



First-year medical students arrived last month for orientation. **Page 4**

Scientists home in on origin of human, chimp facial differences

By Krista Conger

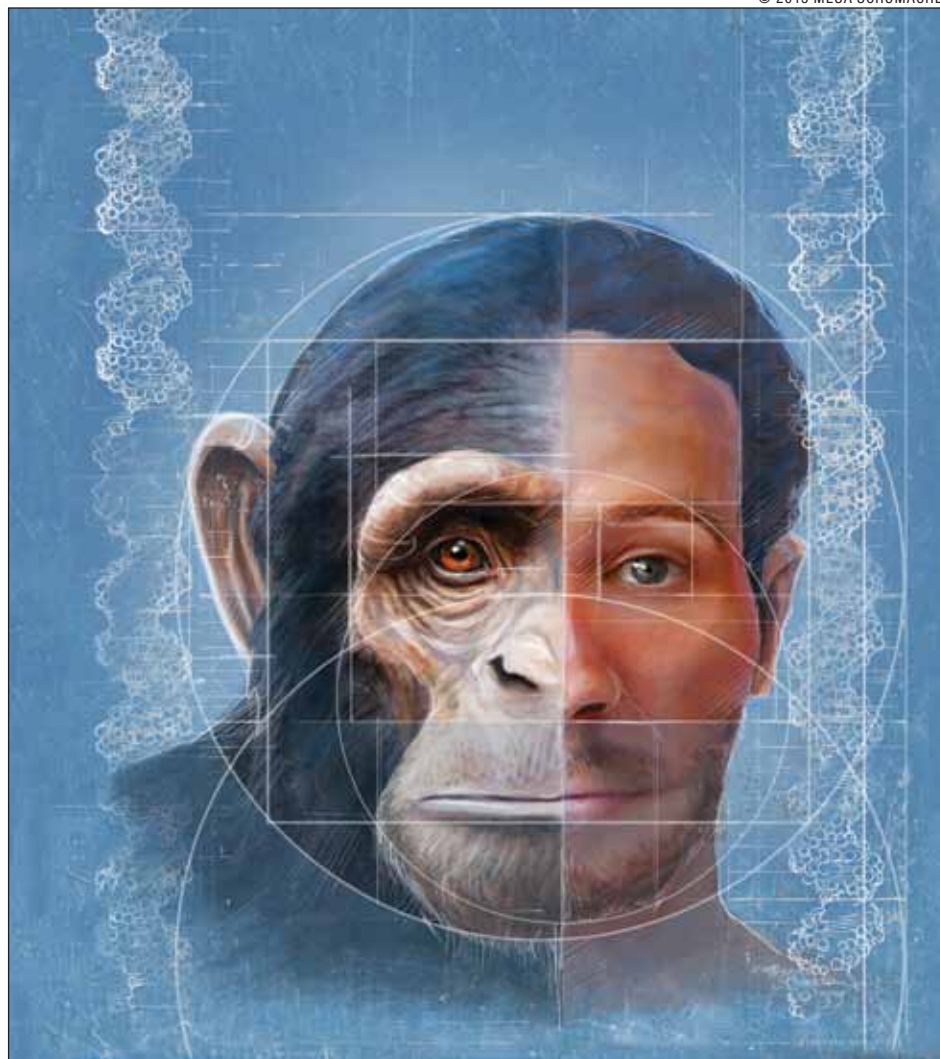
The face of a chimpanzee is decidedly different from that of a human, despite the fact that the apes are our nearest relative in the primate tree. Now researchers at the School of Medicine have begun to pinpoint how those structural differences could arise in two species with nearly identical genetic backgrounds.

The key lies in how genes involved in facial development and human facial diversity are regulated — how much, when and where the genes are expressed — rather than dissimilarities among the genes themselves. In particular, the researchers found that chimps and humans express different levels of proteins known to control facial development, including some involved in jaw and nose length and skin pigmentation.

“We are trying to understand the regulatory changes in our DNA that occurred during recent evolution and make us different from the great apes,” said Joanna Wysocka, PhD, associate professor of developmental biology and of chemical and systems biology. “In particular, we are interested in craniofacial structures, which have undergone a number of adaptations in head shape, eye placement and facial structure that allow us to house larger brains, walk upright and even use our larynx for complex speech.”

The researchers coined the term “cellular anthropology” to explain how some steps of early primate development can be mimicked in a dish, and thus used to study gene-expression changes that can shed light on our recent evolutionary past.

A study describing the research was published online Sept. 10 in *Cell*. Graduate student Sara Prescott is the lead author. Wysocka and senior research scientist Tomasz Swigit, PhD, share senior authorship of the study.



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Although chimps and humans have almost identical genomes, their genes make different amounts of proteins known to control facial development, including some involved in jaw and nose length.

The role of enhancer regions

For their comparison, the researchers focused on areas of DNA known as enhancer regions in human and chimpanzee genomes. These regions contain chemical tags and proteins bound to the DNA that control when, where and how nearby genes are expressed. Prescott and her colleagues wondered whether differ-

ences in the way proteins bind to these enhancer regions during development could explain morphological differences between humans and chimpanzees.

“We wanted to look at how the activity of these enhancer regions may have changed during recent evolution,” said Wysocka. “Many recent studies have shown that changes in the DNA sequences of enhancers **See FACE, page 6**

Study: Math anxiety relieved in children who get tutoring

By Erin Digitale

Anxiety about doing math problems can be relieved with a one-on-one math tutoring program, according to a new study from the School of Medicine. The tutoring fixed abnormal responses in the brain’s fear circuits.

The study, published Sept. 9 in *The Journal of Neuroscience*, is the first to document an effective treatment for math anxiety in children.

“The most exciting aspect of our findings is that cognitive tutoring not only improves performance, but is also anxiety-reducing,” said the study’s senior author, Vinod Menon, PhD, professor of psychiatry and behavioral sciences. “It was surprising that we could, in fact, get remediation of math anxiety.”

Even if they are good at math, many children feel anxious about doing math problems. For some, the anxiety persists throughout life, discouraging them from pursuing advanced math and science classes as well as careers that rely on mathematical expertise. Yet almost no attention has been paid to how

See MATH, page 7

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Using star power to teach Indian kids about HIV/AIDS

By Ruthann Richter

At Zilla Parishad High School in the south Indian metropolis of Hyderabad, more than 100 students in blue and white uniforms sit cross-legged on the stone floor, faces gleaming and eyes riveted on an animated video featuring Nagarjuna, a revered star of south Indian cinema.

The video, featuring an avatar of the handsome, mustachioed actor, doesn’t aim to entertain but to teach the students some basics about HIV/AIDS that could help protect their health and possibly save their lives.



Piya Sorcar

“I never knew HIV existed,” one 13-year-old student, Dharana, said after viewing the 22-minute video. “I learned a lot. Now I have an awareness. I want to go to the hospital before marriage and have my groom get an HIV test.”

Though India **See AIDS, page 6**

Trail gets hotter in hunt for cause of ALS

By Krista Conger

A defect in how proteins are transported inside cells may be at least partially responsible for some symptoms of amyotrophic lateral sclerosis, according to a study by researchers at the School of Medicine.

The researchers found that cells with a mutation associated with the disease were hampered in their ability to move proteins into and out of the nucleus, a cell’s command center. The findings are among the first to open a window into the molecular causes of the deadly condition.

Also known as Lou Gehrig’s disease, ALS is a progressive neuromuscular disorder. Although it’s unknown what causes many cases of the disease, a genetic stutter in a region of DNA called C9orf72 has been associated with the development of both ALS and another related neurodegenerative disorder called frontotemporal dementia. In this region, the DNA sequence is made up of a six-nucleotide pattern, which repeats abnormally in some people with



KOYA979 / SHUTTERSTOCK

A mutation linked to amyotrophic lateral sclerosis interferes with the transport of proteins in and out of a cell’s nucleus.

ALS or FTD.

“Healthy people have two to five repeats of this six-nucleotide pattern,” said Aaron Gitler, PhD, associate professor of genetics. “But in some people, this region is expanded into hundreds or thousands of copies. This muta- **See ALS, page 7**

Girls and boys with autism differ in behavior, brain structure

By Erin Digitale

Girls with autism display less repetitive and restricted behavior than boys do, according to a study by researchers at the School of Medicine.

