Medicine@Yale

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Advancing Biomedical Science, Education, and Health Care

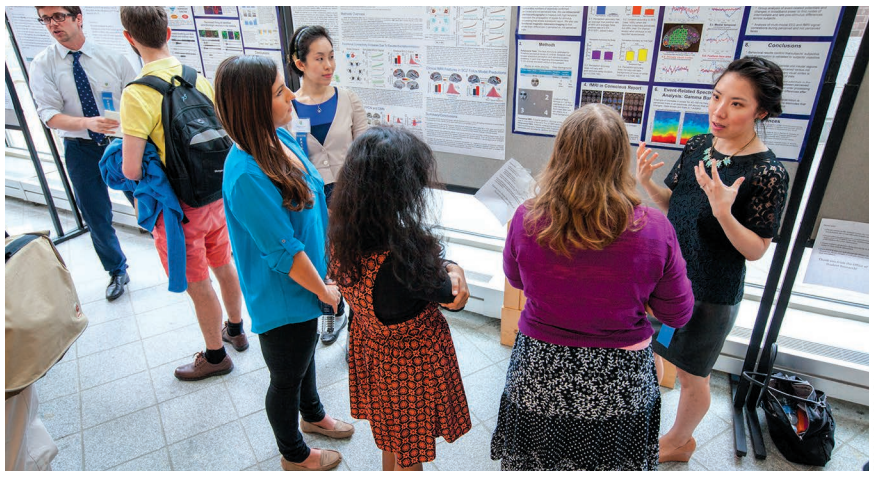
A foundation's gift paves the road for future scientists

Gift benefits trainees 'who excel both in research and in the practice of medicine'

The living human brain is a puzzle to scientists, in part because its inner workings are so hard to observe. Wendy Xiao, a student in the medical school's Medical Scientist Training Program (MSTP)—known on campus as the M.D./PH.D. Program—is helping to lift the veil with research that maps activity in the brain as it forms a conscious experience. She is also the inaugural recipient of a fellowship award established at Yale by the Gustavus and Louise Pfeiffer Research Foundation.

Xiao and her colleagues in the lab of Hal Blumenfeld, M.D., PH.D., the Mark Loughridge and Michele Williams Professor of Neurology and professor of neuroscience and neurosurgery, showed human subjects a degraded image of a human face set in various contexts, while measuring electrical activity across the brain. "The intriguing thing is that our equipment registered the stimulus as it entered the primary visual cortex, whether the subject reported awareness of the face or not," Xiao says. "Yet corresponding activity in other parts of the brain varied dramatically. There seem to be 'gates' that control the entry of

// Foundation *(page 7)*



TERRY DAGRADI

Wendy Xiao, a student in the medical school's M.D./PH.D. Program, discusses her work on conscious perception at Student Research Day. A recent gift from the Gustavus and Louise Pfeiffer Research Foundation is supporting a new generation of physician-scientists at Yale.

An epidemiologist's best weapon: math

Two philanthropists support math modeling in public health research

As a high school student Alison P. Galvani, PH.D., wrote a letter to the British evolutionary biologist Richard Dawkins. She told him she enjoyed his book *The Blind Watchmaker*, but took issue with his point that speciation—the evolutionary process through which new species form—can occur only gradually. In his reply Dawkins praised her argument and encouraged her to apply to the University of Oxford in the United Kingdom. Galvani heeded this advice, and earned her bachelor's degree in biological sciences from Oxford and stayed there to earn a doctorate under theoretical biologist Robert May in 2002.

As a graduate student Galvani took the plunge into epidemiology and gained a foothold in the research methods that she's taken further in the years since. While at Oxford, she met the philanthropist Charles Ryland Burnett III and his friend William A. Stender.

TERRY DAGRADI

Burnett and Stender were impressed with Galvani's research. Her innovative approaches to studying disease transmission particularly interested Burnett. In 2015 Burnett and Stender came together to endow the Burnett and Stender Families Professorship of Public Health, to

// Chair *(page 8)*

Alison P. Galvani, the Burnett and Stender Families Professor of Epidemiology, uses complex epidemiological models and statistical analyses to predict the spread of viruses, including the 2014 Ebola virus outbreak. Pictured at a symposium celebrating her appointment to the new professorship are (from left) William A. Stender, Galvani, Charles Ryland Burnett III, and School of Public Health Dean Paul D. Cleary.

A new leader and a boost in funding for Yale neuroscience

Pietro De Camilli, M.D., the John Klingenstein Professor of Neuroscience, professor of cell biology, and a Howard Hughes Medical Institute investigator, has been named chair of the Department of Neuroscience and director of the Kavli Institute for Neuroscience at Yale. His appointment in September 2015 coincided with a pledge by The Kavli Foundation to commit $5 million to the institute's endowment, the third such commitment since the institute's founding in 2004. The Foundation has contributed a total of more than $16 million to the endowment.

The California-based Kavli Foundation aims to promote research that will advance science for the benefit of humanity and increase public understanding and support for scientists and their work. The Kavli Institute for Neuroscience at Yale is one of seven Kavli-supported university institutes that specialize in neuroscience.

// Neuroscience *(page 8)*

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HAROLD SHAPIRO

David Hafler delivered the 2015 Raymond D. Adams Lectureship at the annual meeting of the American Neurological Association in Chicago. "When colleagues give you an award like this," he says, "it's like having someone thank you for the effort you've put into research."

Cracking the immune system's code

Innate curiosity fuels a lifelong quest to better understand disease

Through the lens of his first microscope, a young David A. Hafler, M.D., witnessed white blood cells rushing to attack unwelcome viruses and bacteria. "How could that not be interesting to a child?" he said recently.

Hafler wasted no time acquainting himself with the intricate ecosystem that makes up human blood. At age 10, unable to find an immunologist in the phonebook, he showed up alone for an appointment with a hematologist in his Teaneck, N.J., neighborhood. A skeptical receptionist asked his mother's whereabouts. Undeterred, Hafler managed a one-on-one conversation with the physician and went home with a hematology textbook.

As an undergraduate chemistry major at Emory University in Atlanta, Hafler continued to follow his passion for immunology. A mentor there, Dale McFarlin, M.D., introduced him to multiple sclerosis (MS)—in which a person's own immune system attacks the protective myelin sheaths covering his or her nerves.

At that time, the autoimmune disease's cause and workings remained largely mysterious. "When I started in 1970, there was absolutely nothing for MS patients. They were in wheelchairs," Hafler says.

Over the next decade, he earned his medical degree from the University of Miami School of Medicine, completed a neurology residency at what was then called Cornell Medical Center/New York Hospital, and worked in the lab of Henry G. Kunkel, M.D., at The Rockefeller University, before joining the Harvard Medical School faculty in 1984.

In 2009 Hafler joined the School of Medicine as chair of the Department of Neurology and neurologist-in-chief at Yale New Haven Hospital. By then he had helped contribute paradigm-altering ideas to the field. For example, in the 1980s, Hafler and colleagues found that MS activates the body's entire immune system, just like HIV. Working with another group, Hafler conducted research suggesting that MS patients maintain a higher number of T cells, which in turn seem to react to a particular region of a protein that makes up nerve-covering myelin.

This untangling of the major mechanisms of action within MS has allowed Hafler, now the William S. and Lois Stiles Edgerly Professor of Neurology and professor of immunobiology, to tackle ever-intricate aspects of the disease. In 2013, he and colleagues suggested in *Nature* that increased levels of salt contribute to higher levels of a particular type of T cell, which led mice to develop a disease called autoimmune encephalomyelitis, the mouse equivalent of MS.

In November, Hafler and colleagues published a study in *The Journal of Clinical Investigation* that details how a high-salt diet likely impairs the ability of T regulatory cells—a subtype of T cell that guards against autoimmune reactions in the body—to function well. Thousands of years ago "we lived in Sub-Saharan Africa on 200 mg of salt [per day]," Hafler says. "Today the average American eats five grams of salt daily." He recently began a Phase I clinical trial to monitor the effects in humans of switching from a very low-salt diet to a high-salt one.

MS patients today can choose from among 12 medications to keep their chronic disease in check. Despite years of research that has led to better care for patients, Hafler says he has "one big experiment left to do." He wants to identify the epigenetic factors—environmentally caused, heritable modifications to the way cells *read* DNA—that could be responsible for the development of MS in the first place.

Center provides researchers access to highly specialized tools

If a researcher needs highly the specialized expertise and equipment required to investigate a blood disease, where does she go?

Answer: the Yale Cooperative Center of Excellence in Hematology Specialized Core Center (YCCEH). The National Institutes of Health has designated Yale as one of three universities nationwide to receive a $5 million, five-year grant. The others include the University of Washington and Indiana University.

"It's a big honor that Yale is one of the three centers nationwide, and it puts us on the map for being experts in top-notch hematology research," says Diane S. Krause, M.D., PH.D., professor of laboratory medicine, cell biology, and pathology, and associate director of the Yale Stem Cell Center.

Diane Krause

Patrick Gallagher

Krause is the grant's co-principal investigator. The other principal investigator is Patrick Gallagher, M.D., professor of pediatrics, genetics, and pathology.

The grant provides money for pilot and feasibility studies, guest seminars, and staff members for each of its four core centers who handle research and training requests.

The specialized core, which opened last September, facilitates cell preparation and analysis, imaging, gene expression and genomics, and animal modeling.

Additionally, the three universities have special sharing priviledges.

More information on the YCCEH is available at medicine.yale.edu/labmed/ycceh/.

Immunologist is associate dean for scientific affairs

Ruth Montgomery

Ruth R. Montgomery, PH.D., associate professor of medicine, has been named associate dean for scientific affairs. In this role Montgomery will oversee core research facilities, institutional grants and site visits, research policies and regulation, as well as school-wide planning related to research space. She succeeds Sarah Rockwell, PH.D., professor emeritus of therapeutic radiology and pharmacology.

