Yale’s new Research Accelerator will bring scientists together

As a pulmonologist who conducts a great deal of translational research on diseases of the airway and lung, Geoffrey L. Chupp, M.D., associate professor of medicine and director of the Yale Center for Asthma and Airway Disease, often finds himself in unfamiliar scientific territory. “I’ll find a molecule that’s interesting or I’ll come upon some piece of data where I don’t really know what I’m dealing with,” Chupp says.

But in the fast-moving world of biomedical research, finding people with specific expertise using traditional methods—searching the literature or Internet, for instance—are often inefficient. “There may be people in my own building that I don’t even know about whom I could work with or get information from,” Chupp says.

Chupp hatched an idea for a Web-based resource that would make interdisciplinary scientific collaboration quicker and easier. In 2008, he approached longtime friend Steven Greenberg, a Westport, Conn.-based journalist and attorney who recently launched Jobs4.0, an online employment resource designed to help people over age 40 find meaningful work in a tough economy.

Chupp and Greenberg built a prototype, which they demonstrated for Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine. As director of the Yale Center for Clinical Investigation (YCCI), Sherwin oversees many of the School of Medicine’s efforts to accelerate the pace of clinical and translational research.

“We presented our site to Dr. Sherwin because we felt that the goals of YCCI and discovery—every life scientist seems to be making use of it in one way or another, and it is hard for those who overuse sequencing facilities to keep up with the demand. For researchers today, a single human genome won’t do—they want many, and they want to be able to compare them in detail.

At Yale, scientists can now obtain this 21st century research staple from the Yale Center for Genome Analysis (YCGA), a new high-speed sequencing facility that opened in January. Housed in a newly renovated space perched atop a hill at Yale’s West Campus, the YCGA is

Homecoming for a top cell biologist is packed to rafters

For several years, the School of Medicine’s Department of Cell Biology has invited a distinguished scientist to Yale each year to deliver the George Palade Lecture, named in honor of a beloved former Yale faculty member and Nobel Prize winner whose integration of electron microscopy and biochemistry helped lay the foundation of modern cell biology. Following Palade’s death at age 95 in 2008, the department decided to “elevate the status of the lecture-shup to a university-wide event, a major international lectureship renamed the George E. Palade Memorial Lectureship in Cell Biology,” says Chair James E. Rothman, Ph.D., the Fergus F. Wallace Professor of Biomedical Sciences.

In a fitting tribute, on April 4, the inaugural Palade Memorial Lecture was given before a standing-room-only crowd by world-renowned cell biologist Marilyn G. Farquhar, Ph.D., Yale’s professor of cellular and molecular biology, a Distinguished Professor of Molecular and
Turning the tide on type 2 diabetes

Work on insulin resistance sparks researcher’s hopes for prevention and a cure

Gerald I. Shulman, M.D., Ph.D., a world-renowned authority on diabetes, says he can’t remember a time when he wasn’t interested in science and medicine. He was partly inspired by his father, a Detroit physician who occasionally took the younger Shulman on hospital rounds. But as a biophysics major at the University of Michigan, Shulman “fell in love with physics and biochemistry,” he says, and knew that research would figure prominently in his career.

After his second year of medical school at Wayne State University, Shulman took a break to study in the laboratory of Alan D. Cherrington, Ph.D., at Vanderbilt University School of Medicine. There, Shulman administered the newly discovered hormone somatostatin to animals to suppress the pancreatic secretion of glucagon and insulin, allowing him to eliminate the effects of these two hormones and show that the amount of glucose produced by the liver can be affected by changes in blood glucose levels alone.

Following a residency in internal medicine at Duke University Medical Center, Shulman did his endocrine fellowship training at Massachusetts General Hospital. During the research portion of the fellowship, he studied the insulin receptor but he was keen to return to studies of metabolism in animals, such as those he had done at Vanderbilt.

