Evolution of anatomy illustration traced by Lane Library archivist

By Kris Newby

Drew Bourn, PhD, the historical curator at Lane Library’s Medical History Center, gently placed his favorite book in front of a group of art students. It was one of the last surviving volumes of The Comprehensive Book in the Art of Medicine, written by the famous Arab physician Ibn al-Nafis in the 13th century.

As Bourn turned its yellowed and frayed pages, he told the students that it was written after most of the world’s medical knowledge had been destroyed in the 1258 Mongol siege of the city of Baghdad, which at the time was an intellectual center for astronomy, mathematics and medicine. If al-Nafis hadn’t dedicated the rest of his life to reconstructing this medical information, it would’ve been lost forever, historians say.

“This is the eightieth year that Gail Wight, MFA, an associate professor of art and art history, has brought students in her Art and Biology course down to the archive reading room in the basement of the School of Medicine’s Lane Medical Library, a bookshark catacomb where Bourn curates the center’s more than 7,000 rare publications.

Wight originally called Bourn to see if he’d show her students at the time the archive’s first edition of De humani corporis fabrica, the groundbreaking book on anatomy written in 1543 by the Flemish anatomist-physician Andreas Vesalius.

“I believe that historical stories can have a big impact on people’s lives,” said Bourn, who comes from a family of historians and librarians.

Changed how medicine was taught

Speaking to the current group of students, Bourn told them that Vesalius’ Fabrica was more than an anatomy textbook; it changed the way medicine was taught. In 1537, Vesalius graduated with what was then a classical European medical education. In anatomy courses, his professors would read straight from the works of the ancient Greek physician Galen, who was born in 129, while an assistant dissected a cadaver to illustrate the structures discussed in the text. Galen’s teachings were considered the gold standard for more than 1,000 years, and they were above reproach.

Then Vesalius moved to Padua University to teach surgery. And after he began dissecting

In-home care of dementia patients falls mainly on women, experts say

By Tracie White

The responsibility of providing care to the vast number of patients with dementia expected over the next 20 years will disproportionately fall on working women, according to researchers at the School of Medicine.

“The best long-term care insurance in our country is a conscientious daughter,” the authors wrote in a perspective piece published today in JAMA Neurology. The article points to a lack of affordable in-home care options in the United States other than unpaid family members, primarily women.

As more baby boomers reach retirement age, experts predict a corresponding surge in cases of dementia: By 2030, an estimated 8.4 million Americans are expected to be suffering from some form of the disease.

Today, most of the care for these patients — 83 percent — is provided by unpaid family members, two-thirds of whom are women, the authors wrote.

“Wives are more likely to care for husbands than vice versa, and daughters are 28 percent more likely to care for a parent than sons,” the authors wrote, adding that

Scientists assemble working human forebrain circuits in lab dish

By Bruce Goldman

Peering into laboratory glassware, School of Medicine researchers have watched stem-cell-derived nerve cells arising in a specific region of the human brain migrate into another brain region. This process recapitulates what’s been believed to occur in a developing fetus, but has never previously been viewed in real time.

The findings, and the techniques used to obtain them, carry potential for the personalized study of individuals’ psychiatric disorders. The investigators saw the migrating nerve cells, or neurons, hook up with other neurons in the target region to form functioning circuits characteristic of the cerebral cortex.

These observations also showcase neuroscientists’ newfound ability to monitor, assemble and manipulate so-called neural spheroids, generated from human induced pluripotent stem cells, to study the normal development of the human forebrain during late pregnancy.

“We’ve never been able to recapitulate these human-brain developmental events in a dish before,” said the study’s senior author, Sergio Pasca, MD, assistant professor of psychiatry and behavioral sciences, “The process happens in the second half of pregnancy; so viewing it live is challenging. Our method lets us see the entire movie, not just snapshots.”

In the study, published online April 26 in Nature, the scientists were able to attribute, for the first time, defects in neuronal migration to Timothy syndrome, a rare condition that predisposes people to autism, epilepsy and cardiac malfunction. Postdoctoral scholars Fikri Birey, PhD, Jimena Andersen, PhD, and Chris Makinson, PhD, share lead authorship.