From 2004 to 2013 Montgomery served as director of confocal microscopy for the department of internal medicine. In 2013 she launched a new cytometry Time of Flight (CyTOF) core at the School of Medicine. CyTOF enables cells to be tagged with heavy metal-coupled antibodies and analyzed by time-of-flight mass spectrometry, making it possible to resolve more than 40 cell types and functional markers in a single assay. She remains director of the CyTOF core and active in her research lab.

Montgomery earned her bachelor's degree in biology at the University of Pennsylvania and her doctorate at the Rockefeller University, where she studied macrophage biology. She came to Yale in 1988 for postdoctoral training, and stayed on as a research scientist in rheumatology.

Montgomery has become well-known for her studies of human immune responses to the tick-borne bacteria *Borrelia burgdorferi* and to West Nile Virus, and the effects of aging on the innate immune system. Her research has been widely recognized for the use of novel technology to explore immune-related mechanisms in primary human cells.

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ADVANCES
Health & Science News

Modeling a flavor's path to our senses

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Smell is closely linked to taste. We perceive flavor when we exhale food particles held in our airway, but the reason for this has been elusive.

An interdisciplinary Yale team recently set out to learn why and how sense of taste is tied to exhalation but not inhalation. Led by Gordon Shepherd, M.D., D.PHIL., professor of neuroscience, the team used a computerized tomography (CT) scan of a healthy airway to create a 3D-printed model of the anatomy. Sending water and fluorescent particles through the model, researchers visualized the path air and food particles take when we breathe through our noses.

Inhaled air, they found, creates a barrier that keeps food particles from traveling to the lungs. Exhaled air, however, travels through a virtual cavity, where it picks up the odor particles and carries them out through the nostrils. The findings, published in *Proceedings of the National Academy of Science* in November, suggest humans may have adapted this pathway to sense whether food is safe without taking its aroma into the lungs.

Creating better cellular factories

Novel, or recombinant, proteins have been used to develop groundbreaking medications for numerous conditions including diabetes, cancer, and hemophilia, but until now biomolecular engineers have faced a limitation. Cells typically require 20 amino acids to produce a protein. Engineers have been able to include only one, or perhaps a few, synthetic amino acids among them. This has limited the number of novel proteins scientists have been able to build.

Recently, a team of Yale researchers removed the translational machinery from *E. coli* bacterial cells whose genome was entirely recoded. The machinery translated the code for specific amino acids and their corresponding proteins. Removing it helped establish a free channel through which the cell can code new, synthetic amino acids. The research was published in November in the journal *Nature Biotechnology*.

"Now we can introduce dozens of new synthetic building blocks with user-defined precision to produce new compounds to improve drugs or functionalized polymers for new materials, [such as] biocompatible glue," said Farren Isaacs, PH.D., assistant professor of molecular, cellular and developmental biology and senior author of the study.

Institute reveals secret life of microbes

A team of scientists uses cross-displinary tools to discover how microbes function and interact with their environment

Of Earth's nearly countless species of microbes—bacteria, fungi, viruses, and protozoa—we've studied only a few in depth. They can resist stress by congealing into a tough, glassy material. They have observable social behaviors, like sharing public goods. In our own bodies, they outnumber human cells by 10 to one. They affect our health, the economy, and the environment in ways we're still just beginning to grasp.

"It's wise to study microbes because they really impact everything we care about," says Christine Jacobs-Wagner, PH.D., the William H. Fleming, M.D. Professor of Molecular, Cellular, and Developmental Biology and a Howard Hughes Medical Institute investigator.

Jacobs-Wagner is the director of the Microbial Sciences Institute on Yale's West Campus. She and four other institute faculty work at the interface of disparate disciplines, studying microbes with tools from computational, life, and physical sciences. Each has a primary appointment at the School of Medicine or the Faculty of Arts and Sciences, and their collaborators outside the institute include geneticists, chemists, ecologists, evolutionary biologists, computational scientists, and engineers.

With its faculty united by a common interest but not by methods or training, the institute flips the traditional concept of the academic department, Jacobs-Wagner says. "In the past, in a department of biochemistry, you would attract people [who] focus on biochemical approaches to address questions on anything," she says. "We wish to do the opposite ... We address a variety of microbial questions, but they are all microbial questions, and our goal is to attract people with training in various disciplines."

Not long ago, scientists studying microbes were largely limited to the few species that grow in culture media. But in recent years, as genetic sequencing has grown much more affordable, researchers can sequence the genetic material of hundreds of microbial species from an environmental sample at once, producing vast datasets that give a glimpse of how communities interact with each other and their environments. This technique is called metagenomics. Other tools like bioinformatics and advanced microscopy have also helped to transform microbiology by opening a window on microbial behavior and evolution.

Andrew Goodman, PH.D., associate professor of microbial pathogenesis, studies the role human-associated microbial communities play in host disease and health. Goodman's interests include how the beneficial bacteria that live in the intestine—collectively known as the gut microbiome—interact with each other and their host. In 2015 his team reported in *Science* on a gene that beneficial gut microbes can use to survive host inflammation events, and in a 2016 paper in *Proceedings of the National Academy of Sciences* uncovered direct warfare between our friendly bacteria. His ongoing research projects are examining a different aspect of host-microbe interaction: his lab is working to understand how our gut microbes could influence the metablism and function of important medical drugs.

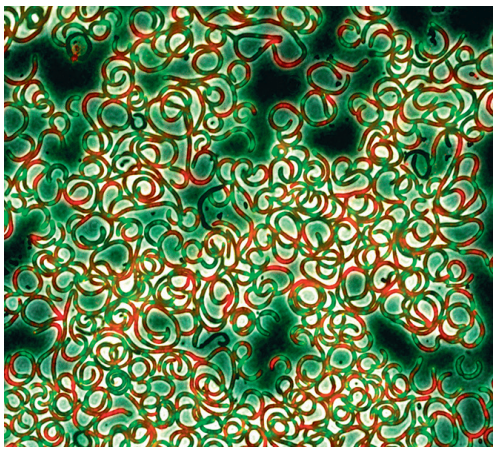
Eduardo A. Groisman, PH.D., professor of microbial pathogenesis, studies how bacteria adapt to new conditions by adjusting which genes they express. For instance, the gastroenteritis-causing bacteria *Salmonella enterica* lives inside host immune cells. Groisman's team found that within those cells, these bacteria produce cellulose—a substance commonly found in plants but that also helps bacteria cling to surfaces in groups—and that as it dials down cellulose production, it becomes more virulent.

This helps explain how *Salmonella* modulates growth inside host cells. The results appeared in a 2015 article in *Proceedings of the National Academy of Sciences*.

Biophysicist Alvaro Sanchez, PH.D., currently a junior fellow at Harvard's Rowland Institute, studies how microbial communities evolve. A focus of his lab is the evolution of "public goods" production in these communities—for instance, when microbes secrete enzymes that break complex sugars into simple ones. His team assembles and cultures microbial communities, with some microbes engineered to display particular behaviors, then uses mathematical models to study their community dynamics. In a 2013 paper in *PLOS Biology*, his team described how a population of cooperative, resource-sharing yeast that is invaded by non-contributing "cheaters" can still reach a stable equilibrium—but the community is less able to resist outside stresses. Sanchez will join the faculty of the institute and of Yale's Department of Ecology and Evolutionary Biology in July.

In Jacobs-Wagner's lab, bacteria help illuminate how cells self-replicate. "We share an evolutionary link with microbes, so they can be a really fantastic model system to study basic biological function," Jacobs-Wagner says. For replication to occur, many intricate events have to occur in the right order. Yet bacteria can proliferate very quickly, with some able to divide every 20 minutes—"and it virtually never fails, which means that the system is very robust," Jacobs-Wagner says. Her lab also explores how bacteria organize their inner components in space.

BELOW: COURTESY OF CHRISTINE JACOBS-WAGNER; RIGHT: CARL KAUFMAN



Researchers at the Microbial Sciences Institute on West Campus investigate the role of microbes everywhere, from the gut microbiome to oil spills. The institute's core faculty include (above, from left) Nikhil Malvankar, Andrew Goodman, Christine Jacobs-Wagner, and Eduardo Groisman. The microscopy image at left shows chromosome segregation protein ParA (red) and a cell division regulator (green) found in a freshwater bacterium called *Caulobacter crescentus*.

"Before we started we thought they were just tiny bags of molecules floating around. Our lab has contributed to the [finding] that their cells are actually spatially organized, and that this organization is critical for cellular function and behavior," Jacobs-Wagner says.

Shocking news: Some bacteria have hairlike projections that conduct electricity. Nikhil Malvankar, PH.D., the institute's newest faculty member, is an assistant professor of molecular biophysics and biochemistry who is a physicist by training. As a doctoral student he developed techniques to study materials with "interesting quantum-mechanical properties," Malvankar says. Then he realized those techniques could be put to a different use.

"Biology is a lot more complex," Malvankar says. "You can really have a breakthrough if you apply these techniques to biological problems instead of conventional physics problems." While a postdoctoral fellow at the University of Massachusetts, Malvankar was part of a team that found certain soil-dwelling bacteria sport hairlike protein "wires" called pili that dump excess electrons. That discovery has potential implications for developing bioenergy sources, as well as for understanding how certain infections begin. He was the first to use a technique called electrostatic force microscopy to visualize these electrons traveling along bacterial proteins.

"I'm really excited to be here," says Malvankar. "It's an amazing idea, putting all the people working on microbes under one roof."

