Medicine@Yale

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Advancing Biomedical Science, Education, and Health Care

A cause close to home inspires a gift with universal reach

To combat mood disorders, a new professorship and seminal research

Hope Furth and her husband John, of the Yale College Class of '52, are passionate about advancing understanding of developing brains because of their devotion to children's causes and excitement about emerging science. But their strongest motivation is even closer to home.

Searching for information that would help two of their grandchildren with special needs, they met the School of Medicine's Hilary Blumberg, M.D., professor of psychiatry, of diagnostic radiology, and in the Child Study Center, and director of Yale's Mood Disorders Research Program. "We were terribly impressed by the research that she's doing," said John Furth. "Hilary is looking for answers to the questions that most concern us: What is the cause of very serious mental and emotional problems in children? And how do we develop effective treatments?"

In December the Furths created the John and Hope Furth Professorship of Psychiatric Neuroscience with a $3 million gift. Blumberg has been named the inaugural Furth Professor.

"This is a partnership between people with a passion for knowledge and a belief that it can improve lives," said Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "The Furths' vision advances neurodevelopmental psychiatry and promises to make a tremendous difference for people with mood disorders."

Researchers like Blumberg have brought psychiatry to a "transitional moment," said John H. Krystal, M.D., the Robert L. McNeil Jr. Professor of Translational Research and

// Gift *(page 8)*

COURTESY OF HOPE AND JOHN FURTH

To support research on developing brains, Hope and John Furth have endowed a new professorship in psychiatric neuroscience.

Building a legacy of support for science

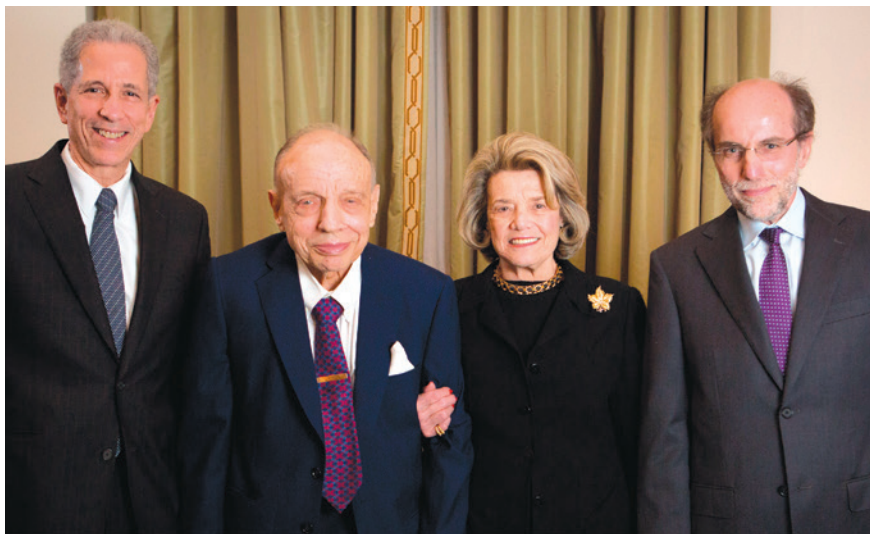
In supporting neuroscience, a five-generation Yale family honors a patriarch

Asked to reflect on the life and career of her husband, Pat Klingenstein smiles warmly. "John has always been his own man, speaking his mind, and following his own path wherever it has led. And, I'm proud to say, that path has led to a career of real significance." In talking about John Klingenstein, now 86, Pat gets to the heart of a man whose influence on medical science has been undeniable.

Inspired by his grandfather Frederick Adler, an 1891 graduate of Yale College, and an uncle, Milton Steinbach, of the Class of 1924, Klingenstein graduated from Yale College in 1950 as an engineering major. A first-rate student, John was elected to the engineering honors society Tau Beta Pi as a junior. He pursued a career in engineering for several years, including a stint at Westinghouse, where he was a member of a team working on the first jet propulsion engines. Then, at the urging of his father, Joseph Klingenstein, a co-founder of the storied New York investment firm Wertheim & Co., he headed to Wall Street, joining the firm in 1959. As a partner for many years, he worked alongside his brother Frederick, Yale College '53, who later succeeded Joseph as CEO.

The Klingenstein family's influence extends beyond the world of finance. For more than three decades, the School of Medicine has been a beneficiary of the family's support of medical science. In the early 1970s, John was named president of the Esther A. and Joseph Klingenstein Fund, the family's primary philanthropy. John brought to the Fund a business discipline, the precise thinking of an engineer, and a keen interest in

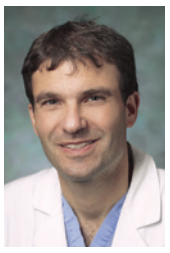
// Neuroscience *(page 8)*



JULIE BROWN HARWOOD

The School of Medicine has been a beneficiary of the Klingenstein family's support of medical science for more than three decades. The family's most recent gift supports an endowed chair held by Pietro De Camilli (right) honoring John Klingenstein (second from left). Also pictured are Dean Robert Alpern (left) and John's wife, Patricia Klingenstein.

Two clinical leaders join medical school as administrators



Jeff Geschwind

Mary O'Connor

Two School of Medicine departments gained new leadership this spring. In May, Mary I. O'Connor, M.D., an accomplished orthopaedic surgeon and researcher, became the inaugural director of medical school's new Musculoskeletal Center. And in July, Jean-Francois (Jeff) Geschwind, M.D., an internationally known radiologist and a recognized leader in the field of liver cancer, joins the faculty as chair of the Department of Diagnostic Radiology at the School of Medicine and chief of diagnostic radiology at Yale-New Haven Hospital (YNHH).

Geschwind comes to Yale from The Johns Hopkins University (JHU) School of Medicine, where he was vice chair of its Russell H. Morgan

// Leaders *(page 4)*

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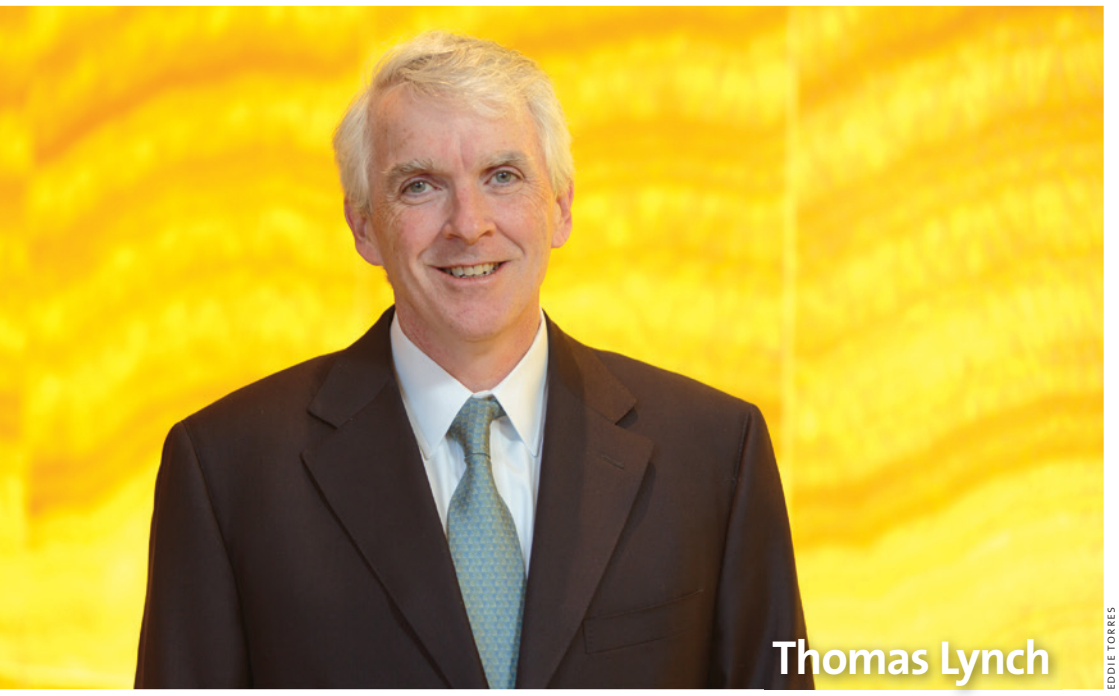

EDDIE TORRES

Thomas Lynch brought the molecular profiling of cancer out of obscurity and into standard protocols at Smilow Cancer Hospital at Yale-New Haven. Widespread access to clinical trials is key to continued progress, he says.

A commitment to care, basic science

Clinical trial access means better patient care and more clinical research

Early cancer drugs killed indiscriminately, going after the body's healthy cells as relentlessly as its cancerous ones. Today, hundreds of anticancer drugs target the specific genetic mutations that drive cancer. Pinpointing those mutations and pairing patients with targeted drugs has become standard at Smilow Cancer Hospital at Yale-New Haven, thanks in large part to the work of Thomas J. Lynch Jr., M.D., the Richard Sackler and Jonathan Sackler Professor of Medicine.

According to the National Cancer Institute (NCI), nearly 41 percent of Americans will be diagnosed with cancer in their lifetimes. Growing up in New Jersey as the son of a hematologist, Lynch says, "I knew even as a kid that I wanted to make [addressing] that my life calling."

Lynch received his bachelor's degree from Yale College, and his medical degree and his start in cancer research at the School of Medicine. As an undergraduate he worked in the lab of John S. Lazo, PH.D., associate professor of pharmacology, studying a drug for head and neck cancer. "Seeing the applicability of what happens in the lab and how it impacts patients got me really excited about the research angle of what we do," he says.

Lynch's forays into personalized medicine took place in Boston. He completed his internship and residency at Massachusetts General Hospital (MGH) and a fellowship in medical oncology at the Dana-Farber Cancer Institute. In 1993 he joined the faculty at Harvard Medical School (HMS), where he progressed to professor of medicine and chief of hematology/oncology at MGH Cancer Center.

Lynch specialized in the biggest cancer killer in America: lung cancer. When he began researching the disease, it was a death sentence. In the early 2000s he was giving his patients a drug called Iressa. The drug worked in 10 percent of patients and did virtually nothing for the other 90 percent.

Then came a turning point. A colleague, Daniel A. Haber, M.D., PH.D, professor of oncology at HMS and the director of MGH Cancer Center, found a mutation in the epidermal growth factor receptor gene in nearly every one of Lynch's patients that responded to Iressa. Lynch now had a test that could identify the patients who would respond to a specific drug. Personalized medicine in lung cancer was born.