Culturing neurons in a lab dish is old hat. But the two-dimensional character of life lived atop a flat glass coverslip doesn’t sit well with cells designed for three-dimensional existence. Neurons cultured in monolayers mature only partially, tend to die fairly quickly and interact suboptimally.

The need for 3-D models

In a 2015 study, Pasca and his colleagues described their method for producing neural spheroids. Neural precursor cells generated from IPS cells are placed in culture dishes whose bottoms are coated to make it impossible for neurons to attach. The cells float freely in a nutrient-rich broth, ultimately developing into hundreds of almost perfectly round balls approaching 1/16 of an inch in diameter and consisting of over 1 million cells each. These neurons can live for up to two years, and they mature fully.

The spheroids created in the 2015 study recapitulated the human cerebral cortex’s six-layer-thick architecture, and the neurons they contained were of the type that arise in and dominate the cerebral cortex. They’re called glutamatergic neurons because they secrete the excitatory chemical glutamate.

But the cerebral cortex’s glutamate-
California handgun sales spiked after two mass shootings, study finds

By Beth Duff-Brown

After the 2012 mass shooting of children and teachers at Sandy Hook Elementary School in Connecticut, a leader of the National Rifle Association proclaimed, “The only thing that stops a bad guy with a gun is a good guy with a gun.”

It would seem that many Californians agreed, according to a new study by researchers at Stanford and two other universities.

In the six weeks after the Newtown shootings — when a man fatally gunned down 20 children and six adults reached across a variety of fields of medicine, from oncology to neurology to heart disease. Projects delved into topics such as stem cell research, heart health care policy, bioinformatics and global health. They explored diseases such as pulmonary arterial hypertension, sepsis and carcinoma.

The range of projects is terrific,” said Laurence Baker, PhD, director of the Schol­arly Concentration Program, a required program of study for medical students that pro­motes in-depth learning and research scholarship. Each Stanford medical student is required to complete at least one quarter’s worth of research, but must do more, he said. Some, like Souza, take a research year away from medical school to work on their projects.

Fire hazard

Souza’s research showed that the most common burn wounds in rural Nepal were to the hands of small children, who often fell into open fires used for cooking. Usually it’s years before the children get surgery to repair the deformities to their fingers, which curl up into fists as the wounds heal. The hand splint successfully keeps the fingers from retracting again in the months following surgery.

The 4-year-old who fell while playing in his mother’s shoes successfully recovered 100 percent of the use of his hands using the hand splint post-surgery, Souza said. “I took a year off to research this,” said Souza, who is a new head into her last year of medical school. “I’ve always had an inclination toward global health. There’s such a huge disparity globally. I believe health care is a human right.”

For their projects, the students work with faculty members, who provide mentorship and guidance through the potential pitfalls and successes of medical research. “Many of these projects will eventually be published,” Baker said. “Our goal is to make research part of the medical school experience at Stanford.”

‘Not black and white’

Kuo-Kai Chin, a second-year medical student, chose to explore a new area for him: health policy. For his project he ventured into the world of epidemiology and statistical analysis. “It’s been a big learning experience,” said Chin, a self-described math and science guy, laughing about the ups and downs of the journey. “I’ve learned that research is not black and white.”

Chin set out to investigate the use of two anti-seizure medications, gabapentin and pregabalin, that have been shown to work well as possible alternatives to opioids for post-surgery pain medications.

“Everyone knows about the opioid epidemic,” Chin said. He project set out to discover whether use of these adjuvant analgesics instead of morphine after knee replacement surgeries was increasing at Stanford as concerns about the national opioid epidemic increased.

His results showed that from 2008-15, the use of these drugs did, in fact, increase significantly. “Physicians are thinking about the opioid crisis and what other alternatives are available,” said Chin, who will be presenting results of the study at a health policy conference in New Orleans this summer.

