multiple sclerosis, say researchers at the School of Medicine.

Exactly why this happens is still unclear. It may be, in part, that blocking expression of the protein, SIRT1, enhances the transmission of cells that make the insulating myelin sheath necessary for the transmission of nerve signals. This myelin coating is damaged in autoimmune diseases such as multiple sclerosis and Guillain-Barré syndrome.

Although much more research is needed, the findings support the notion that one day be possible to induce remyelination in the brains of patients with myelin-associated diseases or injuries to heal themselves by selectively interfering with the activity of SIRT1.

“We are excited by the potential implications our study has on demyelinating diseases and injuries,” said Anne Brunet, PhD, an associate professor of genetics. “It’s intriguing because activating SIRT1 is typically considered to be beneficial for metabolism and health, but in this case, inactivating SIRT1 can provide protection against a demyelinating injury.”

Brunet, who is also a member of the Stanford Cancer Institute, is the senior author of the research, which was published online May 5 in Nature Cell Biology. Postdoctoral scholar Victoria Rafalski, PhD, is the lead author of the study.

Blocking SIRT1 expression appears to work by promoting the development of neural stem cells in the brain into a type of cell called an oligodendrocyte precursor. These cells, in turn, become the mature oligodendrocytes that wrap the long arms of neurons with myelin — a fatty material necessary to facilitate the transmission of electrical signals from one nerve cell to another. In humans, most myelination occurs during infancy and adolescence.

Diseases such as multiple sclerosis wreak havoc in the central nervous system by damaging this protective myelin coating and impeding communication between nerve cells.

Because SIRT1 is more highly expressed in the brains of mice with an inducible form of multiple sclerosis, Brunet and her colleagues wondered what role the protein might play in the generation or inhibition of oligodendrocytes. To find out, they created a laboratory mouse in which the gene for SIRT1 is selectively disrupted in neural stem cells when the mouse is injected with a drug called tamoxifen. This technique allows the researchers to effectively turn SIRT1 expression off at will in neural stem cells.

Researchers found that, over time, a subset of the nerve stem cells in which SIRT1 expression had been eliminated began to make proteins indicative of oligodendrocyte precursor cells and eventually began to look like typical oligodendrocytes. Growing the neural stem cells in culture yielded similar results; genetically engineered cells lacking active SIRT1 (or unmodified cells treated with a drug that specifically inhibits the activity of the SIRT1 protein) resulted in a marked increase in the proportion of cells expressing an oligodendrocyte-specific protein marker.

When normal mice and those with inhibited SIRT1 expression were injected with a compound that causes the demyelination of nerve cells, the SIRT1-inhibited mice recovered more quickly. Furthermore, they were protected for a time from the paralysis that develops after the onset of the multiple-sclerosis-like disorder.

“Our work suggests that SIRT1 may normally limit the proliferation of oligodendrocyte precursors and that it has to be inactivated to transiently increase the number of these myelinating cells,” Brunet said.

To understand more about how SIRT1 works in these processes, “As is always the case, every time you discover something, you discover new questions,” he said. “This funding expands our capacity to pick apart that neural circuit. It’s fantastic.”

Deisseroth’s laboratory recently developed a technique called CLARITY, supported in part by his HHMI Early Career Scientist funding, that can convert biological systems (such as entire, intact mammalian brains) into a fully transparent form. This technology allows researchers to track neural pathways across the brain, and identify the molecular composition of these pathways within the intact brain. It’s a process that could revolutionize how neuroscientists study the brain. Beginning in 2004, Deisseroth also developed optogenetics, an equally revolutionary technique that allows scientists to control individual types of neurons in living animals. That technique is now used by thousands of neuroscientists.

“We’ve taken some high risk approaches, and sought to develop technologies that seemed to have a low expected probability of success,” said Deisseroth, who also holds the D.H. Chen Professorship. “Both optogenetics and CLARITY, because they were such high-risk projects, underscore the importance of the kind of support HHMI provides.”

His next steps will be to develop new techniques that allow scientists to control individual types of neurons in living animals. That technology is now used by thousands of neuroscientists.

“Both Deisseroth and Moore noted that HHMI’s support freed them to undertake more audacious projects. “HHMI supports people who are willing to take substantial risks; since the possible benefits are so extraordinary, why this kind of support is important for the community,” said Deisseroth.

