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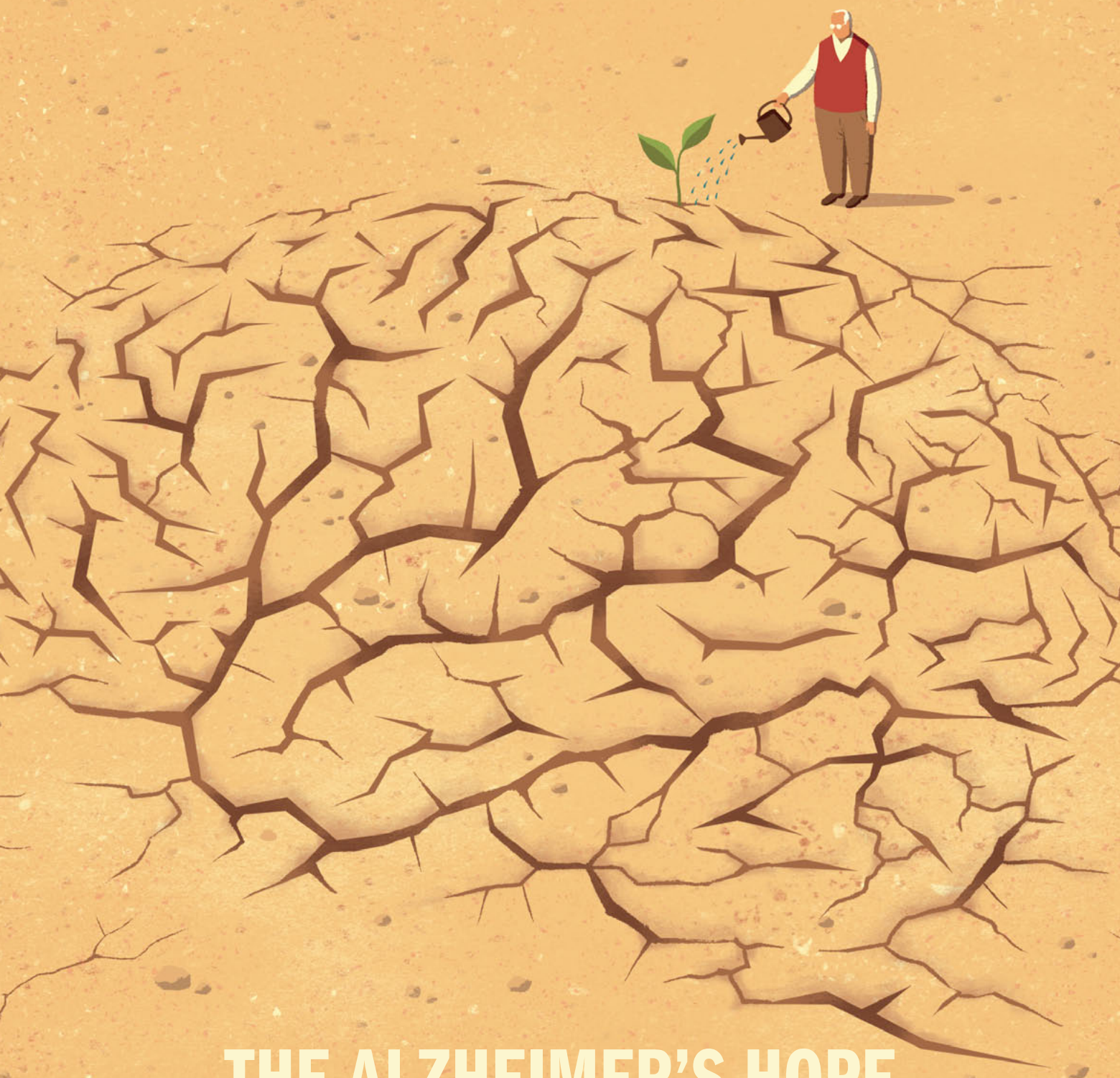
Tufts Medicine



THE ALZHEIMER'S HOPE

SMALL ACHIEVEMENT

Nikolai Klebanov, E14, M18, was a bright high school kid from Newton, Massachusetts, trying to make himself useful when he emailed Charles Sykes, an associate professor of chemistry at Tufts, looking for a summer job. Sykes said yes.

"I had no idea you could do that," Klebanov says with surprise. Next thing he knew, the enterprising teenager was part of a team in Sykes' lab intent on creating the world's smallest electric motor—one the size of a molecule. The effort succeeded, and by September 2011 had made the *Guinness Book of World Records* in that infinitesimal category.

Klebanov came to the lab with certain advantages. Born in Moscow to parents who were both electrical engineers, he is at ease in areas hard to imagine for most of us. "The definition of a motor is something that turns in one direction more than another," he says at the start—in other words, a motion that is controlled rather than random. In Sykes' lab, the butyl methyl sulphide molecule's spinning on a copper plate was achieved through an electric charge at the tip of a scanning tunneling microscope.

Klebanov sees his professional future most likely being devoted to medical engineering, where miniature mobile devices of all kinds may be used to whisk medicines to targeted sites throughout the body, delivering keener treatment efficiencies along the way. -BRUCE MORGAN

PHOTO: JOHN SOARES

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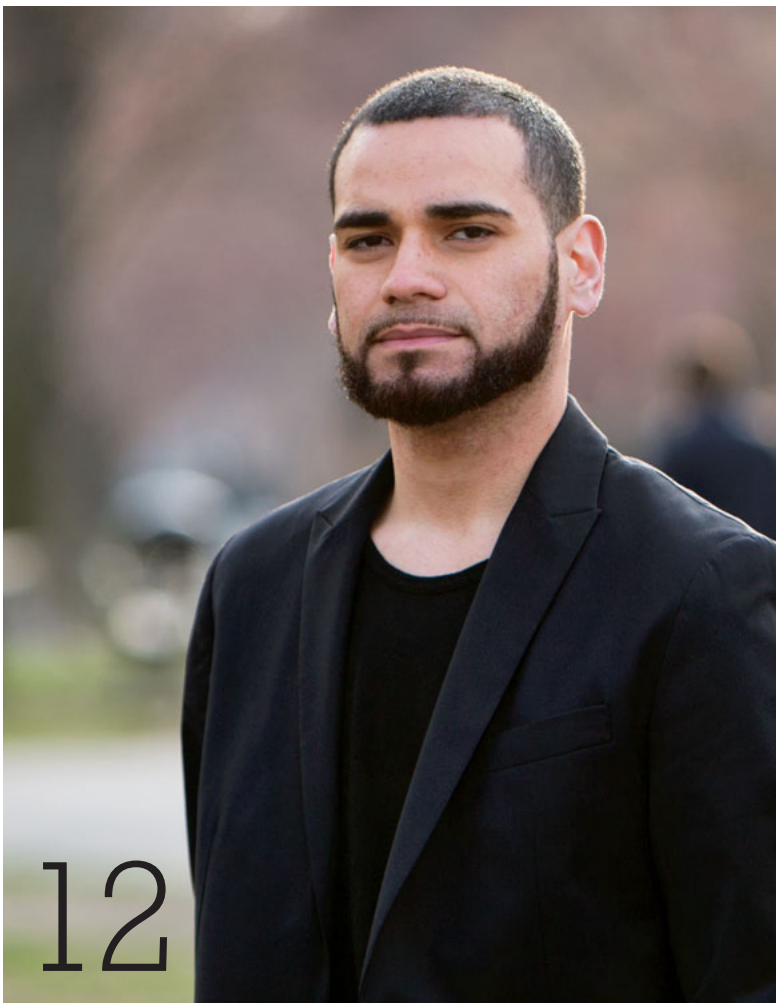
COVER STORY First, neuroscientist Philip Haydon made himself an expert in a little-known area of brain science. Now he is testing a revolutionary new approach that shows great promise for the treatment of this dread modern disease.
BY BRUCE MORGAN

20 THE GIFT
When it comes to live-donor liver transplants, Lahey Hospital & Medical Center has seen more patients than anyone else in the country. One of those patients had his life saved thanks to a donation by his son, a Tufts medical student. Here, in their own words, is the story of that procedure. **BY BRUCE MORGAN**



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Cover art by
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ILLUSTRATION: AMANDA GLEESON

DOCTORING, THEN AND NOW

Although this photo of medical school life from the Tufts University archives is undated, one can easily place it sometime in the mid-20th century based on its lineup of all white men. Without any doubt, this was typical of the period. In 1945, for example, there were 103 doctors in our graduating class, and all but five of them were men. Some 70 years later, the world has changed. Members of the Tufts Medical School Class of 2019, the most recent for which we have data, are mostly female, consisting of 109 women and 92 men. Racial and ethnic diversity has also seen a shift, with nine Black or African American, 13 Hispanic and 36 Asian students in the latest mix. -BRUCE MORGAN

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PHOTO: COURTESY OF TUFTS DIGITAL COLLECTIONS AND ARCHIVES

THE ART OF CONNECTING

WHEN I FIRST became dean of the medical school, I imagined that the part of the job I would dislike the most would be the fund-raising—all those meetings and meals and conversations taken up with talk about money. But in fact, I'm finding I love that the most. I'm out there meeting interesting people who want to do good things for Tufts. After a while, you get to know these prospective donors as friends.

The payoff can be substantial. It goes without saying that any future success we may find in our fund-raising efforts must build on the foundation of relationships we have cultivated over the years. This is true wherever we happen to be meeting people, shaking hands with them and starting a new conversation.

I have just returned from another intriguing trip to mainland China, Macao and Hong Kong, and find the intimate and collegial process of making connections on my mind more than ever. I'm happy to report that our medical school now has more friends, and I would venture to say, better friends, in Asia than we have ever had before. Let me touch on just three highlights from these annual Asian trips.

In Taiwan, which I visited most recently in 2014 and 2015, we are in dialogue with leaders at that nation's largest engineering school, an institution generally considered to be "the MIT of Taiwan." They are interested in potentially launching an international-quality medical school there, and have approached us as prospective mentors and guides along that path.

This overture was no accident. I have visited Taiwan five times now, and the people I've met have come to trust us. We have put our heads together and are deepening our relationship month by month as tentative plans for the new medical school proceed.

A second opportunity for collaboration on Taiwan stems from our school's growing familiarity—our "name recognition," if you will—among people in positions of power and influence there. Over the years, I have become friends with a man named Dr. Wen-Ta Chiu, whom I first met when he was president of one of Taiwan's leading medical schools, Taipei Medical University. He went on to become Taiwan's minister of health and welfare, and I visited with him a couple of times when he was in that position.

Now, in his postministerial life, he has been advising a major industrialist in Shanghai who has an interest in branching out into the health-care and education fields. Because this industrialist is familiar with Tufts, Dr. Chiu has recommended to him that an affiliation with us could be beneficial for both sides. And that set the stage for the wonderful visit to Shanghai we had in January.

Our collaboration with this individual is still tentative, but here again, having become a familiar name in a foreign milieu has helped improve our chances to connect with a newfound partner. To show his appreciation, the Shanghai industrialist has pledged a substantial gift to the medical school to support both education and research.

None of these connections would have happened without the wonderful assistance of two members of our board of advisors, Olivia Cheng and Ajay Sondhi, both of whom have taught us a good deal about China and Taiwan and have advised and assisted us in developing these international relationships.

Personally, one aspect of all this traveling has been a deepening appreciation for what the ongoing business of fund-raising entails. They call it "development," and that's a perfect term. With each visit and each conversation, we and our potential partners steadily develop an understanding and respect for each other.

Soon our sense of common purpose—our sense of family, really—is enlarged. And this can only be seen as a good thing.

HARRIS A. BERMAN, M.D.
Dean, Tufts University School of Medicine

PHOTO: KELVIN MA

Pulse

Uranium tailings, such as these being removed from a mill site in Utah, have long been recognized as a public health hazard, but now uranium from natural sources is raising the risk.

Danger in Your Drink

The toxic metal uranium has found its way into public water supplies throughout California's farming regions

BY BRUCE MORGAN

RADIOACTIVITY ISN'T THE only thing to fear about uranium. Ingested, traces of the toxic metal can damage kidneys and boost the risk of cancer when consumed over a year or more. Now a recent investigation by the Associated Press has shown that many thousands of people living in California's agricultural areas are taking in uranium at levels considered unsafe by state and federal standards.

"Uranium, the stuff of nuclear fuel for power plants and atom bombs, increasingly is showing up in drinking water systems in major farming regions of the U.S. West—a naturally occurring but unexpected byproduct of irrigation, of drought and of the over-pumping of natural underground water reserves," according to the story, published late last year. The AP focused on California's central farm valleys, an area roughly 250 miles long and encompassing major cities, citing a claim from the U.S. Geological Survey that as many as one in 10 public water systems in the region had elevated levels of uranium.

Schools in the area have stopped using public drinking fountains and are trucking in bottled water instead. "We don't have a choice," said one elementary school principal quoted in the story. "You do what you have to do."

Geologists and other experts are still trying to figure out exactly how the uranium has spread through public water systems and private wells the way it has, but they suspect the rise of farming over the past 150 years has been a contributing factor. Mountain snowmelt in California washes uranium-laced sediment down to the flatlands. Irrigated plants leech uranium from the soil, and the metal eventually sinks down into aquifers tapped by wells.

Doug Brugge, a professor of public health and community medicine at Tufts, has been concerned for years about the deleterious effects of uranium on people exposed to it. "We should not have any doubts as to whether drinking water with uranium in it is a problem or not. It is," he told the AP. "The larger the population that's drinking this water, the more people that are going to be affected."

Research teams at Tufts and the University of New Mexico have joined forces to explore uranium's health impacts in more detail. "There has not been an appreciation of the number of people exposed"—the issue has not drawn the attention it deserves, said University of New Mexico researcher Johnnye Lewis. Early findings suggest that long-term exposure to uranium also can lead to reproductive and genetic damage, among other problems.

PHOTO: JUSTIN SULLIVAN/GETTYIMAGES.COM

Body and Mind

A new program at Cooley Dickinson Hospital in Northampton, Massachusetts, is making it easier for primary-care patients to find mental health services right where they are, according to MassLive.com. Peter Halperin, associate clinical professor of psychiatry, is heading up the initiative.

Studies have shown repeatedly that integrating mental health into a primary-care setting leads to better health outcomes for patients, according to the National Center for Biotechnology Information. More psychotherapists are expected to be added to the Cooley Dickinson staff.