OUT & ABOUT

October 3 The **¡ANDA! 5K For HAVEN Free Clinic** drew a crowd of runners, volunteers, and spectators despite an unseasonably cold day. The event raised $36,900 for supplies and services for the Fair Haven-based clinic. **1. Peter J. Ellis**, M.D., MPH, assistant professor of general medicine (left) with his daughter, **Malaya**, after the race. **2.** School of Public Health students (back, from left) **Monica Guo** '17, **Rebecca Valderrama** '17, **Grace Carroll** '17, **Rachel Clare** '17, **Marlene Edelstein** '19, and **Eric Strubel**, crew coach of Moorestown High School in Moorestown, N.J.; and (front, from left) **Emma Stein**, '17 and **Kira DiClemente** '17. **3.** Runners jockey for positions at the start of the race. **4.** Race volunteers included (from left) physician associate student and clinic board member **Trisha Blake** '16 and medical students **Mehida Alexandre** '17 and **Jennifer Fischer** '18, also a member of the Fair Haven-based clinic's board.




JOHN CURTIS (4)

October 9 A **Reception** was held to honor the biochemist and molecular biologist Aziz Sancar, M.D., PH.D., of the University of North Carolina-Chapel Hill, who received the 2015 Nobel Prize in chemistry. Sancar is a former postdoctoral fellow in the Yale lab of **W. Dean Rupp**, PH.D., professor of therapeutic radiology. **1.** (from left) **James E. Hansen**, M.D., assistant professor of therapeutic radiology; **Faye A. Rogers**, PH.D., associate professor of therapeutic radiology; **K. Brooks Low Jr.**, PH.D, professor (adjunct) of therapeutic radiology; **Douglas E. Brash**, PH.D., senior research scientist in therapeutic radiology and dermatology; **Ranjit S. Bindra**, M.D., PH.D, assistant professor of therapeutic radiology and pathology; Rupp; **Ryan B. Jensen**, PH.D., assistant professor of therapeutic radiology and pathology; **Susan J. Baserga**, M.D., PH.D., professor of molecular biophysics and biochemistry, genetics, and therapeutic radiology; **Peter M. Glazer**, M.D., PH.D., chair and the Robert E. Hunter Professor of Therapeutic Radiology and professor of genetics; **Ravinder Nath**, PH.D., professor of therapeutic radiology; **Zhong Yun**, PH.D., associate professor of therapeutic radiology; **David Joel Carlson**, PH.D., associate professor of therapeutic radiology; and **Zhe (Jay) Chen**, PH.D., professor of therapeutic radiology and chief physicist at Smilow Cancer Hospital at Yale New Haven. **2.** (from left) Glazer; **Daniel C. DiMaio**, M.D., PH.D., Waldemar Von Zedtwitz Professor of Genetics and professor of molecular biophysics and biochemistry and of therapeutic radiology; and **Joan A. Steitz**, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry.


JOHN CURTIS (2)

October 20 The theme for this year's **Junior Principal Investigator Retreat** was "Team Building and All That Jazz." Sponsored by the School of Medicine Dean's Office and the Office of the Provost, interspersed information sessions with live jazz entertainment for an audience of junior faculty. **1. Jeffrey Ernstoff**, ED.M., of the Wisconsin Institute for Discovery at the University of Wisconsin-Madison, presents a jam session demonstrating innovative collaboration. **2.** (from left) **Andrew Goodman**, PH.D., associate professor of microbial pathogenesis, **Valentina Greco**, PH.D., associate professor of genetics, cell biology and dermatology, and **Stefania Nicoli**, PH.D., assistant professor of medicine, participate in a moderated session. **3. Ann Kuhlman**, director of the Office of International Students and Scholars, discusses topics relevant to international scholars, including visas and immigration status.



TERRY DAGRADI (3)

Foundation's support helps young physician-scientists excel

Janice Jin Hwang, M.D. is using magnetic resonance imaging (MRI) to understand how the brain changes in diabetes and obesity. This research may lead to better treatments for diabetes and weight management. However, Hwang, an endocrinologist and instructor in medicine, balances her work with the demands of being a parent. "Sick days and school closings come up," says Hwang, who has two children under the age of five. "But the research doesn't stop," she says.

Like Hwang, most junior faculty struggle to balance the often competing demands of family and research, but some additionally face extraordinary caregiving demands such as caring for a child or a parent with a new diagnosis of severe illness. A new program aims to help physician-scientists with extraordinary caregiving needs excel. The Yale Center for Clinical Investigation (YCCI) has received a grant from the Doris Duke Charitable Foundation through its Fund to Retain Clinical Scientists to support early-career physician-scientists who are also caregivers.

The program will provide supplemental research funding, mentoring opportunities, and access to support staff in such areas as data management and grant writing. The goal, says Robert S. Sherwin, M.D., C.N.H. Long Professor of Medicine and director of YCCI, is to relieve faculty of some of the pressure to seek grants in the short term while providing them with resources that will help them achieve discoveries that draw significant support in the long term. "I know how hard it is to start a career," Sherwin says. "When people finish their training their kids are still young, and it's not a simple thing to be successful," he says.

This program is a step toward retaining young women on the faculty, says Ana-Claire L. Meyer, M.D., assistant professor of neurology and one of the project's co-directors. However, she emphasizes that the project must be part of a larger effort. Only 34 percent of the School of Medicine's faculty are women, though women make up 47 percent of the faculty at the instructor or assistant professor level, and research indicates that heavy workloads and demands at home contribute to junior faculty abandoning academic medicine.

"Improved support for junior faculty with extraordinary caregiving needs, whether for young families or eldercare, meets an important need at a critical time for all faculty and can be a key component of a more comprehensive program to achieve a more diverse senior faculty," Meyer says. "We are deeply grateful for the Doris Duke Charitable Foundation's critical investment in our efforts to increase gender and racial diversity among faculty at Yale School of Medicine."

JERRY DOMIAN

A new program supported by the Doris Duke Charitable Foundation aims to smooth the road for young physician-scientists, particularly women. Its directors include (from left) Rajita Sinha, Eugene Shapiro, Kimberly A. Yonkers, Ana-Claire Meyer, Robert Sherwin, and Marcella Nuñez-Smith (not pictured).

Diversity is not only an issue of equity: it changes the nature of research. "Increased diversity among scientific investigators and leaders has the potential to benefit science with regard to the questions that scientists ask, the way scientists teach and mentor, and the relevance of our research to a diverse world," Meyer says.

In keeping with YCCI's mission to support research that leads to improvements in patient care, the program is limited to faculty conducting human investigations. The time is ripe for clinical science with impact on human health, says Sherwin, an endocrinologist who played a critical role in developing insulin pump therapy. "We're just beginning to have the capacity to look at the molecular level," Sherwin says. "It's important to retain people who are bright and capable of taking this work forward."

ADVANCES
Health & Science News

Homing in on hereditary deafness

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Maternally inherited nonsyndromic deafness is caused by a defect in mitochondria—the organelles within cells in which respiration and energy production occur—and can cause premature deafness in humans.

Now, a team of Yale scientists led by Gerald S. Shadel, PH.D., professor of genetics, has shed light on the dysfunction and found a potential target for future therapies.

The researchers genetically altered mice to model mitochondrial deafness, in which hearing loss was caused by dysfunction in specialized tissues in the inner ear. The team found that activation of the stress-response enzyme AMPK triggered this dysfunction. They also found that genetically reducing AMPK activity had no impact on mice with normal hearing, but inhibited hereditary hearing loss in the deafness-model mice.

The study, published in *The American Journal of Pathology* in December, points to possible strategies for preventing or treating deafness associated with mitochondrial dysfunction and aging in humans.

A link between estrogen and autism

Drugs approved for autism, a neurodevelopmental disorder characterized by repetitive behaviors and social shyness, likely do not target its underlying mechanisms. Because those remain a mystery to researchers, drug discovery works by testing hundreds of molecules on autistic animal models and watching for clues. Recently, a Yale-led team of scientists identified a potential winner: estrogen.

The team reported in February in *Neuron* that the flavonoid biochanin A, along with three other estrogenic compounds, seemed to reverse abnormal behavior in zebra fish carrying mutations in an autism risk gene.

To observe the drugs' effects, the researchers, led by Ellen J. Hoffman, M.D., PH.D., assistant professor in the Child Study Center, and Antonio J. Giraldez, PH.D., professor of genetics, analyzed movements of zebra fish carrying a mutated gene called *CNTNAP2*, which is strongly linked to autism and epilepsy in Amish families. Estrogenic molecules suppressed hyperactivity at night—a manifestation of the disorder in zebra fish—but at no other time. This suggests the drugs were targeting a specific, though unknown, pathway of the disorder.

"These findings open the door to studies about how estrogen affects brain development," Hoffman says.

Study hints at fingerprints for the brain

Scientists observing brain images find that individuals display differing 'signature' patterns when processing information

Great minds think alike, the saying goes. But a new study by School of Medicine researchers suggests something else: every mind thinks a bit differently. A team led by R. Todd Constable, PH.D., professor of radiology and biomedical imaging, has discovered that subtle individual variations in brain function define one-of-a-kind "fingerprints" that distinguish one person from another.

Constable and colleagues constructed diagrams using data from functional magnetic resonance imaging (fMRI), a non-invasive technique that detects brain activity. The data indicated which parts of the brain were effective in tandem at any given time, and the connectivity patterns turned out to be highly distinctive.