Tirin Moore, Karl Deisseroth named HHMI investigators

By Rina Shaikh-Lesko

Two Stanford researchers are among 27 scientists appointed May 9 by the Howard Hughes Medical Institute as investigators. They were chosen through a competitive selection process from a pool of more than 1,000 candidates.

The new investigators are Tirin Moore, PhD, associate professor of neurobiology, and Karl Deisseroth, MD, PhD, professor of biochemistry and biomedical sciences and of bioengineering. Both Moore and Deisseroth received HHMI Early Career Scientist appointments in 2009.

HHMI will provide both researchers with flexible support for their research over a five-year renewable appointment, including full salary and benefits, a research budget as well as payment for research space and critical equipment. The organization supports creative, innovative approaches to medical research by employing researchers, rather than simply providing grants for specific research projects. Researchers are able to take risks or change research directions if necessary.

“We at Stanford Medicine are grateful to the Howard Hughes Medical Institute for their support and for sharing our commitment to highly creative scientists and paradigm-changing science,” said Lloyd Minor, MD, dean of the School of Medicine. “We are proud of the accomplishments of Dr. Deisseroth and Dr. Moore, and look forward to even greater achievements.”

With today’s appointments, Stanford now has 20 HHMI investigators, 17 of whom are faculty of the medical school. (Deisseroth is part of the Department of Bioengineering, which is jointly operated by the School of Medicine and the School of Engineering.)

Moore’s research focuses on understanding how neural circuits control visual attention, or the ability to filter our unimportant and distracting stimuli and to focus on what’s important. He noted that this capacity is compromised in people with conditions like attention deficit hyperactivity disorder.

His HHMI Early Career Scientist funding helped him answer key questions about which visual features are classified in these processes. "As is always the case, every time you discover something, you discover new questions,” he said. “This funding expands our capacity to pick apart that neural circuit. It’s fantastic.”

Deisseroth’s laboratory recently developed a technique called CLARITY, supported in part by his HHMI Early Career Scientist funding, that can convert biological systems (such as entire, intact mammalian brains) into a fully transparent form. This technology allows researchers to track neural pathways across the brain, and identify the molecular composition of these pathways within the intact brain. It’s a process that
By Erin Digitale

Preparing babies, those with birth weights hovering around 2 pounds, are prone to bleeding in the brain that can lead to permanent brain damage. Lucy Schoen, a second-year medical student at Stanford, has designed and conducted an experiment that she hopes will eventually provide a way to help physicians determine in advance which babies are at greatest risk for this condition.

“Newborns’ brains are not developed enough to show on the outside what’s happening on the inside,” Schoen said.

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“Until relatively recently, we could only provide supportive care for full-term babies who suffered brain injury in the labor process,” Van Meurs said. “About 25 percent of neonatal mortality is due to birth asphyxia, so controlled hypothermia has the potential to have a big impact.” Packard Children’s participated in one of the earliest clinical trials of hypothermia and has offered it since 2000, she noted.

After Jackson’s body temperature was returned to normal, he received a magnetic resonance imaging scan to check for signs of brain damage. Use of MRIs for newborns’ brains is also in its infancy, she noted. The Neuro NICU and elsewhere has shown that, if begun within six hours of birth, cooling slows damaging metabolic processes and gives the brain time to heal.

“Newborns’ brains are not developed enough to show on the outside what’s happening on the inside.”

“Schoen, who plans to continue the pilot study we found this association. It was weak, but it was there,” said Schoen, who plans to continue her research, conducting measurements on larger numbers of babies.

Schoen was one of 45 MD and MD-PhD students at the School of Medicine who presented their research projects during the symposium in Berg Hall, at the Li Ka Shing Center for Learning and Knowledge. From future stem cell researchers to budding international health experts, the crowd of aspiring physicians were available next to their poster boards to describe their work in detail for the crowd of faculty, staff and fellow students — a medical condition in premature infants in which portions of the bowel undergo necrosis (tissue death). It is one of the most common causes of morbidity in premature infants in developing countries.

Nearby, second-year medical student Katherine Ransohoff, working together with her sister Julia Ransohoff, a high-school student, discussed their research project involving the use of new immunosuppressive therapies to increase cell survival rates in mice receiving cardiac stem cell treatments.

“Cell survival increased from 10 days with traditional therapy to 35 days with the use of novel blockade agents,” Ransohoff said. The young authors have submitted the study to a journal for publication.