Combining research and medical school at the same time is a challenge, Chin said. “There are a lot of dead ends. School sometimes gets in the way, but I’ve learned a lot about research.”
Researchers seek adults with peanut allergies for two studies

By Emma Hoiński

Researchers at the School of Medicine are seeking adults with peanut allergies to participate in two clinical trials of drugs that may reduce the severity of allergic reactions.

One is a phase-1 trial that will test the tolerability of a vaccine-based treatment intended to lessen the severity of allergic reactions. The other is a phase-2 trial examining the effectiveness of an antibody drug aimed at reducing the inflammatory response.

Millions of people in the United States are allergic to peanuts, one of the most common and deadly food allergens. There is no pharmaceutical treatment for this allergy. Oral immunotherapy, in which patients consume tiny amounts of the food allergen, such as peanut proteins, may help desensitize the immune system — but support from the highest levels of government would be needed, according to a recently published report from the National Academies of Sciences, Engineering and Medicine.

Although eradication is rarely possible, in 2016 the World Health Assembly passed a resolution to set a goal to eliminate viral hepatitis as a major public health problem by 2030, and asked each nation to develop national strategies for elimination.

Our committee believes it is feasible to eliminate hepatitis B and C as a public health problem in the United States by ending transmission and preventing the morbidity and mortality among people with chronic hepatitis. Similar global elimination efforts have been mounted against neonatal tetanus and trachoma, an infection that causes blindness.

There is no better time to act. With the new hepatitis B medications, over 95 percent of people with chronic hepatitis B are cured after only two to three months of treatment. Hepatitis B is preventable with vaccination, and hepatitis B antiviral treatments — although not curative — can prevent disease progression and most of the related deaths. Our report found that if diagnosis and care for chronic hepatitis B and C are increased, 90,000 deaths in the United States would be averted by 2030, and new hepatitis C infections would drop by 90 percent.

Why hasn’t eliminating hepatitis B and C in the United States been a priority?

It’s unfortunate that most people, including polyclinicians, philanthropic foundations and many leaders in academic medicine and global health, are not well-informed or aware of the prevalence and seriousness of chronic hepatitis B and C infections, their link to rising rates of liver cancer and the opportunities for elimination. Despite being a major national and international public health problem, viral hepatitis receives less than 1 percent of the National Institutes of Health research budget.

To address the obstacles to eliminating hepatitis, our center has worked diligently in collaboration with leaders in national governments, the Centers for Disease Control and Prevention, the World Health Organization and donors to build the case for elimination. So, I am really excited that we are finally talking about national and global elimination of hepatitis B and C.

What are a few of the biggest challenges you see?

Chronic viral hepatitis is a silent disease and most of the infected have no symptoms. In the United States, an estimated two-thirds of people infected with hepatitis B and half of those with hepatitis C are not aware they are infected.

Among the biggest challenges are diagnosing people who are living with chronic hepatitis B and C and providing them with access to care and antiviral treatment. Although screening is covered by the Affordable Care Act and by Medicare, health care providers rarely suggest it. And most primary care providers have not been trained to screen and provide care and treatment for patients with chronic viral hepatitis.

A major challenge in hepatitis C elimination is access to treatment, due to the cost of the most effective medication. As a result, only five of the estimated 700,000 hepatitis C patients on Medicaid, in correctional facilities or covered by Indian Health Services have received treatment. The report discussed ways possible to pro-

Assessing efficacy, tolerability of antibody

The other Stanford study is a phase-2 clinical trial of an antibody drug, ANP8020. The trial will assess the safety and tolerability of the drug. ANP8020 may be able to reduce the immune response to allergens, like peanut proteins. The antibody targets an important molecule in the immune response pathway known to reduce sensitivity to multiple allergen types, according to the drug developer, AnaptyBio Inc. The company is recruiting up to 20 adults aged 18 and older with a diagnosed peanut allergy and no history of life-threatening anaphylactic reactions. Participation will span about 60 days, and participants will undergo an allergy response test before and after the treatment. This trial is sponsored by AnaptyBio Inc. A phase-1 clinical trial has already been completed in Australia.