Lynch returned to Yale in 2009 as director of Yale Cancer Center (YCC) and physician-in-chief at Smilow Cancer Hospital. He has overseen the standardization of molecular profiling in cancer patients, the establishment of an early drug development unit, and the re-designation of YCC as a comprehensive cancer center by the NCI. He has also worked to narrow the gap between research and patient care.

"Yale always had great clinical care and great basic science. But it lacked that translational connection between the laboratory and the clinic," says Lynch, who has recruited top translational scientists to build programs that link the clinical care offered at Smilow—where patient satisfaction scores are high—with the innovative research occurring in Yale's labs.

Lynch is also committed to advancing treatment by improving patients' access to clinical trials. Today YCC has 200 open clinical trials, and Lynch has established 10 Smilow Care Centers around Connecticut to bring greater access to patients. Citing progress made in breast cancer and melanoma outcomes, he hopes these trials will someday lead to cures.

"It's a daunting challenge," Lynch says, "but unless we make that our goal, we're never going to get there."

Endocrinologist honored with Leffell Prize praises his staff first

Silvio Inzucchi, M.D., professor of medicine and medical director of the Yale Diabetes Center, is the 2015 recipient of the David J. Leffell Prize for Clinical Excellence. The prize is given to individuals who demonstrate the highest level of clinical expertise, commitment to teaching, and compassion for patients.

At a ceremony on April 13, Inzucchi called the prize "a great honor," then quickly passed the praise along to his colleagues and support team. One of these colleagues, Ania M. Jastreboff, M.D., PH.D., assistant professor of medicine and pediatrics, said Inzuccchi "taught us to think in a logical, grounded manner, considering each patient as a unique individual, focusing on the nuances of each patient's diagnosis."

Inzucchi is director of the Yale Affiliated Hospitals Program and associate chief for clinical affairs in the Section of Endocrinology. He received his medical degree from Harvard Medical School and completed an internship and residency in internal medicine and a postdoctoral fellowship in metabolism at Yale-New Haven Hospital.

The Leffell Prize was established in 2008 with a gift from David J. Leffell, M.D., the David P. Smith Professor of Dermatology and professor of surgery, and his wife, Cindy, in honor of Leffell's 30th Yale College reunion. It inclues a monetary award and a framed citation to be displayed in the Sterling Hall of Medicine.

JERRY DOMIAN

Silvio Inzucchi, pictured with Dean Robert Alpern (left) and David Leffell (right), received the Leffell Prize for Clinical Excellence in April.

Medical school alumnus is named surgeon general

Vivek Murthy

Vivek Murthy, M.D., MBA, a 2003 graduate of the School of Medicine and the School of Management, has been named the nation's 19th surgeon general.

Murthy was officially sworn in by Health and Human Services Secretary Sylvia Mathews Burwell in December.

"I applaud the Senate for confirming Vivek Murthy to be our country's next Surgeon General," said President Barack Obama in a White House statement. "As 'America's Doctor,' Vivek will hit the ground running to make sure every American has the information they need to keep themselves and their families safe."

After graduating Yale, Murthy co-founded two organizations and jumpstarted international outreach projects to provide patients better health access and improve healthcare awareness. In 2010, he co-founded TrialNetworks, an online platform for coordinating clinical trials, which was acquired by DrugDev in 2014. In the lead-up to the Affordable Care Act, he served as president and co-founder of Doctors for America, which works to provide healthcare access to the general public.

Murthy, the first Yale alumnus to serve as U.S. Surgeon General, completed his residency in internal medicine at Boston's Brigham and Women's Hospital. He is an attending physician and an instructor in medicine at Harvard Medical School. Howard P. Forman, M.D., professor of diagnostic radiology and director of Yale's M.D./MBA Program, wrote in a blog post that the position will provide Murthy "but one more opportunity ... to apply his considerable talents."

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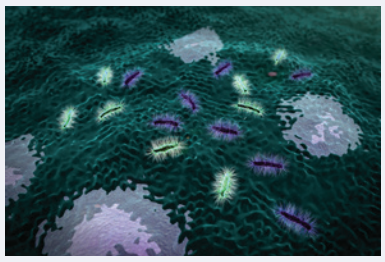
ADVANCES
Health & Science News

How fasting lessens inflammation



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When mice with inflammatory diseases are put on low-carb diets or forced to fast, their symptoms start to disappear. Now, scientists know why.

A team of scientists was studying the compound beta-hydroxybutyrate (BHB), which the body produces during starvation, dieting, or intense exercise. It's been known that the brain uses BHB for energy when blood sugar is low, but the team found something else: BHB blocks the protein NLRP3, which is part of a complex called the inflammasome and has been implicated in inflammatory diseases.

When mice were given BHB, the team reported in *Nature Medicine* in February, NLRP3 stopped activating their inflammasomes. Moreover, healthy mice with high blood levels of BHB did not develop disease when researchers mutated their NLRP3 gene.

Designing drugs that elevate BHB could help treat inflammation-related diseases in humans, says Vishwa Deep Dixit, DVM, PH.D., professor of comparative medicine and immunobiology and senior author of the study.

Shedding light on skin cancer

With a lifetime risk of 20 percent among Americans, skin cancer is the most prevalent form of cancer. Exposure to UV light accounts for the majority of skin cancers. UV radiation produces cyclobutane pyrimidine dimers (CPDs), which cause carcinogenic mutations in skin cells.

Our current understanding of the mechanism implies that damage only occurs during sunlight exposure. But in the Feb. 20 issue of *Science*, Douglas E. Brash, PH.D., clinical professor of therapeutic radiology, and colleagues reported a novel pathway by which UV damage to DNA can also occur in the dark. When they exposed melanin-producing melanocytes in the skin to UV radiation, the cells generated "dark" CPDs for more than three hours afterwards. When they inhibited the UV-induced reactive oxygen and nitrogen species, CPD production after exposure was suppressed. Additional experiments suggested that UV-induced reactive radicals combine to excite an electron in melanin fragments, producing "dark" CPDs.

The finding "implies that UV-induced DNA damage continues even after the exposure to UV rays has ended, [which] has important implications for melanoma formation," says Sanjay Premi, PH.D., associate research scientist in therapeutic radiology and lead author of the study.

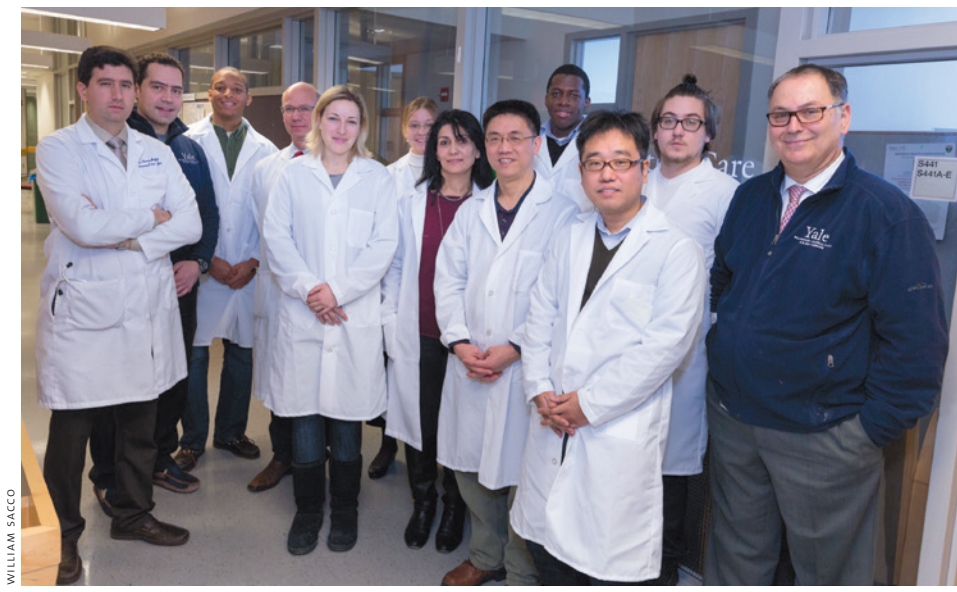
Knocking the wind out of lung disease

State-of-the-art research programs and an emphasis on bioinformatics are pushing pulmonary research at Yale forward

The January unveiling of President Obama's Precision Medicine Initiative—to fund research that better predicts which treatments will be most effective for which patients—highlights the increasing importance of personalized medicine today. But while physicians and scientists have made strides in tailoring treatments to patients with cancer and diseases caused by mutations in a single gene, similar advances in other diseases have lagged behind.

Members of the School of Medicine's Section of Pulmonary, Critical Care and Sleep Medicine (PCCSM) are changing that paradigm. By applying high-throughput RNA sequencing technologies and genomic methods to the study and treatment of chronic lung diseases like pulmonary fibrosis and asthma, they are unraveling the underlying mechanisms of these illnesses and developing targeted approaches to help patients.

Pulmonary fibrosis is a respiratory disease in which uncontrolled scarring damages the lungs and impairs breathing. Patients typically survive three to five years after being diagnosed, but, as with many diseases, how well they do can vary widely. Until recently, doctors had nothing to offer in the way of treatment short of a lung transplant.



WILLIAM SACCO

Members of the School of Medicine's Section of Pulmonary, Critical Care and Sleep Medicine (PCCSM) include (from left) Jose Herazo-Maya, Argyrios Tzouvelekis, Tony Woolard, Geoffrey Chupp, Milica Vukmirovic, Vera Nezgovorova, Farida Ahangari, Qing Liu, Adrian Wyllie, Koji Sakamoto, Giuseppe Deluliis, and Chief of PCCSM Naftali Kaminski.

Research by Naftali Kaminski, M.D., the Boehringer Ingelheim Pharmaceuticals, Inc. Professor of Medicine and chief of PCCSM, has shed light on the disease, revealing that it is an active process of destruction and rebuilding with many pathways. Kaminski's approach to developing personalized treatment has focused on analyzing gene expression in pulmonary fibrosis to help predict which patients progress more quickly. His lab identified a family of microRNAs—small RNA molecules which do not code for proteins but instead regulate which genes are turned on and off—that are changed in patients with pulmonary fibrosis. Last year he showed that supplementing mice with a molecule that mimics miR-29, a microRNA decreased in fibrosis, not only blocked fibrosis but could potentially reverse it.