“Newborns’ brains are not developed enough to show on the outside what’s happening on the inside.”

Jackson Thomas, who was oxygen deprived at birth, underwent controlled hypothermia at Packard Children’s to help him. Diana Powell is a nurse in the hospital’s neonatal intensive care unit.

“The challenge and exciting thing about treating these tiny babies is that the brain is developing on a literally day-by-day basis,” said Courtney Wusthoff, MD, a neonatologist at Packard Children’s. Wusthoff arrived at the hospital in September 2012 to help launch the Neuro NICU.

In addition to bringing Wusthoff on board, the hospital has purchased a wide array of new diagnostic and monitoring equipment for babies’ brains, and is providing specialized training for all its NICU practitioners on the latest research and treatments in infant neurology. The options for protecting and nurturing babies’ quickly changing brains are expanding rapidly, Wusthoff said. “We have more and more opportunities for interventions.”

In early 2012, the Thomas family of San Jose benefited from several such interventions after their younger son’s unexpectedly difficult birth at a hospital in San Jose. When she arrived in labor, Heather Thomas was found to have suffered a placental abruption. The baby was not getting any oxygen and needed to be delivered immediately. Upon delivery, baby Jackson did not breathe. He had a seizure within one minute of birth. After Jackson was resuscitated by a physician, she and husband Gary asked their son to Packard Children’s to receive controlled hypothermia, a recently developed treatment for preventing brain injury after oxygen deprivation. In this procedure, the infant is placed on a blanket impregnated with tubes that carry cool water. The baby’s body is cooled to 92.3 degrees Fahrenheit for three days. Research conducted at Packard Children’s and elsewhere has shown that, if begun within six hours of birth, cooling slows damaging metabolic processes and gives the brain time to heal.

“Newborns’ brains are not developed enough to show on the outside what’s happening on the inside.”

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The abstract form of *Three Fold*, by Alyson Shotz, allows viewers to imbue it with their own meanings. 

“Three-D modeling allows me to go to a level of geometric detail that would be impossible otherwise. When I first began, I saw that on the computer I could make complicated folded shapes in digital space viewable from all angles that were virtual sculptures but were also like drawings — they start as lines on a grid. I then wanted to make those drawings into real physical sculptures.”

After deciding on the sculpture’s form, Shotz worked with a computer programmer to figure out how hundreds of pieces of aluminum would fit together like a puzzle to make the model a reality. Shotz took this information to a fabricator — DCM Fabrication in Brooklyn — where the aluminum and acrylic were cut and the pieces assembled into sections that together form the three parts making up the sculpture.

The sections were loaded into a 53-foot tractor-trailer and hauled across the country, arriving at Stanford in January 2013. Shotz and a team of art-installation specialists worked for two weeks assembling the sections, peeling the protective film off the sculpture’s surfaces, mounting the sculpture on cables and raising it into position.

Shotz named the sculpture when the installation was nearly complete, as is often the case for her. She chose *Three Fold* in part, she said, because each of the sculpture’s three parts began in the same shape, which she folded and stretched in different ways to create the three distinct forms. She likes the title’s open-ended meaning: “It implies three forms as well as an experience three times greater. It also implies that each of the three parts multiply each other — or are more than themselves.”

Shotz has an abiding fascination with science. As a college student at the University of Colorado, she initially studied glaciology before switching to art. So it’s no wonder that she gravitates toward scientific imagery, with much of her work attempting to visualize invisible forces like space and gravity.

The sculpture’s abstract form allows viewers to imbue it with their own meanings. Some see it as the frame of a boat, or a skeleton, perhaps of a dinosaur or a whale. Others say that it brings to mind astronomical imagery compels us to view it differently each time we encounter it, “reminding us of the importance of being receptive to new insights and opportunities.”


The medical school’s art committee chose Shotz for the installation in October 2011 after considering slides of works by about a dozen highly respected artists from around the world selected by Buell, an art adviser at the San Francisco firm Zlot Buell + Associates.

“It was unanimous. No second choice. We all loved her,” said Ralph Greco, MD, the committee’s chairman and a professor of surgery. The Li Ka Shing Foundation, five medical school departments, and more than a dozen medical school faculty and their partners helped fund the acquisition of the piece, its installation and associated construction.