The study also found that brain differences between boys and girls with autism help explain this discrepancy.

The study, which was published online Sept. 3 in *Molecular Autism*, gives the best evidence to date that boys and girls exhibit the developmental disorder differently.

“We wanted to know which specific clinical manifestations of autism show significant gender differences, and whether patterns in the brain’s gray matter could explain behavioral differences,” said the study’s senior author, Vinod Menon, PhD, professor of psychiatry and behavioral sciences. Knowledge of the difference could help clinicians better recognize and treat autism in both sexes, he added. “Understanding this is really quite crucial clinically.”

“We found strong evidence for gender differences in autism,” said postdoctoral scholar Kaustubh Supekar, PhD, the study’s lead author. The researchers used two large, public databases to examine nearly 800 children

with high-functioning forms of autism in the United States, he said.

Repetitive and restricted behavior is perhaps the most widely recognized of the three core features of autism. It can show up as a child’s preoccupation with a narrow interest, inflexibility about routines or repetitive motions such as hand-flapping. The other core features of autism are social and communication deficits.

More boys with high-functioning autism

Among children diagnosed with the high-functioning form of autism, boys outnumber girls by four to one. Scientists were interested in comparing the expression of core features of the disorder between sexes because they have long suspected girls with autism may display symptoms differently, causing them to be underdiagnosed or making it harder for them to get the most appropriate treatment.

“Autism has primarily been studied from the viewpoint of boys with the disorder,” said Menon, who holds the Rachael L. and Walter F. Nichols, MD, Professorship. “Understanding gender differences can help in identifying the behavioral skills that are most important to remediate in girls vis-a-vis boys.”

The study examined the severity of autism symptoms in 128 girls and 614 boys registered with the National Database for Autism Research. The children ranged in age from 7 to 13, had IQ scores above 70, and had been evaluated with standard tests for autistic behavior. The boys and girls were matched for age, and had the same average IQ. Girls and boys had similar scores for social behavior and communication. But girls had lower scores on a standard measurement of repetitive and restricted behaviors.

The researchers then examined data from the Autism Brain Imaging Data Exchange that included structural MRI brain scans of 25 boys with autism, 25 girls with autism, 19 typically developing boys and 19 typically developing girls. The individuals among the groups were matched for age and IQ. The researchers again found that girls and boys did not differ on social behavior and communication skills, but that girls

had less-severe repetitive and restricted behaviors. “This replication provides the strongest evidence to date for gender differences in a core phenotypic feature of autism,” Menon said.

Brain-structure differences

The brain-scan analysis revealed several gender differences in brain structure between typically developing boys and girls, consistent with the findings of earlier studies.

Children with autism, however, had a dissimilar set of gender differences in their brains — specifically, in the motor cortex, supplementary motor area and a portion of the cerebellum. These regions affect motor function and planning of motor activity. The researchers noted that many repetitive behaviors, such as hand-flapping, have a motor component. The study demonstrated that patterns of gray matter in these motor regions could accurately distinguish girls from boys with autism, Supekar said. The researchers found that parts of the motor system that contributed to individual scores for repetitive and restricted behaviors were different in boys and girls.

“Girls and boys with autism differ in their clinical and neurobiological characteristics, and their brains are patterned in ways that contribute differently to behavioral impairments,” Menon said.

“The discovery of gender differences in both behavioral and brain measures suggests that clinicians may want to focus diagnosis and treatments for autistic girls differently than boys,” Supekar added.

This research was supported by a NARSAD Young Investigator Award, an Atherton Investigator Award, the National Institutes of Health and the Simons Foundation.

Creation of the ABIDE data set was supported by the National Institute of Mental Health, the Leon Levy Foundation, Joseph P. Healy, and the Stavros Niarchos Foundation. Menon is a member of the Stanford Child Health Research Institute.

Stanford’s Department of Psychiatry and Behavioral Sciences also supported the research. **ISM**

ALTANAKA / SHUTTERSTOCK



A new study shows that there are gender-based differences in the behaviors displayed by children with autism.

When families of patients prefer Spanish at the hospital

By Erin Digitale

Spanish-speaking families are more satisfied with and better understand their children’s surgical care when they communicate with the surgical team in their native language, according to a new study from the School of Medicine and Lucile Packard Children’s Hospital Stanford.

The study, which appears in the September issue of the *Journal of Pediatric Surgery*, examined outcomes in the Hispanic Center for Pediatric Surgery at the children’s hospital. All staff members at the center, including the receptionists, triage staff, nurse practitioners and pediatric general surgeon, interact with patients and their family members in fluent Spanish. Families thus receive all of their medical care without the need for an interpreter.

“Even though the interpreters are great, being able to look someone in the eye and tell them how we feel, and hear directly how they feel about us, makes

for such a different interaction,” said the study’s senior author, Matias Bruzoni, MD, assistant professor of surgery. Bruzoni is the surgeon for the center, which is part of Stanford Children’s Health.

Hispanics form a large and growing part of the U.S. population, particularly in California, and 25 percent speak little to no English. Although professional medical interpreters can help bridge the language gap, there are drawbacks to using an interpreter compared with communicating in the patient’s native language: For instance, less information can be communicated in the same-length appointment because everything that is said must be interpreted.

The study compared patient satisfaction among three groups of families whose children received surgical care at the hospital between November 2011 and July 2013. The two experimental groups were made up of Hispanic, exclusively Spanish-speaking families, 43 of which communicated with their English-speaking caregivers via a medical inter-

preter, and 78 of which communicated directly in Spanish with their caregivers. The control group was 56 English-speaking families of any race or ethnicity who spoke with their caregivers in English.

The verbal interaction between the caregivers and families included patient registration; the intake exam, history and physical; explanation of the patient’s diagnosis and management plan; surgical consent; and pre- and post-operative instructions for the parents and patient.

All families included in the experiment answered a questionnaire to assess their general satisfaction with their care, their feelings about the importance of speaking the same language as their child’s caregivers, and their feelings about the quality of information they received from hospital staff.

Interacting in Spanish

Spanish-speaking families that discussed their children’s care in Spanish reported a higher level of satisfaction and higher ratings of the quality of information they received compared with the families in the control group and those that worked through an interpreter. Spanish-speaking families rated the importance of discussing care in their native language more highly than English-speaking families, the study found.

Although socioeconomic status was not assessed in this study, Bruzoni noted that Hispanic families of low socioeconomic status may have an even greater need than others to receive care in their native language. “There is a big cultural barrier,” Bruzoni said. “Because of these patients’ circumstances, it is even more important to work with them using their own language.”

He said he wants to encourage other clinics and hospitals, particularly those

that serve large numbers of Hispanic patients, to create similar teams catering to Spanish speakers. “Not only is the patient population growing, the physician population is growing,” he said, adding that he sees a growing number of surgical

STANFORD CHILDREN’S HEALTH



Matias Bruzoni is the senior author of a study that found Spanish-speaking families were more comfortable when they were able to communicate with surgical teams in their native language, without the need for interpreters.

fellows of Hispanic background receiving training. “We need bilingual and bicultural staff to help improve our ability to provide patient-centered care.”

Other Stanford-affiliated authors of the study are medical students Jonathan Dunlap and Joshua Jaramillo; Raji Koppolu, a nurse practitioner in surgery; Robert Wright, a social science research assistant in pediatric surgery; and Fernando Mendoza, MD, professor of pediatrics and a member of Stanford’s Child Health Research Institute.

The research was funded by the Hispanic Center of Excellence at Stanford and the School of Medicine’s Medical Scholars Research Program.

Stanford’s Department of Surgery also supported the work. **ISM**

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Send letters, comments and story ideas to John Sanford at 723-8309 or at jsanford@stanford.edu. Please also contact him to receive an e-mail version of *Inside Stanford Medicine*.