With a new five-year, $7.1 million Centers for Advanced Diagnostics and Experimental Therapeutics (CADET) grant from the National Heart, Lung and Blood Institute (NHLBI), Kaminski's team is taking its findings to the next level. Awarded last July, the grant is enabling the team to develop the evidence needed to support the use of miR-29 mimics as FDA-approved drugs. They will evaluate miR-29 as a therapeutic agent for pulmonary fibrosis in humans and identify biomarkers to show which patients will benefit from the treatment. "The aim in five years is to have both a molecule [for drug development] and a target population," he said.

Kaminski's passion for pursuing personalized medicine is shared across his section by colleagues both junior and senior. Working in the Kaminski lab, Jose Herazo-Maya, M.D., instructor in medicine, was able to identify a gene expression signature in the blood of patients with pulmonary fibrosis that indicated which patients' disease would likely progress more quickly. Such information could be useful in light of two drugs recently approved by the U.S. Food and Drug Administration that can slow disease progression. "We think that the use of gene expression profiles in the blood of patients with pulmonary fibrosis may be helpful to actually get these patients on the drugs faster and to predict when lung transplants will be needed," Herazo-Maya says.

Geoffrey L. Chupp, M.D., associate professor of medicine, uses an approach similar to Kaminski's to treat asthma patients. He developed a system for collecting sputum that provides a window into the lung. After isolating cells from the airway and analyzing the gene expression of those cells, he has identified three sub-groups of patients whose genetic profiles correlate with the severity of their disease. He has also identified a gene expression signature in the blood that he has validated in both adult and pediatric asthma patients.

"In asthma there's a revolution of [therapeutic] biologics coming down the pipeline," says Chupp, also director of the Yale Center for Asthma and Airways Disease and the Pulmonary Function Laboratory at Yale-New Haven Hospital. He and his colleagues are conducting more than a dozen clinical trials to study these biologics—antibody-based therapies that bind to specific targets—and identify which therapies work best in which patients. Chupp is also the recipient of an NHLBI-funded CADET grant that he is using to develop a biologic that binds to and blocks YKL-40, a protein that is typically elevated in those with severe asthma.

Kaminski and Chupp are co-directors of the Center for Precision Pulmonary Medicine (P²MED), a new program that houses genomic technology and expertise within PCCSM. Technology alone cannot, of course, provide the kinds of insight required for precision medicine. "The idea is to create a skilled critical mass of pulmonary physician-scientists who are well versed in clinical medicine, as well as in genomics, bioinformatics and computational biology—the trade tools of precision medicine" Kaminski says.

> "Big data can provide hints about why and how patients respond to a drug."
>
> —Xiting Yan

Genetic analysis generates a massive amount of data—what scientists call "big data"—that require expertise to decipher, a process central to developing personalized treatments. "When you look at outcome data you can gain some insights, but you don't know exactly why some patients are responding while others are not," says Xiting Yan, PH.D., assistant professor of medicine and director of the P²MED Data Analysis and Bioinformatics Hub. "Big data can provide hints about why and how patients respond to a drug."

The location of P²MED within PCCSM affords scientists easy access to its resources and computational expertise. Meanwhile, Yale's clinics and hospitals provide a wealth of clinical information for faculty members to harness in their quest to develop targeted therapies. Each year more than 8,000 patients visit PCCSM's outpatient facility, the Winchester Chest Clinic, for example, and Chupp and Kaminski look forward to the day when each of them will benefit from the genomic discoveries now taking place. "We put in infrastructure very close to the clinical setting," Kaminski says. "That's the way you generate the next generation of physicians who will have the skills to understand genomic information and use it for the benefit of our patients."

OUT & ABOUT

September 11 A gathering marked the establishment of **The Daniel Jordan Fiddle Foundation Adult Autism Research Fund** by the medical school's Child Study Center (CSC) and The Daniel Jordan Fiddle Foundation (TDJFF) to support research projects related to adults living with autism spectrum disorders. (From left) **Roger J. Jou**, M.D., PH.D., assistant clinical professor in the CSC; **Linda J. Walder**, **J.D.**, founder and executive director of TDJFF; **Kevin Pelphrey**, PH.D., Harris Family Professor of Child Psychiatry in the CSC and professor of psychology; **Fred R. Volkmar**, M.D., Irving B. Harris professor in the CSC and professor of pediatrics, psychiatry, and psychology; and **Frederick J. Fiddle**, founder and treasurer of TDJFF.

COURTESY OF THE DANIEL JORDAN FIDDLE FOUNDATION

JOHN CURTIS (3)

February 19 At this year's **Second Year Show**, "How the Grinch Stole the Yale System," the Class of 2017 carried on a 66-year tradition, poking fun at the medical school's faculty and administration. **1. William Meyerson** (right), playing the narrator, introduces the Grinch, played by **John Andrews**. **2.** Andrews with **Lauren Provini**, playing Cindy-Lou-Who-Swift. **3.** The ensemble dances in the finale, a parody of Taylor Swift's "Shake It Off." (From left) **Emily Yin**, **Talia Robledo-Gil**, Provini, **Frances Javier**, **Eunice Martins**, and **Karrin Weisenthal**.

CARL KAUFMAN

November 17 The **New Haven Mental Health Outreach for Mothers (MOMS) Partnership** held a press conference at the Stop & Shop supermarket on Whalley Avenue to announce an expansion following a new $3.7 million federal grant. Under the direction of **Megan V. Smith**, PH.D. (left), assistant professor of psychiatry, the project has provided mental health services to 3,000 low-income single mothers in New Haven.

JERRY DOMIAN

December 9 A celebration of the election of **W. Mark Saltzman**, PH.D., Goizueta Foundation Professor of Chemical and Biomedical Engineering, to the **Institute of Medicine** was held in the medical school's Historical Library. Pictured are (from left) Dean and Ensign Professor of Medicine **Robert J. Alpern**, M.D.; Saltzman, who is also chair of the Department of Biomedical Engineering; and **T. Kyle Vanderlick**, PH.D., dean of the School of Engineering and Applied Science and the Thomas E. Golden Jr. Professor of Chemical and Environmental Engineering.

JOHN CURTIS (4)

March 20 Each spring, medical students across the country eagerly await **Match Day**, when students receive word of acceptance in residency training programs. **1. Jennifer Guo** (left) and **Ruth Wang'ondu**. **2. Emily Thomas** (left) and classmate **Jennifer Quon**. **3.** (From left) **Auguste H. Fortin VI**, M.D., MPH, associate professor of medicine; **Marcella Nuñez-Smith**, M.D., MHS, associate professor of medicine and of epidemiology and public health and director of the Equity Research and Innovation Center (ERIC); **Terri-Ann M. Thompson**, PH.D., associate research scientist; and **Damaris Faustine**, coordinator for ERIC. **4. Serene Chen** and **Daniel Hart**, M.D., a resident in emergency medicine.

// Leaders *(from page 1)* Department of Radiology. His research focuses on improving image-guided therapies for liver cancer and discovering new therapeutics for cancer in general, targeting tumor metabolism.

A native of France, Geschwind earned his M.D. at Boston University School of Medicine and completed his residency training in a National Institutes of Health-sponsored scholars program at the University of California, San Francisco. He completed a fellowship in vascular and interventional radiology at JHU in 1998 before joining the JHU faculty. In 2007 Geschwind was promoted to professor of radiology, surgery, and oncology at JHU. He succeeds T. Rob Goodman, M.B., B.CHIR., professor of diagnostic radiology and chief of pediatric imaging, who served as interim department chair.

O'Connor comes to Yale from Mayo Clinic College of Medicine, where she was professor of orthopaedic surgery and program director of the adult reconstructive fellowship at Mayo Clinic in Florida.

O'Connor earned her bachelor's degree from Yale College and her M.D. from the Medical College of Pennsylvania. She completed an internship and residency in orthopaedics and a fellowship in orthopaedic oncology, both at Mayo Graduate School of Medicine.

At her Mayo practice, O'Connor treated orthopaedic oncology patients and adults needing complex reconstructive surgeries for degenerative joint diseases. She is co-investigator on a pilot study to determine if injecting a patient's stem cells into his or her knee joint will slow the progression of arthritic changes.

Similar to Yale Cancer Center, the new Musculoskeletal Center will coordinate interdepartmental clinical and research programs at the medical school and hospital. As a clinical and research center, it brings together specialists in orthopaedics, neurosurgery, neurology, rheumatology, rehabilitation, biomedical engineering, and other specialties to provide a wide range of services, including joint replacement, pain management, and advanced treatment for arthritis, spine disorders, multiple sclerosis, Parkinson disease, and other conditions.

"Mary O'Connor and Jeff Geschwind bring extraordinary strengths and track records to the medical school," said Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "I look forward to the growth of these programs under their leadership."

ADVANCES
Health & Science News

To trigger brain cell production, a switch

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It's a common mistake to say that you're born with all the brain cells you'll ever have. In fact, stem cells deep in your hippocampus—which controls memories—can make new brain cells throughout your life. But scientists have not fully understood how and when these stem cells are activated to churn out new neurons.

Now, a team led by Jean-Leon Thomas, PH.D., M.SC., associate professor of neurology, and Anne Eichmann, PH.D., M.SC., Ensign Professor of Medicine and professor of cellular and molecular physiology, has uncovered a molecular switch that triggers neuron production.

Stem cells in the hippocampus, the team reported Feb. 19 in *Cell Reports*, have a receptor for the vascular growth factor VEG-FC. When VEG-FC binds to the receptor, the stem cells are signaled to convert into dividing progenitors that make new neurons. When the team bred mice lacking the receptor, the mice produced fewer new brain cells throughout their lives.

The findings could lead to new drugs for neurological diseases that coax the brain to make new cells.

Delivering a death blow to HIV

Antiretroviral drugs, though effective in suppressing an HIV infection, do not completely eradicate the disease. Instead, the virus acquires "escape mutations" that allow it to evade an attack by cytotoxic T lymphocytes (CTLs), the body's virus-specific immune mechanism, and becomes latent in CD4+ T lymphocytes.

New research by Yale scientists suggests that programming CTLs to recognize and kill the infected T cells holds promise for developing a cure for HIV. In the journal *Nature* on Jan. 7, Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology, and colleagues reported that boosting CTL response might hold the key to virus eradication.

The scientists identified CTLs that target unmutated regions of HIV and demonstrated in "humanized" mice harboring an HIV patient's immune system that these CTLs were able not only to control infection, but also to clear the circulating virus. The study is the first to show that broadly reactive CTLs are effective against latent HIV.

"We reconstructed a human patient in a mouse and demonstrated that the body's natural defense, when boosted, can clear HIV infection," says Priti Kumar, PH.D., assistant professor of medicine and microbial pathogenesis and a co-author of the paper. "A finding like this gives the research field a new direction."