The committee members were also unanimous in the decision to dedicate the artwork to Pizzo, who stepped down last fall after 12 years as dean, “It made sense — because of his strong support of art at the medical school, and to recognize his tenure as dean,” Greco said.

Pizzo created the art committee in 2011, which not only commissions works but organizes rotating exhibits featuring art created by members of the medical school’s community. The current exhibit of four artists’ work, also in the Li Ka Shing Center, will continue through the summer.

“A reminder of the beauty of science, Alyson Shotz’s *Three Fold* is stunning sculpture and a fitting tribute to Phil Pizzo’s dynamic and visionary leadership,” said Lloyd Minor, MD, dean of the School of Medicine.

Upon receiving the offer to submit a proposal, the Brooklyn-based artist quickly came to Stanford to examine the space. She then returned to her studio to develop her concept, flew back to Stanford for its presentation, which the committee also loved, and then returned to Brooklyn to complete the job.

“Like much of Shotz’s work, *Three Fold* was born on a computer. ‘I could not have made or even visualized the sculpture without the computer,’” Shotz said.

“Alyson Shotz is a widely respected artist and has had many important commissions. This will be another ‘go-to’ piece for Stanford — like the Chihuly and Andy Goldsworthy’s *Stone River*.”

“This is the biggest project she’s done to date,” said Sabrina Buell, a Stanford alumna who serves on the medical school’s art committee. “To have it at Stanford is a very special thing.”

Shotz’s work is exhibited at some of the world’s most prestigious art museums, including the Solomon R. Guggenheim Museum in New York, The Hirshhorn Museum and Sculpture Garden, The Whitney Museum of American Art and the San Francisco Museum of Modern Art. Her upcoming solo exhibitions are scheduled for, among other venues, the Edythe and Eli Broad Museum in East Lansing, Mich., and the Wellels Museum in Clinton, NY.

2. A worker helps to install the sculpture. 3. Shotz, far left, oversees a crew of art-installation specialists. It took two weeks to assemble and mount the sculpture. 4. Workers lift a part of the sculpture.
Registration now open for Stanford Medicine X conference

By Lia Steakley

Registration is now open for the 2013 Stanford Medicine X conference, which will bring together innovative thinkers to exchange ideas about how social media and mobile computing are sparking new ways to deliver health care and advance the practice of medicine.

The conference runs Sept. 27-29 and features presentations and panels covering a range of topics, including patient-centered design, participatory medicine, crowdsourcing for health projects and the impact of information technology on biomedical research.

"Medicine X is a conference of ideas and a chance for the Stanford community to come together in a global forum to explore the cultural shifts taking place at the intersection of technology and health care," said Lawrence Chu, executive director of the conference. "We are building on the work that began last year and continue to examine ways social media and participatory medicine can empower all health-care stakeholders to work together to improve health."

Delivering the opening keynote at the conference is Maryland high school student Jack Andraka, winner of the 2012 Intel International Science and Engineering Fair and the Smithsonian American Ingenuity Award. Andraka invented a novel paper sensor that detects pancreatic, ovarian and lung cancers in five minutes and costs a mere 3 cents.

Also delivering a keynote speech is John Sculley, former president of PepsiCo and past CEO of Apple Inc. One of America's best-known business leaders, Sculley is a vocal advocate for health innovation and mentor to an elite group of health-care entrepreneurs.

New to this year's conference is the Medicine X Master Class program, a series of small-vendue seminars taught by experts in specific disciplines. Confirmed master-class speakers include Roni Zeiger, CEO of Smart Patients; Susannah Fox, an associate director of the Pew Research Center's Internet & American Life Project; Sonny Vu, CEO of Misfit Wearables; Bertalan Meskó, MD, founder of Wevibric; Wendy Sue Swanson, MD, pediatrician and author of the Seattle Mama Doc blog; Bryan Varzata, MD, assistant professor of pediatrics at Baylor College of Medicine; and patient advocate and artist Regina Holliday.

"Medicine X is a relationship-based conference focused on an entire experience, rather than a single lecture," Chu said. "Our new master-class program expands on this goal by bringing in acclaimed experts to provide once-in-a-lifetime learning experiences and help attendees gain new skills in a participatory and interactive classroom setting."

The conference will be preceded by the IDEO Design Challenge on Sept. 26. Held at the headquarters of design firm IDEO, in Palo Alto, the daylong workshop will offer patients the opportunity to collaborate with designers, technologists, researchers and health-care providers to develop solutions to enhance patient care.