MEDICAL SOCIETY HONORS

Deeb Salem, physician-in-chief at Tufts Medical Center, has been honored by the Massachusetts Medical Society as the 2016 recipient of its Special Award for Excellence in Medical Service. The award honors a physician who has made a distinguished demonstration of compassion and dedication to the medical needs of his or her patients and the general public.

Salem, a cardiologist, has guided medical students and residents as professor and chair of the Department of Medicine since he joined Tufts Medical Center (formerly called Tufts-New England Medical Center). With more than 170 publications to his name, he is a recognized expert in coronary artery disease and congestive heart failure. His positions at the center include service as chief medical officer and interim president. He was named physician-in-chief and the Sheldon M. Wolff Professor and chair of the Department of Medicine in 1999.

EASY DOES IT

PEOPLE WHO MAY need to exercise the most for better health often talk themselves out of it, thinking it's either too hard or too time-consuming. But a recent large-scale study out of Tufts shows that these concerns are exaggerated.

The study analyzed the daily activities of 4,207 Americans who were 73 years old. Participants were followed for a decade. The findings revealed that walking faster than three miles per hour on regular rounds cut the risk of coronary heart disease (CHD) and cardiovascular disease (CVD) by 50 percent in both men and women. Risk of stroke was trimmed by 53 percent.

In addition, walking an average of as short a distance as seven city blocks reduced CHD by 36 percent, stroke by 54 percent and CVD by 47 percent. Lawn mowing, raking and gardening were other simple, routine activities that lowered the risk of these same ailments.

"Our study of older Americans shows that even late in life, moderate physical activity such as walking is linked to lower incidence of cardiovascular disease," said Luisa Soares-Miranda, a study author and a postdoctoral student at the University of Porto in Portugal. Senior author Dariush Mozaffarian, dean of the Friedman School of Nutrition Science and Policy at Tufts, added: "The results were especially relevant because with advancing age, the ability to perform vigorous types of activities often decreases."

PHOTO: KELVIN MA; ILLUSTRATION: ELISE GUILLEN

HALL OF FAMER

VIVIAN PINN, a physician, professor and researcher who has spent her career advancing women's health issues and working to eliminate health care disparities, and who had a legendary impact as assistant dean of students at the medical school from 1970 to 1982, was inducted into *Modern Healthcare*'s Health Care Hall of Fame in March. The ceremony took place in Chicago.

Upon entering medical school at the University of Virginia in 1963, Pinn found herself to be the sole woman and only African American in her class. She graduated with honors. At Tufts, she quickly earned a reputation for her close attention to students, especially minority women, and became a valued mentor.

She was the first African American woman to chair an academic pathology department in the U.S., at Howard University College of Medicine. She also served as the first full-time director of the Office of Research on Women's Health at NIH, beginning in 1991. At a special ceremony on the Boston campus in 2011, the medical school's Office of Student Affairs, was dedicated in her honor and a new scholarship fund was created in her name. Pinn now serves on the Board of Advisors of Tufts Medical School.

OBESITY TRIGGER

SOMETHING LIKE TWO-THIRDS of American adults are overweight, and the way they eat when they step out for a meal may be partly to blame, scientists have concluded.

Researchers at Tufts determined that 92 percent of American restaurant meals contain excess calories—enough to make you fat, if eating out is a regular thing. The study examined meals at 123 restaurants in Boston, San Francisco and Little Rock, Arkansas, between 2011 and 2014. Even without drinks, appetizers and desserts, single-meal servings exceeded the recommended level pretty much all the time. The worst culprits were American, Chinese and Italian restaurants, which had mean counts of 1,495 calories per meal for the main course.

Study author William Masters, a professor at the Friedman School of Nutrition Science and Policy, points out that the findings don't carry equal implications for everyone. "Women typically have a lower caloric requirement than men," he notes. "Women, while dining out, typically have to be more vigilant."

Susan Roberts, director of the Energy Metabolism Lab at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts, has some sympathy for people eyeing an overloaded plate and struggling not to eat it all. "More than 100 years ago, the Russian scientist Ivan Pavlov received the first Nobel Prize awarded for integrated systems physiology for discovering the 'cephalic phase of digestion,' which is basically a mechanism designed to make us hungry and tempted when there is available food for the taking," she says.

"All we have to do is see and smell food, and our sympathetic nervous system revs up, insulin secretion drops blood glucose and our stomach relaxes—the goal of these physiological changes being to prepare us to eat all the food within reach," she told a reporter from munchies.vice.com, a website devoted to food. The study appeared in the *Journal of the American Academy of Nutrition and Dietetics.*

PHOTO: MATTHEW MODOONO; ILLUSTRATION: ERIN FARLEY

> "We have a lot of threats to the water supply. And we have lots of really good professionals in the water industry who see themselves as protecting the public good. But it doesn't take much for our aging infrastructure or an unprofessional actor to allow that protection to fall apart."

Jeffrey Griffiths, professor of public health and community medicine and former chair of the EPA's Drinking Water Committee, quoted in a Feb. 8, 2016, *New York Times* story about unsafe lead levels in tap water

TRUMPED AGAIN

JUST HOW HEALTHY a president would 70-year-old Republican candidate Donald Trump be? You can rely on one of our school's graduates to give us the answer.

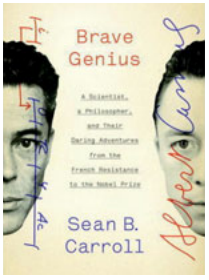
Harold Bornstein, '75, a gastroenterologist based in Manhattan who has been Trump's personal physician since 1980, released the results of the candidate's medical examination in mid-December, stating that "If elected, Mr. Trump will be the healthiest individual ever elected to the presidency."

Bornstein said that Trump had a blood pressure reading of 110/65, no serious diseases or surgeries, and had even managed to shed 15 pounds over the past year—not bad, given all the dietary pitfalls available to him on the campaign trail since he entered the race last June.

Science Writing Prize

Sean Carroll recognized for bridging science and the humanities

Evolutionary biologist, educator and author Sean B. Carroll, a 1983 graduate of the Sackler School, has been awarded Rockefeller University's Lewis Thomas Prize for Writing about Science. The award was given in recognition of Carroll's body of work, including his 2013 book *Brave Genius: A Scientist, a Philosopher and Their Daring Adventures from the French Resistance to the Nobel Prize.*



Named in honor of the noted physician-scientist and perennially graceful essayist Lewis Thomas, the prize was established by the university in 1993. It is designed to recognize "the rare individual who bridges the worlds of science and the humanities, whose voice and vision can tell us about science's aesthetic and philosophical dimensions, providing not merely new information but cause for reflection, even revelation."

Carroll is vice president for science education at the Howard Hughes Medical Institute and a professor of molecular biology and genetics at the University of Wisconsin-Madison. A major player in building the field of evolutionary developmental biology and a prolific writer, he is also a skilled public speaker who appears frequently in the media to discuss new findings. He created the science filmmaking initiative at the Howard Hughes Medical Institute, and in that capacity has served as the host or executive producer of more than a dozen films.

Other recent winners of the Thomas prize include neurologist Oliver Sacks, research physiologist Frances Ashcroft and surgeon Atul Gawande.

Research

The tadpole on the left has regular, symmetrical craniofacial features characteristic of normal development. Researchers interfered with normal bioelectric signaling during development of the tadpole on the right, leading to facial abnormalities.

ELECTRICAL SIGNALING IN CELLS

Findings about craniofacial anomalies could shed light on fetal alcohol syndrome and other conditions

BY JACQUELINE MITCHELL

TUFTS BIOLOGISTS HAVE discovered the bioelectric mechanism by which a rare genetic disorder causes facial abnormalities, a finding that could lead to preventive measures and treatments for a host of disorders, from birth defects to cancer.

For the study, published on Feb. 11 in the *Journal of Physiology* online in advance of print, lead author Dany Spencer Adams, a research associate professor of biology, and colleagues at Tufts, MIT and RMIT University in Australia used an embryonic frog model to demonstrate for the first time that faulty bioelectric signaling is responsible for the craniofacial defects associated with the genetic disorder Andersen-Tawil Syndrome (ATS). Those deformities—a broad forehead and nose, wide-set eyes, low-set ears and a small jaw and chin—are determined during embryonic development.

Patients with ATS have a mutation in the gene that codes for the potassium ion channel known as Kir2.1, a crucial piece of cell machinery that maintains cells' electrical charge by regulating the flow of positively charged potassium ions in and out of cells. If Kir2.1 malfunctions, it affects how facial features develop, among other things. Cardiac arrhythmias and muscle disorders also common in ATS patients had previously been linked to electrophysiology, but the craniofacial defects had not been explained.

The new findings, Adams says, "are not just the first-ever model of why one rare mutation causes craniofacial anomalies. They actually may apply to the very much more common fetal alcohol syndrome."

While only about 100 people in the world have ATS, it's estimated that more than 7 million suffer from fetal alcohol syndrome, she says. Research by other scientists has found that alcohol binds to the Kir2.1 ion channel, leading some to speculate that abnormal ion channel function may cause the distinctive facial features associated with fetal alcohol syndrome, just as it does in ATS.

In their study, Tufts scientists used light to control ion channel activity—the first use of the emerging field of optogenetics to alter embryonic development and probe a disease state by manipulating bioelectric signaling. Using light to precisely manipulate and monitor cells that had been genetically modified to express light-sensitive ion channels, the researchers showed that altering the natural bioelectric patterns within the outer cell layer of the frog embryos during early development caused abnormalities in the skull and face, while bioelectric changes later in development did not.

COMPLEX STRUCTURES

The work bolsters earlier findings by Tufts scientists that bioelectric signaling in many cell types, not only nerves, plays a major role in how cells create and repair complex anatomical structures, says Michael Levin, A92, director of the Tufts Center for Regenerative and Developmental Biology and a coauthor of the study.

With that knowledge, he says, it may be possible to alter bioelectrical signaling to correct the effects of genetic mutations or other developmental defects. "That's the big picture here," says Levin, who is also the Vannevar Bush Professor in the Department of Biology. The research shows that patterns of electrical activity throughout tissues are a key piece of the information exchange by which cells coordinate their activity to produce anatomical

PHOTO: COURTESY ADAMS LAB/TUFTS UNIVERSITY

outcomes, Levin says.

Other researchers have linked a defective Kir2.1 channel to a disruption in the flow of electricity. In Andersen-Tawil Syndrome patients, the muscles, including the heart, don't work properly. Typical symptoms include heart palpitations, fainting and weakness when waking up or after exertion. "People who have this syndrome go to the doctor with cardiac arrhythmia or periodic paralysis—they just kind of freeze," says Adams.

The *Journal of Physiology* study suggests that the ability to exert some control over such ion channels as Kir2.1 could dramatically alter what's going on in the cells of a developing embryo. Treatments to prevent the formation of facial abnormalities, such as those associated with Andersen-Tawil Syndrome and other conditions caused by malfunctioning ion channels, could occur without having to alter the genetic sequence, Adams says, or even necessarily knowing which gene is affected.

"We already have drugs that are approved for human use that alter ion flux," says Adams. "Drugs like Prilosec, Nexium and other proton-pump inhibitors—they all target and change ion movement. Because we have targeted drugs, we already have ways to go in and prevent the problem." Such therapies, Levin says, would target the cells' electrical properties as the key control knob, which can be manipulated by many easily accessible ion channels.

Bioelectricity is also implicated in the development of cancer, says Adams. Cancer cells are too positively charged, compared with healthy cells, and some research has shown that restoring malignant cells' voltage through ion channel regulation tends to return them to a normal, nonmalignant state, she says.

The Adams and Levin labs are two of just a handful in the world studying bioelectricity in cells outside the nervous system. In earlier research, the two teams demonstrated that bioelectric signaling is involved in regulating gene expression and anatomical structure in a range of organs by dictating the fate of cells and tissues during development, regeneration and cancer suppression.

"We have been able to show that it's not just nerve cells that communicate electrically," Levin says. "As embryonic cells are cooperating to form structures like the brain, they exchange information electrically to figure out what pattern they're supposed to be making and whether the current pattern is correct or needs to be repaired or remodeled," he says.

"These bioelectric properties are just as important as biochemical signals," Adams says, "and in some ways are much easier targets for therapy than the genetics."

HOW TEETH COULD HELP SAVE EYESIGHT

Cells from dental pulp could be used to treat macular degeneration

BY DAVID LEVIN

MORE THAN 15 million Americans suffer from age-related macular degeneration. Over the course of months or years, lumps of cellular debris and new blood vessels can form in the retina, damaging tissue and causing progressive blindness—and in many cases, the effects of the disease are irreversible.

Researchers at Tufts are trying to improve those odds. They are exploring new ways to replace damaged retinal tissue using cells from an unlikely source: a patient's own dental pulp.

"[Dental] pulp cells and retinal cells share a common progenitor in the body," says stem cell biologist Behzad Gerami-Naini, an assistant professor at the School of Dental Medicine who is leading the research. "As an embryo develops, certain stem cells differentiate into retinal tissue, fat cells, bone cells or tooth pulp—so all those cell types are actually related on some level." Because the cells share the same origin, Gerami-Naini says, it may be possible to "reprogram" them in the lab, gently coaxing them into becoming retinal cells.

The key to this cellular transformation, he adds, lies in manipulating a set of genetic instructions that tell stem cells which genes

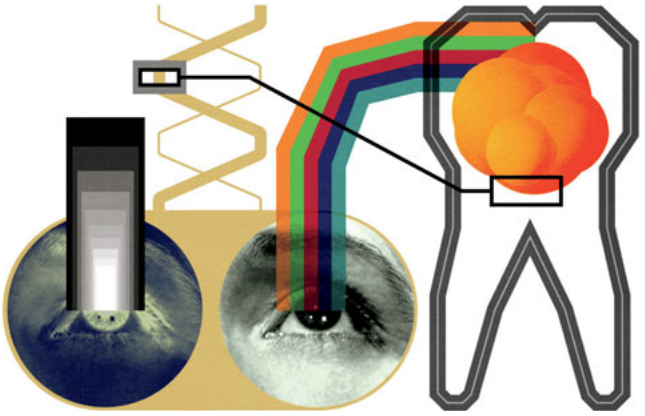


ILLUSTRATION: STUART BRADFORD

should be turned on or off at any given time. These instructions, called the "epigenome," effectively act like a series of molecular bookmarks, flagging snippets of DNA that contain the recipe to make a nerve cell, retina, tooth pulp or other specialized tissue. By rearranging those bookmarks, he says, it's possible to alter which "recipe" a cell uses to determine its final form.