In both clinical trials, participants will be randomized to receive either the treatment or a placebo and will not know which Compound they receive until the treatment period is over.

For more information, email sncpcenter@stanford.edu, or visit ClinicalTrials.gov. At ClinicalTrials.gov, the identifier for the vaccine (AS08092) trial is NCT02851277, the identifier for the antibody (AND020) trial is NCT02920021.

Handgun

continued from page 2

common, such as federal elections, new firearm safety laws and terrorist attacks.

Urging further research

Taken as a whole, these events may drive significant increases in overall firearm prevalence, which may in turn increase the risk for firearm-related morbidity and mortality in the long run, they wrote. The authors urge further research to explore the cumulative effects and temporary shifts in acquisition patterns, their causes, and their implications for public health, crime and social cohesion.

Other Stanford co-authors are researchers Yifan Zhang, PhD, and Jonathan Redden, PhD, professor of political science.

A researcher at Monash University in Australia also co-authored the study.

Stanford’s Department of Medicine supported the work.
Report offers recommendations to U.S. president on mitigating climate change's impacts on human health

By Jennie Dusheck


And since the arrival of Asian tiger mosquitoes in Memphis in 1983, the insects — capable of spreading Zika, dengue and West Nile Virus — have invaded 37 states. In the densely populated Northeast, Asian tiger mosquitoes are poised to triple their range before 2045 — doubling the number of people potentially exposed to these diseases from 18 million to more than 30 million.

In every case, the root cause is climate change.

But we’re not helpless against such threats, according to a recent report co-authored by researchers at Stanford University. A few weeks before the 2016 election, the authors presented the report to the two presidential transition teams. Titled “Health: The Human Face of Climate Change, Perspective and Recommendations for the Next U.S. President,” the report recommended that a future administration initiate a formal, decade-long emergency response to climate change, managed by the U.S. State Department, and frame climate change as a global health security issue — in other words, an acute public health threat to populations across the globe.

“The Human Face of Climate Change” report was one of a series of 14 other climate reports that came out of a 2016 conference at Stanford titled “Setting the Climate Agenda for the Next U.S. President,” the report recommended that a future administration initiate a formal, decade-long emergency response to climate change, managed by the U.S. State Department, and frame climate change as a global health security issue — in other words, an acute public health threat to populations across the globe.

“One of the report’s three authors, Katherine Burke, MM, MSc, who is deputy director of the Center for Innovation in Global Health and president emerita of Wellesley College. Burke, along with other chronic diseases who are at risk. In a warmer world, the number of days when it’s too hot to safely work outside are expected to increase dramatically. Places like Texas, which once had 10 to 20 days a year of temperatures greater than 100 degrees, might see more than 100 a year by the end of the century, according to the National Oceanic and Atmospheric Administration.

Defining the problem

Experts agree that the Earth is warming dangerously and that this warming is due to the burning of fossil fuels and other human activities. The damage in ecosystem disruptions, rising sea levels and ever-more intense storms are all well-documented. So, increasingly, are the rapidly changing climate’s effects on human health.

Both greater average temperature and rising heat waves have immediate effects on morbidity and mortality through heat-related illnesses such as heat stroke and heat exhaustion. “The single thing that’s clearest is the impact of rising ambient temperature,” said Mark Cullen, MD, professor of medicine and of biomedical data science. “With every degree centigrade rise in summer high temperatures, there’s a predictable increase in total mortality.”

Added Cullen, who did not contribute to the report but is an expert on population health, “Most of it is a reappearance of old problems, which is to say, it’s less often completely healthy people who suffer or die; it’s people with other chronic diseases who are at risk of dying sooner during heat waves.”

In addition, healthy people who normally work outdoors during the heat of the day can be sickened or even killed by extreme heat. Farm workers, road workers and roofers are among those at risk. In a warmer world, the number of days when it’s too hot to safely work outside are expected to increase dramatically. Places like Texas, which once had 10 to 20 days a year of temperatures greater than 100 degrees, might see more than 100 a year by the end of the century, according to the National Oceanic and Atmospheric Administration.