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Paul Costello
Chief communications officer

Susan Ipaktchian
Director of print & Web communications

John Sanford
Editor

Robin Weiss
Graphic designer



5 QUESTIONS

an occasional feature in which an expert answers five questions on a science or policy topic

Jim Laflin discusses his role as ombudsperson

Jim Laflin, JD, is an attorney specializing in mediation and conflict resolution who came to the School of Medicine a year ago as its ombudsperson. He is the founder of Concilium, a San Francisco-based mediation firm through which he mediated complex civil cases throughout California, the Northwest and Alaska for 20 years. He also has worked as a consultant for UC-San Francisco's Worklife

Resource Center and Office of the Ombuds, helping to resolve a variety of academic and workplace disputes. He has taught courses on mediation and negotiation, published papers on the issues and lectured widely.

In a recent interview with writer Ruthann Richter, he discussed his job at the medical school and the services offered through his office.

1 What is the role of the school's ombudsperson and how does he/she help the medical school community?

LAFLIN: The Office of the Ombudsperson serves as a confidential resource for the entire medical school community, including faculty, staff, students, graduate students and post-docs, regarding any School of Medicine-related problem or issue that arises. Typical examples are workplace conflicts arising between colleagues and/or supervisors, mistreatment, harassment and bullying, authorship and scientific misconduct disputes, re-appointment and promotion concerns, favoritism and/or discrimination (based on age, race, gender, religion, national origin, etc.), and unfairness in the application of school policy, among other things.

The ombudsperson acts informally, as a neutral and independent voice for fairness, not as an advocate, but in the interests of all sides. Some refer to this as being multipartisan.

So, what does the ombudsperson do? First and foremost, I listen. My office is a safe place where visitors can be heard without worrying about repercussions. Sometimes that's all visitors want. Beyond that, I can provide information concerning school policies and formal processes and explain how those policies and processes might apply in a specific situation. I don't advise individuals what to do but help them understand their options. By helping to identify and clarify options, visitors can decide and choose for themselves how best to proceed. So self-determination is a major principle here. Sometimes that can entail further involvement of the ombudsperson, and sometimes not. Where it does,



Jim Laflin

that involvement can take the form of mediation, facilitated conversations, dialogue, shuttle diplomacy, coaching or some combination thereof. Importantly, the office does not become involved in formal processes, such as investigations, grievances and appeals. Nevertheless, I can offer explanations of those processes and how to engage them.

2 Why is it important to have an ombudsperson?

LAFLIN: It's important to have an ombudsperson so that problems are addressed in a timely, effective and fair way for all parties concerned. This simply doesn't happen unless organizations such as the medical school proactively create and support informal channels, such as the ombudsperson, specifically focused on that goal. I'm not arguing that formal investigatory, appeal and grievance processes aren't legitimate or that they don't have their place. They are and they do. However, the informal tools of the ombudsperson are far more appropriate and effective when it comes to improving communication, restoring trust, building more responsible relationships and cutting through bureaucratic red tape to achieve good outcomes. Otherwise, individuals

and the organization suffer the consequences of festering conflict, such as attrition, lost productivity and lawsuits.

3 Do most medical schools have an ombudsperson or is Stanford unusual in this respect?

LAFLIN: I believe most medical schools now have an ombudsperson. To Stanford's credit, it was among the

first to establish such an office.

4 What are the biggest challenges of the job?

LAFLIN: Some of the biggest challenges involve trust and default thinking. Trust because it's the foundation of the relationship between the ombudsperson and the individuals who come for help. It's something I never take for granted. I have to earn it with every person I work with. And that takes time, effort, honesty and compassion.

Default thinking is another big challenge. By the time most people reach out to the ombudsperson, they've exhausted pretty much all the options they can see for themselves; they can't think of anything else to do. This is a normal result of how our minds work, especially in stressful circumstances; we replay the same internal narrative over and over again. I call this default thinking, and I work to help people get out of this box so that they can take a fresh look at their circumstances and consider making some different choices. So this is another big part of what I do: supporting best thinking and moving beyond default thinking.

5 I imagine that people might shrink from a phone call or visit from you, as they expect you to be the bearer of bad news. How do you manage socially?

LAFLIN: This is a great job, one that I'm grateful for and that I thoroughly enjoy coming to every day. Once people understand what it is that I do, they're nearly always appreciative — not only of me personally but more importantly of the School of Medicine and what it says about the values of the leadership and institution that they care enough about this community to devote the resources required to support the office. **ISM**

Carlos Bustamante named chair of new Department of Biomedical Data Science

By Jennie Dusheck

Carlos Bustamante, PhD, professor of genetics and founding director of the Stanford Center for Computational, Evolutionary and Human Genomics, has been appointed chair of the new Department of Biomedical Data Science.

The department will build on the School of Medicine's strengths in using information technology to advance precision health and work to find common solutions to the challenges of analyzing biomedical data from varied sources, including biosensors, electronic medical records and genomic sequencing.

Bustamante, who was involved in planning the department, said he is enthusiastic about his new position. "It's really a dream come true," he said. "Bringing together our exceptional faculty with expertise in statistics, biomedical informatics and 'big data' analysis creates amazing opportunities for advancing precision health. Our goal is to marry rigorous methods development, large-scale biological data sets, and clinical outcomes to uncover the mechanisms of disease and improve health and well-being," he said.

Lloyd Minor, MD, dean of the School of Medicine, said he is pleased that Bustamante will be heading the department. "Leadership in this area is fundamental to Stanford Medicine's vision for making precision health a reality," Minor said. "Carlos has an inspiring vision for the future of biomedical data science, one that is enthusiastically shared by the founding faculty."

The dean also announced that Philip

Lavori, PhD, professor of health research and policy, has also agreed to serve as vice chair of the new department. Lavori will step down as chair of the Department of Health Research and Policy to take on this new role. Bustamante and Lavori will begin their terms on Oct. 1.

Bustamante is pre-adapted for developing the new department, which was created in June. "I've been interested in large-scale data analysis since I was in graduate school," he said. He is a population geneticist whose work has encompassed analyzing genome-wide patterns of variation within and between species. He has used such genomic analysis to answer basic questions in biology, anthropology and medicine, and has long worked at the interface of genomics, computational biology and mathematical genetics.

After earning a doctoral degree in biology at Harvard in 2001 and completing a postdoctoral fellowship in mathematical genetics at the University of Oxford in 2002, Bustamante was on Cornell University's faculty in the departments of Statistical Sciences and Biology Statistics and of Computational Biology. He joined Stanford's faculty in 2010. He has received multiple honors and awards, including a Marshall-Sherfield Fellowship, a Sloan Research Fellowship and a John D. and Catherine T. MacArthur Fellowship.

Bustamante said he plans to begin populating the new department with a core of 15-20 faculty from across the medical school and add five to 10 "amazing investigators," in the coming five years to build up a premier department that engages Stanford's strengths in biostatistics, bioinformatics and computational science. **ISM**



Carlos Bustamante

Sino-U.S. Symposium on Medicine set for Oct. 15-16

By Jennie Dusheck

The Ninth Sino-U.S. Symposium on Medicine in the 21st Century will be held Oct. 15-16 at the Li Ka Shing Center for Learning & Knowledge on the Stanford campus. Hosted by Stanford Medicine, the two-day event will include panel discussions on precision health, mobile health, population health and genomics, with breakout sessions on ethics, cancer, brain mapping, neuroscience, immunology and infectious disease.

"Stanford Medicine is honored to welcome our Chinese partners to the Stanford campus this year. Together we will work to find answers to some of health care's most pressing questions," said Lloyd Minor, MD, dean of the School of Medicine, who will be a keynote speaker at the symposium.

Partnering with Ruijing Hospital, the Shanghai Jiao Tong University School of Medicine and the Salk Institute of Biological Studies, Stanford Medicine will host researchers, clinicians, industry experts and policymakers from China and the United States. Participants

will discuss such challenges as translating medical research into practical benefits for patients, containing health-care costs, expanding patient access, providing new care delivery models for aging populations and the increasing incidence of chronic conditions.

The theme for this year's event is big data in health care and how to use large-scale computing and data analysis to improve health. The symposium also aims to foster long-term collaborations among researchers and clinicians in the United States and China.

Other keynote speakers include Xu Tianle, PhD, president of the basic medicine faculty at Shanghai Jiao Tong University; Bill Brody, MD, PhD, president of the Salk Institute; and Michael Levitt, PhD, Stanford professor of structural biology and 2013 Nobel laureate in chemistry.