Fortuitously, magnetic resonance spectroscopy (MRS) was just beginning to blossom. Based on the same principles as MR imaging, MRS allows scientists to noninvasively create precise, real-time chemical profiles of small regions of tissue in live animals, including humans. For Shulman, who was searching for a noninvasive method to study intracellular metabolism in living systems, MRS was the answer. In 1984 he persuaded his Mass General mentors to let him travel to Yale to complete his fellowship, since Robert G. Shulman, Ph.D. (no relation), an MRS pioneer, had just joined the faculty. “It’s been 25 years,” jokes Shulman, who has been at Yale ever since, and is now the George R. Cowgill Professor of Physiological Chemistry. “And they keep asking me when I’m coming back.”

In two decades of research that has earned him election to the National Academy of Sciences and many other honors, Shulman, also professor of medicine and of cellular and molecular physiology, and a Howard Hughes Medical Institute investigator, has combined MRS studies of patients with experiments using transgenic mice to elucidate the mechanisms of insulin resistance, the metabolic dysfunction at the core of type 2 diabetes.

His group has found that insulin resistance in muscle is mainly caused by defective insulin-stimulated glucose transport, which reduces glycolysis. On the other hand, increased synthesis of glucose from amino acids and lactate in the liver is the main cause of the fasting hyperglycemia seen in type 2 diabetes.

In a novel unifying hypothesis of insulin resistance, Shulman and colleagues have proposed that an imbalance between the delivery and oxidation of fatty acids in liver and muscle cells causes biochemical changes that block insulin signaling. Recently his group identified two common genetic variants that predispose individuals to nonalcoholic fatty liver disease (NAFLD) and insulin resistance, providing new insights into gene–environment interactions that promote the development of type 2 diabetes.

His work is revealing new drug targets and exercise and dietary strategies to “melt fat away” from liver and muscle, which will reverse insulin resistance and prevent type 2 diabetes.

Shulman is optimistic that type 2 diabetes—an illness that is the leading cause of blindness, end-stage renal disease, and nontraumatic loss of limbs in the U.S., currently costing the U.S. economy more than $182 billion annually—will be beaten. “Just about every drug that we currently have to treat type 2 diabetes was discovered serendipitously,” he says, “and just treats the symptom of diabetes: hyperglycemia. Now that we are beginning to understand the cellular mechanisms of insulin resistance, which is at the root of type 2 diabetes, we have better therapeutic targets, and I’m quite excited about it.”

Insulin pump innovator receives high honor for diabetes research

The American Diabetes Association (ADA) has selected William V. Tamborlane, M.D., to receive its Outstanding Physician Clinician Award, one of the highest honors bestowed by the ADA each year. A professor of pediatrics and a world-renowned figure in the understanding and treatment of childhood diabetes, Tamborlane is chief of pediatric endocrinology at the School of Medicine.

Tamborlane’s major achievements have included pioneering work in the development of insulin pump therapy, continuous glucose monitoring, sensor-augmented pumps, and, most recently, designing a prototype of an artificial pancreas. Tamborlane has also demonstrated the role of insulin resistance in pediatric metabolic disorders, including obesity and type 2 diabetes.

In late 2009, Tamborlane was one of six members of the YSM faculty elected to the Connecticut Academy of Science and Engineering, in recognition of his original contributions to “theoretical or applied science or engineering.” Tamborlane will be presented with the award at the annual ADA meeting in Orlando, Fla., in June.

Diabetes expert is named head of endocrinology

Robert S. Sherwin, M.D., an internationally renowned diabetes researcher and director of the Yale Center for Clinical Investigation (YCCI), has been appointed chief of endocrinology in the department of internal medicine at Yale-New Haven Hospital (YNHH) and Yale School of Medicine. The endocrinology section at YNHH provides diagnosis and therapy to people with hormonal and metabolic diseases.

Sherwin, the C.N.H. Long Professor of Medicine, has been an attending physician at YNHH since 1974, as well as a consulting physician at the VA Connecticut Health-care System in West Haven, Conn. In addition to his role at YCCI, Sherwin directs the medical school’s Diabetes Endocrinology Research Center, and he has served as the program director of Yale’s General Clinical Research Center.