The anatomy of autoimmune disease

By analyzing data from dozens of genomic studies, a team of scientists zeroes in on the molecular links among related diseases

What do diabetes, Crohn's disease, psoriasis, and multiple sclerosis have in common? From the outside, not much: they affect different organs and have vastly different symptoms. But each is an autoimmune disease, and new research, identifying genes and cell types responsible for such diseases, reveals just how much they have in common.

"What we showed is that, to some extent, autoimmune disease is one fundamental entity with many variations," says David A. Hafler, M.D., chair and the William S. and Lois Stiles Edgerly Professor of Neurology, professor of immunobiology, and a senior author of the paper.

In all autoimmune diseases, the body's immune system gangs up on a person's own cells. If the immune system attacks skin cells, the redness and itching of psoriasis can result; if it attacks pancreas cells, type 1 diabetes; if it turns against cells lining the intestines, ulcerative colitis or Crohn's disease. As a whole, autoimmune diseases—which affect an estimated 50 million Americans—are tricky to treat, and their causes are poorly understood.

Previous research on individual autoimmune diseases have used genome wide association studies (GWAS) to narrow down which areas of DNA within the human genome are linked to disease. But the areas of the genome identified in GWAS can contain many genes.

Hafler and his colleagues at the Broad Institute of MIT and Harvard wanted to home in on specific genes linked to autoimmune diseases. To do so, they analyzed 39 previous GWAS studies, spanning 21 different diseases, using new software and data analysis techniques. Says Hafler, "We went from a large region of DNA that's implicated in a disease to the precise gene change that's likely responsible. I call this a post-GWAS understanding of disease."

By mapping certain molecular features within these areas, the team discovered that many autoimmune diseases aren't caused by variations in genes that encode proteins, but by changes to "enhancers," elements in the DNA that can turn on nearby genes. If an enhancer is altered, a whole slew of genes it controls can be flipped on or off at once. In the case of many autoimmune diseases, the scientists reported February 19 in the journal *Nature*, the affected enhancers go on to affect immune genes. And, they found, many genes overlapped between diseases—affecting both Crohn's disease and rheumatoid arthritis, for example.

But the team didn't stop with the identification of genes and enhancers associated with the autoimmune diseases. Next, they studied which cell types each genetic change was active in. "If you have a genetic change in a region where the DNA is tightly wound up, that change is unlikely to make a difference to that particular cell," Hafler explains. But in other cells, the DNA containing the genetic variant could be more "open" and thus accessible for DNA transcription, suggesting that the variant is influencing the cells' function.

Some findings were expected: the DNA regions linked to ulcerative colitis, for instance, were activated in immune cells and mucosal cells lining the digestive system. But others were more surprising—the genetic variants associated with multiple sclerosis seemed to be inactive in brain cells, only making a difference in immune cells themselves.

MICHAEL MARSLAND

David Hafler and colleagues recently published research in *Nature* showing significant genetic overlap in the causes of diverse autoimmune diseases. The research also suggests that many autoimmune diseases are triggered by specific elements within DNA called "enhancers," and not by variations in the genes that encode proteins, as previously thought.

"What this work does is provide, for the first time, a landscape as to how genetic variants are causing autoimmune disease," Hafler says. "That landscape—the molecular events and cell types involved—is a critical step in understanding disease."

While that step of pinpointing important genes and cell types requires more refinement to more fully reveal the cause of autoimmune diseases, it does pave the way toward drugs that can block the immune system from its unwarranted attack, Hafler says. It also shows just how effective new techniques can be at moving from GWAS results to specific genetic changes that cause disease. And that, he says, is useful for studying not only autoimmune disease, but everything from heart disease and Alzheimer's to cancer.

Yale's partnership with Johnson & Johnson promotes data sharing

In January 2014, the Yale Open Data Access (YODA) Project began a collaboration with Johnson & Johnson to establish an independent process promoting data sharing. Since then the YODA Project has fielded more than a dozen requests for clinical data from researchers and played a key role in pushing the clinical research field toward a more open way of operating.

Part of Yale's Center for Outcomes Research and Evaluation (CORE), the YODA Project began in 2012 with the mission of promoting scientific inquiry and lowering barriers to data access. The partnership with Johnson & Johnson gives the YODA Project all decision-making authority over the release of the company's pharmaceutical trial data.

The idea is to make these data available to researchers who can put it to good use. But there is also a larger aim, says Joseph S. Ross, M.D., M.H.S., co-director of the YODA Project: "We're trying to create a paradigm shift in the way clinical research is done," Ross says. "It's about honoring the commitment the patients have made to research, [and] about making sure all of the evidence that could potentially inform a decision about whether a patient should use or a physician should prescribe a given therapy is available."

Harlan Krumholz

Joseph Ross

Investigators requesting data must submit a research proposal to the YODA Project. The application and review process is key to the idea of promoting responsible research, says Ross, also associate professor of medicine and assistant professor of public health.

Studies have found that up to half of all clinical data are never published—data that could move medicine forward. The YODA Project aims to shift this paradigm, and to take decision-making power about data sharing "out of the hands of these large companies that had a major investment in what happens with the data," Ross says.

In January of this year, on the same day that Johnson & Johnson announced it expanded its collaboration with the YODA Project to include data from clinical trials of medical devices, a committee of the Institute of Medicine (IOM) called on stakeholders in the medical research process to "foster a culture where data sharing is the expected norm." The committee recommended that all stakeholders in clinical trials commit to "responsible strategies aimed at