To learn more or to register for the conference, visit <http://med.stanford.edu/sino-us.html>. The registration cost is \$195 for university faculty, postdoctoral scholars, students and trainees, and \$295 for the general public. **ISM**

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New medical students ponder life-and-death ques

By Tracie White

Silence fell in Berg Hall when Alvaro Galdos stood amid a crowd of new medical students and their family members and recalled the decision to end life support for his youngest son, Luis, who was 8 year old.

“Eleven years ago we lost a son at a hospital in Texas due to a congenital heart defect,” Galdos said. His oldest son, Francisco, a first-year medical student at Stanford who was 11 at the time, hopes to become a pediatric cardiologist.

“As much as we loved him, we didn’t want him to suffer anymore,” Galdos said. “We knew the end of his life was coming. We made the decision to stop everything. Was this euthanasia? We still wonder.”

What is and isn’t euthanasia? Is there a line between euthanasia and murder? How does a physician always uphold the Hippocratic Oath, which includes a pledge to abstain from doing harm?



NORBERT VON DER GROEBEN

A group of new medical students pose for a selfie at the stethoscope ceremony Aug. 21 on Alumni Green.

These were the types of questions raised during an hour-and-a-half discussion among this year’s class of new medical students and their family members; Lloyd Minor, MD, dean of the School of Medicine; and Charles Prober, MD, senior associate dean for medical education.

Donning the white coats

The discussion, inspired by the book *Five Days at Memorial*, a grim recounting of the horror at a New Orleans hospital following Hurricane Katrina 10 years ago, was part of a three-day orientation for new students in preparation for the start of classes Aug. 24. The book was assigned summer reading.

Each year, new medical students receive their white

coats and stethoscopes during a ceremony on the last day of orientation. Then they stand together as a group and read the Stanford Affirmation, which is a pledge written in the spirit of the Hippocratic Oath — an ancient vow to uphold certain ethical standards of caregiving.

The new cohort of 90 students was chosen from an applicant pool of 7,200. Twenty-six were born outside the United States. Nine entered with graduate degrees — eight with master’s degrees, one with a PhD — and 40 have published in peer-reviewed journals.

Most had not yet faced the responsibilities they will encounter routinely as physicians. It was the ethical and emotional challenges ahead that Minor and Prober hoped to explore during the book discussion. “I think one of the key lessons from this book: If we’re going to make progress in medicine, we’re going to have to face realistically when we make errors,” Minor said. “Progress only occurs when we are able to frankly address those situations and acknowledge those errors.”

The book describes health-care workers treating patients in a way that could arguably violate tenets of the Stanford Affirmation. “You will be reciting this later today after you receive your white coats and stethoscopes,” Prober said. “Hopefully, the affirmation will have more meaning to you. It will help you to reflect more deeply on the words as you ponder it into the future.”

Written by Pulitzer Prize-winning investigative reporter and Stanford-trained physician Sheri Fink, *Five Days at Memorial* is filled with ethical conundrums about what constitutes humane health care.

The book describes how medical staff and patients in the flooded hospital had to fend for themselves in the days following Hurricane Katrina. After the waters receded, authorities discovered that 45 patients had died at the hospital. Three health-care professionals, including one physician, were arrested for murder. A New Orleans grand jury ultimately refused to indict them on charges of involuntary euthanasia and murder, but exactly what happened during those five days, when temperatures soared, sleep was rare and proper sanitation was nonexistent, remains unclear.

What is clear, as Prober described it, is that the lack of planning, communication and panic worsened an already unimaginable situation, one that no physician ever wants to face.

“As I read the book, I imagined how horrible it would have been to live through this tragedy,” Prober said. “It’s amazing they stayed after abandonment by the federal government.”

The book, which Fink herself said she hoped would inspire discussions, captured the imagination of Prober and Minor, who described how they met over dinner to discuss it.

“When we met, it became very clear what we could talk about,” Prober said. “Did the care providers do the right thing? ... The question is whether or not it was



Clockwise from above: Xylen Washington, 5, tries out the stethoscope belonging to a new medical student. New medical students read the Stanford Affirmation, the School of Medicine’s stethoscope ceremony. First-year medical student Yekaterina Shpanskaya greets a family member.

kindness or at the other extreme, murder.”

According to the book, it is clear that physicians administered life-ending injections of morphine or the sedative midazolam, or both, in about half of the patients. The Louisiana Attorney General maintained that a number of the dead were victims of homicide.

“It was definitely hard to know what was right or wrong,” Minor said. “They showed a lot of courage staying behind and working. Lack of communication and leadership was a big problem. If there is a villain in this book, it was the parent hospital chain for Memorial. The crew was told, ‘We can’t do anything. You have to wait for the military and the Coast Guard.’”

Can euthanasia be justified?

Prober and Minor posed the question to the audience, “Is involuntary euthanasia ever justifiable?” The general consensus was that involuntary euthanasia is

Stanford Health Library, in new digs, marks its 25th anniversary this year

By Ruth Schechter

When her son was diagnosed with a serious kidney and urinary tract defect, Cathy Draper struggled to find information about his condition. “At that time it was very difficult to get the information we needed — not only to explain the defect, but to help us in making treatment decisions,” she said. “I did not have a place to go for scientifically based health information.”

That changed just a few years later, when she donated a kidney for her son’s transplant and helped a family member who had just been diagnosed with ovarian cancer.

“By that time I had heard about the Stanford Health Library,” said Draper, a dental hygienist who has been a volunteer at the library for the past 20 years. “It was an invaluable resource while I researched both of the medical conditions I was dealing with. Patients are often overwhelmed with difficult choices or complex diagnoses. I know only too well the need for trustworthy resources so that people can better understand their condition and treatment.”

The Stanford Health Library, which celebrates its 25th anniversary this year, is a free community resource for medical and health information. Started in a small storefront in the Stanford Shopping Center, the library’s main branch now is housed in the Hoover Pavilion, a landmark Art Deco building, at the corner of Quarry and Palo roads, that was once Palo Alto Hospital. The building currently houses the Stanford Neuroscience Center and many of Stanford’s primary care clinics.

Renovation challenges

“Our move here was a confluence of two major changes,” said library director Nora Cain, who oversees satellite branches in the Stanford Cancer Center, Stanford Hospital, East Palo Alto and the new Stanford Cancer Center South Bay. “Our building in the shopping center was being torn down, and the Hoover Pavilion was being restored. We were the ideal entity to respect that space and to accommodate the public.”

The 2,244-square-foot library, located in what was the main lobby of the

former hospital, boasts 14-foot ceilings, fluted columns and expansive windows that had been hidden behind drywall. Its stairway entrance is of high-quality terrazzo, a polished composite handmade by mixing stone particles into concrete.

Originally, the first floor of the building held the emergency room, kitchen, labs, morgue and locker rooms for staff. Stairs led to a formal front door on the second floor, where visitors could wait in a reception area before being allowed in to visit patients. Over time the role of the building changed, as did public taste. Though the exterior did not change dramatically, a major renovation in the early 1960s removed most of the deco elements from the interior.

“There was not much to save inside,” said George Tingwald, MD, AIA, a credentialed architect, surgeon and director of medical planning for Stanford’s adult and children’s hospitals. “There were very few remnants of the original design. So much had been taken down and destroyed.”

The team of architects and planners

had hoped to uncover the plaster murals and handmade metalwork shown in archival photos and architectural plans. But these features, as well as the original terrazzo floors, had been all but demolished in the 1960s redesign.

“Our goal was not to re-create the 1930s but to take elements of that style and develop it for continuity. We brought in materials to support the look without trying to replicate the original design,” Tingwald said. “While the outside was meticulously restored, we approached the lobby with a sense of adaptive reuse. The Health Library was the perfect fit.”

The designers eliminated several small rooms to open up the space and fabricated new columns to match the ones outside. They reconstructed the plaster ceiling to match the few original ceiling panels that remained and installed new overhead fixtures to complement the 85-year-old building’s style. They fitted the main room with comfortable chairs for reading, eight computer stations, built-in bookshelves, movable furniture and enough floor

tions at stethoscope ceremony

NORBERT VON DER GROEBEN



ing to his father, Gabriel Washington, a first-year medical
Medicine's version of the Hippocratic Oath, during the
ts medical school Dean Lloyd Minor during the ceremony.

never OK, even in dire circumstances. But questions remained.