Sherwin received his undergraduate degree from Union College and in School of Medicine, New York, and his M.D. from Albert Einstein College of Medicine. He did his residency at Mount Sinai Hospital and was a clinical associate at the NIH before becoming a fellow in medicine (metabolism) at Yale. He is a former president of the American Diabetes Association (ADA) and a winner of the ADA’s Banting Medal for lifetime scientific achievement in diabetes. He has published over 100 papers in scientific journals, edited textbooks and book chapters related to diabetes, and has served on national professional committees for the past 30 years.

In a novel unifying hypothesis of insulin resistance, Shulman and colleagues have proposed that an imbalance between the delivery and oxidation of fatty acids in liver and muscle cells causes biochemical changes that block insulin signaling. Recently his group identified two common genetic variants that predispose individuals to nonalcoholic fatty liver disease (NAFLD) and insulin resistance, providing new insights into gene–environment interactions that promote the development of type 2 diabetes. His work is revealing new drug targets and exercise and dietary strategies to “melt fat away” from liver and muscle, which will reverse insulin resistance and prevent type 2 diabetes.

Shulman is optimistic that type 2 diabetes—an illness that is the leading cause of blindness, end-stage renal disease, and nontraumatic loss of limbs in the U.S., currently costing the U.S. economy more than $182 billion annually—will be beaten. “Just about every drug that we currently have to treat type 2 diabetes was discovered serendipitously,” he says, “and just treats the symptom of diabetes: hyperglycemia. Now that we are beginning to understand the cellular mechanisms of insulin resistance, which is at the root of type 2 diabetes, we have better therapeutic targets, and I’m quite excited about it.”

The American Diabetes Association (ADA) has selected William V. Tamborlane, M.D., to receive its Outstanding Physician Clinician Award, one of the highest honors bestowed by the ADA each year. A professor of pediatrics and a world-renowned figure in the understanding and treatment of childhood diabetes, Tamborlane is chief of pediatric endocrinology at the School of Medicine.

Tamborlane’s major achievements have included pioneering work in the development of insulin pump therapy, continuous glucose monitoring, sensor-augmented pumps, and, most recently, designing a prototype of an artificial pancreas. Tamborlane has also demonstrated the role of insulin resistance in pediatric metabolic disorders, including obesity and type 2 diabetes.

In late 2009, Tamborlane was one of six members of the YSM faculty elected to the Connecticut Academy of Science and Engineering, in recognition of his original contributions to “theoretical or applied science or engineering.” Tamborlane will be presented with the award at the annual ADA meeting in Orlando, Fla., in June.
If proteins were celebrities, oct4 would be on the A-list. In 2007, in a dramatic advance, several researchers showed that the gene could be turned on in adult cells and that a new class of genes could be reanimated in adult skin cells to stem cells capable of generating any tissue in the body. But in addition to the vast healing potential of stem cells, some fear that therapy may cause tumors, and others believe that tumors regrow in cancer patients when a tiny number of stem cells in tumors survives therapy and continues regenerating.

"Oct4 is commonly expressed in germ cell tumors (GCTs), such as testicular cancer and some ovarian cancers. In the April 17 online edition of Proceedings of the National Academy of Sciences, a team led by Madhav V. Dhodapkar, M.D., the Arthur H. and Isabel Bunker Professor of Hematology, found that the immune system commonly targets this protein and that this immune response correlates with the development of GCTs. Only 35 percent of newly diagnosed GCT patients had an immune response to oct4, compared to more than 80 percent of healthy humans. Interestingly, after chemotherapy, an anti-oct4 immune response was seen in 83 percent of the GCT patients."

"The work could lead to trials of immune therapies for cancer that target pathways involving stem cells."