Gerami-Naini is no stranger to working with stem cells in this way. His team has already shown that it's possible to "reboot" human skin cells, sending them back into an embryonic-like form, called an induced pluripotent stem cell (iPS), which has the potential to become any type of cell in the human body. Using iPS cells as a starting point, the team has been able to grow healthy retinal cells that theoretically could be implanted into the eye to repair damage from macular degeneration.

There's a catch. The iPS process, which Japanese researchers pioneered in 2006, normally uses a lab-made virus to inject new genes into a cell's DNA that erase existing genetic bookmarks. The use of such viruses can create stumbling blocks to approval from the FDA, because they have the potential to cause unpredictable changes to a cell's genetic code.

"There are still many safety concerns," says Benjamin Chan, D10, DG13, a clinical instructor of orthodontics at Tufts who is a collaborator on the research. "In order to perform clinical trials, you have to first show there won't be any [unintended] viral effects [to the genome]."

Dental pulp stem cells, however, may help avoid those complications. Instead of relying on viruses, the Tufts team believes it may be possible to manipulate the pulp cells' DNA—effectively forcing them to change their form—by using existing chemicals and growth media.

Creating virus-free cells is just one part of the challenge, however. "Treating macular degeneration isn't as simple as just injecting new retinal cells into the eye," says team collaborator Sheldon Rowan, a scientist in the Nutrition and Vision Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts. "The retina is a complex structure. Each cell has a specific orientation that needs to be maintained to keep the tissue healthy in the long run."

In order to create tissue that could be used for implantation, Rowan says, the research team first needs to grow its cells on a microscopic scaffold that mimics the underlying membrane of the retina. They're working with David Kaplan, director of Tufts' Tissue Engineering Resource Center, to build a series of tiny silk structures that recreate the weblike structure of the retina membrane. The researchers plan to grow their cells on these scaffolds to see whether they can generate a healthy piece of three-dimensional retinal tissue.

Gerami-Naini is quick to note that the research is still in the early stages, but the results look promising. If the team is successful, that could be good news for patients diagnosed with age-related macular degeneration, he says.

BUILDING AN ARTERY

3D models that mimic blood flow through tissues could lead to new medical devices

BY DAVID LEVIN

SQUISHY AND IMPERFECT

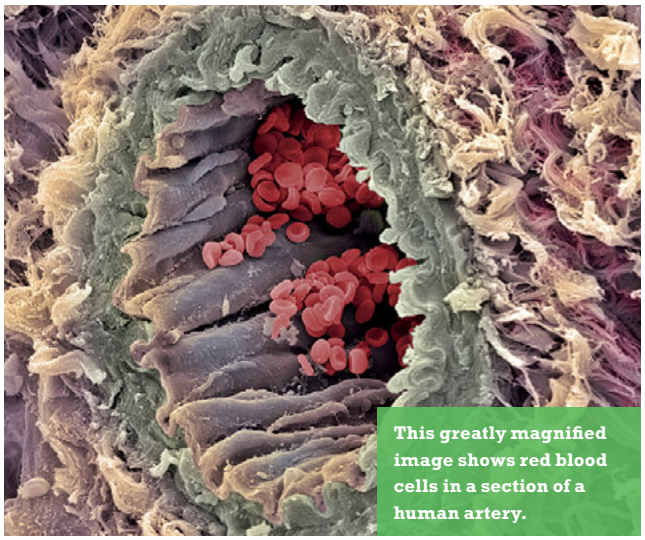
though it may be, the human body is a beautifully complex machine. Every movement, from lifting a finger to taking a step, relies on a broad array of biological levers, pulleys, cables and springs. And as with any other machine, the forces required to operate each part can be measured and quantified, at least in theory. In practice, however, gathering data on mechanics inside the body can be a huge challenge.

"Almost no information is available about blood flow in most arteries," says Erica Cherry Kemmerling, an assistant professor of mechanical engineering at Tufts.

She should know. Kemmerling studies the dynamics of fluids such as blood and air—yes, air counts as a fluid—inside the body. She's working to slowly reveal the exact ways those fluids behave in a living tissue, accumulating data that could be the key to developing new medical devices and procedures.

In the past, researchers used cadavers or lab animals to test new treatment ideas. Although that approach can be useful, says Kemmerling, it has its limitations. A cadaver, after all, isn't living, so its tissues gradually lose their elasticity. Using lab animals allows researchers to experiment on living tissue, but not living tissue that accurately reflects the inner workings of humans. In addition to these complications, there's another major issue that Kemmerling wants to avoid—the tissue in different animals or cadavers has slightly different properties, making controlled experiments a challenge.

In order to test treatments—and explore the dynamics of cardiovascular disease—in a controlled, repeatable manner, Kemmerling is building three-dimensional models of arteries and other structures. If she does her job just right, she says, she and other researchers might be able to use these simulations to get more accurate experimental data than would otherwise be possible, and simultaneously avoid the added costs and training required to work with animals and cadavers.



This greatly magnified image shows red blood cells in a section of a human artery.

With an understanding of the mechanical properties of human arteries, she adds, her team could design and 3D print a lifelike plastic model of an artery suffering from stenosis. They could then use the model to test different devices, such as stents, that help improve blood flow.

"We could optimize the design of it by trying a few different combinations of shapes and materials to test which one holds the artery open most effectively," she says. "You could never, never do that in a person. But a model that's a piece of plastic, who cares if you break it?"

It's a tantalizing idea. Testing devices on a lifelike replica of human tissue might help reduce the time and expense required to get approval from the FDA, the main regulating body for medical devices in the U.S. The practice could even have a major impact on the way new lifesaving treatments are developed. The main challenge Kemmerling faces is that the human body is inherently complex.

ENGINEERING BLOOD FLOW

Replicating the exact shape and surface features of a blood vessel can be tough—and finding materials to mimic its mechanical properties can be even tougher. In addition to developing plastics that mirror the strength and elasticity of a human artery, Kemmerling is trying to create fluids that approximate the behavior of blood itself.

Blood, she notes, is what's known as a "non-Newtonian fluid." Like ketchup or quicksand, its viscosity can change depending on the forces exerted upon it. It flows easily through blood vessels, but can change its properties, slow down and become more viscous as cells within it run into each other.

In the future, Kemmerling's team hopes to start using a specialized type of synthetic "blood"—a viscous mix of water, glycerin and microscopic particles of nylon—inside their 3D artery models to obtain even more detailed information about how blood moves inside a real human artery.

At the moment, their work takes place on a relatively small scale: Each model is less than a foot in length. But Kemmerling has a grander plan—she wants to scale up from small benchtop tests and build a working model of the entire human circulatory system.

That's no small task. There are billions of capillaries in the body—tiny tubes, less than 10 microns in diameter. "It'd be impossible to build all of those," she notes. "If you spent five minutes on each capillary, it'd take you years. I'm not planning on keeping my graduate students here that long." Instead, she says, her lab will find the ideal balance. They'll have to identify the minimum number of features they'll need to add to the model to get accurate data. They'll also have to determine which ones they can leave out to avoid unnecessary complexity.

It's an ongoing struggle, but one that Kemmerling relishes: "One of the beauties of engineering is that you can make something that will help people within your lifetime. You can watch it change the way health care works."

OUR NON-HUMAN DNA

Ancient fragments could advance understanding of how viruses evolved

SCIENTISTS AT THE medical schools at Tufts and the University of Michigan have found 19 new pieces of nonhuman DNA lurking between human genes, apparently from viruses that infected our ancestors hundreds of thousands of years ago.

One stretch of DNA, found in about 50 of the 2,500 people studied, contains an intact genetic recipe for an entire virus. That one might "allow us to study a viral epidemic that took place long ago," said Tufts virologist John Coffin, the senior author on the study that was published in the *Proceedings of the National Academy of Sciences*. The new research, he explained, "provides important information necessary for understanding how retroviruses and humans have evolved together."

Other studies have tried to link DNA sequences derived from a virus to cancer and other diseases, but their occurrence is rare. "This is a thrilling discovery," said co–first author Julia Wildschutte, who began the work as a Ph.D. student in Coffin's lab. "It will open up many doors to research."

PHOTO: SPL/SCIENCE SOURCE

always the new kid

My life as a minority of one has made me stronger and inspired me in ways I never could have imagined

BY ANTHONY KULUKULUALANI, '17
PHOTOGRAPH BY JOHN SOARES

THE WEATHER WAS FRIGID. SNOW FELL LIGHTLY ONTO THE windshield of the van as my dad sped down the highway to our new home. Strange music played softly over the car speakers as I gently tugged on my coat. I was just 7, and I hated this big puffy coat my mom made me wear. It was an unfamiliar garment, but at least it kept me warm.

We had moved from Hawaii to North Carolina because my dad was in the military. It was a change that shaped the trajectory of my life. As a Native Hawaiian raised in the South by a Hawaiian mother and African American father, my cultural identities were virtually unknown to those around me. I was a minority among minorities. Not only was it extremely rare to encounter a fellow Hawaiian here, but it was nearly impossible to meet someone with my distinctive background.

Memories of my home in Hawaii resurfaced as I got used to my new life in Fayetteville. Our temporary housing at the army base in this small, solemn military town was quite a contrast to the life I was accustomed to back in Honolulu. This made me miss my home even more. There, the chocolate melted in its box, exposing the macadamia nut. This traditional candy was my favorite on a hot summer day.

Back home, my grandmother would scrape together change to give to the young lady who sold her cosmetics. I never understood why, at the age of 60, my grandmother still needed these things. I decided to ask. Her reply was simple, "Because, Keoni, everyone here is family, and we need to help each other out when we can. That is what family does." My family calls me Keoni, Hawaiian for John, which is my middle name.

I anticipated that college might be an opportunity to make cultural connections in a diverse student body, but as an undergraduate at North Carolina State University, I was still the new kid on the block.

Recently, a close friend said to me, "You will always be an army of one," with that one referring to my cultural background. Since childhood, I have often found myself forced to assimilate to my surrounding communities, because I never can establish a group with a background similar to mine. As a kid, this was especially difficult to deal with. My new home didn't feel like home—the food was weird, the sudden changes in weather were bizarre, and the people talked funny.

I had to learn to adapt quickly. Despite obvious differences between myself and others, I can now find similarities so that I am able to better relate to people. This has helped me let go of that long-ingrained feeling of being different. My ability to relate to a diversity of people has encouraged me to develop my leadership skills. Since high school, I have pursued various leadership opportunities that have strengthened my communication skills, honed my capacity to work effectively in team settings, heightened my self-awareness and social awareness, and provided the motivation to continually improve myself.

As I have gotten older, I have continued to serve in leadership positions. I have taken on roles that continue to teach me how to integrate my cultures into the mainstream. Although persistently being the outsider was difficult to process as a child, I since have been able to use my background and personal experiences to my benefit by developing adaptive coping skills to help narrow that cultural distance that I so often felt as a young man.

ANTHONY KULUKULUALANI is the 2015-16 president of the Student National Medical Association, or SNMA, a 7,800-member organization that has represented the interests of minority medical students in the U.S. since 1964.

Anthony Kulukulualani, ’17

BY BRUCE MORGAN ILLUSTRATION BY DAVIDE BONAZZI

the Alzheimer's hope

First, neuroscientist Philip Haydon made himself an expert in a little-known area of brain science. Now he is testing a revolutionary new approach that shows great promise for the treatment of this dread modern disease.

A few years ago, I was out in Denver visiting my mother in her condo, sitting at the end of her couch in the living room, working through the day's newspaper. It was late afternoon. I noticed my mother, still in her bathrobe and seated beside my younger brother, Gary, in an adjacent kitchen area, perhaps 15 feet away. She was peering in my direction. "My," she said finally in a stage whisper to my brother, "our neighbor is being awfully quiet today." Gary, who was used to this sort of thing, corrected her. "That's not your neighbor," he told her quietly. "That's your son, Bruce."

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The excitement began on a small scale, with unexpected signals coming from a laboratory dish in the middle of Iowa. The dish held brain cells. Phil Haydon, a neuroscientist conducting research at Iowa State University in Ames, had killed off the neurons in the dish and left the glia—long considered by scientists to be little more than glorified packing material for the brain's all-powerful neuronal networks. He expected that the glia would fall silent along with the neurons.

But they did not. Instead, the glia kept emitting chemical signals. The year was 1994, and these signals were one half of a conversation that the world had never seen before. The glia, Haydon was shocked to discover, were not passive or inert, as they had been thought to be by medicine for more than a century. Rather, they were active participants of some kind in the brain's functioning. "We were off on one path in science, and there was an observation we could not explain," Haydon later told a Tufts audience. "Over the course of two or three months, we figured out what was going on, changed the direction of research in the lab 180 degrees and said, 'It's time to take a risk.' "

Those faint signals in the dish raised big, immediate questions. What was the precise nature of glial involvement, and what might the implications of their role be for optimal human health?

Some of Haydon's most promising work over the past decade concerns his quest to modify glia on the surface of the human brain to create a bold new treatment for the scourge of Alzheimer's disease, which afflicts one-third of Americans over age 85 and some 50 million people around the world. Haydon's revolutionary approach, derived from his expertise in a still-obscure area of brain science and—in stark contrast to all other comparable trails to date—already tested successfully on human subjects, may upend the Alzheimer's apple cart for good.

Haydon, who is now the Annetta and Gustav Grisard Professor and chair of neuroscience at Tufts School of Medicine, after seven years on faculty at the University of Pennsylvania, likes a good analogy as well as the next person. He says that when you picture the brain, imagine it as a dense bush with cables running through it. The cables are the neuronal system; the bush represents the glia, spidery filaments of connective tissue. Glia, meaning "glue," make up as much as 80 or 90 percent of the human brain by volume.

Neurons and glia "speak different languages," says Haydon, with the former brain components reliant on electrical and the latter on chemical signaling methods. They differ in other ways as well. Neurons need physical connections resembling a plug in a socket to function properly, whereas glia merely require being in the vicinity of their recipients to get their signals through. R. Douglas Fields, a senior investigator in neuroscience at NIH who wrote a 2011 book on glia called *The Other Brain: From Dementia to Schizophrenia, How New Discoveries About the Brain Are Revolutionizing Medicine and Science*, and has also collaborated with Haydon on a number of occasions in the relatively small field they share, likens the twin signaling methods to cell phones (glia) and land lines (neurons).

How exactly are the two systems talking to each other? This is an area where Haydon may know the answers better than anyone. "Phil's pioneering work has to do with glial influence on synapses," Fields told me, speaking in technical terms and leaving me a bit confused. "Imagine a car race," Haydon explained later, offering another analogy. "The cars [neurons] get all the attention, but the car needs a pit crew. That pit crew is the glia. They are tuning the brain for peak performance."