Infectious disease will also get worse, as disease vectors such as mosquitoes and ticks grow in numbers and spread. And climate change has hundreds of other indirect effects on health. For example, our cattle and chickens are as vulnerable as we are to 100-plus-degree temperatures that increasingly persist for days or weeks.

Ocean warming and acidification are together killing coral reefs and collapsing marine fisheries, the primary food source for some 2 billion people in Asia and the Pacific. Valuable agricultural lands around the world are threatened by drought or, in places such as Bangladesh, inundation from rising seas and flooding. As your food basket isn’t producing, then your city is going to be in serious trouble,” said Burke.

The consequences of shocked food supplies spread outward, causing economic privation, social upheaval, food shortages and the displacement and forced migration of millions. These in turn lead to violence, trauma and physical and mental health disability.

For example, an extreme drought in Syria between 2006 and 2009 — which experts believe was due to climate change — caused influenza-like symptoms which, in turn, triggered the migration of 1.5 million people from farms to cities. Such displacement played a role in the subsequent uprising against President Bashar al-Assad in 2011, experts have argued.

What is being done?

The health care community already recognizes that tracking, studying and addressing the health impacts of climate change are critically important to strengthening the resilience of societies around the world.

Many institutions have begun integrated programs to consolidate what is known and what questions need to be answered. For example, The Lancet, a medical journal, has instituted an international research collaboration called "Lancer Countdown: tracking progress on health and climate change.”

The American Public Health Association — a 25,000-member organization of public health professionals — designated 2017 the year of climate change and health. And in March, The New England Journal of Medicine published an appeal to the administration to stay the course on climate change and health.

The Stanford report recommends the establishment of a State Department-based Presidential Emergency Response to Climate Change, conceptually similar to the 2001 Presidential Emergency Plan for AIDS Relief, which has saved millions of lives. Climate change’s impacts on human health compare to that of the AIDS epidemic, said Walsh, one of the report’s three co-authors. “Climate change is a huge threat to humanity, a threat to world security and a threat to health security. We have to see it on that scale,” she said.

With a $90 billion budget over 10 years, the report’s authors suggested, a federal climate change and health program could develop initiatives including a global climate health surveillance system; vulnerability maps and tools to create projections and early warning systems; and public health awareness campaigns.

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It’s not game over; it’s game on.
Mitigating effects of climate change on human health

The table, too. Hospitals in the United States are second only to restaurants in the intensity of their energy use. The Stanford report recommended reducing the health sector’s carbon emissions by powering it with renewable energy and increasing energy efficiency, as well as making hospitals and clinics more resilient to storms.

The human face of climate change

The report also recommended framing climate change as a human health issue — partly because it is a health issue and partly to better engage the public and the health care community in action that will slow the root cause. Americans recognize that climate change is a major threat, said Burke. But the subject lacks immediacy, and it’s often low on people’s lists of concerns. Talking about current impacts on health is a way to engage the public’s support for action. “It’s no longer an abstract thing” — not vaguely about the health of future generations, Burke said. “It’s now. It’s our own children and grandchildren; they are growing up in a very different world.”

At a recent climate policy meeting, Emily Wimberger, chief economist at the California Air Resources Board, said that when it comes to action, people respond most readily to direct threats to human health and security. People who don’t necessarily want to talk about climate change, she said, will pay more attention to the problem when it’s framed as a matter of keeping everyone healthy. For instance, as California reduces fossil fuel use, CARB frames the issue as both a way to slow climate change and also a health-centric reduction in smog — one that lowers population risks for asthma, heart disease and dementia.

Looking forward

Experts agree that addressing the health aspects of climate change needs to depend on the federal government; it can happen at the level of cities, states, local governments, businesses or institutions, as well as through regional collaborations. “It’s not game over; it’s game on,” said Wimberger.