"Isn't it equally morally reprehensible letting someone die without care?" said incoming medical student Mari-posa Garth-Pelly.

Another student added, "I feel like in the reality of the world, [health-care professionals] are also human beings that have needs."

"I don't know that I would have made a different decision," said another student.

The conversation lingered over the book's vivid description of the helicopters landing in a poorly lit, precarious spot on an aging landing space where health-care workers struggled to carry patients up stairs and through a tunnel to evacuate them. One health-care worker was badly injured while transporting a 300-pound patient to a helicopter. The workers feared

some patients would be left behind alone without care following a mandatory evacuation. Panic reigned.

"Mistakes were made," Minor said. "But progress only occurs when we acknowledge those shortcomings and hopefully grow as a person and as a physician."

At the end of the discussion, the students and their families walked outside to Alumni Green, where they accepted their white coats and stethoscopes during a ceremony. Parents clicked photos and shed tears. Then the entire class stood together and recited the Stanford Affirmation, which begins: "On my admission to the practice of medicine, I pledge to devote my life to the service of humanity." **ISM**

NORBERT VON DER GROEBEN



NORBERT VON DER GROEBEN



New bioscience graduate students begin classes soon

By Tracie White

As 112 new graduate students in the biosciences prepare to begin classes Sept. 21, Will Talbot, PhD, professor and chair of developmental biology, is settling into the position of senior associate dean for graduate education and postdoctoral affairs.



Will Talbot

Talbot was appointed to the post Sept. 1, replacing Daniel Herschlag, PhD, professor of biochemistry.

"I am very excited about my new role," Talbot said. "We are all inspired by the accomplishments of our graduate students and postdoctoral fellows, at Stanford and beyond. It is privilege to have a role in their training."

Lloyd Minor, MD, dean of the School of Medicine, said, "Will has shown a strong commitment to graduate education and postdoctoral training. Under his leadership, I am confident that the Office of Graduate Education and Postdoctoral Affairs will enjoy a bright future and will continue guiding and empowering the next generation of leaders and innovators in academia and industry."

The first-year students were selected from a pool of 1,985 applicants. Seventy of the students are men, and 42 are women. Twenty-four of the 112 students were born outside the United States, including Myanmar, the Ukraine and Ghana, and 31 are considered underrepresented minorities in the biosciences. Eighteen hold advanced degrees, including 11 with master's degrees and two with doctorates in veterinary medicine.

"The arrival of our new graduate students is a wonderful way to start our academic year," Talbot said. "This incoming class represents our most diverse cohort ever, and we are all excited about the great discoveries they will make as students and in the future."

The Office of Graduate Education, in collaboration with Alumni Affairs, will hold the annual PhD lab coat ceremony Sept. 30 at the Li Ka Shing Center for Learning and Knowledge. At the event, each new student is introduced by his or her program chair and presented with a lab coat. **ISM**

space to accommodate seating for an ongoing series of free community lectures by Stanford physicians.

"There are so many people in the community who were born in this building. They come up to me and thank me for bringing it back. The library brings people back into the building and makes it a real community resource again," Tingwald said.

Community service

"We started in a nonclinical setting to provide evidence-based information people could trust," Cain said. "We have access to libraries and databases not available to the general public and can customize packets to any level of expertise."

The library staff respond to about 600 requests a month, with most inquiries revolving around cancer, aging, nutrition and chronic conditions like diabetes, arthritis and heart disease.

Requests come in by phone, by email and in person, with the library's resources available to anyone in the community — not just patients and their families, Cain said. Librarians and volunteers also work closely with several Silicon Valley companies' wellness programs.

"I'm amazed how different it is now," said Laura Markman, who has been a library volunteer for 17 years. "I remember this spot as the hospital lobby, so it's wonderful to me that it is still being used by the public. There are no space issues here, and it's easy to sit right next to a patron to help them learn how to use the computer or navigate a website."

The new location also allows the library team to work closely with Stanford's coordinated care clinic, located on the building's fourth floor, where clinicians treat patients with chronic conditions.

"It's a model of integration, with clinical care that lets us develop aspects of our collection and offer self-manage-

ment classes that address the needs of these patients," Cain said. "We hope to expand that model to other specialties. A resource like this is especially important at a place like Stanford, where treatments may be groundbreaking." **ISM**

Ruth Schechter is a freelance writer and editor.

LANE LIBRARY



The lobby of the Hoover Pavilion — left, as it looked in the 1960s — is now home to the Stanford Health Library, right, a free community resource for medical and health information.

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Face

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may mediate morphological differences among species.”

To conduct the study, however, Prescott and her colleagues had to obtain a specialized type of cell present only in very early primate development. The cells, called cranial neural crest cells, originate in humans within about five to six weeks after conception. Although they first appear along what eventually becomes the spinal cord, the neural crest cells then migrate over time to affect facial morphology and differentiate into bone, cartilage and connective tissue of the head and face.

“These cells are unique,” said Prescott. “If we want to understand what makes human and chimp faces different, we have to look to the source — to the cell types responsible for making these early patterning decisions. If we were to look later in development or in adult tissues, we would see differences between the species but they will tell us little about how those differences were created during embryogenesis. But accessing early cell types like neural crest cells can be quite difficult, especially when studying primates.”

To obtain this elusive cell type, the researchers used induced pluripotent stem cells, or iPS cells, made from chimpanzees. IPS cells, which are made from easy-to-obtain skin or blood samples, can be coaxed to become other tissues. Although iPS cells from humans have been well-studied, they’ve only recently been made from chimpanzees in the laboratory of Fred Gage, PhD,

a professor of genetics at the Salk Institute for Biological Studies and a co-author of the study.

Prescott and her colleagues coaxed human and chimpanzee iPS cells to become cranial neural crest cells by growing them in the laboratory under a specific set of conditions. They then examined enhancer regions throughout the genome, looking for those that were not just active and therefore likely to be involved in craniofacial development, but also those whose patterns or degrees of activity seemed to vary between human and chimpanzee cells.

“Of course, humans and chimps are very closely related,” said Wysocka. “Most of the regulatory elements are the same between the two species. But we did find some differences. In particular, we found about 1,000 enhancer regions that are what we termed species-biased, meaning they are more active in one species or the other. Interestingly, many of the genes with species-biased enhancers and expression have been previously shown to be important in craniofacial development or associated with normal intrahuman facial variation.”

Snout length and shape

In particular, the researchers found that two genes, PAX3 and PAX7, known to affect snout length and shape in laboratory mice, as well as skin pigmentation, were expressed at higher levels in chimpanzees than in

humans. Humans with less than the normal amount of PAX3 have a condition called Waardenburg syndrome, which includes craniofacial, auditory and pigmentation defects. Genomewide association studies in humans have identified PAX3 as a region involved in normal facial variation.

In contrast, another gene known to be involved in determining the shape of the beaks of finches and the jaw of a fish called a cichlid was expressed at higher levels in humans than in chimpanzees. In mice, overexpression of this gene, BMP4, in cranial neural crest cells causes a marked change in face shape, including a rounding of the skull and eyes that are more near the front of the face.

“We are now following up on some of these more interesting species-biased enhancers to better understand how they impact morphological differences,” said Wysocka. “It’s becoming clear that these cellular pathways can be used in many ways to affect facial shape.”

Another Stanford-affiliated author of the study is research assistant Rajini Srinivasan.

The research was supported by the National Institutes of Health, the California Institute for Regenerative Medicine, the W.M. Keck Foundation and the Innovation Fund.

Stanford’s departments of Chemical and Systems Biology and of Developmental Biology also supported the work. **ISM**



Joanna Wysocka

AIDS

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has the third-highest number of AIDS cases in the world, knowledge about the disease is very low. Sex, the primary mode of HIV transmission, is a taboo subject, and there is no sex education in the schools, so students know precious little about a virus that has infected more than 2 million people in India, according to the United Nations Joint Programme on HIV/AIDS.

TeachAIDS, a nonprofit organization that began as a graduate student’s thesis project at Stanford, aims to fill that gap

but they are in countries where talking about these things has been taboo or very, very limited. And she’s done it in this very culturally sensitive, appropriate way. It’s really impressive.”