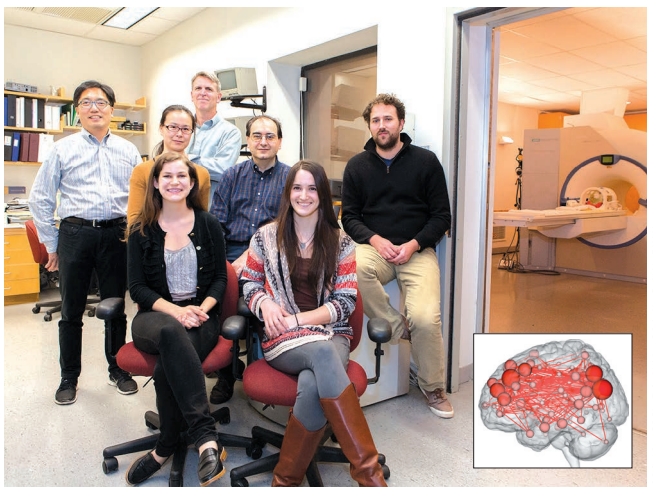
"That was an unexpected finding, just how unique these brain systems are," Constable says. The differences were apparent even between identical twins, he says. The results were published in *Nature Neuroscience* in October.

In the study, two Constable lab members, neuroscience graduate student Emily Finn and Xilin Shen, PH.D., associate research scientist, analyzed fMRI data from 126 healthy young adults who were scanned multiple times over 2 days. By measuring the strength of more than 35,000 connections between 268 different brain regions, Finn and Shen produced what they call connectivity profiles for each person in the study. The surprise came when they compared all those profiles: they found that each was different enough that they could identify with confidence any one person based solely on the person's profile. The profiles identified people consistently, even when the scans were done on different days or while subjects were doing some kind of mental task, rather than just resting in the scanner.

The connectivity profiles were not just unique: they were also informative. The researchers found connectivity fingerprints that tracked how people scored on a test of fluid intelligence, the type of brainpower used for on-the-spot problem solving. "It's not just that everyone has a different pattern of these connections, but also that they are relevant to some kind of real world output of the brain," Finn says.

In a second study, also published in *Nature Neuroscience*, Finn and psychology graduate student Monica Rosenberg teamed up to apply the same profiling approach to look at a different cognitive ability, the capacity for sustained attention. They found a set of brain connections associated with high or low performance on an attention test among Yale student volunteers. Then, they showed that the same fMRI-based profile could predict the presence and severity of symptoms of attention deficit hyperactivity disorder (ADHD) in adults and children in China, who were scanned completely independently.

Finn says she is interested in whether the connectivity profiles might be useful to predict something even harder



GROUP: JERRY DOMIAN, BRAIN: EMILY FINN

A team led by Todd Constable (back, center) found that functional connections in the brain can be distinguished among individuals. Pictured with Constable are (second row, from left) Marvin Chun, Xilin Shen, Xenophon Papademetris, and Dustin Scheinost, and (front, from left) graduate students Monica Rosenberg and Emily Finn.

to measure than intelligence or attention, like the risk of future disease or the trajectory of disease. She says she and her colleagues are now looking at another set of scans from people at high risk of developing schizophrenia. "They were scanned before they developed the full blown illness, and we are asking if we can use connectivity profiles to predict who went on to develop the illness," Finn says.

One open question is whether a person's connectivity fingerprint is fixed, or whether it could change over time. "We do know that connectivity patterns change a lot through development and as a function of age," Constable says. "But would your pattern change enough so that we could no longer identify you? We don't know that yet."

New federally funded program energizes lung cancer research

Armed with an $11 million grant from the National Cancer Institute (NCI), Yale Cancer Center and Smilow Cancer Hospital at Yale New Haven will launch a new research program in non-small cell lung cancer (NSCLC), one of the world's most prevalent and lethal forms of cancer.

Known as a Specialized Program of Research Excellence, or SPORE, the new research program harnesses the strengths of academic cancer centers by bringing together experts in oncology, immunobiology, pharmacology, molecular biology, pathology, epidemiology, and addiction science to collaborate on projects.

"The only way to approach a problem as big as lung cancer is to have experts in basic, translational, and clinical research working on several fronts taking the research from the lab to the clinic and back again to develop even newer insights," said principal investigator Roy S. Herbst, M.D., PH.D., Ensign Professor of Medicine, chief of medical oncology at Smilow Cancer Hospital, and associate director for the Translational Research Program at Yale Cancer Center. "This effort represents tremendous teamwork by investigators to combat this very common and all-too-fatal disease."

Nearly 90 percent of lung cancers worldwide are NSCLC cases, which are largely incurable once they become metastatic. While most cases are linked to smoking, experts are increasingly identifying mutations in light smokers and non-smokers that are treatable.

"This is an exciting time to do cancer research in areas like immunotherapy," said Lieping Chen, M.D., PH.D., the United Technologies Corporation Professor in Cancer Research and professor of immunobiology, dermatology, and medicine. "With this award from the NCI, we hope to make a big difference in treating and preventing lung cancer."

The Yale SPORE will conduct projects in immunotherapy, precision medicine, drug development, and smoking cessation. Teams will also work to identify new translational research avenues and train young physician-researchers for careers in lung cancer. Frank J. Slack, PH.D., director of the Institute for RNA Medicine at the Cancer Center at Beth Israel Deaconess Medical Center, will co-lead

PETER BAKER

Roy Herbst, chief of medical oncology at Smilow Cancer Hospital, is the principal investigator on a new SPORE grant focused on non-small cell lung cancer. Research efforts will be heavily team-based in order "to combat this very common and all-too-fatal disease," he says.

a project examining microRNAs as therapeutics for lung cancer. Slack was formerly on the faculty at Yale School of Medicine and retains an affiliation.

Yale is one of four institutions in the country with a SPORE devoted to lung cancer and one of 13 institutions to house more than one SPORE.

The other SPORE focuses on skin cancer, and the NCI originally awarded the grant in 2006. Ruth Halaban, PH.D., senior research scientist in dermatology, is the principal investigator of the project. The research focuses primarily on the skin cancers basal cell carcinoma and melanoma.