Hospitals and health care systems have some specific challenges to tackle, according to the Stanford report. “When a crisis such as a deadly heat wave or a hurricane occurs in a community, two things happen,” said Walsh. “First of all, it puts stress on the health care system when the system needs to be able to respond quickly and effectively. But secondly, it’s the place that people turn to. It can be a kind of resource. It’s a 24/7 organization that is still there and still running when everything else is uncertain.”

“Hospitals can be a kind of beacon in a community, a place people can turn to,” she added.

Need resilient health systems

Health care systems need to be especially resilient in times of crisis. Hospitals may need to be able to withstand Katrina-type hurricanes, floods and heat waves. For example, in recent decades, hospitals in Chicago and New Orleans have had to deal with patients developing heat stroke while in hospital beds because of insufficient air conditioning. Staff reportedly couldn’t distinguish patients who were suffering from overheating from those who had fevers from infections. Organizationally, a health care system needs to be able to continue to function effectively when things are at their worst.

Some of the solutions will come from the technology sector, others from an understanding of how organizations work and how people function during crisis. Just establishing what the questions are will take research.

Cities also need to think ahead. Cullen, who is also a professor of health research and policy, said that the effects of heat waves can be anticipated and mitigated. “For example, some big cities, like Chicago, have developed air conditioning shelters for elderly people in urban areas to deal with heat waves,” he said. Chicago also has cooling buses that can pick people up wherever they live.

Walsh said that while she was doing research prior to the election, contacts at the U.S. State Department told her that they “liked the idea in our report of a big coordinated effort that would bring together all these pieces — the data and trying to define more precisely where the vulnerabilities are, including which populations are most at risk and what those risks are.”

“And that’s a big-data, population problem, something that Stanford does well. This could be a place where Stanford could lead,” she said.
Anatomy
continued from page 1

His own cadavers, he made a shocking discovery: Some of Galen’s ‘facts’ were inaccurate because, for religious reasons, he’d never dissected a human body — only pigs, oes, dogs and monkeys.

But, at age 23, Vesalius meticulously began separating fact from fiction in Galen’s anatomical works. For example, he discovered that the human jaw is one bone, not two, and the breastbone has three segments, not seven.

An illustration from De humani corporis fabrica, by Andreas Vesalius.

One of the last surviving volumes of The Comprehensive Book in the Art of Medicine, written by the famous Arab physician Ibn al-Nafis in the 13th century, is held by Lane Medical Library.

Dementia
continued from page 1

because women now make up almost 50 percent of the workforce, these burgeoning demands will disproportionately fall on them — and put at higher risk for lowering or exiting their career trajectory.

“Hard-fought gains toward equality in the workplace are at risk,” they wrote.

Health care dilemma

Concern about this troubling health care dilemma grew out of research by a team of design fellows at Stanford’s Clinical Excellence Research Center. They were investigating ways to provide better care at lower costs for patients with dementia and other cognitive disorders.

As CERC fellows dug below the surface of the disease, they discovered that it was relentless. It was so hard on my mom.

The authors noted that while caregiving for loved ones with dementia can certainly be meaningful, the amount of time required — an average of 171 hours per month, according to the article — combined with the unpredictability of the job’s demands and unrelated tasks, such as toileting and bathing, can be overwhelming. The article also asserted that “it’s not likely that men will step up and share in the caregiving anytime soon.”

If nothing is done to plan for this shift in caregiving demands, not only women and their families suffer but costs will fall on employers from a new level of accuracy and artistry. Because he lived in northern Italy during the Renaissance, he had access to some of the most talented artists of the times. Historians believe that he outourced the illustrations in Fabrica to artists working in master painter Titian’s studio.

The resulting woodcuts were both amazing works of art and disturbing, showing cadavers staged in dramatic poses with layers of skin peeling off to reveal muscle and bone, often drawn with bucolic Italian landscapes in the background. They looked more like storyboards sketches for a zombie apocalypse movie than scientific illustrations.

Woodcuts ‘convey complex attitudes’

‘Artists are still referring to Fabrica today, primarily through restaging these now iconic poses in a contemporary context,’ said Wight, a new-media artist who continues to work in the medium.