The workshop is one of several ways Medicine X will unite health-care stakeholders to identify how advances in technology can be used to transform medicine. In addition to presentations and moderated discussions about data-driven studies and clinical outcomes demonstrating how web-based and mobile computing applications can improve health, the conference will include talks by "e-patients" — health consumers who use digital tools to get information about and help manage their medical conditions.

"Bringing patient voices to the conference is an essential part of this goal," Chu said. "We continued that objective this year by creating the e-patient track for presenters to discuss important uses and research relating to participatory medicine."

Conference registration fees start at $1,119 for the general public, $779 for academics and $499 for students. The early registration deadline is June 15, Medicine X 2012 sold out, and space is limited for this year's event. To register, visit http://medicinex.stanford.edu. Keynote speeches and video presentations from Medicine X 2012 are available online at http://medicinex.stanford.edu/video/talks. To learn more about the upcoming conference program, visit http://medicinex.stanford.edu or follow the conference on Twitter at @StanfordMedX.

"Medicine X is a project of the Stanford University School of Medicine Anesthesia Informatics and Media Lab, and is sponsored in part by the school's Department of Anesthesia. Other sponsors include Stanford Hospitals & Clinics, the Agency for Healthcare Research Quality and the Stanford Hospital Corporate Partners Program."

Registration now open for Stanford Medicine X conference
comparative medicine at Stanford and senior author of the paper. The Stanford scientists collaborated with colleagues at San Francisco State University on the study, which was published May 15 in PLOS ONE.

The fungal pathogen, known as *Batrochochromis denrobrachiatus*, has been implicated in frog epidemics in a number of countries, including the United States, United Kingdom, France, Spain, Germany, Portugal, Italy, Brazil and Japan, as well as throughout Latin America, said Green, who is a frog expert. Along with environmental pollution and loss of habitat, it’s believed to be one of the factors behind the precipitous decline in worldwide frog populations.

The African clawed frog has long been suspected of spreading the dangerous pathogen, which is transmitted through the water. Spores from the fungus may tunnel into the animals’ skin, causing skin thickening, electrolyte imbalance and brain swelling, Green said.

Though the practice was largely discontinued in the late 1970s, some frogs used in the testing process may have been released into the environment. “From a conservationist’s perspective, releasing these frogs into the wild was not a good thing, no matter how well-intended,” Green said.

Today, the frogs are commonly used in biomedical research laboratories because they are hardy and long-lived and because they can continue to lay eggs for a large number of eggs, thus providing scientists with a steady supply of material for studies in developmental biology, medicine and physiology, Green said. However, because they are invasive and are not native to North America, their use, sale and transport are highly regulated in California and 11 other states, she said.

While useful in the lab, once released in the wild they may pose a threat to native amphibians. The frogs, which Green describes as “big, slimy, green, ugly things,” are predators and are carnivorous, devouring everything in their path, including their own species. They can grow as long as 7 inches and are extremely adaptable, often living a decade or more in the wild, where they have few local predators.

To determine their role in the spread of disease, the scientists examined 23 Xenopus specimens collected in California between 2001 and 2010, as well as 178 specimens collected in Africa between 1987 and 2008. All the specimens had been assembled by Stanford biologists, preserved in alcohol and donated to the California Academy of Sciences, which has one of the oldest and largest herpetology collections in North America.

Green and her collaborators, including co-author Stephen Felt, DVM, MPH, an assistant professor of comparative medicine, and three former Stanford undergraduates — Erica Morgan, Andrea Cowen and Sabrina Wilson, all members of the class of 2011 — spent hours in the basement of the academy combing through thousands of specimen jars and swabbing DNA from the skin of preserved frogs. They tested these samples using polymerase chain reaction, a simple, fast technique that allows DNA to be copied repeatedly. Among the African samples, five — or 2.8 percent — were positive for the fungus, including three from Kenya and two from Uganda, the researchers reported.

Among those samples from California, they found three — or 13 percent of those tested — were positive for the fungus, including one frog taken from the Lily Pond in Golden Gate Park and two from San Diego.

The researchers documented the earliest positive case of the disease in a frog collected in Kenya in 1934, reinforcing the theory that the fungus was endemic to Africa long before the frogs were distributed worldwide as part of the live amphibian trade.

Now that the frogs are widely dispersed across the globe, Green said containing the epidemic is a major challenge.