Each version is carefully tailored to the local culture, featuring recognizable local celebrities in local dress speaking local dialects. The organization, supported by private philanthropy, donates the materials to governments, which then distribute them free of charge to schools, hospitals and counseling centers. In 2012, the nonprofit was recognized in The Tech Awards, a signature program of The Tech Museum of Innovation in San Jose that honors large-scale initiatives using technology for philanthropic goals. It also has won the TR35 Award from MIT, which recognizes innovations that could have a dramatic impact on the world.

First launched in the hard-hit countries of sub-Saharan Africa, TeachAIDS began moving into India in 2009, at a time when the disease was rapidly spreading there.

“I was reading reports that India was to be a hot zone for HIV,” said Sorcar, an adjunct affiliate at the School of Medicine and lecturer in the School of Education, in a recent interview over coffee near her office in downtown Palo Alto. “Millions of dollars were poured into this problem, but knowledge levels were very low.... It was disturbing how much was unknown about the basics of transmission.”

On a visit to India that year, she managed to secure a five-minute interview with Nagarjuna, hoping he would agree to be featured in TeachAIDS productions. By sheer coincidence, Nagarjuna’s wife, actress and activist Amala Akkineni, had been embroiled just the week before in a heated public debate over the expulsion of HIV-positive students from the local schools in Hyderabad, India’s fourth-most populous city, with some 7 million people.

Though the AIDS virus cannot be transmitted through casual contact, uneducated parents were demanding that their children not sit side by side in class with children infected with the virus.

Akkineni, herself a mother, managed to persuade the parents to back down from their demands by assuring them that the schools would introduce materials to educate the students about HIV.

Akkineni was at a loss; the government had banned previous HIV materials as pornographic, and some had been burned in public bonfires. She fretted about where to find AIDS information that officials would find acceptable. So Sorcar’s visit could not have been more auspicious: “My husband came home and said, ‘You have to meet this young lady, Piya Sorcar,’” Akkineni said. “It was cosmic.”

Within the year, TeachAIDS had released its first productions in the south Indian state of Andhra Pradesh, which has a population of more than 83 million and one of the highest rates of HIV in the country. Akkineni agreed to serve as trustee for the organization.

Star power

It was not Akkineni’s first foray into the epidemic. Once a major Bollywood actress, she had starred in 54 movies by the time she was in her mid-20s, but then decided to give up full-time acting to devote her time to social activism. An animal lover, she founded Blue Cross of Hyderabad, the city’s first and only animal shelter, in 1992. Shortly after, she was approached by Karl Sequeira, an AIDS activist, who was looking to establish the city’s first AIDS hospice. It was a period in which people living with the disease were literally being wrapped up in blankets and tossed in the garbage, Akkineni said. Sequeira, who died in 2004, was moved by the dire need for humane care.

“I was already known as this notorious ex-actress who was running this hospice for animals,” Akkineni said in an interview in her office at the animal shelter. “So he thought I was a kindred soul.” In one evening, they raised 2.5 million rupees, about \$40,000 in today’s currency, to start the project, among the wide-ranging HIV/AIDS and substance-abuse services provided now by Freedom Foundation.

The state of Andhra Pradesh had a crying need for such services; it claims the highest prevalence rate of AIDS in the country. A high rate of heterosexual sex outside of marriage, low condom use, a large migrant community and a flourishing sex-trafficking industry are among the factors that have contributed to spread of the virus, according to a report by the United Nations Develop-

ment Program.

Akkineni said she is particularly concerned about sex trafficking, in which girls as young as 3 are sold into brothels, where they may contract HIV and serve as reservoirs for the virus.

To promote HIV prevention, TeachAIDS has distributed 25,000 copies of the videos throughout the state, and has shown them on private and government TV channels, Sorcar said. They target schools enrolling preadolescents and teenagers, reaching students at a vulnerable age (most girls marry between the ages of 18 and 20), with messages that are simple and clear.

“For the children, since it’s in animation format, it’s very attractive,” Basaveswara Rao, joint director of information, education and communication with the Telangana State AIDS Control Society, said during the airing of the video at Zilla Parishad High School. “Added to that are the celebrities, who deliver the message.”

TeachAIDS has recruited more than two dozen Indian celebrities to participate in the project, including Amitabh Bachchan. With his signature oversized glasses and renowned voice, he is one of the most influential actors in the history of Indian cinema.

In the Telugu-language version of the video, narrated by Nagarjuna, the actor tells the students that AIDS is a condition that does not have a cure, so it’s important to know how to prevent it. Based on rigorous research and testing, the video provides the suggestion of human intimacy by showing a young couple together, then an image of birds kissing. A woman embracing a baby, her breast fully covered, conveys the concept of breastfeeding, one of the ways in which an HIV-positive mother can transmit the virus to her child.

One of the students, Shirisha, 16, said: “I understood and was very happy because it’s about health, and I can learn how to protect myself and tell my family and friends. Most parents are not educated and don’t know things. I want to take my groom before marriage for an HIV test” — a move that could save her life.

“The kids learn so much and you can see the joy in their eyes to receive these messages from their beloved role models,” Sorcar said. “The exciting part for our team is the palpable energy from the young people every time the software is shown in schools. It’s inspiring to see that using a research-based process matters — and it works.” **ISM**



Students at Zilla Parishad High School, in the south Indian metropolis of Hyderabad, gather to watch an educational video about HIV/AIDS.

with culturally sensitive animated videos, as well as interactive versions for use on computers, that use the voices and faces of celebrity icons to teach the basics of HIV biology, how the virus is spread and how individuals can protect themselves.

Videos in 14 languages

Founded in 2009 by Stanford School of Education graduate Piya Sorcar, PhD, the nonprofit now distributes its videos free of charge in more than 80 countries and in 14 languages. In India, the group plans to take the program national by the end of the year, distributing as many as 30,000 copies in each state where prevalence is high and providing versions in seven different languages, Sorcar said.

“I think what Piya has done is amazing,” said Douglas Owens, MD, professor of medicine, director of the Center for Primary Care and Outcomes Research/Center for Health Policy and adviser to the project. “She started the program as a PhD student and not only are the videos available in 81 countries

ALS

continued from page 1

tion is found in about 40 to 60 percent of ALS inherited within families and in about 10 percent of all ALS cases. This is by far the most common cause of ALS, so everyone has been trying to figure out how this expansion of the repeat contributes to the disease.”

Although the repeat occurs in a region of the gene called an intron, which does not normally carry protein-making instructions, researchers have speculated that a molecular miscue may cause a cell to mistakenly make RNAs and proteins from the expanded repeat.

Gitler is the senior author of the study, which was published online Aug. 26 in *Nature Neuroscience*. Postdoctoral scholar Ana Jovičić, PhD, is the lead author. The Stanford research is complemented by similar findings from two other groups that were published in the Aug. 27 issue of *Nature*.

Toxic proteins

Previous research has shown that proteins made from the expanded section of nucleotides are toxic to fruit fly and mammalian cells and trigger neurodegeneration in animal models. However, it's not been clear why. Gitler and Jovičić used a yeast-based system to understand what happens in these cells. Although yeast are a single-celled organism without nerves, Gitler has shown that, because they share many molecular pathways with more-complex organisms, they can be used to model some aspects of neuronal disease.

Cells make proteins by copying a nucleotide sequence from DNA. This copy, called RNA, is then shuttled to the cell's protein-making factories. Proteins are made, or translated, from the RNA by assembling building blocks called amino acids in a sequence dictated by the order of nucleotides in the RNA string. Every three-nucleotide combination either encodes a particular amino acid or carries a cellular command such as “start” and “stop” to facilitate protein production.

Often, genes include strings of intervening nucleotides called introns that don't contain instructions to make proteins. These introns are usually removed from the RNA before it is translated.

However, researchers have speculated that cells with introns harboring expanded repeats (as in the C9orf72 gene) may mistakenly make protein from the repeated section even in the absence of a traditional “start” command. Although it's not known exactly why this abnormal protein translation may occur, previous research has shown it does sometimes happen in regions of the genome with repeated nucleotide sequences.