Grants and contracts awarded to Yale School of Medicine

January 2015–June 2015

Federal

Fuad Abujarad, DHHS, *Patient Centered Virtual Multimedia Interactive Informed Consent (VIC)*, 2 years, $300,000 • **Serap Aksoy**, NIH, *Control of Tsetse Fly Transmitted Diseases in Kenya*, 5 years, $3,466,803 • **Andrei Alexandrov**, NIH, *Identification of New Human Targets to Inhibit Decay of PTC-containing mRNAs*, 2 years, $374,625 • **Heather Allore**, NIH, *Individualized Absolute Risk Calculator for Persons with Multiple Chronic Conditions*, 3 years, $989,843 **Karen Anderson**, NIH, *Exploring Novel Targeting Strategies for AIDS Protozoal Pathogens*, 5 years, $2,300,208 • **David Assis**, NIH, *The Role of Macrophage Migration Inhibitory Factor in Autoimmune Hepatitis*, 4.9 years, $764,370 **Sviatoslav Bagriantsev**, NSF, *Molecular Basis of Mechanosensitivity in Tactile Foraging Birds*, 5 years, $832,500 • **Rachel Barnes**, NIH, *Novel and Scalable Internet Supplemented Weight Loss Treatment in Primary Care*, 2 years, $166,500 • **Anton Bennett**, NIH, *MKP5 in Dystrophic Muscle Disease*, 4.9 years, $2,049,957 **Ranjit Bindra**, NIH, *Development of a Novel Assay to Measure DSB Repair at Endogenous Loci in Cells*, 2 years, $166,500 • **Anne Black**, NIH, *Using EMA to Assess the PTSD-HIV Risk Behavior Relationship in OEF/OIF Veterans*, 2 years, $294,525 • **Angelique Bordey**, NIH, *Astrocytes Contribution to Tuberous Sclerosis Pathology*, 2 years, $457,875 • **Sonia Caprio**, NIH, *Metabolic Markers and Predictors of Childhood Obesity*, 5 years, $2,550,580 • **Nicholas Carnevale**, NSF, *Bilateral BBSRC-NSF/BIO: Collaborative Research: ABI Development: Seamless Integration of Neuroscience Models and Tools with HPC - Easy Path to Supercomputing for Neuroscience*, 3.3 years, $129,624 • **Joseph Craft**, NIH, *Follicular Helper T Cells in Immunity, Allergy and Autoimmunity*, 2 years, $422,910 • **Michael Crair**, NIH, *Mechanisms of Visual Map Development in the Thalamus and Superior Colliculus*, 4 years, $1,332,000 • **Peter Cresswell**, NIH, *Molecular Aspects of Human CD1d Functions*, 5 years, $2,229,305 • **John Davis**, NIH, *Mobile Health for Implementation of Home-based TB Contact Investigation in Uganda*, 3 years, $1,663,411 • **Daniel DiMaio**, NIH, *Cell Transformation by Bovine Papillomavirus*, 5 years, $2,582,904 • **Kyle Draheim**, NIH, *Determining the Functional Significance of the CCM Complex*, 2 years, $117,928 • **Chenguang Fan**, NIH, *Expanding the Genetic Code in* Salmonella, 2 years, $457,875 • **David Fiellin**, NIH, *Safety and Comparative Effectiveness of New Medications for Unhealthy Alcohol Use in HIV*, 3 years, $1,239,550 • **Susan Fink**, NIH, *Role of Ire1alpha in Resistance to Viral-Induced Apoptosis*, 5 years, $899,370 • **Ellen Foxman**, NIH, *Cell Death and Cross-Protection in Rhinovirus Infection*, 5 years, $899,370 • **Jorge Galan**, NIH, *Campylobacter Jejuni Colonization and the Resident Microbiota*, 2 years, $457,875 • **David Glahn**, NIH, *1/3: Pedigree-Based Whole Genome Sequencing of Affective and Psychotic Disorders*, 4 years, $1,161,737 • **Kylia Goodner**, NIH, *Mechanism of Endosomal Membrane Penetration by Human Papillomavirus 16*, 2 years, $72,400 • **Murat Günel**, NIH, *Integrating the Genomics of Autism Spectrum Disorders (ASD) in Consanguineous and "Idiopathic" Families*, 3.8 years, $2,427,873 • **Adrian Haimovich**, NIH, *Development of Co-translational Phosphotyrosine Incorporation to Elucidate Mechanisms of Src Activation*, 3 years, $103,560 • **Karen Hirschi**, NIH, *Specification of Hemogenic Endothelial Cells*, 3.9 years, $2,594,689 • **John Hwa**, NIH, *Platelet Mitochondrial Function in Health and Disease*, 4 years, $1,665,000 • **Jeannette Ickovics**, DHHS, *Maternity Care: Variability in Utilization/Cost by Delivery Mode and Risk Status*, 1 year, $100,000 • **Akiko Iwasaki**, NIH, *Immunity to Genital Herpes Simplex-2*, 5 years, $1,873,125 • **Xiaoyun Ji**, NIH, *Molecular Basis of HIV Restriction by SAMHD1*, 2 years, $209,390 **Erdem Karatekin**, NIH, *Membrane Fission During Sporulation*, 4.8 years, $1,245,184 • **Joan Kaufman**, NIH, *A GEWIS Study of Smoking, Hazardous Drinking, and Other Health Risk Behaviors*, 3 months, $249,260 • **Barbara Kazmierczak**, NIH, *Intrabodies that Prevent or Disrupt Biofilms*, 2 years, $457,874 • **Mustafa Khokha**, NIH, *New Mechanisms of Heterotaxy and Congenital Heart Disease: Nucleoporins at Cilia*, 3.8 years, $3,153,039 • **Martin Kriegel**, NIH, *Human Gut Commensal Cross-reactivity in Antiphospholipid Syndrome*, 5 years, $2,096,614 • **Ivana Kuo**, NIH, *Non-Hypertensive Cardiac Disorders in Polycystic Kidney Disease*, 2 years, $181,500 **Themis Kyriakides**, NIH, *MCP-1 and Attenuation of the Foreign Body Rresponse*, 3.9 years, $1,849,344 • **TuKiet Lam**, NIH, *An Ultra-Performance Liquid Chromatography System to Support Metabolomics at Yale University*, 1 year, $135,183 • **Rachel Lampert**, NIH, *Exercise in Genetic Cardiovascular Conditions*, 5 years, $4,764,465 • **Brett Lindenbach**, NIH, *Bacterial Effectors as Probes to Study (+) RNA Virus-Host Cell Biology*, 2 years, $457,875 • **Elan Louis**, NIH, *Patholog-Omics - Essential Tremor in the Broader Context of Neurodegeneration*, 5 years, $3,296,886 • **Robert Malison**, NIH, *Glutamate-Glutamine Cycling (Vcyc) in Cocaine Abstinence Using 13C-MRS*, 2 years, $905,753; NIH, *Identifying Methamphetamine Risk Variants by Extreme Phenotype Exome Sequencing*, 4.8 years, $3,589,350 • **Goran Micevic**, NIH, *Role of DNA Methylation in Melanoma Formation and Tumor Heterogeneity*, 4 years, $103,560 • **Yann Mineur**, NIH, *Cholinergic Pathways in Depression*, 1.8 years, $166,500 • **Christopher Moore**, **Judy Burleson**, DHHS, *Minimizing Unnecessary Irradiation from Renal Colic CT Scans in the United States*, 5 years, $1,224,666 • **Evan Morris**, NIH, *Validation of Quantitative 11C-Erlotinib PET for Imaging EGFR-Mutant Lung Cancer*, 3 years, $513,590 • **Ismene Petrakis**, NIH, *Microglia as a Treatment Target for Alcohol Use Disorder*, 2 years, $343,613 • **Virginia Pitzer**, NIH, *Model-Guided Assessment of Rotavirus Vaccine Impact in Developing Countries*, 5 years, $1,893,416 • **Katerina Politi**, NIH, *Targeting the Immune System in Mouse Models of Lung Adenocarcinoma*, 3 years, $1,781,413 • **Karin Reinisch**, NIH, *Pathophysiology of Plasma Membrane PI4P Generation*, 4.2 years, $2,046,827 • **Lawrence Rizzolo**, **Ron Adelman**, DoD, *Maturation and Implantation of Engineered Retinal Tissue Grafts*, 3 years, $999,998 **Faye Rogers**, NIH, *Gene-Targeted Apoptosis as a Treatment for HER2-Positive Breast Cancer*, 2 years, $398,352 • **Douglas Rothman**, NIH, *Console and Gradient Upgrade for a 9.4 T 16 cm* in vivo *MR System*, 1 year, $600,000 **Craig Roy**, NIH, *Biogenesis of the Coxiella-Containing Vacuole*, 5 years, $2,084,874; NIH, *Rab Protein Functions that Impact Coxiella Intracellular Replication*, 2 years, $457,875 **Carolyn Sartor**, NIH, *Distinctions Between Black and White Young Women in the Course of Alcohol Use*, 4 years, $1,261,496 • **Curt Scharfe**, NIH, *Technology Development for Rapid Detection and Diagnosis of Metabolic Disorders*, 2.1 years, $784,081 • **Dongju Seo**, NIH, *Multimodal Neuroimaging of Stress, Arousal, and Alcoholism Risk*, 5 years, $880,371 **Nenad Sestan**, NIH, *2/2 Somatic Mosaicism and Autism Spectrum Disorder*, 4.8 years, $3,503,796 • **Gerald Shadel**, NIH, *Inducible Mouse Models of Mitochondrial ROS Signaling and Environmental Stress*, 2 years, $453,438 **Frederick Shic**, NIH, *Neural Correlates of Biological Motion Perception in Children with ASD*, 4 years, $707,579; NIH, *A Multimedia Screening System for Early ASD Identification in Diverse Populations*, 1.9 years, $457,875 • **Michael Simons**, NIH, *Arteriogenesis and Branching*, 4 years, $2,194,534 • **Rajita Sinha**, NIH, *Chronic Alcohol and Brain Stress Circuit Response*, 5 years, $2,968,476 • **Andrew Smith**, NIH, *Systems Genetics of Smoking*, 3 years, $120,036 **Carlo Spirli**, NIH, *Cross Talk Between Epithelial, Inflammatory and Mesenchymal Cells in the Development of Portal Fibrosis*, 3.8 years, $1,498,500 • **Joan Steitz**, NIH, *Viral Non-Coding RNAs and Cell Transformation*, 11 months, $271,516 • **Bing Su**, NIH, *The Function of MEKK3 Interaction with CCM2*, 4 years, $1,282,052 **Nancy Suchman**, NIH, *Fostering Mothers Emotionally Responsive Parenting*, 4.8 years, $2,962,798 • **Alexander Svoronos**, NIH, *Developing a Novel System for Cancer Therapy: Tumor-Targeted Inhibition of Oncogenic MicroRNAs*, 3 years, $93,240 • **Mary Tomayko**, NIH, *B Cell Memory Regulation by Bone Morphogenetic Protein Receptor 1A*, 5 years, $2,172,166 • **Jeffrey Townsend**, NSF, *Collaborative Research: Evolution of Systems Biology Underlying Fruiting Body Development in Fungi*, 3 years, $600,000 • **Flora Vaccarino**, NIH, *Somatic Mosaicism in the Brain of Tourette Syndrome*, 4.8 years, $5,094,723 **Anthony Van den Pol**, NIH, *Dopamine Excites Orexigenic AgRP/NPY Neurons, but Inhibits Anorexic POMC Neurons*, 5 years, $1,873,125; NIH, *Lassa-vsv Targets and Kills Glioma, and is Not Neurotoxic*, 5 years, $1,883,644 • **Shiyi Wang**, DHHS, *Development and Evaluation of a Decision Analysis Based Decision Aid*, 5 years, $753,538 • **Zuoheng Wang**, NIH, *Novel Methods for Longitudinal Study of Gene-Environment Interplay in Alcoholism*, 5 years, $862,583 **Jason Weinstein**, NIH, *Transcriptional Regulation of T Follicular Helper Cells in Lupus*, 5 years, $640,575 • **Yong Xiong**, NIH, *Recognition of Viral DNA by APOBEC3 Proteins and their Antagonization by HIV Vif*, 5 years, $2,073,977 **Xiao Xu**, DHHS, *Hospital Variation in Costs and Outcomes of Care for Childbirth*, 3.5 years, $870,633 • **Ke Xu**, NIH, *Genome-Wide DNA Methylation in HIV Infected Drug Users*, 2 years, $261,800 • **Qin Yan**, NIH, *Targeting Epigenetic Regulators to Suppress Breast Cancer Metastasis*, 2 years, $181,068; NIH, *Identifying Epigenetic Changes Critical for Trastuzumab Resistance*, 2 years, $398,352 • **Lawrence Young**, NIH, *DDT and CD74 Receptor Activation Prevent Cardiac Injury*, 3.9 years, $1,665,000 • **Jun Yu**, NIH, *ER-Associated Protein Reticulon in Atherosclerosis*, 3.9 years, $1,665,000 • **Dejan Zecevic**, NIH, *Electrical Role of Dendritic Spines*, 4.8 years, $2,008,913 • **Huiping Zhang**, NIH, *Salivary MicroRNAs as Biomarkers for Alcohol Dependence*, 2 years, $343,613