That's fine when all systems are working well—but what happens when they malfunction? Broken or frayed connections within the brain are now known to be significant contributing factors in a host of human ailments, including MS, epilepsy, depression, schizophrenia, ALS, and Parkinson's and Alzheimer's diseases, among others. Over the past 25 years, Haydon has been working to understand the role that glia play, not just in these ailments, but in normal, healthy human functioning as well.

Take sleep as one example. In 2009, Haydon and his team published the results of a study in the journal *Neuron* showing that glia are involved in creating sleepiness. To do this, they blocked the effects of glia in a group of sleep-deprived mice and found that these mice did not require as much catch-up sleep as expected, while retaining the full memory function of well-rested mice. "Glia are altering sleep," Haydon concluded.

Every brain function has its glial contributor, as

PHOTO: JAKE BELCHER

Phil Haydon

Haydon sees things. Talking with him on the subject can entail a sudden, dizzying drop into philosophy or cosmology or God knows what. "How is it that you can bring your thoughts to focus on a given task?" he inquires at one point, suggesting it may have to do with glia controlling the strength or weakness of signals at certain neuronal junctions. Then, a moment later, he muses aloud: "Some memories may be created in the glia."

THE LIMITATIONS ON WHAT GLIA MAY OR MAY NOT DO in the human brain are yet unknown—or, rather, in the process of becoming known. When asked to specify the nature of any substantive criticism that he has drawn from colleagues in his fast-emerging field, Haydon compares it to people disputing the color of the wall in his office. "Is that wall off-white, gray or beige?" he asks with an irritated wave of his hand. "That's the kind of argument we're having these days: Exactly how much control do the glia have in the system?"

In fact, many of the early reactions Haydon heard at professional gatherings were blunt and dismissive. "There is no way that glia do anything of importance," one colleague told him to his face. "What are you trying to do," another scientist asked Haydon rather plaintively, "make our understanding of the brain more complicated?"

The answer to that one was yes**.** A study that Haydon published in *Nature Neuroscience* in May 2010 showed that a reaction that occurs in glial cells in a variety of brain diseases such as epilepsy hinders their interaction with neurons, likely contributing to the cognition, learning and memory impairments that often accompany neurological dysfunction. Several decades ago, the problem likely would have been seen to be purely neuronal; now, with Haydon's series of findings, the problem is more precisely understood as a breakdown in glia-neuronal signaling, like a conversation between two people that all too suddenly fades away.

His field may be opening up more and more with each new discovery—and Haydon is quick to point out that there are known to be four main types of glia, with multiple subtypes waiting to be found, so the work is just beginning. But he concedes it has not been an easy professional path for anyone leading the charge. "Twenty or so years ago, it was not in vogue," Haydon observes. In fact, he admits he initially hesitated to submit any of his findings to established journals for fear of ridicule.

Fields, from NIH, explains that there was a self-reinforcing loop of obscurity at play in the 1990s that made general acceptance difficult: People hadn't heard of glia, so funding for glia research was hard to come by. Because there was no funding, little got published; because little was published, no one knew about glia, and so on. "This is what always happens in new fields of science," Fields says. "The new area becomes a backwater. But the field has been transformed lately as people are realizing that we had overlooked half the brain."

Even observers in a position to know weren't necessarily aware of this radical shift. Fields relates that when he submitted a general-interest feature on glia to *Scientific American* in 2004—where it ended up being the cover story for April that year—the editors called him and said, "This sounds interesting, but what is this 'glia' you talk about? " As Fields points out, "People didn't even know the word."

Over the past 10 or 15 years, glial research has quietly

caught fire, generating excitement, "especially among young people who want to come into an area that's unexplored," Fields suggests. As one example, Fikri Birey, a postdoctoral research fellow in psychiatry at Stanford Medical School, and a guy young enough to sport an earring, gave a 2013 TEDx talk—which remains available online—that crackled with impatience.

Birey began by reviewing the conventional medical understanding of the human brain. "Glia, 90 percent of your brain, was reduced to being bubble wrap, just lifeless glue holding neurons together, or an uninspiring scaffold to hold the evolutionary wonder that is neurons," he said near the start of his TED talk, an edge of sarcasm coloring those last six words. "But things are changing, and they're changing fast. Today we realize that age-old disorders of the brain such as ALS, Alzheimer's, MS, epilepsy, even brain cancers all have an imprint of glial dysfunction on them."

Alzheimer's presents a special case. In good health, the body produces protein fragments called amyloid that collect on the brain, where they are broken down and eliminated. However, the volume of amyloid produced in a person with Alzheimer's overwhelms the brain's regular maintenance system, with the result that protein fragments accumulate to form hard, insoluble plaques. These plaques block cell-to-cell signaling and often trigger damaging inflammation as well. With time, cognition—the ability to think clearly, function and make sense of the world—steadily declines.

Haydon's breakthrough came from a chance remark at a professional conference in 2008, when he heard a colleague say that he had identified a protein that caused certain glia cells to remove the brain's unwanted surface accumulations. This was a moment that Haydon was primed and ready for. He reasoned that if he stimulated the protein in question, it might help clear the excessive levels of amyloid plaque found in Alzheimer's. "What we did was realize we could recruit a natural process to our benefit," says Haydon. He promptly tested the idea on mice and found that it worked.

Haydon used a small molecule dubbed GC021109 that brought two simultaneous benefits: It sped up plaque removal from the brain's surface while also tamping down inflammation that hampered the ability of glia to function efficiently in their regular maintenance role. That was fine for the mice, but would the approach work on people, too?

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About 30 years ago, Mom was driving us through the high Rockies on twisting roads in good weather. We were looking for the highest local peak, a favorite of hers. We got stopped at one spot where a gang of mountain goats came clambering down a ledge-filled cliff and picked their way across the road in a waterfall of hooves and horns. Moments later, my mom and I descended the mountain through a sudden blinding snowstorm that's common at that altitude, a jagged rock wall on one side, a 1,000-foot drop on the other. Mom, hunched over the steering wheel, never flinching, said out of the side of her mouth, without turning her head, "We're having an adventure, kid."

I don't think I ever loved my mother more than right then; her comment was so much the way she lived her life.

On a subsequent visit, 15 years later, I caught a first glimpse of something new. We were tooling along a major highway on our way to lunch when she abruptly pulled off the road into the grid of a suburban neighborhood, made a few quick turns and stopped the car. We were facing a chain-link fence surrounding a small airport. We sat there a while. "Mom?" I said quietly. Her hands hadn't left the steering wheel. "What's this place?" she asked me in total confusion. "How do I get back on that road we were on?" Step by step—"OK, first back up the car, now go straight to the corner, turn the wheel left, now left again"—I led her around the block, tracing our return to the general flow of traffic.

COULD THIS SMALL, NONDESCRIPT PILL REALLY REPRESENT A MILESTONE ALONG THE ROAD TOWARD RELIEVING SO MUCH PERSONAL AND FAMILIAL AND SOCIETAL MISERY? IT'S POSSIBLE.

Bridging the gap between animal and human models has been the insurmountable obstacle for anyone pursuing a therapy for Alzheimer's, says Peter Reinhart, founding director of the Institute for Applied Life Sciences at UMass-Amherst. Formerly a tenured professor in neuroscience at Duke University Medical Center, Reinhart has held senior roles in research at pharmaceutical giants Pfizer and Wyeth and most recently served as chief scientific officer and head of corporate development and new products at Alzehon, a biotech company focused on brain health, memory and aging, and development of treatments for Alzheimer's disease and other neurodegenerative disorders.

Reinhart explains that the prevailing pharmaceutical approach has been to try to prevent amyloid plaque from forming and accruing on the brain in the first place—to head off what he calls, rather poetically for such a terrible process, "the amyloid cascade." Haydon, in contrast, wants to intervene once the amyloid has formed. "His approach has put him in a unique position," says Reinhart, who knows Haydon personally and has followed his career for some time.

The Proof of Concept Phase 1b clinical trial for Haydon's idea began in February 2015, and included 36 human patients with mild to moderate Alzheimer's disease. In the form of multiple increasing doses, the subjects each were given daily pills that resembled something you might come across in the multivitamin section of your local pharmacy. I've seen a sample, and the pill's modest size, oblong shape and light beige coloration left me feeling shortchanged. Could this small, nondescript pill really represent a milestone along the road toward relieving so much personal and familial and societal misery? It's possible.

After nearly a year, the results were in. According to the usual biomarkers' readout, patients with Alzheimer's disease saw rapid reversal of the amyloid cascade. "Although this was a small sample size, we are highly encouraged by the results," Haydon said, speaking for his research team, in the official press release last December 14. (Less formally, in our conversation a week or two later: "Lots of beer was consumed that night.") Reinhart considers the test results "extremely promising."

Levels of brain amyloid—readily determined through the amount of amyloid in a subject's cerebrospinal fluid—changed to a "statistically significant" degree, according to the statement from GliaCure, the privately held biotechnology company Haydon has formed and with which Tufts University holds exclusive licensing arrangements for the GC21109 compound and related technology. There's still some distance to go, of course. Haydon is busy raising funds for a Phase II trial of his Alzheimer's treatment that will involve 240 people and take two years. With any luck, he says, his company could have an Alzheimer's pill on the market by 2022-23.

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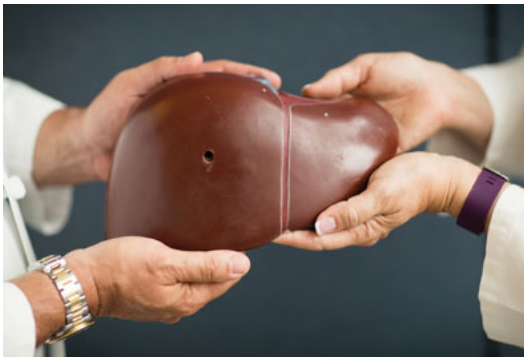
Once, when I was little, my mother, brother and I spent an afternoon on the eastern shore of Lake Michigan. The sand dunes were bigger than I had ever seen. My older brother, Craig, and I had to go up them as soon as the family car came to a stop in the parking lot, and we did, eagerly climbing, pawing with our hands as the sand gave way under us. At the top of the dune, I turned—Craig already having raced ahead to where he disappeared over a rise—and glanced back down. My mother was a small, distant figure, waving up at me. Then I turned again, back toward the lake, took one grainy, sinking step, and she was gone.

Wind off the dark lake blew over me atop the dunes. I couldn't see anyone; it was just me, I was 7 or 8 years old, and the wind was in my face, and all at once I felt like crying. Years later, my mother told me she had felt it, too, the immense, piercing loneliness of the place. "When I couldn't see you, that was as frightened as I've ever been," she said with a small shudder.

Now she has gone over the lip of her own personal, late-life dune, reached the crest and taken one step more, the known world, cloaked in wind and sky, falling off behind her.

BRUCE MORGAN is the editor of this magazine.



THE GIFT

BY BRUCE MORGAN PHOTOGRAPHS BY KATHLEEN DOOHER

Over the past 30 years, the live-donor liver transplant program at Lahey Hospital & Medical Center has treated more patients than any comparable program in the country. One of those patients had his life saved thanks to a donation by his son, a Tufts medical student. Here, in their own words, is the story of that experience.

Scott Linscott and Josh Linscott, '18

Not many people will ever need a liver transplant, but for those who do, the live-donor option may save their life. That's what happened in May 2012, when Joshua Linscott, '18, gave part of his liver to his father, Scott. Performing that transplant were Elizabeth Pomfret, a professor of surgery at Tufts Medical School and chair of the Department of Transplantation at the Tufts-affiliated Lahey, and her husband, James Pomposelli, an associate professor of surgery at Tufts. What follows has been edited and condensed for clarity.

SCOTT LINSCOTT: I'm 52 years old and live in Westbrook, Maine. I'm a photographer, and now also minister of a church. Back in 2005, I had a gallbladder surgery. Also at that point I was morbidly obese, almost 320 pounds. During that procedure, they saw that my liver was pitted and showing some scarring. The diagnosis was fatty liver disease.

The doctor said we needed to start monitoring it, because it could end up that one day I would need a transplant. Over the next six years, I would have annual checkups where they would either do an endoscopy or an ultrasound. Nothing really changed. In 2009, I changed my lifestyle and started losing weight. By 2011, I was feeling good. I was able to ride my bike 15 and 25 miles at a time and was down to about 245 pounds. That's when some other complications started rearing their head, and my liver was clearly going downhill.

JOSH LINSCOTT, '18, SCOTT'S SON: At first it was a "He may need a transplant" type of thing. But as he continued to decline, I became more and more worried—first, about whether he might become too sick to do the transplant, and then if we would have everything lined up in time to be able to take care of him before things were kind of too late.

In May 2011, it was determined that Scott Linscott would need a liver transplant.

SCOTT: Josh volunteered to donate his liver immediately. They had nine people who volunteered to go through the whole testing process to be a donor, but we never had to go any further than Josh, because he was a perfect match.

JOSH: When I got the call from my mom saying that he needed a transplant, I just knew it was going to be me.

SCOTT: Josh and I have always been close, from my coaching him through all the levels of baseball, and driving him to gigs when they had a band, and doing all that stuff.

ELIZABETH POMFRET, PROFESSOR OF SURGERY AT TUFTS AND CHAIR OF THE DEPARTMENT OF TRANSPLANTATION AT LAHEY: The first successful living donor liver transplant happened in 1989 at the University of Chicago. It used to be that you needed a whole liver from somebody who had died. But Christoph Broelch, the man I'm shown with in that photo [she points to a framed image on the wall], took this smaller part of a mother's liver and transplanted that into her baby daughter. About 60 percent of the time in a live-liver donation, the patient and the donor are related, and the most common relationship is child to parent. Anyway, that girl has since graduated high school, college, and I think she's engaged to be married.

The liver is unique because it regenerates. It's one of the only organs where you can take a piece of it that functions like the whole. I mean, that's extraordinary—you can't do that with a kidney, for example. So the diseased liver comes out entirely, and you replace it with just a portion of a liver. For a baby, you take a very small amount, typically about 20 percent of a donor's liver. You need a lot more for an adult recipient—typically about 60 percent if you're a larger person, and if you're smaller in size, a 40-percent portion would be OK.

When it comes to live-liver donations, the risks are bigger than with kidneys, and the recovery is longer. With a kidney donor, you've got two kidneys and you're taking one out, and you're not likely to damage the other kidney because it's on the total opposite side of the body. With a liver, you've got one liver that you need to split. There's a significant chance that you could damage the part that's staying there.