“Right now people are still tracking what populations may be affected and may succumb a few years from now,” she said. “Resistant species are surviving with chronic infections and will learn to live with it. While it wipes out most frogs that are not native or indigenous to the source of the fungus, some survive and there is hope that surviving populations will adjust and become resistant to it. But we don’t have enough data to know indeed if that is happening.”

The U.S. Fish and Wildlife Service has considered further restrictions on the importation and interstate transport of the African clawed frogs, though Green said she does not believe such rules would have much effect on the current epidemic.

“In essence, it’s like closing the barn door long after the horse has left,” she said. “Further restricting Xenopus at this point it probably going to have very little impact on the ongoing epidemic, but will certainly have a negative impact on biological and biomedical research.”

The project was funded by a grant from Stanford’s Office of the Vice Provost for Undergraduate Education awarded to Cowen and by a National Science Foundation grant to SFU biologist Vance Vredenburg, PhD, who is the lead author of the study.

The Department of Comparative Medicine also supported the work.
Researchers develop new technique to track cell interactions

By Rina Shaikh-Lesko

Researchers at the School of Medicine have developed a new technique to see how different types of cells interact in a living mouse. The process uses light-emitting technologies that glow when two types of cells come close together.

Using the technique, the team was able to pinpoint where in the body metastatic cancer cells ended up after they broke off from an initial tumor site, using readily available lab reagents. The team chose chemicals that are easily available in most life sciences laboratories because they wanted to develop a technique that could be widely used.

The study was published online May 6 in the Proceedings of the National Academy of Sciences.

Until now, the best way to see cells interacting inside a living animal or person was to implant a microscope. But predicting all the places metastatic cancer cells will proliferate is nearly impossible. “There are currently no great ways to look at early metastasis, where metastases are finding their micro-environments and setting up shop,” said Mark Selenny, MD, PhD, the study’s lead author, who developed the technique as a graduate student working jointly for Christopher Contag, PhD, professor of pediatrics and of microbiology and immunology, and Tom Wandless, PhD, associate professor of chemical and systems biology.

Selenny, who begins a research residency in radiology at the University of Pennsylvania this summer, worked closely with Jennifer Prescher, PhD, a former postdoctoral scholar in Contag’s lab who is now an assistant professor at the University of California-Irvine. “I think it really expands our capabilities, expands the tool box,” Prescher said. “We’re always beholding to the tools available for us in terms of what we can observe. Any time we have a new technology — it can open doors to understanding new aspects of biology.”

Selenny and Prescher genetically altered immune cells and cancer cells — what they call activator and reporter cells, respectively — so the cells would produce two different enzymes. The activator enzyme activated the enzyme B-galactosidase, which can convert a common biological probe called a “caged luciferin” into luciferin, a molecule naturally found in animals like fireflies. The reporter enzyme activated the enzyme luciferase, which splits the luciferin molecule in a chemical reaction that emits light.

After demonstrating the process could work in a cell culture in a petri dish, they used the same method in living mice. The mice were implanted with genetically altered bone marrow cells. After several weeks, the researchers injected a compound that would be converted to light-emitting luciferin.

The researchers could easily see where populations of immune cells got close to populations of cancer cells because those parts of the mouse body would glow. Among other metastasis sites, researchers were surprised to find that in several mice, small populations of cancer cells had started to grow in their noses and just under their lower jaws.

According to a control group of four additional mice were implanted with unaltered bone marrow cells. After several weeks, the researchers injected a compound that would be converted to light-emitting luciferin.

The researchers could easily see where populations of immune cells got close to populations of cancer cells because those parts of the mouse body would glow. Among other metastasis sites, researchers were surprised to find that in several mice, small populations of cancer cells had started to grow in their noses and just under their lower jaws.

Currently, the technique can’t be used in people, but the researchers hope it will be used to study a variety of cell interactions in laboratory mice. Contag is planning to use the technique to study how immune cells migrate to sites of infection. Cell-cell communication is important for a variety of biological processes. “Knowing the proximity of one cell type to another in the context of the living tissue is key for understanding biology,” Contag said.

The technique requires a minimum population of 1,000 cells for both the activator and reporter cells to work. Prescher is working on improving the precision of the method so that smaller populations with fewer cells can be tracked.

Both Contag and Wandless noted that Selenny’s and Prescher’s interdisciplinary approach was key to developing the technique.