Zeroing in on genes to head off aneurysms

In a massive new genomic study, an international team led by School of Medicine researchers has identified three new regions, or loci, containing variants in genes that increase the risk of intracranial aneurysms, weaknesses in the brain's blood vessels. Ruptured aneurysms occur in 300,000 people worldwide each year, causing hemorhagic stroke, but most have no symptoms. Rupture is fatal in up to 40 percent of cases, and survivors usually have severe neurological damage. The team compared nearly 500,000 variable spots in the genomes of almost 6,000 aneurysm patients with those of 14,000 healthy subjects. In the May issue of Nature Genetics, they describe the new loci and confirm that two previously identified GGT loci are still associated with aneurysm risk.

"A person carrying variants in all five loci is five to seven times more likely to develop an aneurysm than an individual who carries no variants in these five regions, or loci, containing variants in genes that can exist in a fly with mostly normal cells. In an elegant series of experiments reported in the journal Nature in January, Xu and colleagues used this model to demonstrate that interactions between separate cells carrying different mutations are indeed possible, and that they can have a profound effect on how cancers grow and metastasize."

"In the new studies, Xu, along with graduate student Ming Wu, Ph.D., and postdoctoral fellow José Carlos Pastor-Pereja and Ming Wu discovered that distinct genetic mutations occurring in different cells can cooperate to fuel cancer. (Bottom) In the fruit fly brain, cells carrying a cancer-promoting ras mutation alone (panel 1, green) could not die, while a single mutant scribbled gene alone (2) has little effect. When Ras and mutant scribbled are together in cells, tumors invade the entire brain (3), an effect also seen when these genes are each expressed alone in different, but adjacent, cells (4)."

"The most intriguing observation, however, was that when Ras was expressed alone in some cells, and the scrib mutation alone in other, adjacent cells (with most cells being normal, as before), rampant tumor growth and metastasis was seen again, just as when the two mutants occurred together in the same cells (see photo)."

"This phenomenon had never been observed, and indicated that some intercellular interaction between Ras and scrib mutant cells could fuel the growth and spread of cancer. The researchers discovered that the jnk pathway would have caused the cells to die, while simultaneously triggering another pathway in adjacent cells known as jak-stat, which promotes proliferation. This made them wonder if the loss of one of the last key mutant cells in a process known as compensatory proliferation. However, the presence of Ras and the scribbled mutation together in the same cells over- rides the jnk cell-death signal, while preserving the Jak-stat proliferation signal, putting the Ras and scribbled cells on a path to tumor development and progression."

"Xu believes that his group's findings on cell–cell interaction in tumors are a powerful demonstration of how the precise genetic control offered by Drosophila can shed new light on the biology of cancer. "The bad news is that it is much easier for a tumor to accumulate mutations in different cells than in the same cell," says Xu, a Howard Hughes Medical Institute investigator and director of the Institute of Developmental Biology and Molecular Medicine at Fudan University in Shanghai, China. "Better understanding of the underlying mechanism causing cancer allows offering new tools to battle the disease.""
February 19 and 20 The Class of 2012 affectionately mocked faculty while carrying on a 61-year-old tradition at this year’s Second Year Show, entitled “Love in the Time of Swine Flu.” The show’s finale featured the full cast.


3. Julius Oatts ’12, the show’s director, as star-crossed lover Steven.

4. Alyssa Nylander ’12 (in red), the director of choreography, and Oatts (with bow tie) lead a dance number in the Cadaver Ball scene that accompanies the song “Thriller,” choreographed by Carina Preskill ’12 (not pictured).

January 21 The Status of Women in Medicine (Swim) held a reception celebrating the contributions of women to the School of Medicine. From left: Merle Waxman, M.A., associate dean for academic development, ombuds person of the School of Medicine, and director of the Office of Women in Medicine, Swim co-chair Paula B. Ravathas, Ph.D., professor of laboratory medicine, genetics, and immunology; Swim co-chair Jennifer M. McNiff, M.D., professor of dermatology and pathology; Robert J. Alpern, M.D., Dean and Ensign Professor of Medicine, Swim co-chair Joaann B. Swasy, Ph.D., professor of therapeutic radiology and genetics; Carolyn M. Mazure, Ph.D., professor of psychiatry and psychology, associate dean for faculty affairs, and director of Women’s Health Research at Yale, and Nancy H. Ruddle, Ph.D., the John Rodman Paul Professor of Epidemiology and professor of immunobiology.