JAMES POMPOSELLI, ASSOCIATE PROFESSOR OF SURGERY AT TUFTS AND ELIZABETH POMFRET'S HUSBAND: It's a much bloodier operation. The liver is very vascularized, so you can bleed more. A live-liver transplant is one of the more technically challenging operations done anywhere.

POMFRET: Which is why there are only a few places that do it. Imagine the liver as your body's manufacturing plant. That's where all your proteins are made, all your clotting factors. Everything gets detoxified there. That's its job, so when you do something like this—for the donor, taking 60 percent of your liver means acutely dropping your liver function by 60 percent—you put a huge demand on the part that's remaining.

When you're transplanting, that new liver has to kick into gear and start working, and you need to control

Transplant surgeons
Elizabeth Pomfret and
James Pomposelli

it from rejecting when the body realizes it's not the liver you were born with. It's very complicated. But one of the biggest benefits of live-donor liver transplants is that you significantly reduce death on the waiting list. A person who is able to have a live-donor transplant has about 25 percent less chance of dying while waiting for a transplant. That's because, with a deceased-donor transplant, the patient typically has to get sick enough to reach the top of the waiting list. With a living donor, though, you time the transplant to get the person in the best shape possible. In other words, you're starting with a healthier person.

Because of his father's illness, Josh Linscott ended up changing careers.

I remember toward the end of April 2012, Josh called me and said, "Dad, what are you doing next Monday?" I said, "I don't know, just lying on the couch, dying," and he said, "No, we're having our transplant."

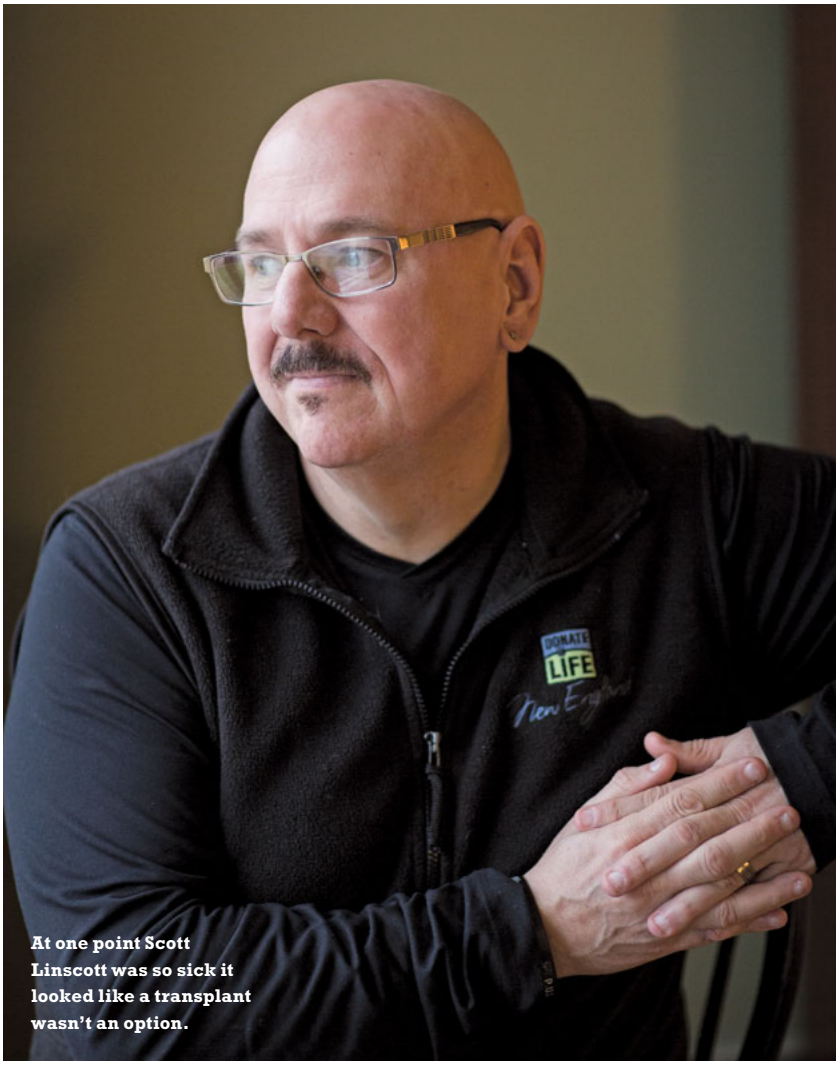
SCOTT: They want to transplant you at a MELD [Model for End-Stage Liver Disease] score of 20 to 22—the lower the better—while you're still healthy, and your recovery tends to be much better. But by the time we hit March of 2012, I was too sick for a live donor. I had a MELD score of 36. I was that sick.

When your liver starts to fail, all your other systems start to fail. They're all connected. So I was having issues with fluid leaking into my lungs so I couldn't breathe. I was having to have my lung cavities drained fairly regularly. I was having to have fluid drained out of my abdomen. I was having issues with cramping and muscle wasting. I was in a mobility chair—one of those scooters. That's when I was taken off the transplant list, for that little blip of time. They're not going to put another liver in you when you're too sick to recover. Especially from a live donor, when you're getting 55 or 60 percent of the donor's liver. You have to be healthy enough to grow that other half of a liver in order to survive. If you're not strong enough, they're not gonna go with a live donor for you. They're going to say, "You're too weak, you need a cadaver donor, you need a full liver, because your body's not going to have the energy or the ability to recover and to grow another half of a liver."

That was the only time in the process that my wife, Robin, lost hope. That's what really turned up the urgency with Josh. He started calling Lahey and saying, "Listen, when can we get this thing done? I'm ready." He was in the Ph.D. program [in pharmacological research] at Weill/Cornell in Manhattan, and they were ready to let him go at any point, give him the time off. It was a nephrologist up here in Maine who, after consulting with Lahey, got me on a medication that regulated my adrenal gland, helped my

kidneys balance the sodium and cleared the infection. That was when my MELD score dropped down to a 27 or 28, which put us in the range of being able to have a live donor again.

I remember toward the end of April 2012, Josh called me and said, "Dad, what are you doing next Monday?" I said, "I don't know, just lying on the couch, dying," and he said, "No, we're having our transplant."



At one point Scott Linscott was so sick it looked like a transplant wasn't an option.

POMFRET: Where the live-donor liver field has peaked is in Asia, because most of Asia believes that taking anything out of your body means you won't be able to go to the afterlife. You have to go as a whole person. Consequently, it was against the law in Asia to do a donor surgery using brain-dead donors.

POMPOSELLI: In this country, however, we depend on brain-dead donors. When people die and the heart stops, you can't get organs out of those people. There are millions of people who die every year, but only about 8,000 people a year die in the U.S. in a way that you can use their organs. They have to be brain-dead. A typical donor whose organs we can use might have had a gunshot wound to the head, or maybe a stroke. So the heart is beating, but the brain is dead.

POMFRET: Asians were really the ones who expanded living donation. They did the first adult-to-adult operations. Hepatitis B and hepatitis C are rampant in that area of the world, so they have a huge amount of liver disease, and they don't have cadaveric donation. So either they were going to make something work with live people, or all these people who needed donations were just going to die. India is a place that's exploding with live-donor transplants.

POMPOSELLI: In China, it's the same thing.

POMFRET: The whole U.S. experience is extremely small in comparison. In Korea, they're doing about 300 people per year. Our program has done 300 total. So the East/West picture is very different. I just finished a term as president of the International Liver Transplantation Society, because our reputation in the world is that we at Lahey clearly have the largest volume for the West.

POMPOSELLI: Immunologically, a live-liver transplant is relatively easy to deal with. A kidney transplant is technically a much easier operation, but immunologically more difficult; the liver is more forgiving.

POMFRET: The risk associated with liver donation is directly related to how much liver you take out of the person: the smaller the amount of liver tissue, the less risk, and the more likely they'll be back to normal quickly. How can we take the smallest amount of liver tissue from this donor and have it be sufficient for that recipient? Another important thing we have to determine for the donor is, can we physically divide their liver in two without harming the part that's staying, and is that enough for the needs of the recipient? And then, do we have all of the correct "plumbing" to be able to take the donor's liver and hook it into the recipient?

To determine all of that, we take a CT scan here and send it electronically to Bremen, Germany, where a group of mathematicians and radiologists has come up with software that makes 3-D models of the liver for us. Then I

can know, OK, this is where we want to divide the liver. And when I ask, "How much liver tissue is that?" they can tell me, for example, "This amount of liver is 183 grams of liver tissue."

POMPOSELLI: Once we're ready to begin the transfer procedure, Liz usually starts with the donor first. I usually wait at least an hour.

POMFRET: There are two staff surgeons. There's also a fellow who's already finished residency. There's usually a resident in the room. There's a scrub nurse and a circulator. Two anesthesiologists. A pump tech. There are probably a dozen people.

POMPOSELLI: We try to time the procedure so that the diseased liver is about to come out when the donor liver is about to come out, so there's no wasted time. Once we're ready, Liz will take the donor liver out; we'll flush it with preservative solution, and bring it over to the recipient room. There we'll take *that* liver out and put the new one in. The donor liver is out of the body for only about an hour, which is another advantage to live donation, because the amount of time the liver is out of the body influences outcomes. With a liver, you can go up to nine or 10 hours, but after that you start getting nervous.

Pomfret and Pomposelli performed Scott's transplant in May 2012.

SCOTT: On the day of my transplant I remember them giving me something to calm me down before the surgery—that's about it. Afterward, I was in the hospital for two weeks, trying to get all my systems working. I was weak. I remember the first time standing next to my bed, and it was a great victory to stand for 30 seconds. Then they're trying to move you to sit in a chair. And being able to sit in that chair—you can only take it for 10 minutes because it hurts too much.

You're going through a reboot, and the pain was beyond anything I had ever experienced. I think it was Dr. Pomposelli who told me, "You've not only been hit by a truck, but the truck backed up and ran over you again. You're gonna hurt for a while." But my wife says that I told her, "This hurts, but for the first time since I can remember, I don't feel sick." I felt different right away, and people remarked that my color was different and that my eyes seemed clearer.

JOSH: My own recovery was fairly rapid and not too complicated. When I did the donation, I was 24 and really healthy. I had been working out and was going into the hospital in good shape. A week later, I could tie my own shoes—which didn't seem like anything to me, but the team kept saying, "Wow, look at how well you're doing!"

SCOTT: I try to mark each anniversary with some accomplishment, so this year, the three-year anniversary, I did the Trek Across Maine, which is a 180-mile bike ride in three days. I got up on my bike as quick as I could after the surgery and started riding. Four-and-a-half months after transplant, I did a 10-mile ride for cancer. Second year, my goal was a 50-mile ride in one day and 100 miles in a week, and I accomplished that goal.

JOSH: Life is going very well, which both my dad and I are blessed to say. Around the same time I was preparing for the transplant, I ended up talking to a woman who is now my wife. We were becoming friends, and I was going through this whole process with my dad. She and I talked more and more, getting closer, and really hit it off.

SCOTT: It's kind of funny, because Josh went to college saying he was going to be a doctor. Then, while he was an undergrad, he talked to doctors who said, "Nah, you don't really want to do that—you won't have a family life." So instead, Josh went into chemistry and got his Ph.D. in pharmacological research. While we went through the transplant together, he says it became clear to him that he had to be a doctor. Because he was lying there in his room, and with Lahey being a teaching hospital, the Tufts students would come and he'd hear them outside his room talking about cases, and then one or two each day would get to come into the room with the doctor. Josh said to himself at that point, "No, this is what I've always wanted to do. This is what I'm going to do."

JOSH: I think my dad's heard me tell that story several times, but it really was like that.

SCOTT: So he accelerated his Ph.D., and now he's in the Tufts medical program, and got accepted into the Maine Track, which means that he and his wife could move back here to Maine, which we were thrilled about. This summer we renovated our basement into an apartment for Josh and his wife. Now we have Josh and his wife, Kristin, living in an apartment in our house, and they just had their first baby nine days ago, so we've got our grandson, Calvin, here.

JOSH: So in going through the transplant, I ended up changing careers, finding a wife, getting to come back to Maine, which was my home, and having a son. It's really worked out a lot better than you would ever imagine having end-stage liver disease would lead you to. It couldn't have ended any better.

BRUCE MORGAN, the editor of this magazine, can be reached at bruce.morgan@tufts.edu.

From All Corners

UNIVERSITY, SCHOOL & ALUMNI NEWS

HUMBLE START

OUR MEDICAL SCHOOL opened in fall 1893 on Boston's Boylston Street in the building shown here with lettering on its side. A brief account written in 1908 by Charles Thayer, the school's first professor of anatomy and one of its seven founders, recalled "the paucity of our equipment, the stained platform, the uncomfortable straight-backed chairs and the beggarly array of apparatus" that nonetheless made possible "a School, the growth and success of which is without parallel in the history of medical education."

PHOTO: COURTESY OF TUFTS DIGITAL COLLECTIONS AND ARCHIVES

Police sergeant Jeremiah Nicastro drives through a cemetery in Gloucester, Massachusetts, where a relative who died of a heroin overdose is buried.

Assault on the Opioid Crisis

Massachusetts medical schools confront a growing public health problem

BY BRUCE MORGAN

WHEN IT COMES to opioid use in Massachusetts, things are bad and getting worse, says epidemiologist Thomas Stopka, an assistant professor of public health and community medicine at Tufts. Deadly drug use that might once have been associated with poverty and crime has changed over the past decade and now touches just about everyone. "More and more, rural, suburban and younger populations are falling prey to it," he says. "We're seeing it everywhere now."

In response to the changing landscape, Tufts is part of a concerted effort launched by Massachusetts Gov. Charlie Baker aimed at unifying the state's four medical schools in curricular reform to ensure that newly minted physicians are prepared to meet the growing challenge of patients and communities afflicted by opioid addiction.

The Medical Education Working Group on Prescription Drug Misuse, as the collaborative effort is called, has worked with the Massachusetts Medical Society and the Massachusetts Department of Public Health to develop a series of "core competencies" that each of the state's 3,000 medical students should acquire during their training. The idea is to unify standards in a state that saw 1,173 opioid-related deaths in 2014, the most recent statistic.

Of the four medical schools—the University of Massachusetts, Boston University, Harvard and Tufts—only Tufts had a course on addiction medicine already in place. Associate Professor Emmanuel Pothos has taught the course to first-year students for more than a decade now.