// Sharing *(page 7)*

Grants and contracts awarded to Yale School of Medicine

March 2014–August 2014

Federal

Nii Addy, NIH, *CaV 1.3 L-type Calcium Channel Mechanisms in Cocaine Seeking*, 2 years, $475,319 • **Amy Arnsten**, NIH, *mGluR2/3 Influences in Primate Prefrontal Cortex: Potential for Therapeutics*, 2.9 years, $1,498,500 • **Jeremy Baskin**, NIH, *Mechanisms Controlling Phosphoinositide Synthesis at the Plasma Membrane*, 2 years, $180,000 • **Choukri Ben Mamoun**, NIH, *Development of Novel Therapeutics for Babesia Microti Infection*, 2 years, $457,875 • **Steven Bernstein**, NIH, *A Network Analytic Model of Adherence and Abstinence*, 3 years, $696,367 • **Hal Blumenfeld**, NIH, *Deep Brain Stimulation to Prevent Impaired Consciousness in Epilepsy*, 2 years, $457,875 • **Linda Bockenstedt**, NIH, *A New Cytokine-Based Immunoassay for the Diagnosis of Lyme Borreliosis*, 3 years, $1,446,052 • **Titus Boggon**, NIH, *Upgrade of a Home Source Macromolecular X-ray Diffraction System*, 1 year, $459,619 **Alfred Bothwell**, NIH, *Regulatory T Cell Control of Intestinal Tumorigenesis*, 5 years, $1,727,440 **Richard Bucala**, NIH, *MIF and Host Response to Infection*, 1 year, $426,423; NIH, *Inflammatory Suppression of Adaptive Immunity by Plasmodium MIF*, 5 years, $2,081,250 • **Sarah Calabrese**, NIH, *Intervention to Promote PrEP Awareness and Equitable Prescription among Providers*, 4 years, $633,763 • **Lloyd Cantley**, NIH, *Defining the Polycystin-Dependent Macrophage Responses that Accelerate Cyst Growth in ADPKD*, 5 years, $1,810,690 • **Sandy Chang**, NIH, *Understanding Alternative Non-Homologous End Joining Repair in Telomere Dysfunctional Breast Cancer*, 2 years, $398,352 **Tian Chi**, NIH, *CaM-Regulated Chromatin Remodeling: Mechanisms, Generality and* In Vivo *Functions*, 2 years, $457,875 • **Michael Choma**, NIH, *Massively Parallel Interferometric Confocal Microscopy using Degenerate Lasers*, 2 years, $409,330 • **Daniel Colon-Ramos**, NSF, *Dissection at Single Cell-Level of the Thermotaxis Behavioral Circuit in* C. elegans, 4.3 years, $680,000 • **Joseph Contessa**, NIH, *Targeting N-linked Glycosylation to Enhance Radiation Therapy*, 4.9 years, $2,013,043 • **Justin Cotney**, NIH, *Identification of Human Orofacial Enhancers and Their Role in Orafacial Clefts*, 2 years, $217,706 • **Emerson Crabill**, NIH, *Functional Analysis of a* Coxiella burnetii *Effector Protein that is Required for Intracellular Replication*, 2 years, $104,812 • **Pietro De Camilli**, NIH, *Molecular Mechanisms in Synaptic Vesicle Recycling*, 3 years, $1,248,750 • **Isabelle Derre**, NIH, *ER-Chlamydia Inclusion Membrane Contact Sites*, 5 years, $2,081,250 • **Ralph DiLeone**, NIH, *A Role for Lipoprotein Lipase in Mesolimbic Function*, 2 years, $406,077; NIH, *A Role for Vitamin D in Drug Addiction*, 2 years, $354,750 **Maria Diuk-Wasser**, **Adalgisa Caccone**, **Katharine Walter**, NSF, *Dissertation Research: Invasion Phylogeography of* Borrelia burgdorferi, *a Tick-Borne Pathogen*, 1 year, $21,146 **Jackie Fretz**, NIH, *Regulation of Podocyte Differentiation by the Transcription Factor EBF1*, 2.9 years, $726,969 • **Kara Furman**, NIH, *Investigating the Role of D2 in Feeding and Obesity*, 3 years, $102,144 • **Jorge Galan**, NIH, *Virulence Factors of* Salmonella Typhi, 1 year, $486,262 **Alison Galvani**, NIH, *Dynamic Data-Driven Decision Models for Infectious Disease Control*, 4.7 years, $3,377,995 • **Paul Geha**, NIH, *Neural Mechanisms of Obesity in Chronic Low Back Pain*, 5 years, $876,837 • **Mark Gerstein**, NIH, *Gene Regulatory Elements and Transcriptome in iPSCs and Embryonic Human Cortex*, 3 years, $156,018 • **Steven Gore**, NIH, *Targeting Epigenomics in Myeloid Neoplasms*, 1.9 years, $551,780 • **Fred Gorelick**, NIH, *Exocrine Pancreatic Zymogen Activation*, 5 years, $1,182,330 **Daniel Greif**, **Anne Eichmann**, NIH, *Mural Cell TGF-Beta-Mediated Signaling and Neonatal Intracerebral Hemorrhage*, 2 years, $457,875 **Carlos Grilo**, NIH, *Treatment of Loss of Control Eating Following Bariatric Surgery*, 5 years, $2,231,474 • **Jaime Grutzendler**, NIH, In Vivo *Cellular Imaging of Myelin Plasticity and Regeneration in Cortical Gray Matter*, 2 years, $457,875; NIH, *The Role of Astrocytes in Myelin Maintenance and Regeneration*, 2 years, $457,875 • **Murat Gunel**, **Kaya Bilguvar**, NIH, *Disease Gene Discovery in Structural Brain Disorders*, 2 years, $1,485,239 • **Kathryn Hacker**, NIH, *Rodent Population Dynamics and Leptospirosis Infection in Urban Slum Environments*, 2 years, $54,580 • **Marc Hammarlund**, NIH, *A Novel Mechanism that Inhibits Axon Regeneration*, 1 year, $416,250 • **Jeanne Hendrickson**, NIH, *Immunoprophylaxis to KEL RBC Alloimmunization During Pregnancy*, 10 months, $172,756; NIH, *Protecting Fetuses and Newborns from Maternal RBC Alloantibodies*, 5 years, $2,130,430 • **Kevan Herold**, NIH, *Phase II Trial of HOKT3gamma 1 (ALA-ALA) in Type 1 Diabetes*, 4 years, $1,332,837 • **Howard Hochster**, **Peter Glazer**, **Thomas Rutherford**, NIH, *YCC Cooperative Group Support Grant*, 4.9 years, $2,757,500 **Mark Hochstrasser**, NIH, *Degradation of Short Lived Regulatory Proteins In Yeast*, 4.8 years, $1,814,782 • **Jonathon Howard**, NIH, *Control of Microtubule Length by Polymerases and Depolymerases*, 3.8 years, $1,620,308 • **Karl Insogna**, NIH, *A Novel SATB2 Mutation Illuminates Bone Anabolism*, 2 years, $402,930 **Shuta Ishibe**, NIH, *KUH Undergraduate Summer Research Program at Yale*, 5 years, $493,020 **Natalia Ivanova**, NIH, *Novel Differentiation Repressor Module in Human ES Cells*, 4 years, $1,265,400 • **Ania Jastreboff**, NIH, *Effect of Insulin on Brain Activation, Food Craving, and Food Intake in Obesity*, 2.8 years, $467,079 **Elizabeth Jonas**, NIH, *Role of DJ1 in Mitochondrial Biogenergetics and Neuronal Metabolism*, 5 years, $2,205,298 • **Mustafa Khokha**, NIH, *A System Approach to the Analysis of Heterotaxy Candiate Genes*, 4.7 years, $2,707,778 **Mustafa Khokha**, **Engin Deniz**, **Martina Brueckner**, **Michael Choma**, NIH, *Cardiac Phenotyping of CHD Candidate Genes in Xenopus*, 2 years, $454,122 • **Kenneth Kidd**, NSF, *Ongoing Development of a Human Population Genetics Resource*, 2 years, $379,240 • **Steven Kleinstein**, NIH, *Computational Tools for the Analysis of High-Throughout Immunoglobulin Sequencing*, 4 years, $1,782,027 • **Anthony Koleske**, **Jaime Grutzendler**, NIH, *Laminin Control of CNS Dendrite and Dendritic Spine Development*, 4.9 years, $1,801,220 • **Anthony Koleske**, NIH, *Control of Actin Dynamics and Dendritic Spine Stability by Arg and Cortactin*, 2 years, $353,813 **Harlan Krumholz**, DHHS, *Yale-CORE Career Development Program in Patient-Centered Outcomes Research*, 5 years, $3,403,262 **Priti Kumar**, NIH, In Vivo *Genomic Editing of Hematopoietic Cells for HIV Resistance*, 4 years, $2,073,619 • **Brian Leaderer**, NIH, *Indoor Nitrogen Dioxide Exposure and Children with Asthma: An Intervention Trial*, 5 years, $4,584,829 • **Daeyeol Lee**, NIH, *Learning and Selection in the Basal Ganglia*, 1.9 years, $451,225 • **Ifat Levy**, NIH, *Neural Mechanisms of Decision-Making under Uncertainty in PTSD*, 2 years, $457,874 • **Janghoo Lim**, NIH, *Investigating the Pathogenesis of Cerebellar Neurodegeneration*, 5 years, $1,821,095 • **Chenxiang Lin**, **Charles Lusk**, **Thomas Melia**, NIH, *Generating Nuclear Pore Complex Mimics with DNA Origami*, 2.2 years, $457,875 • **Chi Liu**, NIH, *Low-Dose SPECT/CT for Imaging Chemotherapy-Induced Microvascular Cardiotoxicity*, 4.7 years, $3,217,654 • **Yuchen Liu**, NSF, *Collaborative Research: Unraveling Sulfur Networks in Methanogenic Archaea*, 3 years, $392,011 • **Elias Lolis**, NIH, *Structure of the Chemokine Receptor CXCR3*, 2 years, $457,874 • **Patricia Lorusso**, NIH, *VikTriY Early Clinical Trials Consortium (ECTC)*, 4.6 years, $5,891,923 • **Arya Mani**, NIH, *Genetic Regulation of Arterial Wall by Canonical Wnt Signaling*, 3.8 years, $2,164,500 • **Kathleen Martin**, NIH, *Epigenetic Control of Vascular Smooth Muscle in Cardiovascular Disease*, 4 years, $1,665,000 • **Diane McMahon-Pratt**, NIH, *Translational Research Training on Leishmaniasis and Emerging Infectious Diseases*, 4.7 years, $1,140,049 • **Peggy Myung**, NIH, *The Role of Non-Cell Autonomous Wnt Activation in Hair Follicle Growth and Cancer*, 4.9 years, $640,575 • **Michael Nathanson**, NIH, *Training Program in Investigative Hepatology*, 5 years, $1,348,717 • **Don Nguyen**, NIH, *Epigenetic Modulation of Lung Cancer Metastasis By a Novel Long Intergenic RNA*, 2 years, $398,352 • **Laura Niklason**, NIH, *Research Training in Anesthesia*, 5 years, $961,897 • **A. David Paltiel**, NIH, *Novel Approaches to the Design and Evaluation of Combination HIV Prevention*, 4.8 years, $3,309,826 • **Joao Pereira**, NIH, *Cellular and Molecular Analysis of B Lymphocyte Development and Selection*, 5 years, $2,063,528 **Marina Picciotto**, NIH, *Anatomical Basis for Nicotine Addiction*, 5 years, $1,956,375 • **Pasko Rakic**, NIH, *Origin of Cortical Species-Specific Distinctions*, 5 years, $3,582,124 • **Karin Reinisch**, NIH, *Cargo Recognition by the Retromer Sorting Complex*, 1.8 years, $166,500 • **Douglas Rothman**, NIH, *13C MRS Studies of Brain Mitochondrial Metabolism in Insulin Resistance*, 5 years, $2,094,810 • **Lauren Sansing**, NIH, *Modulating Monocyte Responses to Reduce Injury after Intracerebral Hemorrhage*, 2.2 years, $457,875 • **Alessandro Santin**, NIH, *Integrated Genomic Analysis of Racial Disparities in Endometrial Cancer*, 5 years, $1,741,765 **William Sessa**, NIH, *Endothelial NOS by Protein to Protein Interactions*, 4.8 years, $2,359,915 **Gordon Shepherd**, NIH, *SenseLab: Integration of Multidisciplinary Sensory Data*, 5 years, $3,374,215 • **Frederick Sigworth**, NIH, *Fluctuations in Ionic Current Through Membrane Channels*, 4.9 years, $1,591,747 • **Charles Sindelar**, NIH, *Structural Basis of Motility by Dimeric Kinesin Motor Proteins*, 5 years, $1,581,750 **Satinder Singh**, NIH, *Structure and Function of a Serotonin Transporter*, 2 years, $2,876,536 **Christal Sohl**, NIH, *The Molecular Mechanism of Isocitrate Dehydrogenase (LDH) Mutations in Cancer*, 2 years, $178,596 • **Michael Strambler**, **Walter Gilliam**, Department of Education, *Researcher-Practitioner Partnerships in Education Research*, 2 years, $199,989 • **Joann Sweasy**, NIH, *DNA Polymerase Beta and Mutagenesis*, 4.8 years, $1,652,226 • **Susumu Tomita**, NIH, *Identify Functional Modulators of Ionotropic Neurotransmitter Receptors in Brain*, 3 years, $1,030,216 • **Derek Toomre**, NIH, *New Toolkit for Imaging and Controlling Early Ciliogenesis*, 2 years, $457,875 • **Christian Tschudi**, NIH, *Mechanism of Infectivity Acquisition in African Trypanosomes*, 5 years, $2,081,250 **Federico Vaca**, NIH, *Automated Bilingual-Computerized Alcohol Screening & Intervention in Latinos*, 5 years, $3,160,607 • **Flora Vaccarino**, NIH, *Gene Regulatory Elements and Transcriptome in iPSCs and Embryonic Human Cortex*, 3 years, $1,760,570; NIH, *Gene Regulatory Elements and Transcriptome in iPSCs and Embryonic Human Cortex*, 3 years, $33,415 • **Penghua Wang**, NIH, *A Critical Role of NLRP6 in West Nile Virus Pathogenesis in Mice*, 2 years, $457,875 **Li Wen**, NIH, *Dendritic Cells in Immuno-Metabolic Disorder in Mouse and Man*, 3.8 years, $1,442,795 • **Jeffrey Wickersham**, NIH, *Training in Drug Abuse and HIV Prevention for Female and Transgender Sex Workers*, 5 years, $837,825 • **Adam Williams**, NIH, *Identifying lincRNAs Critical in Asthma Pathogenesis*, 2 years, $457,875 • **Dianqing Wu**, NIH, *Investigating Cellular Function and Biochemical Mechanism for STK24-CCM3 Complex*, 4.8 years, $1,581,750 • **Guanqing Wu**, NIH, *To Explore and Study Domain Functions of Fibrocystin using Animal Models*, 1.3 years, $342,305 • **John Wysolmerski**, NIH, *PMCA2 Regulates Mammary Gland Involution*, 5 years, $1,798,439 • **Ke Xu**, NIH, *Longitudinal Exome-Focused GWAS for Alcohol Use in a Cohort with and without HIV*, 2 years, $343,613 • **Zhong Yun**, NIH, *Malignant and Radioresistant Nature of Hypoxic Tumor Cells*, 5 years, $1,727,440 • **Alexei Zelenev**, NIH, *Modeling HIV and Substance Abuse: Correcting Sampling Bias and Cost Effectiveness*, 5 years, $837,825 • **Zhenwu Zhuang**, NIH, *Molecular Imaging of Factor XIII in a Mice Model of Coronary Microvascular Disease*, 1.7 years, $457,875