“The training in biology allowed them to identify an important problem in the area of cell interactions and their ability to incorporate chemistry allowed Mark and Jenn to design and develop a new technique that would be out-of-the-reach to the majority of classical biology labs,” Wandless said.

Other Stanford authors of the study include postdoctoral scholar Laura Brorsenti, PhD, and visiting scholar Hiroshi Imoto, MD, PhD.

The study was supported by the National Institutes of Health, the NIH Medical Scientist Training Program and the Susan G. Komen Foundation.

The Stanford Molecular Imaging Scholars Program also supported the research.

Rina Shaikh-Lesko is a science-writing intern for the medical school’s Office of Communication & Public Affairs.

Cigal Kadoch, Jerry Crabtree and Diana Hargreaves identified a protein complex that, when unmutated, as a tumor suppressor is further emphasized by the fact that, in some cases, a mutation in one subunit is sufficient to initiate cancer development.

“For example,” said Kadoch, “a type of mutation called a chromosomal translocation in the gene encoding one of these newly identified subunits, S18, is known to be the hallmark of a cancer called synovial sarcoma. It is clearly the driving oncogenic event and very often the sole genomic abnormality in these cancers.”

Kadoch and Crabtree published a study in March in Cell uncovering the mechanism and functional consequences of BAF complex perturbation in synovial sarcoma.

The startling prevalence of mutations in the BAF complex was discovered when Kadoch conducted a series of experiments to determine exactly which proteins in the cell were true subunits of the complex. (“Protein complexes are the fundamental building blocks of the cell. If you can ascertain the exact subunits, you can start to figure out how the complex is organized.”) Kadoch used an antibody that recognized one core component to purify intact BAF complexes in various cell types, including embryonic stem cells and skin, nerve and other cells. She then analyzed the various proteins isolated by the technique.

Using this method, Kadoch identified seven proteins previously unknown to be BAF components. She and Hargreaves then turned to previously published studies in which the DNA from a variety of human tumors had been sequenced because those parts of the mouse body would glow. Among other metastasis sites, researchers were surprised to find that in several mice, small populations of cancer cells had started to grow in their noses and just under their lower jaws.

CURRENTLY, THE TECHNIQUE CAN’T BE USED IN PEOPLE, BUT THE RESEARCHERS HOPE IT WILL BE USED TO STUDY A VARIETY OF CELL INTERACTIONS IN LABORATORY MICE. CONTAG IS PLANNING TO USE THE TECHNIQUE TO STUDY HOW IMMUNE CELLS MIGRATE TO SITES OF INFECTION. CELL-CELL COMMUNICATION IS IMPORTANT FOR A VARIETY OF BIOLOGICAL PROCESSES. “KNOWING THE PROXIMITY OF ONE CELL TYPE TO ANOTHER IN THE CONTEXT OF THE LIVING TISSUE IS KEY FOR UNDERSTANDING BIOLOGY,” CONTAG SAID.

The technique requires a minimum population of 1,000 cells for both the activator and reporter cells to work. Prescher is working on improving the precision of the method so that smaller populations with fewer cells can be tracked.

Both Contag and Wandless noted that Selenny’s and Prescher’s interdisciplinary approach was key to developing the technique.

“The training in biology allowed them to identify an important problem in the area of cell interactions and their ability to incorporate chemistry allowed Mark and Jenn to design and develop a new technique that would be out-of-reach to the majority of classical biology labs,” Wandless said.

Other Stanford authors of the study include postdoctoral scholar Laura Brorsenti, PhD, and visiting scholar Hiroshi Imoto, MD, PhD.

The study was supported by the National Institutes of Health, the NIH Medical Scientist Training Program and the Susan G. Komen Foundation.

The Stanford Molecular Imaging Scholars Program also supported the research.

Rina Shaikh-Lesko is a science-writing intern for the medical school’s Office of Communication & Public Affairs.
Mom gets in shape to give kidney to daughter with rare illness

By Winter Johnson

Lori Vargas, mother of 15-year-old Taylor Simpson, said that donating a life-saving kidney to her daughter wasn’t that big of a deal, even though it was.

“There’s nothing you wouldn’t do for your child to make them healthy,” Lori said. She said she never had any doubts, even committing herself to lose almost 40 pounds — climbing stairs “like a madwoman” so that she would be fit enough to give a kidney to her only child.