Non-federal

Albert Arias, Real-Time Analyzers (NIH), *Saliva Analyzer for Diagnosing SRD Patient Drug Use*, 10 months, $50,724 • **Will Bailis**, Cancer Research Institute, *Identification and Characterization of Immune Escape Mechanisms in Leukemia*, 3 years, $164,500 • **Jeffrey Bender**, Fondazione Cariplo, *Targeting Myeloid Cell Migration and Differentiation at Sites of Chronic Inflammation: Role of the Stress Activated Protein Kinase Network*, 2 years, $169,473 • **Kim Blenman**, Melanoma Research Alliance, *In Situ Tumor Microenvironment Profiles for Immunotherapy Responders*, 3 years, $75,000 • **Angelique Bordey**, Brain & Behavior Research Foundation (formerly NARSAD), *Exosomes as Carriers of Disease Spread*, 1 year, $99,834; Citizens United for Research in Epilepsy, *Exosomes as Carriers of Circuit Alterations in Epilepsy*, 1 year, $49,126 • **Elizabeth Bradley**, **Leslie Curry**, Commonwealth Fund, *Achieving Value: Strategies for Managing Populations with Complex, High-Cost Health Needs*, 2 years, $281,289 • **Richard Bucala**, Massachusetts General Hospital (DoD), *Development of a T Cell-Based Vaccine for Q Fever*, 1 year, $199,365 • **Richard Carson**, Pfizer, U.S. Pharmaceuticals Group, *Preclinical Evaluation of [11C]Valsartan*, 1 year, $220,779 • **Eda Cengiz**, The Leona M. and Harry B. Helmsley Charitable Trust, *Investigating Blood Glucose Variability and Insulin Action during Menstrual Cycle in Females with Type 1 Diabetes to Design Innovative Therapies*, 3 years, $1,436,436 **Ignacio Cerdena**, American Society of Tropical Medicine and Hygiene, *Developing a Community Health Worker TB Screening Intervention and Testing its Effectiveness in a Latin America Prison: A Quasi-Experimental Trial*, 3 months, $1,000 • **Sreeganga Chandra**, Connecticut Innovations, *Human Embryonic and Patient-Derived Induced Pluripotent Stem Cell Models of Neuronal Ceroid Lipofuscinosis*, 2 years, $200,000 • **Oscar Colegio**, Robert Leet and Clara Guthrie Patterson Trust, *Defining Metabolic Communication in Melanoma*, 1 year, $100,000 • **Zachary Cooper**, National Institute for Health Care Management Foundation, *Do Higher Priced Providers Deliver Higher Quality Care? An Analysis of the Price/Quality Relationship Using HCCI Data*, 1.8 years, $68,656 • **Joseph Craft**, **In-Hyun Park**, **Insoo Kang**, Connecticut Innovations, *Studying the Therapeutic Role of IPSCs in Human Lupus*, 4 years, $1,200,000 • **Joseph Craft**, Alliance for Lupus Research, *Characterization and Function of CD4 T Cell Subsets in Lupus*, 3 years, $567,567 • **Larry Davidson**, Patient-Centered Outcomes Research Institute, *Broadening Stakeholder Involvement in Behavioral Health Research*, 2 years, $248,263 • **Madhav Dhodapkar**, University of Pittsburgh (NIH), *GVL Resistance: Immune Selection, T Cell Ignorance and T Cell Exhaustion*, 3 months, $42,511 **Margarita Dominguez-Villar**, Benaroya Research Institute (NIH), *Epigenomic Analysis of Regulatory T Cells*, 1 year, $114,885 • **Marie Egan**, Cystic Fibrosis Foundation Therapeutics (CFFT), *2015 TDN Spring Meeting*, 6 months, $3,024 • **Donald Engelman**, Breast Cancer Alliance, Inc., *Chemotherapeutic Delivery Targeted to the Acidic Microenvironment of Breast Tumors*, 1 year, $100,000 • **Shawn Ferguson**, The Bluefield Project to Cure Frontotemporal Dementia, *Role of Lysosomes in Progranulin-Linked Frontotemporal Dementia*, 1.5 years, $170,000 • **Erol Fikrig**, New York Medical College (NIH), *A Critical Role of NLRP6 in West Nile Virus Pathogenesis in Mice*, 1 year, $49,950 **Brian Forsyth**, Ummeed Child Development Center, *Implementation of the International Guide of Monitoring Child Development (GMCD): An Individualized Technology-Aided Approach to Promoting Early Childhood Development in a Low Income Setting in Mumbai*, 1.5 years, $28,305 • **Abigail Friedman**, Robert Wood Johnson Foundation, *Behavioral Experiments in Improving Medicare Coverage Choices*, 1 year, $71,500; Robert Wood Johnson Foundation, *How Do A.C.A Smoking Penalties Affect Insurance Enrollment and Smoking Cessation*?, 6 months, $61,962 • **Joel Gelernter**, University of Connecticut (NIH), *Quantitative Methods to Subtype Drug Dependence and Detect Novel Genetic Variants*, 3.8 years, $9,866 **Mahboobe Ghaedi**, Connecticut Innovations, *Engineering Patient-Specific Tracheas Using IPSC-Derived Airway Epithelial Cells*, 2 years, $199,892 • **Sourav Ghosh**, University of Arizona (NIH), *Functional Restoration through Salivary Progenitor Label Retaining Cells*, 9 months, $13,567 • **Walter Gilliam**, **Angela Maupin**, W.K. Kellogg Foundation, *Understanding Race and Gender Bias Contributing to Preschool Expulsions and Suspensions to Inform Anti-bias Policies and Teacher Training*, 1.5 years, $375,000 • **David Glahn**, University of Texas Rio Grande Valley (NIH), *Whole Genome Sequencing to Identify Causal Genetic Variants Influencing CVD Risk*, 1.8 years, $55,396 **Jordan Grapel**, Autism Science Foundation, *Autism Science Foundation Undergraduate Summer Research Award*, 1 year, $3,000 **Daniel Greif**, American Heart Association, *Endothelial-Smooth Muscle Cell Interactions and OCT4 in Pulmonary Hypertension*, 2 years, $150,000; March of Dimes, *Specialized*