Wight will teach a special variation on her Art and Biology class in the winter quarter of 2018, as part of Stanford’s Francis Kenneth Bright/200 celebration. The course, which usually includes a short section on monsters, will focus entirely on the bizarre, monstrous, mythological and medical perceptions of all things monstrous.

Lane Library’s Medical History Center is open to the Stanford community and the public. Contact Bourn at dbourn@stanford.edu for research assistance or to schedule a visit.

Taube Philanthropies gives $3 million for Huntington’s disease research

Scientists at the School of Medicine and the Gladstone Institutes have received a $3 million gift from Taube Philanthropies to fund Huntington’s disease research.

The donation will support the first efforts to use gene editing and stem cell therapies to ameliorate Huntington’s disease, a progressive, inherited neurodegenerative disease that presently lacks approved drugs to slow its progress and for which there is no cure.

The research team is composed of Matthew Porteus, MD, PhD, associate professor of pediatrics at Stanford School of Medicine, who will lead the work; Frank Longo, MD, PhD, professor of neurology and neurosurgery; and Sean Finkbeiner, MD, PhD, of the Gladstone Institutes’ Tauke-Koret Center for Neurodegenerative Disease Research.

The team will also collaborate with clinical efforts at the UCSF Memory and Aging Center.

Tad Taube, founder and chairman of Taube Philanthropies, has contributed to research on neurodegenerative diseases in the past. Approximately 30,000 people in the United States have symptoms of Huntington’s disease, and another 200,000 people are at risk of developing it.

The View-Master is a reminder of how fast the medium has changed, and how quickly the view of human physiology changed through it at colorful photographic dissection images captured with Kodachrome film, a medium that is practically obsolete with the advent of digital photography.

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Photographed in the 1950s and 1960s by Stanford anatomy instructor David Lee Bassett, the 1,554 image slides were captured with Kodachrome film, a medium that is practically obsolete with the advent of digital photography.

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MIGRATION JUMPS.

In the new study, the researchers separated their spheroids into two batches and observed them to become different regions of the human brain. They cultured one batch in a medium that induces cortexlike spheroids containing glutamatergic neurons. They placed the second batch in dishes whose broth steers the spheroids toward the circuitry responsible for the brain's most advanced and usually epileptic regions. Their migration pattern, the scientists noted, was halting: They would move toward the target spheroid for a little while, then stop for an extended period, then start up again in stuttering jumps.

On reaching their destination, the GABAergic travelers underwent a transformation, sprouting dendrites — brain cell branches — that receive inputs from other neurons and forming working connections with the glutamatergic neurons. Electrophysiological tests revealed that GABAergic and glutamatergic neurons were successfully forming circuits and signaling to one another.

INSIGHT INTO TIMOTHY SYNDROME

The scientists had access to tissue samples from patients with Timothy syndrome, an extremely rare and severely cardiac abnormalities once spelled ultra-short life expectancies, but now can be ameliorated with pacemakers. However, survivors usually have autism and frequently have epilepsy.

The investigators generated both types of neural spheroids from their Timothy-syndrome tissue samples. They fused them and watched to see what would happen. What they saw was this: The GABAergic neurons, which seemed to develop normally, exhibited aberrant start-and-stop migration patterns. Their forward movements were more frequent, but far less efficient, than those of normal neurons.

The mutation behind Timothy syndrome increases the likelihood that the calcium channel for which it codes will let calcium ions flow through it. So, the researchers reasoned, a drug impeding the channel's activity could halt the migration jumps.

To test this idea, they turned to a drug inhibiting a calcium ion channel. It reduced the fraction of normal neurons in the spheroid samples from their Timothy-syndrome tissue samples. The spheroids from their Timothy-syndrome tissue samples more frequently have epilepsy.