Non-federal

David Assis, Cystic Fibrosis Foundation, *Improving GI and Liver Care for Adults with Cystic Fibrosis*, 3 years, $96,992 • **Alexander Au**, KCI USA, *External VAC Therapy Improves Perfusion in a Pig Model*, 2 years, $29,119 • **Alexia Belperron**, L2 Diagnostics, LLC (NIH), *A Serologic Assay to Measure Successful Lyme Borreliosis Antibiotic Therapy*, 1 year, $366,302 • **Joerg Bewersdorf**, G. Harold and Leila Y. Mathers Charitable Foundation, *Nanoscale Observation and Manipulation in Cells and* In Vivo, 4 years, $1,500,000 **Vineet Bhandari**, Hartwell Foundation, *Surfactant-Enhanced Delivery of Silencing Ribonucleic Acid to Prevent Bronchopulmonary Dysplasia*, 3 years, $300,000 • **Michael Bloch**, Tourette Syndrome Association, *FAAH Inhibitor Trial for Adults with Tourette Syndrome*, 1 year, $74,985 • **Linda Bockenstedt**, L2 Diagnostics, LLC (NIH), *Diagnostic Assays for Early Lyme Borreliosis Using* In Vivo *Expressed Antigens*, 1 year, $368,393 • **Titus Boggon**, Emory University (NIH), *Signaling and Targeting of 6-Phosphogluconate Dehydrogenase in Human Cancers*, 10 months, $2,671 • **Elizabeth Bradley**, Management Sciences for Health, *Sustainable Leadership, Management, and Governance*, 1.9 years, $457,506 • **Clemente Britto-Leon**, Cystic Fibrosis Foundation, *Program for Adult Care Excellence (PACE)*, 3 years, $81,000 **Robert Bruce**, University of Pennsylvania (NIH), *Pharmacogenetics of Opioid Agonist Therapy*, 1 year, $68,906 • **Emanuela Bruscia**, Cystic Fibrosis Foundation, *Role of the HO-1/CO Pathway in CF Macrophage Function*, 2 years, $194,400 • **Jessica Cardin**, McKnight Endowment Fund for Neuroscience, *Mechanisms of State-Dependent Cortical Network Regulation*, 3 years, $225,000 • **Richard Carson**, Eli Lilly and Company, *PET Ligand Development and Nonhuman Primate Imaging*, 2 years, $348,152; Taisho Pharmaceuticals, *Work Order #1-11C-TASP0410699 on NHP*, 1 year, $497,086; Research Foundation of (SUNY) State University of New York (NIH), *Lithium's Molecular Mechanism of Action and the Pathology of Bipolar Disorders*, 1 year, $413,715 • **Nancy Carrasco**, Fibrolamellar Cancer Foundation, *Fibrolamellar Cancer Foundation Project*, 1 year, $126,700 **Kachun Cheung**, Uniting against Lung Cancer, *Treating Metastasis by Differentiation Therapy: Identifying Druggable Pathways*, 2 years, $100,002 • **Theodore Cohen**, Bill and Melinda Gates Foundation, *Mathematical Models to Improve Drug Dosing for Limiting Persistence in M. Tuberculosis*, 1.2 years, $120,766 • **Joseph Contessa**, American Cancer Society, Inc., *Targeting N-linked Glycosylation in Non-Small Cell Lung Cancer*, 4 years, $792,000 • **Joseph Craft**, Rheumatology Research Foundation, *Studying Monocytes and iPS Cells in RA*, 2 years, $400,000 • **Michael Crair**, Simons Foundation, *Disrupted Network Activity in Neonatal Cortex of Mouse Models of Autism*, 2 years, $250,000 **Pietro De Camilli**, Michael J. Fox Foundation for Parkinson's Research, *The Function of Parkin-mediated Ubiquitination in Synaptic Function*, 1 year, $125,000 • **Daniel DiMaio**, Brown University (NIH), *Structure-Function Based Development of Therapeutics for JCV Induced Disease*, 10 months, $366,300 • **Edward Faustino**, American Heart Association (Founders Affiliate), *Epidemiology of Deep Venous Thrombosis in Critically Ill Adolescents (National)*, 2 years, $154,000 • **David Fiellin**, University of Pittsburgh (NIH), *Comparative Effectiveness of Alcohol and Drug Treatment in HIV-Infected Veterans*, 2 years, $152,542 • **Richard Flavell**, AbbVie, Inc., *Rerouting Pathogenic T Cells to Regulatory T Cells to Cure Autoimmune Disease*, 4 years, $1,665,000 • **Anna-Rachel Gallagher**,