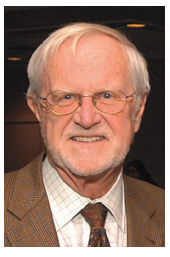
Arteriole Smooth Muscle Cells: Primed to Muscularize in Pulmonary Hypertension?, 3 years, $289,000 • **David Hafler**, Brigham and Women's Hospital (NIH), *TIM Family of Genes: Role of T Cell Immunity and Tolerance: Project 2*, 1 year, $216,450; National Multiple Sclerosis Society, *Collaborative MS Research Center Award: Systematic Genome Editing of the Risk Variants in Multiple Sclerosis*, 5 years, $825,001; Benaroya Research Institute (NIH), *Signatures of Autoreactive T Cells Across Diseases: CGSADP Pilot*, 1 year, $155,634 • **Kevan Herold**, Benaroya Research Institute (NIH), *Preclinical Studies of IL2-Tregs: Benaroya Research Institute*, 10 months, $74,925 • **Michael Higley**, The Brain Research Foundation, *Determining the Cell-Autonomous Role of GABAergic Inhibition in Visual Processing*, 2 years, $80,000 • **Dewan Syed Fahmeed Hyder**, Rutgers, the State University of New Jersey, *Mitochondrial Facilitation Treatment in Mild TBI and its Integrated Translatable Monitoring*, 1 year, $41,965 **Melinda Irwin**, American Institute for Cancer Research, *A Mail- and Video-Based Weight Loss Trial in Breast Cancer Survivors*, 2 years, $165,000 • **Natalia Ivanova**, Connecticut Innovations, *Dissecting Human Embryonic Stem Cell Pluripotency with Functional Genomics Approaches*, 3 years, $550,200 • **Peter Jatlow**, University of Connecticut Health Center, *UConn Health Personal Service Agreement*, 8 months, $4,920 • **Christoph Juchem**, National Multiple Sclerosis Society, *In Vivo Metabolomics of Oxidative Stress with 7 Tesla Magnetic Resonance Spectroscopy*, 3 years, $633,900 • **Susan Kaech**, Albany Medical Center (NIH), *A New Humanized Mouse Model of Chronic Hepatitis B*, 1 year, $51,442 • **Samuel Katz**, Connecticut Innovations, *Use of Human Embryonic Stem Cells and Murine Neural Stem Cells to Elucidate Pro-Apoptotic Signaling in Glioblastoma*, 2 years, $200,000; March of Dimes, *Control of Craniofacial Development by BCL-2 Multi-Domain Pro-Apoptotic Family Members*, 2 years, $150,000 **In-Jung Kim**, E. Matilda Ziegler Foundation for the Blind, *The Role of GABAergic Interneurons in the Development of Retinal Circuits*, 2 years, $100,000 • **Steven Kleinstein**, Mount Sinai Medical Center (NIH), *Modeling Early Immunity to Human Influenza Infection*, 1 year, $65,989 **Sanjay Kulkarni**, Greenwall Foundation, *Balancing Non-Maleficence and Autonomy: Establishing Ethical Risk Thresholds for Living Kidney Donors*, 1 year, $139,977 • **Csaba Leranth**, University of California, Davis (NIH), *Fluoxetine: Sensitive Ages & Genotypes for Adverse Effects in Juvenile Monkeys*, 1 year, $132,400 **Chiang-Shan Li**, Peter F. McManus Charitable Trust, *Noradrenergic Basis of Cognitive Control Deficits in Cocaine Addiction*, 1 year, $49,522 **Judith Lichtman**, University of Miami Miller School of Medicine (NIH), *Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD)-CMS*, 1 year, $133,188 • **Haifan Lin**, **Diane Krause**, Connecticut Innovations, *Continued Support and Technology Development for Shared Core Facilities at the Yale Stem Cell Center*, 1 year, $499,974 • **Chi Liu**, General Electric Healthcare, *Quantification of Cardiac Sympathetic Activity and Myocardial Blood Flow using Dual-Isotope Dynamic SPECT with MIBG and Tefrofsomin*, 10 months, $4,000 • **Yifei Liu**, Connecticut Innovations, *Investigating the Role of RlFl in Human Embryonic Stem Cells*, 2 years, $200,000 • **Steve Martino**, Research Triangle Institute (NIH), *Motivational Interviewing for Comorbid HIV and Substance Use*, 3 months, $14,785 • **Thomas Melia**, Columbia University (NIH), *Autophagy and Neurodegeneration*, 1 year, $206,045 • **Wang Min**, Connecticut Innovations, *TNFR2-Bmx Signaling in Cardiac Stem Cells and Cardiac Repair*, 5 years, $750,000 • **Walther Mothes**, Scripps Research Institute (NIH), *Structure and Dynamics of Native HIV-1 Envelope Trimers*, 1 year, $166,500 • **Angus Nairn**, Brown University (NIH), *Serine/Threonine Phosphatases in Neurological Diseases*, 1 year, $24,691 **Chimaeze Ndumele**, Brown University (DHHS), *Medicaid Managed Care and the Quality of Care for Women and Children: Evaluating a Randomized Trial of Enrollment in a Medicaid-Focused or Commercial Health Insurance Plan*, 1 year, $33,598 • **Kevin O'Connor**, Benaroya Research Institute (NIH), *Immune Responses to Human Commensal Bacteria in Patients with T1D and MS*, 1 year, $40,646; Guthy Jackson Charitable Foundation, *B Cell Tolerance Defects in NMO*, 1 year, $54,257 • **Pasquale Patrizio**, EMD Serono, *Identification of Novel Markers of Human Oocyte Aging Via Non-Invasive RNA-Sequencing Analysis of Cumulus Cells*, 2 years, $198,000 **John Persing**, Icahn School of Medicine at Mount Sinai (ISMMS) (NIH), *Craniosynostosis Network*, 1 year, $23,727 • **Robert Pietrzak**, SUNY Stony Brook (NIH), *A Life Course Approach to PTSD and Cognitive Aging: A Cohort of 9/11 Responders*, 9 months, $10,030 • **David Pitt**, Medimmune, Inc., *Medimmune Pilot Research Agreement Pilot*, 4 years, $12,950; National Multiple Sclerosis Society, *Using Patient-Specific Induced Pluripotent Stem Cells to Model the Effect of Glutathione S-Transferase Polymorphisms on Neurodegeneration in Multiple Sclerosis*, 1 year, $44,000 • **Christopher Pittenger**, Nancy Taylor Foundation for Chronic Diseases, Inc., *Targeted Neurofeedback: A Novel Non-Pharmacological Treatment for Obsessive-Compulsive Disorder*, 1 year, $115,000 • **Angelica Ponguta**, **Chin Reyes**, AGA Khan University, *Pakistan Early Child Development Scale Up (PEDS) Trial Phase III*, 1.7 years, $71,606 • **Lori Post**, Rutgers, the State University of New Jersey, *A Research Strategy to Understand the Impacts and Impact Pathways of Food, Agriculture and Nutrition Policies in Feed the Future (FtF) Countries*, 1 year, $85,305 • **Yibing Qyang**, Brigham and Women's Hospital (NIH), *Iron-Sulfur Deficiency as a Critical Pathogenic Cause of Pulmonary Hypertension*, 5 months, $22,458 • **Cristina Ramirez-Hidalgo**, American Heart Association, *Role of miR-148a in Controlling LDLR Activity and Plasma LDL Levels*, 4 years, $308,000 • **Chin Reyes**, Education Development Center, *Literacy and Academic Success for English Learners through Science (LASERS)*, 1 year, $37,500 • **David Rimm**, Cepheid, *Measurement of mRNA in Breast Cancer*, 1 year, $166,000; OncoPlex Diagnostics, *OncoPlex Diagnostics*, 1 year, $166,500; Genoptix, *Development of Multiplexed Fluorescent Tests for Immune Checkpoint Analysis*, 2.1 years, $332,000 **Lawrence Rizzolo**, Connecticut Innovations, *Reconstruction of an Outer Retina for Transplantation and Pharmaceutical Testing*, 3 years, $550,200 • **John Rose**, Albany Medical Center (NIH), *Enhancing Oncolytic Virotherapy with Type Iii Interferon*, 7 months, $20,254 • **Carla Rothlin**, Alliance for Lupus Research, *Protein S: At the Crossroads of Thrombosis and Inflammation in SLE*, 3 years, $569,326 • **Joseph Santos-Sacchi**, Stanford University (NIH), *Synaptic Specializations in Auditory Hair Cells*, 5 years, $41,625 • **Curt Scharfe**, Stanford University (NIH), *Multiplex Clinical Viral Detection in Formalin-Fixed Paraffin-Embedded Tissue Samples*, 1 year, $82,500 • **Gerald Shadel**, A-T Children's Project, *Proof-of-Principle Studies on Using Mitochondrial Antioxidants for Ataxia-Telangiectasia*, 1 year, $75,000 • **Gordon Shepherd**, University of California, San Diego (NIH), *Operation, Support and Strategic Enhancement of Neuroscience Information Framework*, 1 year, $100,000 • **Jodi Sherman**, Anesthesia Patient Safety Foundation, *Environmental and Public Health Impacts of Anesthesia Alternatives*, 2 years, $150,000 • **Gerald Shulman**, Gilead Sciences, *Yale-Gilead Preclinical Mitochondrial Protonophore Collaboration*, 2 years, $795,870 • **Rajita Sinha**, John B. Pierce Laboratory (NIH), *Cognitive and Affective Influences on Taste Processing*, 1.6 years, $33,603; John B. Pierce Laboratory (NIH), *The Gut-Brain Axis: A Novel Target for Treating Behavioral Alterations in Obesity*, 1.4 years, $30,065 • **Megan Smith**, Kresge Foundation, *Evaluate Impact to MOMS Partnership on Two-Generation Outcomes and City-Level Social Capital*, 2 years, $400,000 **Jane Taylor**, Brain & Behavior Research Foundation (formerly NARSAD), *Altered Frontalstriatal Decision Making in Rat: PET and Computational Models of Psychosis Vulnerability*, 1 year, $100,000 **Jeffrey Townsend**, Michigan State University, *Harnessing the Transcriptome of Conidial Germination for Pathogen Control*, 3 years, $197,271 **Flora Vaccarino**, Autifony Therapeutic, *Reversal of Anatomical and Behavioral Phenotype of Trkb KO Mice by the AUT-6 Compound*, 1 year, $129,738 **Martin Vinck**, Human Frontier Science Program Organization, *State-Dependent Recruitment and Impact of Cortical Inhibition*, 3 years, $162,852 **Fred Volkmar**, Nancy Taylor Foundation for Chronic Diseases, *Diagnostic Stability and Early Childhood Predictors of Outcome in Autism Spectrum Disorders*, 1 year, $169,781 • **Narendra Wajapeyee**, Melanoma Research Alliance, *Anoikis Effector as Driver and Drug Target in Metastatic Melanoma*, 2 years, $100,000 • **Lisa Walke**, University of Colorado Denver, *Evaluation of WISE: A Welcoming Interdisciplinary Senior-Friendly Emergency Department*, 1 year, $45,000 **Jake Wang**, Howard Hughes Medical Institute, *Immunization against Malignant Melanoma in a Murine Model using Extracorporeal Photochemotherapy*, 1 year, $41,000 • **Stuart Weinzimer**, Cystic Fibrosis Foundation Therapeutics (CFFT), *The Role of Glucagon in Cystic Fibrosis-Related Diabetes*, 2 years, $216,000 • **Brian Weiss**, West Virginia University (NIH), *Functional Differentiation in Tsetse Species Microbiotas*, 1 year, $34,962 **John Wysolmerski**, Georgia Regents University (NIH), *DiaComp Summer Student Funding Program*, 1 year, $8,163 • **Andrew Xiao**, Connecticut Innovations, *Modeling Pax7-Associated Craniofacial Defects with Human ES Derived Neural Crest*, 4 years, $500,000 • **Xiaoyong Yang**, American Cancer Society, Inc., *Control of Cancer Metabolism by O-linked Glycosylation*, 4 years, $792,000 • **Wendell Yarbrough**, Adenoid Cystic Carcinoma Research Foundation, *Model Development, Cell Culture Characterization, and High Throughput Screening to Advance Treatment for Adenoid Cystic Carcinoma*, 1 year, $73,865 • **Heidi Zapata**, Wake Forest University School of Medicine (NIH), *Effects of Age and HIV Infection on C-Type Lectin Receptor Function*, 1 year, $25,000 **Hitten Zaveri**, Epilepsy Foundation of America, *Brain Implantable Focal Cooling Sensing Array*, 1 year, $25,000; Triton Biosciences, *Energy Harvesting for Next Generation Neurotechnology*, 8 months, $10,580

// Foundation *(from page 1)* information into our consciousness, and we want to understand that."

Late last year the Gustavus and Louise Pfeiffer Research Foundation made a gift of $1 million to support the School of Medicine's M.D./PH.D. Program. The gift currently funds a single fellowship, but it will support more fellows in the future as the endowment fund grows.

"Yale is known for training physician-scientists who excel both in research and in the practice of medicine and thus are positioned to move discoveries from the laboratory into medical practice," said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. "I am grateful to the Pfeiffer Foundation for its generous funding of financial aid for our M.D./PH.D. students."

Xiao credits Yale's M.D./PH.D. Program for making her both a better clinician and scientist. "Very few programs provide students with the opportunity to treat patients in the hospital or clinic while they complete their doctoral work. This keeps our clinical skills sharp and emphasizes individual patient care," she said. "At the same time, being a member of a research university like Yale has ignited my interest in understanding how or why a treatment is implemented not just for one patient but for the larger population."