The study was funded by the National Institutes of Health, the California Institute for Regenerative Medicine, the McKnight Foundation, the Donald E. and Delia H. Baxter Family Foundation, the Kwan Research Fund, the Stanford Child Research Health Institute, the Wishes for Elliot Foundation, a Walter V. and Ingrid Berry Batedological Fellowship, the Stanford School of Medicine Dean's Office, the UC-San Francisco Program for Breakthrough Biomedical Research and the Sandler Foundation.

Stanford's Department of Psychiatry and Behavioral Sciences and the Stanford Center for Sleep Sciences and Medicine also supported the work.

Christopher Dawes is president and CEO of Stanford Children's Health.

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Christopher Dawes is president and CEO of Stanford Children's Health.
For 40 years, creating sock monkeys for pediatric patients

By Kate DeTrempe

Forty years ago, flyers appeared around town calling on volunteers to join in some “Monkey Business” to ben-
etify young patients at Children’s Hospital at Stanford, as Lucile Packard Children’s Hospital Stanford was then known. The advertisement read:
The Los Altos Senior Citizens Drop-in Center is forming a new group to sew “Monkey Toys” to be given to the children at Children’s Hospital at Stanford.

Prewashed old hose, bits of yarn and scraps of material will be used for stuffing. If you have some to contribute, please drop off at the Center any Monday, Wednesday or Friday from 10:00 a.m. to 3:30 p.m. or bring it with you on Monday, April 29th, 1977.

Won’t you please come and help us out on this project?

Volunteers arrived at the Los Altos Senior Center that day with sewing and embroidery thread, needles and scissors, and have been coming back ever since to create sock monkeys for the patients at Packard Children’s.

Monday gatherings

On Monday mornings, volunteers gather to create the toys, which are made from red-heeled work socks, nylon hose, yarn and red ribbons. The volunteers add individual characteristics to each doll as they put on the finishing touches, including unique faces, ribbons and pom-pom decorations.

Over the past four decades, volunteers have created about 12,000 sock monkey toys, which have become widely recognized and loved by Packard Chil-
dren’s patients and their families. The toys have never been sold but instead are given as gifts to young patients who need a little extra TLC while staying at the hospital.

Marge Filson, a 95-year-old volun-
tee, has been self-proclaimed “monkey toy lady” for the past 28 years. For her, hearing families tell about the joy their toy monkeys bring them is what it’s all about. “You see these kids receive mon-
keys, and they are so excited,” she said. “Anyone who has received a monkey has been very, very happy. I love seeing the response.”

Filson had a special moment while shopping for monkey toy supplies about 15 years ago. After explaining to the woman the counter that the socks she was buying would be turned into monkey toys, she was met with great enthusiasm. “She told me she had always wanted to talk to a monkey toy lady,” Filson said. “She had spent much of her childhood as a patient at Packard Child-
dren’s, where she received her own sock monkey toy, and she had always wanted to meet someone who made them to say thank you.”

‘A sense of comfort’

Every month, the sock monkeys are picked up at the Los Altos Senior Center and distributed to patients at Packard Children’s by Joe Manfrey, a 90-year-old volunteer who has dedi-
cated more than 25 years to the hospital.

“After four decades, the handmade sock monkeys continue to bring a sense of comfort to our patients as they go through a difficult time in their life,” said Maryellen Brady, the hospital’s director of volunteer services. “We are fortunate to have built a long-lasting relationship with the volunteers of the Los Altos Se-
nior Center, and we are grateful for their dedication to the families who receive these special gifts.”

“Here I am almost 100 years old, and I’ve been at it for over 25 years. It’s very much a joy for me to be involved,” Filson said. “It’s such a wonderful program. I’ve put all my life into it.”

OF NOTE

Students named HHMI medical research fellows

Four Stanford medical students have been named medical research fellows by the Howard Hughes Medical Institute. The program provides $45,000 of grant support to allow promising medical, veterinary and dental students to spend a year conducting biomedical research. This year’s 79 fellows were selected.

The Stanford recipients, and the locations of their fellowships, are:

• Heather deJardins-Park — Stanford
• Mollie Friedlander — Stanford
• Heather desJardins-Park — Stanford

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