Jovičić first constructed a series of yeast strains, each of which expressed one of the proteins thought to be made from the expanded repeat. She found that one of the proteins, made up of the amino acids proline and arginine, was particularly toxic to the yeast cells. Another, with glycine and arginine, was also toxic. The particular toxicity of the arginine-containing proteins in the yeast mirrors what had previously been found in mammalian cells and in fruit flies.

Using a technique known as a genomewide screen, Jovičić then systematically tested whether expressing higher-than-normal amounts of any one of the yeast's proteins could suppress the toxicity of the arginine-containing proteins and allow the mutated yeast to grow like its unmutated peers. Conversely, she used another technique to investigate whether the loss of any one protein could influence the protein's toxicity.

Potential targets for drugs

Jovičić found 27 genes that, when expressed at high levels, suppressed the toxicity of the proline-arginine protein. Mutated yeast strains with higher-than-normal levels of any one of these proteins grew better in the presence of the arginine-containing proteins. She also identified 35 genes

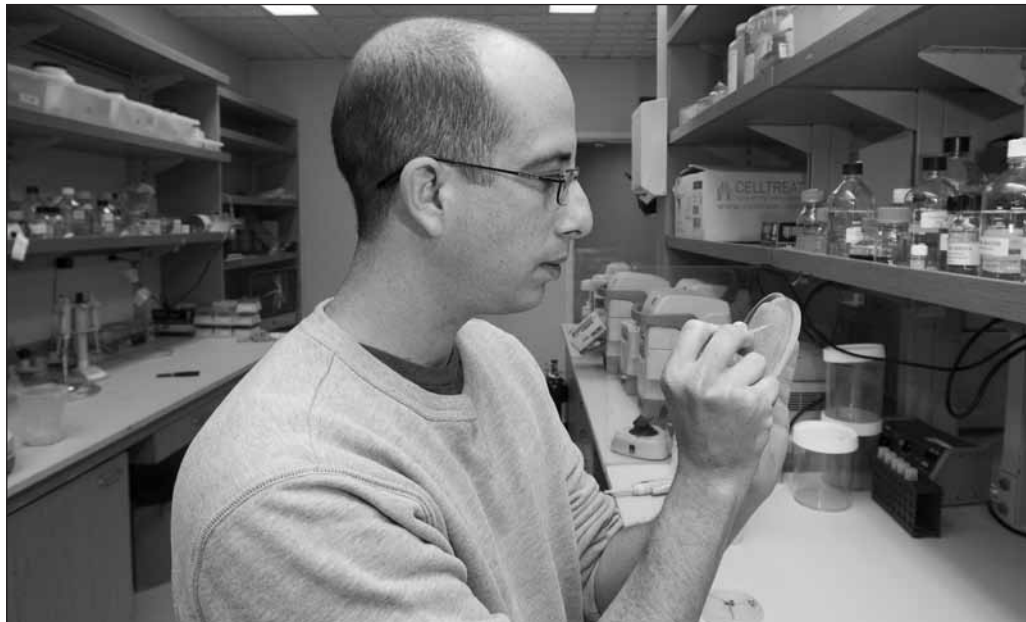
that, when highly expressed, made the arginine-containing proteins even more toxic. Finally, she discovered 16 genes that, when missing from the yeast, rendered the arginine-containing protein less toxic. These deleted genes are of particular interest because they could be potential targets for drug interventions or therapies.

When Jovičić and Gitler examined all

the genes identified in the yeast screens, they found several that encoded proteins responsible for ferrying molecules in and out of the nucleus. In particular, a class of nuclear import proteins called karyopherins appeared important in modulating the effect of the toxic protein. One, called KAP122, was one of the strongest suppressors of toxicity when overexpressed.

the development of ALS and FTD, the fact that the researchers were able to identify specific types of protein families common among yeast, rodent and human cells represents an important step forward in the field, they said. Future work will also focus on disentangling the relative contributions of the RNAs and repeat proteins produced by the mutated C9orf72 gene.

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Aaron Gitler is the senior author of a study that found that cells with a mutation associated with ALS were hampered in their ability to move proteins into and out of the nucleus, a cell's command center.

“We hope that our research may one day lead to new potential therapies.”

Math

continued from page 1

to help alleviate this problem.

“Math anxiety has been under the radar,” said the study's lead author, research associate Kaustubh Supekar, PhD. “People think it will just go away, but for many children and adults, it doesn't.”

Measuring math anxiety

The new research was based on the idea that the principles of exposure-based therapy for treating phobias might also apply to alleviation of math anxiety. Phobias, such as the fear of spiders, can be relieved in affected individuals by repeatedly exposing them in a safe environment to the thing they fear.

The new study included 46 children in third grade. Before receiving tutoring, each child took a test that assessed his or her level of math anxiety. The children were divided into two groups — one with high math anxiety, the other with low math anxiety — based on whether their math anxiety scores fell above or below the median score for all of the children. They also completed standard neuropsychological assessments and were tested on simple addition problems while having their brains scanned via functional magnetic resonance imaging. The brain scans of the children with high levels of math anxiety showed activation in the brain's fear circuits and so-called “fear center,” or amygdala,

before tutoring, replicating a finding that Menon and colleagues published in 2012.

After the first fMRI scan, children participated in an intensive, eight-week tutoring program consisting of 22 lessons involving addition and subtraction problems. Tutors gave the lessons to each child individually. After tutoring, the math anxiety test and fMRI scans were repeated.

All of the children performed better on addition and subtraction problems after tutoring. The children who started the study with high levels of math anxiety had reduced anxiety after tutoring, while those in the low-math-anxiety group had no change in their anxiety levels.

Anxiety alleviated

After tutoring, the fear circuits and amygdala were no longer activated in children who had begun the study with high math anxiety, confirming that tutoring ameliorated the anxiety itself, rather than providing the kids with a coping mechanism that relies on other brain circuits.

“It's reassuring that we could actually help these children reduce anxiety by mere exposure to problems,” Supekar said.

The researchers plan to conduct future studies to figure out what aspects of the one-on-one tutoring were helpful. Menon wants to test whether the interaction

between tutors and students in a social context plays a role, or whether computerized tutoring can result in the same benefits and brain circuit changes.

“The tutoring has a standard protocol, but is also personalized,” said Menon, who holds the Rachael L. and Walter F. Nichols, MD, Professorship. “If a child is stuck at a particular concept, the tutor tries to get the child beyond the bottleneck in a non-negative, encouraging way.” Because the tutoring happens one-on-one, children do not have the opportunity to feel fearful about not performing as well as their peers, which may also help. “We need more research to understand that,” Menon added.

The researchers also want to investigate whether the anxiety-reducing effects of tutoring will persist as children move on to learning more complex problem-solving skills.

Other Stanford-affiliated authors of the study are postdoctoral scholars Teresa Iuculano, PhD, and Lang Chen, PhD. Menon is a member of the Stanford Child Health Research Institute.

The research was supported by the National Institutes of Health, the National Alliance for Research on Schizophrenia and Depression and by an Atherton Investigator award.

Stanford's Department of Psychiatry and Behavioral Sciences also supported the work. **ISM**



Vinod Menon

OBITUARY Thomas Stamey, expert on prostate cancer and PSA test, dies at 87

By Jennie Dusheck

Thomas A. Stamey, MD, a professor emeritus of urology at the School of Medicine and a noted leader in the study and treatment of prostate cancer, died of Alzheimer's disease Sept. 4 at his home in Portola Valley, California. He was 87.

At Stanford, Stamey helped lay the groundwork for the now-controversial PSA blood test for prostate cancer and helped transform urology and surgery from purely clinical fields to research fields. He made major contributions to four areas of medicine: renal hypertension, urinary tract infections, urinary incontinence and prostate cancer. In 1989, he became the first urologist ever elected to the Institute of Medicine. He was also named an honorary fellow of the Royal College of Surgeons Edinburgh.

"Tom Stamey was the founding father of the Stanford Department of Urology and led it for more than 25 years. He was truly one of the giants in academic urology, with his biggest impact in the area of prostate cancer," said Eila Skinner, MD, chair of urology and the Thomas A. Stamey Research Professor in Urology. "His research collaborations with John McNeal formed the basis of much of what we know about prostate cancer today. He trained over 100 residents and fellows, many of whom went on to be leaders in urology in their own right. His influence on the department will go on for many years to come, and I feel privileged to have known him."