It was an impressive commitment, and it led to mom having one of her kidneys removed April 2 at Stanford Hospital & Clinics by surgeon Waldo Conception, MD, who then dashed over to Lucile Packard Children’s Hospital, which is home to America’s No. 1 pediatric kidney transplant program. There, Conception successfully implanted Lori’s kidney into a waiting Taylor.

It was a new beginning for Taylor, and a happy end to a dramatic story. In November 2011, a month before her 14th birthday, Taylor was enjoying a normal teenage life in Watsonville, Calif., when she was hit with sudden, flu-like symptoms. Soon she was vomiting blood. She was rushed to a local hospital and then taken by ambulance to Packard Children’s, where blood tests and CT scans showed Taylor had end-stage kidney failure along with bleeding in her lungs. She was diagnosed with Goodpasture syndrome. “It’s an extremely rare and life-threatening autoimmune disease, and it happens to previously healthy people without warning,” said nephrologist Paul Grimm, MD, medical director of the kidney transplant program at Packard Children’s and a professor of pediatric nephrology at the School of Medicine.

“She was attacking the filters of her kidney and also the blood vessels of her lungs,” the disease was first reported in 1919 by pathologist Ernest Goodpasture.

It was the beginning of a long and exhausting medical journey. Lori and Taylor were soon driving two hours to Packard Children’s for kidney dialysis. There were multiple rounds of immunosuppressant medications and plasmapheresis, a process to purify the blood — all to fight the disease raging through her body.

However, it eventually became clear that the damage to Taylor’s kidneys was too severe to avoid a transplant. Mom was ready. “From the get-go, I planned on being Taylor’s donor,” Lori said.

To receive mom’s kidney, doctors had to be certain that Taylor’s immune system stopped producing the deadly Goodpasture antibodies so there would be no danger of her body attacking the new organ. Plus, she needed to be steroid-free for six months, thus pushing the wait into 2013.

Despite all of her treatments and waiting, Taylor never stopped joking around with Packard Children’s staff and devoting herself to her artwork and homework. She became great buddies with her rheumatologist Nina Washington, MD, and nephrologist Orly Haskin, MD, while keeping up with school via dialysis unit teacher Katie Fennimore and a “Taylor”-made Individualized Education Program.

“The care teams at Packard Children’s treated me like a normal person instead of a sick kid,” Taylor said.

In the meantime, Lori lost the weight and got the thumbs up on Feb. 6 to be a donor. “I think my mom is beyond awesome,” said Taylor, who crossed the finish line of being steroid- and antibody-free this spring, thus being healthy enough for the April transplant.

A big bonus: After plasmapheresis and a strict medication regimen designed to get rid of the antibodies in her blood, Taylor’s lungs have fully recovered.

Now, Taylor and Lori are happily back home in Watsonville, where Taylor is focusing on the dreams that mom’s kidney has made possible. She’s interested in several possible careers — as a bilingual animal rights activist, a yoga teacher or police officer — but first wants to line up some food she has been missing, including potatoes, milk and tomatoes. Taylor couldn’t eat the yummy but potassium-rich foods prior to her transplant, as patients with kidney disease have a hard time excreting potassium in their urine, causing a buildup that could result in cardiac failure, Haskin said.

The high-school freshman has a simple summer plan: “I’m looking forward to going to the beach and finally being able to swim,” Taylor said.

She is rediscovering a normal teenage life again thanks to advanced medical care, organ donation and a loving mom who would do the same thing again and again and again — and not just for her only child.

“If I had more than one kidney I could donate,” Lori said. “I’d keep donating to other patients at Packard Children’s. Taylor and I really know what these kids on dialysis go through while waiting for a new kidney, and I’d like to provide this gift of life to every one of them.”

The Symphonic Body/Medicine

Guillem Pratx

Performing medicine

Cathy Jan, a graduate student in electrical engineering; Baru Atindog, a life science research assistant in dermatology; and Eliver Zhou, a postdoctoral scholar in genetics perform the Symphonic Body/Medicine, a dance of gestures related to the everyday work of physicians and scientists, at the Cantor Arts Center. Choreographed by Ann Carlson, a visiting artist in the Department of Theater and Performance Studies, the work was presented as part of a May 2 symposium, “A Healing Dose of Creativity: Medicine and the Arts,” sponsored by the medical school’s Arts, Humanities and Medicine Program.