James Jamieson

Barbara Kazmierczak, M.D., PH.D., associate professor of medicine and microbial pathogenesis and director of the program, notes that Yale is a national leader in this kind of education. "For a very long time," Kazmierczak says, "Yale has emphasized the training of physicians who are scientists and scientists who function as physicians, so we integrate these two aspects of training very effectively." Since 1969, the program has drawn top students, in part because the university offers graduate work in fields as diverse as public health, medical anthropology, neuroscience, and biomedical engineering. For most of its existence, Yale's MSTP was helmed by James Jamieson, M.D., PH.D., professor of cell biology. Jamieson led the program from 1974 to 2014, with the exception of the years 1983 to 1992, when he chaired the Department of Cell Biology. Kazmierczak succeeded him as director in 2014.

John Krystal

"Our graduates usually establish research careers after they finish their training, and not lucrative private practices. We support their education so they don't graduate with significant debt," Kazmierczak says. The Pfeiffer Foundation's "gift will establish an endowment for long-term support, which is especially meaningful as we expand student enrollment in this important program."

In addition to its support of the M.D./PH.D. Program, the foundation also awarded a grant to the School of Medicine for studies that will advance the development of a new class of antidepressant. This project is led by principal investigator John H. Krystal, M.D., the Robert L. McNeil Jr. Professor of Translational Research, chair of the Department of Psychiatry, and professor of neuroscience. The grant will allow Krystal's team to evaluate the use of ketamine, which works on an entirely different type of neurotransmitter system than current medications do and has proven to be fast-acting and effective for short periods. Treatment with ketamine may allow physicians to treat depression rapidly in combination with long-lasting treatments such as cognitive behavioral therapy.

The Gustavus and Louise Pfeiffer Research Foundation has a long-standing relationship with Yale and has most notably supported the Yale Combined Program in the Biological and Biomedical Sciences and scientific research in several fields.

School of Medicine scientists join National Academy of Medicine

Of 80 scientists to join prestigious body, four are on School of Medicine faculty

TERRY DAGRADI

Dean Robert J. Alpern joined the medical school's inductees into the National Academy of Medicine. (From left) Ronald S. Duman, Murat Günel, Alpern, David A. McCormick, and Laura E. Niklason.

Four School of Medicine scientists have been inducted into the National Academy of Medicine (NAM). Three of the four inductees specialize in neuroscience, and the fourth focuses on biomedical engineering.

Ronald S. Duman, PH.D., has heightened general understanding of neurobiological stress, stress-related disorders, and the treatment of depression within the field of neuroscience. Duman, the Elizabeth Mears and House Jameson Professor of Psychiatry and professor of neuroscience, conducts research focused on molecular and cellular changes inside the adult brain associated with stress, depression, and antidepressant treatments.

Murat Günel, M.D., chair and the Nixdorff-German Professor of Neurosurgery and chief of neurosurgery at Yale New Haven Hospital, has conducted extensive genomic research that has helped underscore genetic risks for brain aneurysms and the multitude of genes necessary for cortical development. Also professor of genetics and of neuroscience, he is considered a pioneer in massive genome analysis studies.

David A. McCormick, PH.D., the Dorys McConnell Duberg Professor of Neuroscience and professor of psychology, has helped to identify neural circuits involved in optimal performance in animals with the goal of better understanding the roots of behavior in healthy and diseased brains. His work explores the cellular and network mechanisms of the cerebral cortex and has led to new findings in areas such as attention deficit hyperactivity disorder (ADHD) and sleep, with the ultimate goal of understanding the roots of behavior.

Laura E. Niklason, M.D., PH.D., professor of anesthesiology and biomedical engineering, has focused on creating engineered blood vessels, lung tissue, and cardiac muscle. She is currently testing engineered arteries in patients with vascular disease and renal failure. In 2010 her research team created artificial lungs that were capable of gas exchange, a fundamental function of the lungs, in an animal model.

"I think Yale's excellence is defined by the excellence of our faculty and the impact of what they do," said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. "We are hiring and nurturing the right faculty at Yale."

The 80 new worldwide members will be inducted into the NAM in October 2016. The NAM changed its name from the Institute of Medicine earlier this year.

// Chair *(from page 1)* which Galvani was appointed in September. "I thought if there was any way I could help promote her work and views, then that was the best thing I could do," Burnett said.

In a short time, Galvani, also professor of ecology and evolutionary biology and director of the Center for Infectious Disease Modeling and Analysis, has tackled diverse public health questions using epidemiological models and statistical analysis, from mapping Chikungunya virus cases to controlling outbreaks of sleeping sickness to Hepatitis C virus screening.

A number of Galvani's research papers have had a direct impact on improving public health policies. Until recently, for example, the United Kingdom's National Health Services (NHS) did not offer rotavirus vaccination as a component of routine childhood vaccination. Based on traditional cost-effectiveness analyses that did not take into account the dynamics of disease transmission, the NHS had deemed rotavirus vaccination to not be cost-effective according to their criteria. Then, Sanofi Pasteur, the vaccines division of the pharmaceutical company Sanofi, expressed interest in Galvani's approaches that integrate transmission dynamics into analyses of cost-effectiveness.

The company approached Galvani and asked her to reconsider the question in anticipation of an NHS policy review. Galvani took into account that vaccination of one baby not only provides protection for that specific baby, but also reduces transmission to the population in general. By accounting for transmission dynamics, Galvani and her team found that rotavirus vaccination of infants in the U.K. would be cost-effective. These results were presented to the NHS, which went ahead and implemented the policy. Because of Galvani's work, babies in the U.K. now receive vaccination against rotavirus.

Burnett said he hopes more students will become interested in the field of public health as a result of Galvani's research and instruction. "Public health is such an important field," he said. "[Galvani's] tenacity and ability to use mathematics to study how diseases are spread [are] uniquely important."

// Neuroscience *(from page 1)* This boost to the Yale institute's endowment is a part of the foundation's campaign to advance the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, a public-private research project launched by President Barack Obama in 2013.

"We are very pleased to join Yale in building the endowment of its Kavli Institute to an even higher level," said Robert W. Conn, PH.D., president and CEO of The Kavli Foundation. "This added investment will result in a substantially increased annual payout from Yale's Kavli Institute endowment. The vast majority of these funds are unrestricted for use in advancing the basic science of the brain and will further empower Yale's great scientists to explore their most exciting new ideas and proposals."

The additional funding will support research and activities relevant to advancing the mission of the institute, according to De Camilli. The contribution will allow Yale's large neuroscience-focused community "to be brought together to foster interdisciplinary research," he says.

"Pietro De Camilli's leadership appointments come at a time when neuroscience at Yale is solidifying and advancing," said Dean and Ensign Professor of Medicine Robert J. Alpern, M.D. "His expertise is ideal for a department that covers basic neuroscience all the way to neuronal circuits and disease." This broad scope is also reflected in the new name of the department. Until last October, the Department of Neuroscience was known as the Department of Neurobiology; the new name reflects its expanded scope.

For more than 30 years De Camilli has studied the dynamics of cell membranes in the nervous system. His research has illuminated the highly orchestrated series of events that leads to the release of neurotransmitters from nerve endings via membranous pouches, called synaptic vesicles, and to the reutilization of these pouches for multiple rounds of secretion. He has become a world-renowned expert on the mechanisms through which all cells secrete substances, take up material from the external environment, and transport it to appropriate intracellular destinations. He has also provided insight into pathological conditions resulting from genetic or autoimmune disruptions of these mechanisms.

In his most recent work, De Camilli has focused on the role of lipids, the main building block of cell membranes, in controlling the traffic and interactions of cell membrane organelles. His research has illuminated how lipids define the identity and properties of membranous organelles and revealed mechanisms underlying the exchange of lipids between them.

Most studies of nervous system function have addressed the role of proteins, but "less is known about lipids—their metabolism and transport," De Camilli says. "This is a field wide open to new exploration." Mutations that occur in enzymes that modify lipids or mediate their transport result in neurological and psychiatric conditions, including neurodegeneration.

A native of the lake region in northwestern Italy, De Camilli earned his medical degree at the University of Milan and completed postgraduate training at the University of Pavia. He came to Yale in 1978 as a postdoctoral fellow in the lab of the renowned pharmacologist Paul Greengard, who received the Nobel Prize in physiology or medicine in 2000. In 1979 he was recruited by the late cell biologist George Palade, M.D., also a Nobel laureate, to what was then called the Section of Cell Biology and subsequently became the Department of Cell Biology. He served as chair of that department from 1997 to 2000.

In 2005 De Camilli co-founded, together with Stephen Strittmatter, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neuroscience, the School of Medicine's Program in Cellular Neuroscience, Neurodegeneration, and Repair. Since the beginning of De Camilli's career, research in cell biology has inspired some of his new ideas about how to better understand neurons, and vice versa. He is the president-elect of the American Society of Cell Biology, which he will lead in 2017.

As chair of neuroscience, De Camilli assumes a role long held by Pasko Rakic, M.D., PH.D., the inaugural director of the Kavli Institute at Yale, the Dorys McConnell Duberg Professor of Neuroscience, and professor of neurology, who was recruited by Palade to found the department and then led it for 37 years. Rakic is well known for his studies on the cellular and molecular mechanisms of proliferation and migration of neurons in the cerebral cortex—the brain's outer layer. which plays a key role in cognition. His elucidation of how cortical cells migrate from their birthplace in the brain's core to their distant, final destinations represent a landmark discovery in neuroscience. Rakic has also contributed one of the most significant tenets of the field—that neurons of the cerebral cortex last for a person's entire life and are irreplaceable.

Through Rakic's vision "the Yale School of Medicine became a beacon of neuroscience research worldwide," Alpern said.