'A strongly knit department'

Born in North Carolina in 1928, Stamey graduated from Vanderbilt University and went on to earn a medical degree in 1952 from Johns Hopkins University, where he also did his internship and a residency. After serving as a urological consultant for the U.S. Army in the United Kingdom, he joined the faculty of Johns Hopkins in 1958. In 1961, he came west to Stanford's medical school as associate professor of surgery and chair of the Division of Urology. In 1990, he was appointed founding chair of the newly created Department of Urology and worked to develop it into one of the top programs in the nation.

Stamey's wife, Kathryn, noted that her husband worked with the late Duncan Govan to create the department. Govan, MD, PhD, a professor emeritus of urology, died in 2007. "They built the department from scratch, and it became, at its high point, the most

sought-after urology residency in the country," Kathryn Stamey said. "It was a very strong, family-oriented department. We had lots of parties, and everybody came with their children. It became a strongly knit department and very successful."

Stamey authored or co-authored more than 225 scientific papers, four books, 30 textbook chapters and seven monographs. Among many other awards, he received the Hugh Hampton Young Award (1972) and the Ramon Guiteras Award (1995) from the American Urological Association and the Valentine Award (1991) from the New York Academy of Medicine.

"He was a giant in the field. His most spectacular achievement at Stanford was making research for surgeons an important part of an academic career, which was not true of departments in many other parts of the country," said Linda Shortliffe, MD, professor of pediatric urology.

Shortliffe, who did her 1977-81 residency with Stamey, said, "People talk about translational medicine now, but he was doing it back then." That research focus was the reason, she said, he was the first urologist and one of the first surgeons to be elected to the Institute of Medicine. "Tom instituted one year of a medical residency to be a laboratory year, where residents worked on research," Kathryn Stamey said.

Authoritative voice

Shortliffe has vivid memories of working with Stamey and, in particular, of his authoritative voice. She said that many of Stamey's former residents wrote to her in response to news of his death, reporting, "I still hear his voice."

"He had a distinct North Carolina accent, which was not that common on the West Coast," she said. "It was like hearing your father's voice all the time, even though we were not that much younger than he was. It was a voice you could hear in your sleep." Even today, she said, many of his former surgical residents say they hear his voice while working in the operating room.

Many of the residents Stamey trained went on to become departmental chairs around the country, said Kathryn Stamey.

Stamey was also one of the first to show the value of

the PSA test for prostate cancer, but then, ironically, his was also a voluble voice against the test's use to justify unnecessary prostate surgery. In the late 1980s, he pioneered the development of the prostate specific antigen, or PSA, blood test for prostate, which allowed physicians to estimate the risk that a male patient had prostate cancer.

PSA levels correspond to the size of the prostate. As men age, it's common for the prostate to become larger, leading to higher levels of PSA in the blood. When surgeons biopsied the prostates of men with high PSA levels, they frequently found cancer. However, what was not obvious at the time was that both an enlarged prostate and small prostate cancers are common among all men and usually not lethal. That is, most men with a prostate cancer will die of something else, and treating the prostate cancer can need-

lessly lead to a much-reduced quality of life. To Stamey's credit, he recognized this, and in 2004 published a study showing that the PSA test predicted the size of the patient's prostate, but not the severity of cancer.

As Stamey said at the time, "Our job now is to stop removing every man's prostate who has prostate cancer. We originally thought we were doing the right thing, but we are now figuring out how we went wrong. Some men need prostate treatment but certainly not all of them." The 2004 paper was one the last papers he wrote, Kathryn Stamey said.

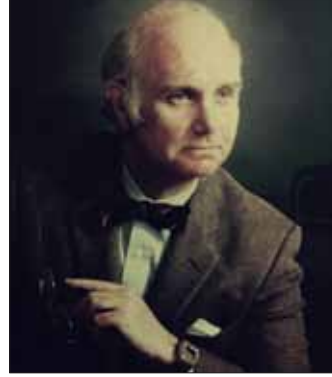
But that kind of strong language was typical of Stamey, Shortliffe said. "There was never any question about where he stood."

"He was a compassionate, kind gentleman," his wife added. "He thought his patients were his heroes, and he loved medicine. He loved learning, he loved everything about his work. He said he never worked a day in his life. He was just a very kind and loving man."

In addition to his work at Stanford, he loved fly-fishing, music and travel, she said.

In addition to his wife, Stamey is survived by his five children — Frederick Stamey, Charline Stamey, Alex Stamey, Theron Cooper and Allison Stamey — and grandchildren Suzi Quist, George Quist, Heather Magrin, Robin Magrin and Alexis Stamey.

A service for Stamey was held Sept. 12 in Menlo Park. ISM



Thomas Stamey

OF NOTE

reports on significant honors and awards for faculty, staff and students

LEAH BACKHUS, MD, MPH, was appointed associate professor of cardiothoracic surgery, effective July 1. Backhus specializes in general thoracic surgery and thoracic surgical oncology. She will lead health services and surgical outcomes research in the Department of Cardiothoracic Surgery. Her research focuses on lung-cancer survivorship and imaging surveillance following treatment for early-stage lung cancer.

SUZAN CARMICHAEL, PhD, was promoted to professor (research) of pediatrics, effective Aug. 1. Her research focuses on nutritional, environmental and genetic risk factors for perinatal outcomes such as birth defects, preterm delivery and stillbirth, and factors affecting the care and outcomes of infants who have birth defects.

STEPHANIE CHAO, MD, has been appointed assistant professor of surgery, effective July 1. Her research focuses on eradicating hepatitis B, which is the leading cause of liver cancer and liver disease globally. Chao works with the Asian Liver Center at Stanford and helped launch the Jade Ribbon Campaign to improve public and physician awareness about hepatitis B.

MICHAEL CLEARY, MD, professor of pathology and of pediatrics, was awarded a 2015 innovation grant from Alex's Lemonade Stand Foundation. This award will provide \$250,000 over two years for his research on the molecular events and



Leah Backhus



Suzan Carmichael



Stephanie Chao



Michael Cleary



Terry Desser

cellular responses associated with the onset of acute leukemia. The grants support experienced researchers with new and promising projects to identify the causes of and cures for childhood cancers.

TERRY DESSER, MD, was promoted to professor of radiology, effective Aug. 1. Desser served as residency program director in the Department of Radiology for 11 years. Her work focuses on identifying the human factors related to success in academic radiology and what drives the choice of specialties among medical students. Her clinical interests lie in the area of cancer overdiagnosis, particularly in ultrasound diagnosis of thyroid cancer.

GREGORY ENNS, MB, ChB, was promoted to professor of pediatrics, effective June 1. Enns' research involves developing ways to detect and monitor mitochondrial dysfunction noninvasively using highly sensitive biomarkers, tandem mass spectrometry and high-dimensional flow cytometry. He also is involved in clinical trials using novel therapeutics to treat inborn errors of metabolism, with an emphasis on mitochondrial disease.

EBEN ROSENTHAL, MD, has been ap-



Gregory Enns



Eben Rosenthal



Ronald Witteles

pointed professor of otolaryngology-head and neck surgery, effective July 1. Rosenthal focuses on developing real-time imaging agents to help surgeons and pathologists visualize cancer during surgery. He recently completed the first clinical trial in the United States for near-infrared optical imaging in cancer and is initiating this technique in a range of tumor types at Stanford.

JENNIFER SHAH, MD, a resident in radiation oncology, has received a 2015 American Society for Radiation Oncology Residents/Fellows in Radiation Oncology Research Seed Grant to study the feasibility of performing a specific type of CT scan on patients undergoing stereotactic ablative radiation therapy for lung

cancer. This grant provides \$25,000 for one year to residents and fellows planning to pursue careers in basic science or clinical research in radiation oncology.

RONALD WITTELES, MD, was promoted to associate professor of medicine, effective June 1. Witteles is program director of the internal medicine residency training program at Stanford, and oversees all fellowship programs within internal medicine. He is also co-director of the Stanford Amyloid Center, the largest center of its kind in the western United States. His research focuses on emerging treatments for systemic amyloidosis, cardiac complications of cancer therapy, and evolving diagnostic/therapeutic strategies for cardiac sarcoidosis. ISM