Opioid addiction in Massachusetts has grown along two main paths: people seeking to relieve chronic pain who become addicted to opioids such as Oxycontin, and others who use the drugs for recreation or self-medication.

Heroin has gotten both cheaper and easier to find than it used to be, worsening the situation, says Stopka.

Rebecca Lee, '16, is among the students gratified to see the curriculum changes happening. She has been involved in serving Boston's homeless population over the past few years, and now her concern has extended more generally to advocacy work on addiction medicine, including better instruction and more exposure to the issue of opioid addiction among students in the state's medical schools.

"I'm also working with Dr. Pothos, who heads the addiction medicine course at Tufts, to try and integrate a naloxone-training session for all first-year medical students into the curriculum," she says. Naloxone is a drug used to reverse the effects of opioids, especially in cases of overdose.

Scott Epstein, '84, dean for educational affairs, describes the spirit of the state's opioid initiative as truly

PHOTO: JOHN MOORE/GETTY IMAGES

collaborative. Beginning late last summer, representatives from the four medical schools have met repeatedly, with as many as 25 people in attendance at each session. Each school will be free to adjust its curriculum in its own way, with all proposed changes set to take effect by September 2016. Meetings will continue on a regular basis "so that we can learn from each other," says Epstein. Collectively, the schools will assess the impact of their new programs.

Tufts School of Medicine will approach the new challenge in two ways, Epstein says—by determining where the topic of opioid misuse might best be integrated into the existing curriculum, and in the longer term, by tracking how appropriate skills are being cultivated among students throughout the four years of medical school.

Internal support for the opioid emphasis is widespread. The medical school's curriculum committee, consisting of 32 faculty members and 16 students, unanimously approved adoption of 10 "core competencies" related to opioid use at its meeting last November.

Epstein says that the Core Collaborators Committee—a group of the six core clerkship directors in the disciplines of family medicine, medicine, obstetrics-gynecology, pediatrics, psychiatry and surgery—will have one or more of the competencies in place by May.

How successful can any curricular efforts be in addressing something as complex as the state's opioid crisis? Even Epstein, with all his time spent in meetings and his evident commitment to the cause, grants that it's hard for any individual school to "move the dial" on a problem like this. The medical school, which graduates about 200 doctors each year, sees fewer than half of them go on to do their residency training in Massachusetts, he notes.

Stopka, the epidemiologist, takes a long-range perspective. "We have to approach the problem from multiple angles and with multiple tools," he says.

CAREER BOOSTERS

PHILIP ELIADES, '16, was on his surgery rotation when the organ transplant team was called into action. He was with them when they rushed to a local hospital to harvest a liver. He was in the operating room when the team paused for a moment of silence before the donor's heart was stopped—and he remembered his own experience as a transplant patient.

In that moment, Eliades was no longer a medical student, but once again a gravely ill 18-year-old whose liver had shut down after being attacked by his immune system. "I could picture my own donor being in a similar situation years earlier," he says. "It was an emotional experience seeing just how my donor had given me the gift of life."

Eliades has made every minute of that gift matter. After completing a premed track at Boston College, he entered Tufts School of Medicine thinking he'd become a surgeon. Instead, he plans on a career in dermatology. It is an unexpected twist on his boyhood dream, but a logical one nonetheless. Turns out immunosuppressant drugs used to prevent organ rejection can increase the risk of skin cancer in transplant survivors.

Intrigued by that connection, he plans to focus part of his career on the nascent field of transplant dermatology and contribute to a better understanding of treating skin cancer in transplant recipients.

Eliades is one of 17 medical students whose careers have received a boost from the Fund for Tufts Medicine Scholarship. Each of them received a partial-tuition scholarship of up to $15,000.

The scholarship was launched a year ago when Willard Dere, a member of the school's board of advisors, and his wife, Julie, both M12P, pledged to make a $50,000 gift to the fund if 500 gifts of any amount were made before June 30, 2015. Alumni, parents and friends surpassed that challenge: 543 gifts. Those contributions, combined with the Deres' pledge, totaled $261,277— a 30-percent increase in annual fund financial aid gifts over the previous year.

"We are deeply grateful to everyone who recognized our effort to support our extraordinary students," says Dean Harris Berman. "Financial aid is a top priority for the School of Medicine, as it is across the university, and we are constantly striving to grow our resources for scholarships. The positive response to the challenge raises hopes that even more remarkable students will be supported through this fund in the future."

Another of those students is **DAVIES AGYEKUM, '17.** Born in Ghana, he moved to Atlanta when he was 11. He decided in high school that he wanted to be a scientist, and went on to earn a Ph.D. in molecular medicine at the Medical College of Georgia.

Agyekum plans on becoming an anethesiologist and has an interest in studying the physiology of sedation and how it relates to our understanding of pain. He says he could not have considered medical school without the Fund for Tufts Medicine Scholarship. "I am both humbled and inspired by those who helped make possible the pursuit of my life ambition." **-LAURA FERGUSON**

PHOTOS: ALONSO NICHOLS; SHAMIT STHANKIYA

Converging on Breast Cancer

Tufts laboratory brings together biologists, chemists and mathematicians to advance our understanding of disease

BY MICHAEL BLANDING

THE LAST DECADE has seen an explosion of new technology in the biological sciences. High-throughput genomics and advanced techniques for sequencing proteins and small molecules have expanded knowledge more than ever before—but they've come with their own problems.

"That explosion has led to massive quantities of data being collected," says Charlotte Kuperwasser, an associate professor of developmental, molecular and chemical biology at the medical school. "As biologists, we are not trained in knowing what to do with all of that data." Since these technologies were developed by engineers, chemists and mathematicians, it's more essential than ever that biologists look beyond the boundaries of their field to deal with the petabytes of data that have emerged.

"We are trying to understand more complex and deeper questions than we were ever able to think about before," says Kuperwasser, who has devoted her career to researching the causes of and potential cures for breast cancer. "That's why collaborations will be essential for the next wave of insight in understanding and treating disease."

Kuperwasser has taken a giant leap forward in creating those collaborations as director of the Raymond and Beverly Sackler Convergence Laboratory, a new effort by researchers at Tufts and other area institutions to pool knowledge, resources and techniques in the treatment of disease. The lab, which launched last year, is concentrating initially on breast cancer research, but its aims are much more ambitious and include tackling other devastating diseases.

Charlotte Kuperwasser heads up a research effort that involves multiple disciplines, but requires a willingness to share in an open exchange of ideas.

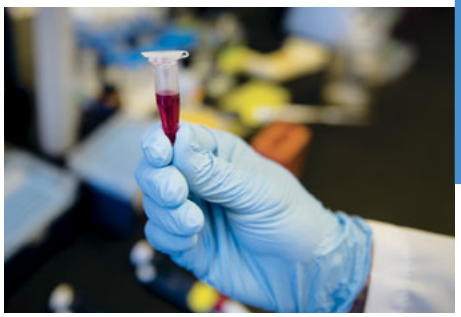
Unlike many breast cancer biologists, Kuperwasser has focused her research not only on the later stages of metastasis, but also on the early events during development of healthy breasts, looking to find those elusive clues that may forecast whether cancer will develop in the future. "I think of cancer as a problem of tissue development and regeneration gone awry," she says.

That perspective makes her ideally poised to take advantage of the vast amounts of biological data that have been generated in the field. One of the scientists Kuperwasser has invited to join the lab is Andrew Beck, a bioinformatician at Harvard Medical School who directs a research laboratory at Beth Israel Deaconess Medical Center in Boston.

Beck has applied computational image analysis to thousands of images obtained from breast biopsies in order to try and tease out precursors of abnormal development. His analysis examines several thousand data points on each slide—everything from the size of a nucleus in a cell to the amount of fat in tissues. "The goal," says Kuperwasser, "is to see whether we can tweak his algorithm to segregate what looks like normal breast tissue into high-risk and low-risk categories for cancer."

PHOTO: ALONSO NICHOLS

In addition to looking at breast tissue in a wide array of patients, Beck is working on examining breast tissue from women identified as having a mutation of the BRCA1 or BRCA2 genes. Research by Kuperwasser and others has shown that the mutation puts women at increased risk for cancer. "We want to see if we can use the computer in a data-driven way to uncover the morphologic and phenotypical changes that may not be visible to the naked eye," Beck says.



MATHEMATICAL LIBERATION

By collaborating on these approaches, says Kuperwasser, the researchers are able to achieve a finer-grade analysis than scientists from any one discipline would have been able to achieve independently.

"The mathematical mind is liberated to a certain extent from the constraints of the biologist," she says. "[Mathematicians] can examine a problem from a purely logical, unbiased approach," she notes. "I am very impressed at how [Andrew Beck] is able to apply computational approaches and computer coding to use a microscope—a tool biologists have been using for centuries—to discover things we haven't been able to see before."

In addition to Beck, the Sackler Convergence Lab team includes researchers from institutions as near as Harvard and MIT and as far away as the University of North Carolina and Arizona State University, as well as two Tufts faculty: David Kaplan, the Stern Family Professor of Engineering and chair of biomedical engineering, and chemistry professor Joshua Kritzer. While all of them are experts in their respective fields, Kuperwasser says she also chose them with specific personality traits in mind.

"We are all open and thoughtful and not hypercompetitive with one another," she says. Those factors are key in having the kind of freewheeling discussions that can lead to productive collaborations, she says. "As director, I am not dictating to the group what we are going to work on; it's about what the interests of the group are and then finding synergy. It may take longer that way, but at the end of the day, we will have something we can pursue with more energy and vigor."

"Collaborations will be essential for the next wave of insight in understanding and treating disease."

Kaplan, whose lab specializes in creating three-dimensional human tissue systems in vitro, has already started working to recreate human breast tissue that could be used by other collaborators in the lab in place of mouse or other animal models. "The collaboration forces people to portion out some time and have very informal and thoughtful discussions, and that's a good thing," he says.

The work cuts both ways—the scientists also end up helping their colleagues in the lab deepen their own research so that it becomes more applicable to real-world problems. Kritzer's lab, for example, focuses on synthetic chemistry, creating molecules out of tiny snippets of proteins in order to target proteins in the body that are "undruggable" by conventional FDA-approved treatments.

"Working with biological collaborators has given me the opportunity that when I find something that works well in the dish, I can put it in mice or rats or other animal models," Kritzer says. The experience of collaborating with Kuperwasser and others has also turned Kritzer on to an entirely new application for his molecules: using them diagnostically to identify breast cancer risk in tissues. "As a chemist, I am so focused on chemicals going in and changing a system, I never thought about my molecules being used just as a sensor," he says.

By taking time to explore with one another and push each other to new insights, the researchers in the Sackler Convergence Lab represent the best aspects of collaboration, where the resulting breakthroughs are much more than the sum of their parts. Kuperwasser hopes that within the next five to 10 years, the researchers will crystallize an understanding of exactly what happens in healthy breast tissue to turn it malignant. "I'd like to be able to define in a specific and concrete manner what takes place in a human breast that poises it to develop cancer," she says.

As a result of early successes in the lab, Kuperwasser envisions expanding into an institute that would bring these innovative techniques to bear on the diagnosis and treatment of a number of cancers and other diseases—setting an example for the future of biological research, where looking outside the discipline to collaborate in analyzing vast amounts of data would not be an anomaly, but the norm.

MICHAEL BLANDING is a Boston-based freelance writer.

"We're going to understand how cells and tissues decide what shape they're supposed to build," says Michael Levin.

$10 Million Life Sciences Investment

Biologist Michael Levin will lead one of two new Allen Discovery Centers in the nation

BY JACQUELINE MITCHELL

TUFTS UNIVERSITY HAS received a $10 million grant, one of only two in the nation given by Microsoft co-founder Paul G. Allen to fund research at the frontier of the life sciences.

Tufts developmental biologist Michael Levin, whose groundbreaking work on the bioelectrical control of development and regeneration could lead to medical breakthroughs in areas such as birth defects, cancer, traumatic injury and degenerative diseases, will lead one of two Allen Discovery Centers—the other is at Stanford University.

The Allen Discovery Center at Tufts University for Reading and Writing the Morphogenetic Code will focus on the role bioelectrical signaling plays in orchestrating how cells communicate to create and repair complex anatomical shapes—an area of inquiry that Levin says is "the key to most problems in biomedicine."

The ability of cell networks to process information and make group decisions is implemented by bioelectrical, chemical and other signals. Errors in this process can give rise to birth defects and cancer. By learning the bioelectrical language that cells use to coordinate their activity toward correct organ shape and placement, researchers will get closer to the control of growth and form in a wide range of applications.

"We're going to understand how cells and tissues decide what shape they're supposed to build, how they figure out what to do in order to make that shape, and how they know when they've achieved that shape and can stop growth," says Levin, A92, the Vannevar Bush Professor in the Department of Biology and director of the Tufts Center for Regenerative and Developmental Biology.

It's been known for a long time that cells in the nervous system relay electrical signals throughout the body via rapid changes in voltage. But in their groundbreaking research, Levin and his colleagues demonstrated that similar communication by many different cell types in the body underlies pattern formation—that is, the complex organization of cells and tissues during embryonic development. They showed that such communication is key to maintaining and fixing cellular and tissue organization in adulthood as well.

Levin's lab is trying to determine how bioelectric communication among cells can be controlled to potentially prevent or reverse birth defects, injury, cancer and even aging (see "Electrical Signaling in Cells, " page 8).

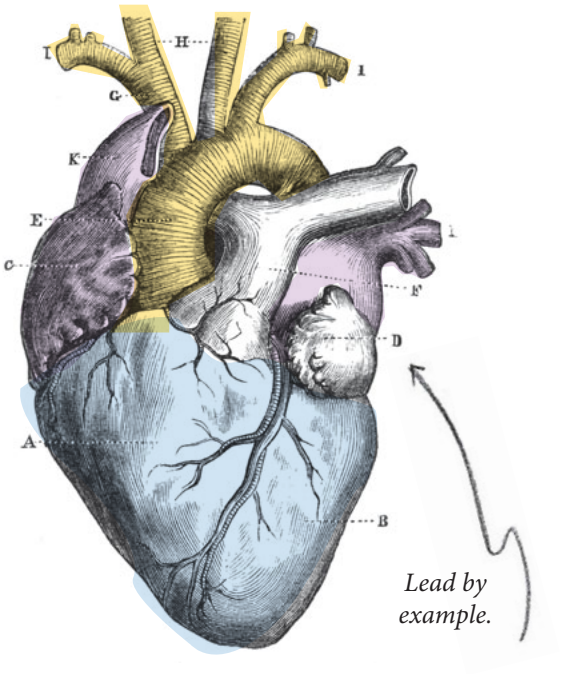
Among their most recent findings, Levin and his team prevented tumors from forming and reversed malignancies after they developed by using light to control electrical signaling among cells.