PKD Foundation, *Investigation of the Biological Basis and Therapeutical Effect of Anti-Tumor Drug 11B Dichloro on PKD*, 2 years, $160,000 **Alison Galvani**, Task Force for Global Health, Inc., *Modeling to Support Lymphatic Filariasis (LF) Elimination Programs: Loa Loa Intensity Modeling*, 7 months, $66,469 • **Joel Gelernter**, University of Iowa (NIH), *Fine Mapping a Gene Sub-Network Underlying Alcohol Dependence*, 1 year, $17,097 • **Mark Gerstein**, University of Massachusetts (NIH), *Racial and Ethnic Diversity in Circulating Human Extracellular RNA*, 4.7 years, $149,855 • **David Glahn**, University of Vermont (NIH), *ENIGMA-Addiction: A Data-Pooling Investigation of Brain and Genetic Correlates of Addiction*, 1 year, $73,000 • **Rosana Gonzalez-Colaso**, Physician Assistant Foundation, *Finding Common Ground: Bilateral Impact of International Rotations for PA Students*, 1 year, $10,000 **Daniel Greif**, American Heart Association (Founders Affiliate), *Aortic Wall Morphogenesis and Disease: Clonal Architecture and Beta Integrins*, 3 years, $198,000 • **Cary Gross**, American Cancer Society, Inc., *Understanding Disparities in the New Era of Personalized Breast Cancer Care*, 3 years, $591,999 • **Jaime Grutzendler**, National Multiple Sclerosis Society, *Cortical Axonal Demyelination and Remyelination Studies with Novel* In Vivo *Microscopy Imaging Tools*, 1 year, $39,999 **Murat Gunel**, Gilead Sciences, *Gilead-Yale Collaboration in Cancer—Therapeutic Effect of the BRD4 Inhibitor Using Brain Tumor Cell Cultures as Well as Xenografts in Mice*, 2 years, $965,800 **David Hafler**, National Multiple Sclerosis Society, *Can a High Salt Diet Drive Induction of Pathogenic T Cells in Humans?*, 3 years, $545,399; Benaroya Research Institute (NIH), *CSGADP Pilot: Utilizing Novel CRISPR Technology to Study Autoimmunity-Associated Genetic Variants*, 1 year, $124,875 • **Mihaly Hajos**, FORUM Pharmaceuticals, Inc. (Formerly EnVivo Pharmaceuticals, Inc.), *Proposal for Electrophysiological Evaluation of Genetic Modeling of Frontotemporal Dementia in Progranulin Transgenic Mice*, 1 year, $85,165 **Stephanie Halene**, State of CT Dept. of Public Health, *Therapeutic Relapse in AML: Clonal Evolution in Patients and Humanized Mice*, 2 years, $400,362 • **Kevan Herold**, University of Michigan, *Brehm Coalition: De-Differentiation During Progression of Beta Cell Loss in Type 1 Diabetes*, 1.7 years, $101,691; University of California, San Francisco, *JDRF Collaborative Center for Treg Biology*, 1 year, $110,000; AbbVie, Inc., *Studies of Inflammatory Bowel Disease in Humanized Mice*, 1 year, $133,200 • **Lawrence Hirsch**, Acorda Therapeutics, Inc., *2014 Epilepsy Research Retreat*, 1 day, $10,000 • **Michael Hoge**, Southern Connecticut State University, *Provide Lecture/Training to DCF Staff on Group Supervision*, 5 months, $25,000 • **Theodore Holford**, National Academy of Sciences, *Health Implications of Raising the Minimum Age for Purchasing Tobacco Products*, 8 months, $25,000 • **Yiyun Huang**, New York University School of Medicine (NIH), *Kappa Opioid Receptor Imaging in Anorexia*, 1 year, $81,666 • **Karl Insogna**, Amgen, Inc., *Amgen Pilot Funding to Pursue SATB2 as a Novel Window on Bone Anabolism*, 2 years, $49,950; Merck Sharp & Dohme, Conference Grant: *The Arthur E. Broadus Skeletal Metabolism Symposium April 3-4, 2014 New Haven CT*, 1 day, $9,983 **Melinda Irwin**, Harvard School of Public Health (NIH), *Exercise and Metformin to Impact Hyperinsulinemia in Colorectal Cancer Survivors*, 1 year, $89,106 • **Bahman Jabbari**, Allergan Inc., *Fellowship in Movement Disorder and Botulinum Toxin Treatment*, 1 year, $28,500; Medtronic, Inc., *Neuromodulation Fellowship DBS Therapy*, 1 year, $25,000; Merz Pharmaceuticals, LLC, *Movement Disorder Fellowship FY2015*, 1 year, $25,000 **Roger Jou**, American Academy of Child and Adolescent Psychiatry, *Neural Disconnectivity in Autism: Distinguishing Fact from Artifact in Diffusion Imaging*, 2 years, $60,000; Roche Translational and Clinical Research Center, *A Multi-Center, Randomized, Double-Blind, 12 Week, Parallel Group, Placebo-Controlled Proof of Concept Study to Investigate the Efficacy and Safety of RO5285119 in Individuals with Autism Spectrum Disorders (ASD)*, 11 months, $175,983 **Amy Justice**, Vanderbilt University Medical Center, *Cardiovascular Disease (CVD) and Other Comorbid Conditions Associated with HIV Infection*, 1 year, $72,608; Vanderbilt University (NIH), *Immune Function and the Risk of CVD among HIV Infected and Uninfected Veterans*, 10 months, $62,339 • **Susan Kaech**, **Joseph Craft, Kevan Herold**, AbbVie, Inc., *Harnessing Inhibitory Checkpoints to Treat Autoimmune Disease*, 2 years, $832,500 • **Edward Kaftan**, State of CT Dept. of Public Health, *Preventive Therapies for the Treatment of Chemotherapy-Induced Peripheral Neuropathy*, 2 years, $247,824 • **Joan Kaufman**, Center for Psychological Consultation, *Computerized Screening for Comorbidity in Adolescents with Substance or Psychiatric Disorder*, 3 years, $298,253 • **Robert Kerns**, Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Pain Care Quality Improvement: From Research to the Marketplace*, 1.6 years, $55,000 • **Steven Kleinstein**, Mayo Clinic of Rochester (NIH), *Development of HIPC Data Standards*, 1 year, $194,757 • **Albert Ko**, L2 Diagnostics, LLC (NIH), *RNA Detection as an Improved Diagnostic Assay for Human Leptospirosis*, 1 year, $103,049 • **Michael Krauthammer**, Elsevier B.V., *Novel Methods for Information Extraction and Knowledge Discovery through Combined Image and Text Mining*, 1 year, $48,289 • **Martin Kriegel**, AbbVie, Inc., *Inhibition in Antiphospholipid Syndrome and Prediction of Response within the Gut Microbiome*, 1 year, $133,200 • **Erica Leifheit-Limson**, American Heart Assoc. (Connecticut Chapter), *Transitions in Care and the Patient Experience within the First 30 Days after Ischemic Stroke*, 2 years, $76,932 • **Mindian Li**, American Federation for Aging Research, *The Role of Pro-Longevity O-GlcNAc Glycosylation in Mitochondiral Bioenergetics*, 7 months, $5,000 **Karel Liem**, PKD Foundation, *Role of Tulp3 and the Hedgehog Pathway in PKD*, 1 year, $80,000 **Janet Lindow**, GORGAS Memorial Institute of Tropical & Preventive Medicine, *Immunopathogenesis in Human Leptospirosis*, 1 year, $21,600 **Chi Liu**, University of Iowa (NIH), *Harmonized PET Reconstructions For Cancer Clinical Trials*, 1 year, $3,000 • **Xavier Llor**, Rush University Medical Center (NIH), *Modeling the Etiology of P53 Mutated Cancer Cells*, 1 year, $111,325 • **Katie Lowther**, Lalor Foundation, *Regulation of Maternal mRNA Translation During Oogenesis by Embryonic Poly(A) Binding Protein (EPAB)*, 1 year, $45,000 • **Xiaomei Ma**, University of Southern California (NIH), *Perinatal Immune Development and Risk of Childhood Acute Lymphoblastic*, 1 year, $88,274 • **John MacMicking**, American Asthma Foundation, *IFN-Inducible GBPs in Asthma Resolution*, 2 years, $300,000 **Ethan Marin**, American Society of Nephrology, *A Novel Mode of Vascular Function Regulation by Protein Palmitoylation*, 2 years, $200,000 **Walther Mothes**, University of Utah (NIH), *Toward the* In Vivo *Visualization of HIV-1 Pathogenesis*, 1 year, $108,000 • **Sukanya Narasimhan**, **John Harris**, L2 Diagnostics, LLC (NIH), *A Multivalent Lyme Disease Vaccine Targeting Tick-Host-Pathogen Interactions*, 1 year, $131,055 • **A. David Paltiel**, Massachusetts General Hospital (NIH), *Optimizing HIV Care in Less Developed Countries*, 1 year, $23,710 • **Wen Pan**, Leukemia and Lymphoma Society, *Determining the Roles of microRNAs in Chemotherapy Response in Leukemia*, 3 years, $165,000 • **Xenophon Papademetris**, Eigen (NIH), *Intra-Procedure Deformable Ultrasound-MRI Fusion for Prostate Biopsies*, 1 year, $119,952 • **Chirag Parikh**, Dartmouth College (NIH), *Novel Biomarkers to Predict Readmission in Pediatric and Adult Heart Surgery*, 10 months, $336,239 • **Abhijit Patel**, LUNGevity Foundation, *Detection of Early-Stage Lung Cancers via Tumor DNA in Blood*, 2 years, $200,000 • **John Pawelek**, Access Business Group International, LLC, *SRA for Access Business Group International*, 3 years, $174,825 • **Melinda Pettigrew**, Research Foundation of (SUNY) State University of New York (NIH), *Pneumococcal Transition from Nasopharyngeal Biofilm Carriage to Otitis Media*, 1 year, $41,625 • **Angelica Ponguta**, Fetzer Institute, *Love, Forgiveness and Peace: Science to Global Policy*, 1 year, $50,000 **Helen Pushkarskaya**, Burroughs Wellcome Fund, *Individual Differences in Human Behaviors Emerging from the Interplay of Cognitive and Emotional Systems—Healthy and Clinical Populations*, 6 months, $8,000 • **Carrie Redlich**, Saudi Arabian Cultural Mission, *MOU Training Program-Khalid Altassan*, 2 years, $299,950 **David Rimm**, Kolltan Pharmaceuticals, Inc., *Assay Development for New Methods of Measurement of mRNA in Situ*, 1.2 years, $150,632 **Michael Robek**, State of CT Dept. of Public Health, *A Safe and Effective Therapeutic Vaccine to Prevent Liver Cancer*, 2 years, $276,449 • **David Ross**, Brown University (NIH), *Promoting Research Training During Psychiatry Residency*, 3 years, $42,700 • **Carla Rothlin**, AbbVie, Inc., *Thrombosis in IBD: Causal or Coincidental?*, 2 years, $453,892 • **Hai-Bin Ruan**, American Heart Association, *O-GlcNAc Signaling in Hunger-Promoting AgRP Neurons Controls Adipose Tissue Browning*, 4 years, $308,000 • **Helena Rutherford**, John Leopold Weil and Geraldine Rickard Weil Memorial Charitable Foundation, Inc., *Investigating the Role of Fetal Attachment as a Protective Factor in Mothers with Addiction*, 2 years, $9,478 • **Alessandro Santin**, Synthon Biopharmaceuticals B.V., *Preclinical Evaluation of SYD985 in Uterine Serous Papillary Carcinoma (USPC)*, 1 year, $166,908 • **Sheela Shenoi**, Robert Leet and Clara Guthrie Patterson Trust, *Avoiding Delay in ART Initiation in Rural South Africa*, 2 years, $100,000 • **Jennifer Sherr**, Juvenile Diabetes Research Foundation International, *Clinical Strategies to Improve Closed Loop System Performance*, 5 years, $749,996 • **Frederick Sigworth**, Princeton University (NIH), *Improved Algorithms for Macromolecular Structure Determination by Cryo-EM*, 1 year, $99,900 • **Matthew Simon**, Searle Scholar Program, *Covalent Tracking of Transient Protein-RNA Interactions*, 3 years, $300,000 • **Albert Sinusas**, University of Virginia (NIH), *MD-INMD A Bioengineering Approach to Gene Therapy for Peripheral Arterial Disease*, 1 year, $281,670; State of CT Dept. of Public Health, *Magnetic Resonance Imaging (MRI) Assessment of Peripheral Artery Disease*, 6 months, $1,296 • **Stefan Somlo**, Allen Foundation Trust, *Discovery of Cilia Dependent Pathways of Cyst Formation in Polycystic Kidney Disease*, 3 years, $330,000 • **Mitchel Stacy**, American Heart Association, *Noninvasive Imaging for Evaluation of Microvascular Perfusion and Treatment Outcomes in Diabetic Patients with Critical Limb Ischemia*, 2 years, $154,000 • **Wenwen Tang**, American Heart Association, *Function and Mechanism of STK24-CCM3 Complex in CCM Pathogenesis*, 4 years, $308,000 • **Edwin Thrower**, State of CT Dept. of Public Health, *Cellular Mechanisms Underlying Cigarette Smoke-Induced Pancreatitis*, 2 years, $268,800 • **Samuel Tomlinson**, Autism Science Foundation, *ASF Undergraduate Summer Research Grant*, 1.2 years, $3,000 • **Richard Torres**, Applikate Technologies, LLC (NIH), *Practical High-Resolution Microscopy of Un-Cut, Un-Embedded Lung Biopsies*, 1 year, $39,345 **Benjamin Turk**, Purdue University (NIH), *Biosensor Assay to Screen for Signaling Pathway Inhibition in Cancer*, 4 months, $22,478 • **Sebastian Urday**, American Heart Association, *Peri-Hematomal Edema in Intracerebral Hemorrhage*, 3 months, $2,000 • **Flora Vaccarino**, Tourette Syndrome Association, *Transcriptome Analysis of the Basal Ganglia in Tourette Syndrome*, 2 years, $149,302 • **Tong Wang**, Cornell University (NIH), *Control of Renal Na and K Excretion*, 4 years, $289,796 • **Xingxing Wang**, Wings for Life Spinal Cord Research Foundation, *Combination of Nogo Receptor Intervention and Neural Stem Cell Transplantation for Spinal Cord Injury*, 1 year, $81,684 **John Warner**, NSF, *Doctoral Dissertation Research: Production and Political Use of Social Science during Extended Periods of Cold War Unrest and Instability*, 1 year, $17,999 • **Stephen Waxman**, Nancy Taylor Foundation for Chronic Diseases, Inc., *Viral-Mediated Approach for the Study and Management of Neuropathic Pain*, 2 years, $253,458 • **Carol Weitzman**, Boston University (NIH), *Early Identification and Service Linkage for Urban Children with Autism*, 10 months, $167,411 **Johanna Withers**, Hope Funds for Cancer Research, *Circumvention of Rapid Nuclear Decay by a Long Noncoding RNA*, 3 years, $154,500 • **John Wysolmerski**, Georgia Regents University (NIH), *DiaComp Summer Student Funding Programs*, 4 months, $8,163 • **Xiaoyong Yang**, State of CT Dept. of Public Health, *Restoring Insulin Sensitivity by O-GlcNAc Signaling through FoxO1*, 2 years, $304,345 • **Yang Yang**, Ovarian Cancer Research Fund, *P53 Aggregation: A New Target to Combat Ovarian Cancer Platinum-Resistance*, 1 year, $75,000 • **Jun Yu**, American Heart Association (Founders Affiliate), *Role of RTN-4B in Macrophage Biology and Artherosclerosis*, 3 years, $198,000

// Sharing *(from page 5)* maximizing the benefits, minimizing the risks, and overcoming the challenges of sharing clinical trial data for all parties." The IOM also recommended the data be made available within 30 days of a product's approval or 18 months after a study's completion.