Levin says the Allen Discovery Center at Tufts will allow him to invest in the people and tools needed to make more breakthroughs in this emerging field.

The Allen Center will likely be a game changer for the life sciences at Tufts. "We expect this center to drive a fundamental change in how we investigate, teach and learn the quantitative biological sciences, and how we extend that knowledge," says President Anthony P. Monaco, who also holds faculty appointments in biology and neuroscience.

The centers at Tufts and Stanford each will receive up to $30 million over the next eight years.

PHOTO: ALONSO NICHOLS



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OUR BASIS OF STRENGTH

Board of advisors' chair hopes to advance translational medicine

ROBERT TEPPER APPROACHES medicine with the compassion of a caregiver, the curiosity of a scientist and the enthusiasm of an entrepreneur. After years heading research and development at Millennium Pharmaceuticals, Tepper cofounded Third Rock Ventures with two colleagues who shared his passion for disruptive technologies that hold promise for the future of medicine. Tufts Medical Center honored Tepper and his cofounders with the Ellen M. Zane Award for Visionary Leadership in March 2015.

Following a decade on the board of advisors to the School of Medicine and the Sackler School of Graduate Biomedical Sciences, Tepper became chair of the board a year ago. He earned his medical degree from Harvard and is an adjunct faculty member there and at Massachusetts General Hospital. He is married to psychiatrist M. Lynn Buttolph, J74.

Tepper spoke with *Tufts Medicine* about his guiding vision for the medical school.

What drew you to get involved in the board of advisors, and what keeps you interested?
Initially, I became interested in joining the board through my longtime colleague, the former dean, Mike Rosenblatt. He and I had taught together at MGH and Harvard, and I was struck by his vision for Tufts. I also got to know Harris Berman quite well and enjoyed his passion for leadership and particularly his affinity for developing medical students into fine physicians.

Through your work you are connected to many different medical schools and other academic institutions. What differentiates Tufts Medical School from its peers?
There are several things. One is the close-knit relationship between faculty and students. You can appreciate that by walking the halls and talking with the students. I've also been struck by the interactions between students. There's a very communal atmosphere.

What do you hope to accomplish as chair of the board of advisors?
One key area that many medical schools, and research institutions in general, are dealing with is the strain on research funding. Overcoming that requires a creative approach. The board and I are thinking about how to broaden the resources available to Tufts researchers.

What should Tufts School of Medicine be thinking about for the future? Where do the opportunities lie?
Research in neuroscience is a unique strength of the medical school and will be important for the future of medicine. Currently there are 5 million Americans with Alzheimer's disease. That number will increase to 10 million by 2025. Based on its expertise in this area, Tufts is in a strong position to have an important impact on Alzheimer's and other neurological diseases (see "The Alzheimer's Hope," page 14).

Another opportunity stems from the school's expertise in population health. It's very important to deliver health care in context of the population that you're dealing with. I've been impressed with the many programs at Tufts that go beyond the treatment of medical disorders to take into consideration the social and economic aspects of health.

As a founder of Third Rock Ventures, you have an innovative approach toward medicine and biomedical research. How does this perspective play into your role as a Tufts advisor?
One of the areas we think about at Third Rock Ventures is how to translate important research into new treatments for patients. Translational medicine is becoming important in education and in allowing discoveries to become great new therapies. I enjoy the opportunity, in my role on the board, to connect Tufts investigators with individuals in the industry who have interest in the area they're studying.

Your bio says that you participated in the 1972 Munich Olympics. Were you an athlete?
(Laughs) I wasn't an athlete—I get a lot of flack from my kids for having that in my bio. The Olympics were hiring young folks from all over the world to help out as ushers and things like that. I got to be exposed to a lot of great things, like how a complex, international event comes together, and I got to know some of the athletes, both current and previous, including Jesse Owens, who had competed in the 1936 Olympics. But it was also the first modern-day Olympics to be struck by a terrorist event. It made an impact on me in a number of ways. I got to see a lot, but I didn't bring home a gold. **–JOANNE BARKER**

PHOTO: ALONSO NICHOLS

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MINDFUL OF OUR PAST

WHEN I WAS a medical student in the 1970s, there were certain attending physicians at the New England Medical Center (as it was then called) that we students held in awe and to some extent fear, since clinical teaching by intimidation was still the norm. Those among my generation will recall Louis Weinstein, Sidney Gellis, Alice Ettinger, Alan Callow and Seymour Reichlin, who were among the many with international reputations.

When I joined the hospital staff in 1980, it was even more awesome to be a colleague of some of these individuals, especially those who had attended Tufts Medical School. This group included Henry Banks, '45, an innovative pediatric orthopedic surgeon who served as dean of the medical school from 1983-90; Thomas Sabin, '62, renowned Boston nephrologist; Andrew Plaut, '62, an internationally respected gastroenterologist, and Sherwood Gorbach, '62, infectious disease expert and discoverer of *c. difficile*.

Among this cohort, Jane Desforges, '45, deserves special mention. She was the second woman, and one of only six women ever to be elected president of the American Society of Hematology. She received the medical school's Outstanding Teacher Award for 13 consecutive years and was the first woman to earn the American College of Physicians Distinguished Teaching Award. She served on the editorial board of the journal *Blood* (founded by the Tufts hematologist William Dameshek) and was also associate editor of the *New England Journal of Medicine*.

Many of you may recall what a great clinician Jane Desforges was. Indeed, I think one might say that she represented why our institution is so great. It is here that great discoveries can be made, but where patient care always remains most important. Individuals like Jane have inspired many of us to pursue careers in academic medicine.

This year at our reunion in early April, we once again celebrated those individuals who have contributed to the eminence of our school through retrospective talks by the biochemist David Stollar, Sol Gittleman, formerly the longtime provost of Tufts University, and me. By reminding you of those who came before and those who mentored us as students, we want to encourage you to pay your alumni association dues and contribute generously to the school's annual fund to ensure that future physicians also get a great start at Tufts School of Medicine.

THOMAS R. HEDGES, '75
President, Tufts Medical Alumni Association
thedges@tuftsmedicalcenter.org

Class Notes

1966

DAVID WELSH of Claremont, California, reports that he and his wife, Arlene, recently returned from their vacation home in Cambria, a small town on the Golden State's central coast, where he was busy making progress on the first draft of his fourth novel. His third novel, *Marburg,* published last fall, concerns six Diana monkeys, imported to the U.S., who carry the Marburg virus. Now retired from his career as a vascular surgeon, Welsh was affiliated with Kaiser Hospital in Fontana, California, for many years. He and his wife have two sons, Joseph and Terence.

1972

JOHN FALLON of Lynnfield, Massachusetts, former chief physician executive and senior vice president of Blue Cross Blue Shield of Massachusetts, the leading health plan in the state, has joined the board of directors of Exact Sciences, a molecular diagnostics company focused on the early detection and prevention of some of the deadliest forms of cancer, including colorectal cancer.

ROGER LANDRY of Wilkes-Barre, Pennsylvania, was a featured speaker at the Sun Health Life Care Community in Surprise, Arizona, in late February, where he gave a talk titled "Successful Aging—A Population Health Necessity." A preventive medicine specialist, Landry is also the author of the best-seller *Live Long, Die Short* and a well-known expert in helping older adults get more out of life.

PHOTO: KELVIN MA

1976

ELAINE HART-BROTHERS, of Durham, North Carolina, received the 2016 Volunteerism Award from the North Carolina chapter of the American College of Physicians in February in recognition of her years of work addressing racial health disparities in her community. She is board president of Community Health Coalition, a nonprofit she founded in 1989 to reduce preventable death and disease among Durham's African-American residents.

RICHARD REINES, A71, A01P, A04P, M05P, of Hollywood, Florida, an ardent, longtime fan of Jumbo, the Tufts University mascot, says that he recently returned from travels abroad and found new tusked friends everywhere. "We have seen more elephants in Sri Lanka than in our other travels in Asia and Africa," he writes. "Jumbo lives on; we were just visiting with all his relatives." Reines spent 10 days in Sri Lanka in January.

1977

CHRISTIAN SEMINE, A03P, A06P, G10P, of Marblehead, Massachusetts, received the Physician of Excellence award from North Shore Medical Center, where he is chair of radiology, in a ceremony in October 2015. The award, the highest honor for the hospital staff, was given in recognition of Semine's efforts in developing the medical center's breakthrough program in low-dose computed tomography lung cancer screening and management.

1980

WILLIAM F. OWEN of Memphis, Tennessee, has been appointed dean of medical sciences at American University of the Caribbean School of Medicine, where he oversees the medical sciences curriculum; he is based on the school's campus in St. Maarten. He was formerly chancellor and senior vice president of health affairs at the University of Tennessee.

1991

JEFFREY MARCHANT, of Medford, Massachusetts, a research assistant professor of integrative physiology and pathology at the Sackler School of Graduate Biomedical Sciences, was part of a five-member team whose 2014 paper on glaucoma, published in *PLOS Biology,* has won the $50,000 Lewis Rudin Glaucoma Prize. The New York Academy of Medicine awards the prize annually for the most outstanding scholarly article on glaucoma published in a peer-reviewed journal during the previous calendar year.

1992

GREGORY CHERR of Buffalo, New York, a vascular surgeon, has been appointed assistant dean for graduate medical education at the University of Buffalo. Five years ago, he was one of six medical educators nationwide to receive an Arnold P. Gold Foundation scholarship to attend the prestigious Harvard Macy Institute for advanced surgical training.

1998

CHRISTOPHER LATHAN of Wayland, Massachusetts, is the new medical director of the Dana-Farber Cancer Institute at St. Elizabeth's Medical Center. He has been a member of the thoracic oncology program at Dana-Farber since 2005 and was appointed the first faculty director of cancer care equity there in 2010. Lathan is a leading researcher at Dana-Farber's Population Sciences Center on issues of race and class disparities in cancer care, and has lectured extensively on the topic.

2001

RAHUL SHARMA of New York City has been promoted to emergency physician-in-chief at New York Presbyterian Cornell Medical. He was formerly executive vice chief for the Division of Emergency Medicine as well as associate professor of clinical medicine at Weill Cornell.

2007

ELIEZER STERNBERG of New Haven, Connecticut, a resident neurologist at Yale-New Haven Hospital, has published a new book, the third in a series he has written on neuroscience and human identity. The *Washington Post* called *Neurologic: The Brain's Hidden Rationale Behind Our Behavior* (Pantheon, 2016) an "audacious, wise and compelling book."

2008

JONATHAN GREENE of Wayland, Massachusetts, has joined Emerson Cardiovascular Associates in Concord, Massachusetts. His clinical interests include coronary artery disease, hypertension, vascular disease and valvular heart disease.

2009

LAURA DOYON of Wayland, Massachusetts, has joined the surgical weight-loss program at Emerson Hospital in Concord, Massachusetts, as a bariatric surgeon. She completed her residency in general surgery at Mount Sinai Hospital in New York City and a fellowship in bariatric surgery at Lahey Hospital & Medical Center, in Burlington, Massachusetts.

VICKI LOSICK of Bar Harbor, Maine, has joined the faculty of the MDI Biological Laboratory, an independent, nonprofit biomedical research institute, as an assistant professor. A molecular microbiologist, she heads a research team devoted to understanding how damaged tissues repair themselves and how the ability to heal declines as we age.

2012

ELINOR MILDER of Malden, Massachusetts, joined Malden Family Health Center in Malden, Massachusetts. She completed her residency at Maine Dartmouth Family Medicine and is board-certified in family medicine. She is active in many volunteer organizations, including Women's Lunch Place and the Animal Rescue League, both in Boston.

In Memoriam

JAMES DEMOPOULUS, '45, J84P, of Dover, New Hampshire, an orthopedic surgeon for many years, died on Nov. 14, 2015, at age 94. He was a U.S. Army captain who served in the medical corps during World War II. He was chief of surgery at Frisbie Memorial Hospital in Rochester, New Hampshire. He is survived by his wife of 55 years, Vasilike, a son, a daughter and five grandchildren.

MELVIN HELLER, A43, M48, G48, J79P, of Haverford, Pennsylvania, died on Jan. 12, 2016, at age 93. Born in Boston to first-generation European immigrants, he rose to become a prominent psychiatrist and psychoanalyst as well as a professor of psychiatry at Temple University School of Medicine. He was the author of many books and journal articles. Among his other works, he published a two-part memoir, *Every Knock Is a Boost*, in his final year of life. He is survived by his three children, David, Joan and Paul; six grandchildren and one great-grandchild.

LAWRENCE MCCARTIN, '53, of Lowell, Massachusetts, a general surgeon and primary-care doctor who ran a busy medical practice in the Merrimack Valley for 60 years and delivered more than 5,000 babies, died on Aug. 5, 2015, at age 87. He served as a captain in the U.S. Army Medical Corps during the Korean War. He was director of the Board of Health in Lowell for 25 years. An optimistic fisherman and skilled equestrian who was also an intrepid private pilot, McCartin approached life as a grand adventure. He is survived by a son, a daughter and four grandchildren.

HUBERT ARONSON, '55, of Coral Gables, Florida, died on Nov. 16, 2015, at age 85. He was a neurosurgeon who moved his young family to Florida in 1963 and practiced principally at South Miami Hospital for nearly 50 years, including his service in roles as chief or neurosurgery and president of the medical staff. He is survived by a son, a daughter, two stepsons, a stepdaughter and eight grandchildren.

RICHARD CHAMBERLIN, '56, of Belgrade, Maine, died on Aug. 26, 2015, at age 84. He was president and chief medical officer of Blue Cross and Blue Shield of Maine, beginning in 1985, and an internal medicine specialist in the state for more than five decades. As his obituary noted, "The loons on Belgrade Lake will cry out a little longer this week in honor of his passing." He is survived by Shirley, his wife of 47 years, two sons, four children from a previous marriage, 12 grandchildren and two great-grandchildren.

RICHARD STOCKWELL, '56, of Farmington, Connecticut, died on Jan. 28, 2016, at age 85. He was a physician, teacher and leader in Farmington for many years, long affiliated with the University of Connecticut John Dempsey Hospital, where he taught physical diagnosis to medical students and tutored medical students in need. He was the town's health director and served on the town's Water Pollution Control Authority, among other roles. He retired in 1997. He is survived by his wife, Beatrice, whom he met on a blind date in Boston in 1954, four sons and 10 grandchildren.

HERBERT RUBIN, A55, M59, A93P, of Worcester, Massachusetts, died on Oct. 21, 2015, at age 81. The first neurologist to open a practice in Worcester, he treated thousands of patients over his 30-year career. He served as a captain in the U.S. Army during the Vietnam War. He is survived by his longtime companion, Ghislaine, two sons and five grandchildren.

ALAN MCCARTNEY, '61, of Rutland, Vermont, and formerly of Chestnut Hill and Wellesley, Massachusetts, died on Nov. 15, 2015, at age 80. An internist and gastroenterologist at Newton-Wellesley Hospital, he was an old-fashioned doctor who made house calls and always made it a practice to treat his patients with compassion and respect. Even after his retirement, he continued seeing patients at a V.A. hospital. According to one obituary, "he relished rounds of terrible puns over dinner and relaxed with Red Sox radio broadcasts. He loved golf, playing cards, singing in the church choir, stout beer and a runaway Patriots win." He is survived by three children and eight grandchildren.

RICHARD STONE, '70, of Rancho Mirage, California, died on Jan. 4, 2016, at age 73. He served on the faculty at the University of California, San Diego, School of Medicine, followed by many years of private practice in nephrology and hypertension at Eisenhower Medical Center. He loved his family, the desert, the Boston Red Sox, playing tennis and going to the movies. He is survived by four children and four grandchildren.

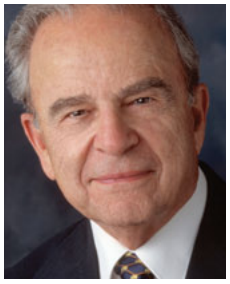
SUSAN MASON, J74, M79, A15P, of Denver, Colorado, died on Jan. 1, 2016, at age 63. She was an infectious-disease specialist in private practice who devoted herself to helping cure people and ease their suffering, beginning in the 1980s with the rise of AIDS. Mason is survived by her husband, Ricke, and her daughter, Julia.

BRUCE REYNOLDS, '85, of Del Mar, California, died unexpectedly on Nov. 15, 2015, at age 56. He was a head, neck and facial surgeon who worked at the Wound Clinic at Ashland Community Hospital in Ashland, Oregon, and at the nearby V.A. hospital. He was loved by his patients for his gentle demeanor, compassionate touch and holistic approach, and enjoyed biking, hiking and long-distance running. He is survived by his two children, Kathryn and Derek.

Faculty

NICHOLAS COE of Hampden, Massachusetts, a professor of surgery and associate director of surgical education at Baystate Medical Center, died on Nov. 27, 2015, at age 69. He was past president of the Association of Surgical Education and a published author, composer and musician who played violin with the Holyoke Civic Symphony in his free time.

PIONEERING ENT SURGEON AND FORMER TRUSTEE



FRED ARRIGG SR., M47, A75P, A77P, M78P, M79P, M82P, of Hampton, New Hampshire, a pioneering surgeon in the Merrimack Valley of Massachusetts for 60 years who served as a trustee of Tufts University for a decade, died on March 15, 2016, at age 93. He was a former president of the Tufts Medical Alumni Association and beloved patriarch of a trio of Tufts-educated physicians.

Arrigg was one of the first surgeons in the world to perform the stapedectomy procedure, which restored the hearing of thousands of patients.

Born in Lawrence, Massachusetts, Arrigg was the son of Lebanese immigrants. Educated in the city's public schools, he graduated magna cum laude from Harvard University in 1944. Following graduation from Tufts School of Medicine in 1947, he completed an internship and residency at Boston City Hospital in pediatrics and ear, nose and throat diseases. In 1950, he opened his practice in Lawrence, where he treated patients with hearing loss, dizziness and balance problems until he retired at age 89. He founded Arrigg Eye and Ear Associates, a multispecialty practice into which he welcomed his three children, Claudia Arrigg, '78; Fred Arrigg Jr., A75, M79, A07P; and Paul Arrigg, A77, M82.

In the Merrimack Valley, Arrigg was often called the "Dean of Medicine" in recognition of his deep knowledge and widespread connections to hospitals in the area. He was active at Lawrence General Hospital and at Bon Secours Hospital (now Holy Family Hospital), where he served as a trustee, chief of staff, chief of the ear, nose and throat department and a member of the executive committee. He also practiced at Boston City Hospital and the Massachusetts Eye and Ear Infirmary.

Arrigg and his wife, Emily, were known for their generous philanthropy in the form of multiple scholarships awarded to deserving students attending high school, college and medical school, including the Dr. Fred and Emily Arrigg and Family Scholarship Fund at Tufts Medical School.

In 1978, Arrigg received the highest honor of the Tufts University Alumni Association, the Distinguished Service Award. The United Lebanese Charitable Society named him Lebanese Citizen of the Year in 1988. In 2001, when Holy Family Hospital presented him with the St. Luke's Award for Outstanding Achievement in Medicine, Arrigg was described as "the heart and soul of our medical community."

Apart from medicine, Arrigg loved reading, travel, history, nature and leading discussions of current events with his grandchildren around the dinner table. In addition to his wife and children, he is survived by nine grandchildren.

Staff

COLLEEN ROMAIN, director of multicultural affairs and student programs for more than 30 years until her retirement in 2013, died on Jan. 26, 2016, at age 66. "Colleen was passionate about assisting students through their medical school journey and served as a motivator, mentor and advocate for a generation of TUSM students," Harris Berman, dean of Tufts School of Medicine, said in a notice sent out to the Boston medical community. "She had a special way of blending compassion with high expectations that helped students flourish." In her term of service, Romain saw more than 750 minority students receive their medical degrees.

PHOTO: DAN GILLAN PHOTOGRAPHY

OUR DIFFERENCE-MAKER

This pharmaceutical innovator 'was a humanitarian above all else'

MICHAEL JAHARIS, H15, M87P, of New York City, an entrepreneur, philanthropist and longtime friend and benefactor of Tufts University School of Medicine, died on Feb. 17, 2016, at age 87 with his family by his side. "His death is a great loss for our school and for our university community," Dean Harris Berman said simply in an email sent to medical school faculty and staff following his attendance at the funeral service in New York.

"Michael was a profound difference-maker at our school and at Tufts University, which awarded him an honorary degree last May," Berman observed. "He served as the chair of our board of advisors and as a trustee of Tufts for many years, lending his guidance and wisdom to us in many ways."

The Jaharis family has been the medical school's most generous donors. Through their family foundation, Michael Jaharis, his wife, Mary, son, Steven Jaharis, '87, a family-medicine specialist practicing in the Chicago area, and daughter, Kathryn, made the cornerstone gift for the Jaharis Family Center for Biomedical and Nutrition Sciences, a milestone in the school's development and a magnificent facility that expanded research space while fostering collaboration among faculty members in medicine, biomedical research and nutrition science. The center opened on the Boston campus in the fall of 2002.

A few years later, the Jaharis family provided the resources to renovate the Sackler Building from top to bottom and make it into a front-line education center. They helped create the Clinical Skills and Medical Simulation Center, enabling students to hone critically important aptitudes in physical diagnosis. The family also endowed the Jaharis Family Chair in Family Medicine as well as the Jaharis Family Scholarship Fund. In his message, Berman called these magnanimous contributions "transformative investments in Tufts."

Jaharis was the son of a Greek immigrant who landed penniless in Boston in 1908. He earned his bachelor's degree from Carroll College, now Carroll University, in Waukesha, Wisconsin, and went on to earn his law degree from Chicago's DePaul University at night while working days as a pharmaceutical salesman for Miles Laboratories. From 1961 to 1972, he was vice president and director of the Ethical Drug Division at Miles.

In 1972, Jaharis became president and CEO of Key Pharmaceuticals. There he led his team to develop such breakthroughs as sustained-release Theo-Dur, which became the nation's best-selling asthma remedy, and Nitro-Dur, the first transdermal sustained-release product to administer nitroglycerine through the skin.

Jaharis has been called a "pharmaceutical maverick" for his ability to recognize and pursue opportunities in the field that others have missed. In 1988, he founded Kos Pharmaceuticals, where he directed the creation of a family of drugs designed to raise HDL, the "good" cholesterol, thereby improving the health of millions.

Outside of the pharmaceutical industry, Jaharis was one of the nation's leading supporters of Greek-American causes, whether religious, cultural or secular. He was intimately involved with the Greek Orthodox Church, serving as vice chair of the Greek Orthodox Archdiocese of America. In that capacity, he volunteered his time in an effort to see New York City's St. Nicholas Greek Orthodox Church, the sole church destroyed in the 9/11 attack at Ground Zero, rebuilt near its original site. When finished, Jaharis told a church council in 2012, the new structure will provide "a shining spotlight on the Greek Orthodox faith and our core values of love, respect, peace, healing and forgiveness." The Greek Orthodox Archdiocese of America made him an "Archon Exarchos of the Order of St. Andrew the Apostle," one of its highest honors.

Michael Jaharis "was a humanitarian above all else," said Peggy Nicholson, executive director of the Jaharis Family Foundation. "He was very passionate about medical research and the arts and was very proud of his Greek heritage."

His family foundation has endowed permanent collections of Greek and Byzantine art at the New York Metropolitan Museum of Art and at the Art Institute of Chicago. In 2013, the family endowed the Archbishop Demetrios Chair in Orthodox Theology and Culture at Fordham University. That same year, the Jaharis Family Foundation pledged $2 million toward hunger and poverty relief in Greece during that country's severe financial crisis.

Jaharis is survived by his wife, Mary; children Steven and Kathryn; and five grandchildren.

"Tufts is where our passion for medicine and the care of others was born, created, and stimulated, enabling us to go on to successful careers. I urge my fellow alumni to remember this, and include Tufts in their own charitable giving."

Joshua Careskey, M77, M13P, M13P, MG13P, knows the importance of education. Not only was he the first doctor in his family, but he was the first to attend college. "My parents instilled in me a love of learning," he recalls. At TUSM, he was inspired by the faculty's work with newborns and children. Now as the director of pediatric surgery at a large medical center in northern New England, he and his wife, Nancy, M13P, M13P, MG13P, feel a deep need to support the school that prepared Dr. Careskey for a career he has "enjoyed tremendously" and also trained two of their three children.

"I feel immense gratitude toward Tufts and want to give back," he says. In order to ensure that future students are able to pursue their passion of patient care, the Careskeys have included TUSM in their estate plans.

The CHARLES TUFTS Society

To learn how you and Tufts can benefit from a gift made through your estate plans, contact the Tufts Gift Planning Office:
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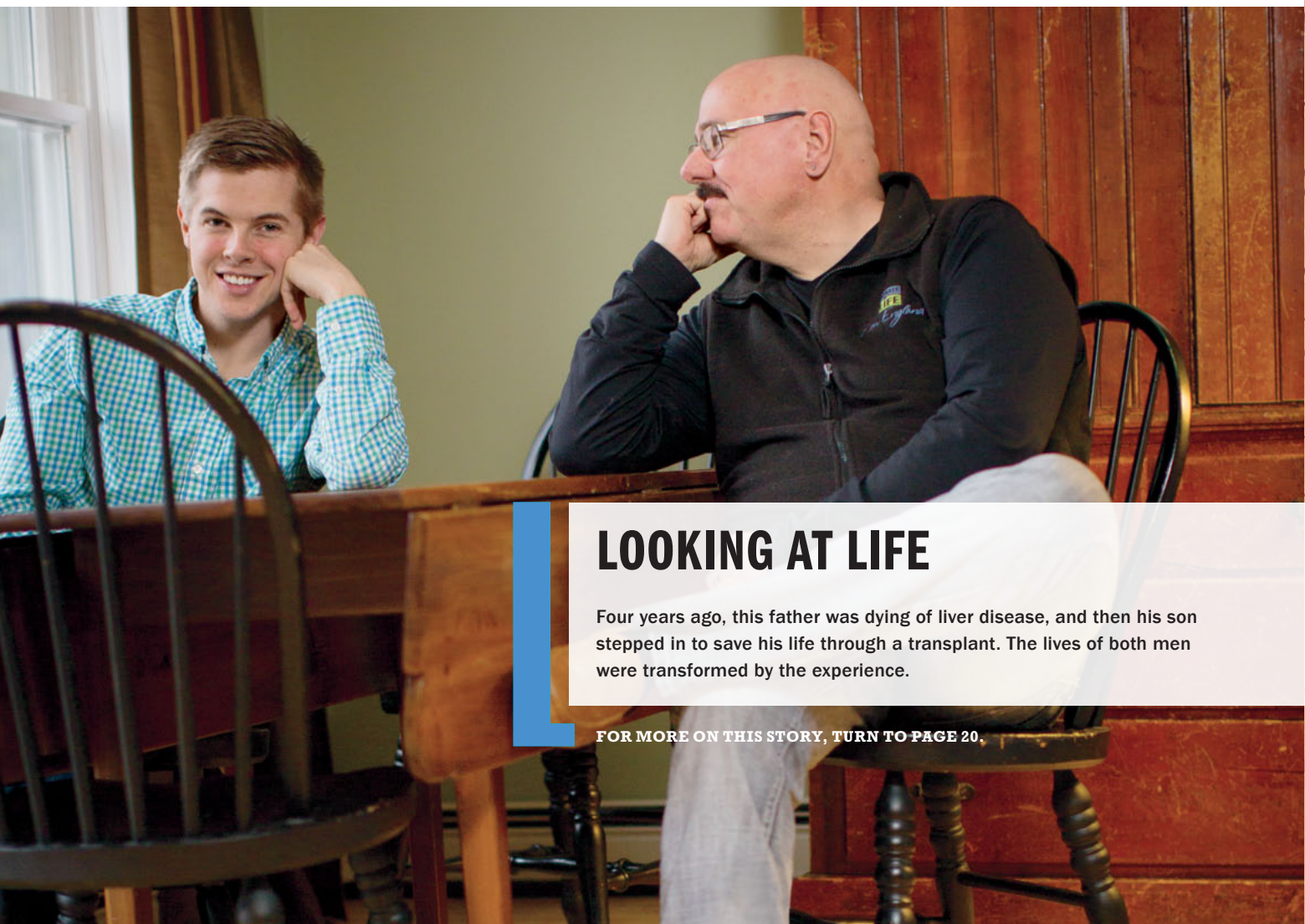

LOOKING AT LIFE

Four years ago, this father was dying of liver disease, and then his son stepped in to save his life through a transplant. The lives of both men were transformed by the experience.

FOR MORE ON THIS STORY, TURN TO PAGE 20.