"I think it's fair to say that YODA has played an important role in moving this issue forward, together with several other organizations," says Bernard Lo, M.D., professor emeritus of medicine at the University of California, San Francisco and the committee's chair. "Sharing clinical trial data strengthens the science that is the basis for good clinical care."

Johnson & Johnson chose to collaborate with the YODA Project "because we wanted a partner with a prominent track record that is known for its leadership in data sharing and that would be able to work with us across every sector of our business," says Joanne Waldstreicher, M.D., Johnson & Johnson's chief medical officer. "Sharing clinical trials data with the wider research community will speed up new medical discoveries and accelerate improvements in public health. Over the next five years, I would expect a more open and collaborative environment across industry, academia, patient groups, and foundations, where data sharing becomes the norm and science accelerates at an even faster pace, all of which is very exciting."

In a *Fortune* magazine ranking of the world's most admired companies in 2015, Johnson & Johnson jumped eight spots to number 11, ranking first in the pharmaceutical category. The article cited a reason for the improvement: "Last year [Johnson & Johnson] became the first large medical device maker to agree to share clinical trial data and diagnostic tests with researchers at Yale University."

A decade ago Ross and Harlan M. Krumholz, M.D., S.M., the Harold H. Hines Jr. Professor of Medicine and principal investigator of the YODA Project, "were kind of like gadflies [urging open science]. Now, the IOM has recommended it, [and] journals are recommending it," Ross says.

Ross envisions a day when data sharing is so commonplace that "when a trial is done, the data [are] deposited, and the processes are in place for making it available on one website," he said. "What I really hope is that we're out of business."

Chair of pharmacology honored by Spanish foundation

Hormones such as insulin and growth factors mediate their many physiological responses by activating a family of enzymes known as tyrosine kinases. Because of their roles as "drivers" of many cancers, tyrosine kinases have become a favorite target within the field of personalized cancer therapy: as of today, 20 cancer drugs targeting them have now been approved by the FDA. Yale's Joseph Schlessinger, PH.D., chair and the William H. Prusoff Professor of Pharmacology, has researched the underpinnings of these enzymes for more than three decades.

The work of Schlessinger and two colleagues has now garnered them the 2015 Frontiers of Knowledge Award in Biomedicine from the Madrid-based Fundación BBVA. Schlessinger shares the award, which carries a €400,000 cash prize, with Tony Hunter, PH.D., of the Salk Institute, and Charles L. Sawyers, M.D., of Memorial Sloan Kettering Cancer Center. According to the Fundación's awards panel, they helped blaze the "path that led to the development of a new class of successful cancer drugs."

For his part, Schlessinger identified how receptor tyrosine kinases are activated, how mutations in receptor tyrosine kinases cause cancer,

Joseph Schlessinger

and how tyrosine kinases can be blocked to treat cancer. He discovered a mechanism, known as receptor dimerization, that explains how receptor tyrosine kinases are activated when a molecule binds at the cell surface. "We found a mechanism for information flow from outside the cell to the interior of the cell, and how this mechanism was hijacked by cancer," Schlessinger says. "We explored the way these signaling pathways operated, and it became clear that if we developed inhibitors we could have drugs to treat cancer."

Schlessinger, also director of the Yale Cancer Biology Institute, has had an exceptional record of research "that reflects a creative experimental approach, spanning molecular, genetic, and structural studies to explore fundamental and important questions in biomedical science," said Dean and Ensign Professor of Medicine Robert J. Alpern, M.D. "He then translated these discoveries into the development of FDA-approved drugs through companies that he founded, Sugen, Plexxikon, and Kolltan."

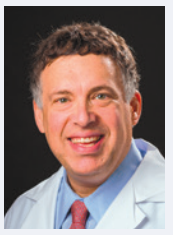
Schlessinger notes that while most drugs in the new class of targeted therapies cannot be considered cures, "they do extend life expectancy, which is a real revolution. These new drugs, moreover, are based on an understanding of what causes cancer. And that is why we can talk about personalized medicine. Even so, we are only scratching at the surface. Cancer is a very complicated disease, and the challenge now is how to overcome resistance."

In 1979 the field experienced a breakthrough with the discovery of the tyrosine kinase that enables the cell to perceive its environment. Like a key, it opens a specific door in the cell membrane and induces a cascade of signals that work to regulate cell proliferation and other processes. The work of the three scientists has shown how aberrant tyrosine phosphorylation enables some cancers and other diseases.

Schlessinger sits on the editorial boards of leading journals such as *EMBO Journal*, *Cell*, and *Molecular Cell*. He is a member of the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences, and the European Molecular Biology Organization. In 2001, the Institute for Scientific Information listed him among the top 30 most cited scientists of the 1990s.

Awards & Honors

Haifan Lin, PH.D., director of the Yale Stem Cell Center, has received the Society for the Study of Reproduction Research Award for his "outstanding contributions to the reproductive sciences." Lin, also professor of cell biology, of genetics, and of obstetrics, gynecology, and reproductive sciences, studies the self-renewal of stem cells. He uses *Drosophila* and mouse germline stem cells to explore the regulation of adult stem cells in the reproductive system.



Roy S. Herbst, M.D., PH.D., Ensign Professor of Medicine and professor of pharmacology, received the Clinical Research Forum's top prize, the Herbert Pardes Clinical Research Achievement Award. The award recognizes research Herbst and colleagues published in *Nature* on how the presence of PD-L1, an immune-suppressing protein in noncancerous immune cells, may predict how patients respond to treatment. Herbst is chief of medical oncology at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven.

// Gift *(from page 1)* chair of the Department of Psychiatry.

The field historically made diagnoses based on behaviors and treated symptoms, but the underlying biology of psychiatric disorders remained largely a mystery. "At a time when bipolar disorder in youth was identified as a major unaddressed public health problem, Hilary Blumberg was the first to identify structural and functional brain differences in adolescents with bipolar disorder," Krystal says.

Hilary Blumberg

Blumberg's research explores the development in adolescence and young adulthood of mood disorders, including bipolar disorder and depression. She also studies these disorders across the lifespan and the associated risk of suicide. She employs multiple brain scanning techniques to study brain circuitry abnormalities.

Blumberg received her bachelor's degree from Harvard. She earned her M.D. at Cornell Weill Medical College, where she also completed her residency in psychiatry and a fellowship in psychiatry with a focus on neuroimaging. She joined Yale School of Medicine's faculty in 1998.

In 1999 Blumberg was one of the first to demonstrate differences in the functioning of the prefrontal cortex during mania in adults with bipolar disorder. In 2003 she was the first researcher to demonstrate differences in the brain in adolescents with bipolar disorder. Blumberg and her research team have since continued to make pioneering contributions to our understanding of brain circuitry in mood and related disorders, identifying risk factors such as genes and early life stress, and developing new interventions to prevent suffering from symptoms and suicide.

"Our long-term hope is that these disorders will be diagnosed earlier for more effective treatment," John Furth says. "We're both just thrilled that we can do this."

The Furth family has a strong tradition of supporting Yale. John is a frequent gift chair for Yale College reunions, is a Class Award recipient, and serves on the Class of 1952 Council. He has served on the Urban Advisory Committee, the Yale Development Board, and the Yale Tomorrow executive committee, and is a member of Yale Legacy Partners and Sterling Fellows. The Furths were instrumental in the creation and growth of the Yale President's Public Service Fellowships. In 1992 they created the John L. and Hope L. Furth Fund for the Public Service Fellowship. They have also supported Yale College, renovations of Silliman College, and bipolar disorder research at the School of Medicine.

John Furth established a charitable remainder trust for the Department of Psychiatry in 2012 in honor of his 40th reunion. He is vice chairman of the financial firm Peter B. Cannell & Co. After graduating Yale College, he served in the U.S. military in Korea and was awarded the Bronze Star. A strong interest in children's welfare has guided his extensive charitable work.

Hope Furth is the former chair of mathematics at Rye Country Day School. A past member of the Smithsonian Libraries Advisory Board, she has served as chair of the White Plains Library and as treasurer of the Westchester County Library System.

// Neuroscience *(from page 1)* medical science and independent education, Pat says. In 1981, he helped establish what's now called the Klingenstein-Simons Fellowship Awards in the Neurosciences, which have supported numerous young investigators engaged in neuroscience research.

Pietro De Camilli

Now, in a tribute to John Klingenstein and in recognition of Yale's strengths in neuroscience, the Klingenstein family—including Pat, sons Tom and Andy, and daughters Nancy and Sally—has endowed the new John Klingenstein Professorship in Neuroscience through a gift from the Fund. Its inaugural holder is Pietro De Camilli, M.D.

The family's motivations were twofold: "We made the gift out of love for my dad and love for Yale," says Andy Klingenstein, Yale College '80 and now the Fund's president.

One could say that Yale runs in the Kingenstein family's blood: in addition to John's grandfather, uncle, brother, and son, his granddaughter Tory Klingenstein graduated from Yale College in 2010.

The family's support of Yale science has enabled advances in basic and clinical research. The family also provided pivotal funding for the Department of Microbial Pathogenesis under the direction of Jorge E. Galan, PH.D., DVM, chair and the Lucille P. Markey Professor of Microbial Pathogenesis and professor of cell biology. Gifts from a related family philanthropy have supported research on attention deficit hyperactivity disorder (ADHD) and depression.

Says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine, "The Klingenstein family's support over the years has made a tangible impact on the medical school. I am especially gratified that the present gift honors John Klingenstein, who has led the philanthropy of a family that has been a stalwart supporter of Yale science for so many years."

The selection of De Camilli as the inaugural Klingenstein Professor, Andy says, was a natural one: "Pietro is an incredible scientist and an even better person."

De Camilli is director of the Yale Program in Cellular Neuroscience, Neurodegeneration and Repair; professor of cell biology and neurobiology; and a Howard Hughes Medical Institute investigator. A prior recipient of the Klingenstein Fellowship Award, he researches the cell biology of neuronal synapses. His work explores the fundamental aspects of the function of cells of the nervous system, with an emphasis on synaptic transmission, the process through which neurons exchange signals with each other. His studies have provided new insights into the molecular events underlying the release of neurotransmitters from nerve cells. More generally, they have advanced knowledge of the mechanisms through which all cells secrete substances, take up material from the external environment, and traffic it to appropriate intracellular destinations.

Prior to being named to the Klingenstein professorship, De Camilli was the Eugene Higgins Professor of Cell Biology and Neurobiology.