January 29 John Allen Jones, an alumnus of Yale College and the Graduate School of Arts and Sciences, made a major gift in support of the student-run Haven Free Clinic. The clinic, which opened in 2005, offers medical services to uninsured patients in the Fair Haven neighborhood of New Haven. From left: Haven student leaders Rachel Jamison ’15, Sara Craig ’12, Audrey Provenzano ’10, Jones, Richard Bellstax, M.D., Harold W. Jockers Professor of Medical Education, deputy dean for education, and associate professor of psychiatry; and Olatokunbo “Toks” Famakinwa ’11.

March 18 Each year, fourth-year medical students experience a welcome sense of relief on Match Day, when they receive word of acceptance in residency training programs. Students from the Class of 2010 matched at top programs across the country, including at Harvard-affiliated hospitals, Yale-New Haven Hospital, the University of California–San Francisco, the Hospital of the University of Pennsylvania, Memorial Sloan-Kettering Cancer Center, Stanford University, New York Presbyterian Hospital, Columbia University, the Hospital of St. Raphael, Johns Hopkins Hospital, and the University of Southern California. Frederick Wang ’10 and Leah McNally ’10, 2. Stephanie Nguyen ’10 (left) and Laura Cooney ’10.

March 19 The Yale Cancer Center’s Oncology Psychosocial Services. Students from the Class of 2010 matched at top programs across the country, including at Harvard-affiliated hospitals, Yale-New Haven Hospital, the University of California–San Francisco, the Hospital of the University of Pennsylvania, Memorial Sloan-Kettering Cancer Center, Stanford University, New York Presbyterian Hospital, Columbia University, the Hospital of St. Raphael, Johns Hopkins Hospital, and the University of Southern California. Frederick Wang ’10 and Leah McNally ’10, 2. Stephanie Nguyen ’10 (left) and Laura Cooney ’10.

// Chupp (from page 4) Yale’s Clinical and Translational Science Award—collaboration, breaking down barriers and resource sharing—were remarkably well aligned with the focus of our new platform,” Greenberg says, and Sherwin agreed. “Our goal is to more effectively link scientists across the Yale campus to promote new interdisciplinary research collaborations,” Sherwin says.

Sherwin provided support that allowed Greenberg and Chupp to proceed on their project, and two years of discussions, consultations, and testing followed. “We spoke to dozens of researchers and clinicians, from lab assistants to department chairs, to make the platform as valuable as possible to the entire Yale scientific community,” says Chupp. Finally, in March, Chupp saw his concept come real, as the new resource—dubbed the VCCl Research Accelerator (RA)—was launched. Since then, more than 300 members of the Yale community have registered to use the RA.

Yale is the first institution to have full access to this type of technology for scientific collaboration and resource sharing. The RA offers Yale scientists a comprehensive online tool they can use to share and discuss research projects, data, lab protocols, results, news of clinical trials, and advances in clinical care.

“A cancer researcher studying a particular gene has no systematic way of finding other researchers, say in immunology, asthma, or even botany, who might be studying the same gene,” Greenberg says. “The VCCl Research Accelerator is designed to facilitate those potentially rewarding collaborations.”

The service uses a novel system called data-driven collaboration to quickly and easily identify potential research partners, Chupp explains. “Other software programs allow researchers to easily find published papers or biographical information,” he says, “but we wanted to create the first-ever platform that identifies potential collaborators on the basis of a mutual interest in the substance of the data or reagents, not on purely social factors.”

Greenberg notes there is great flexibility built into the website, so that each scientist can use it in his or her own way, and each scientist can choose his or her own level of disclosure. In addition, the site can be customized for other institutions, and many institutions can be linked together, so the RA can allow scientists to reach beyond Yale to forge new research connections.

But for the site to be valuable to members of the Yale community, Greenberg says, scientists need to log on and post data. He and Chupp are encouraging all Yale researchers across the university campus to join the RA community.

“The real benefit of having this type of technology is that it will help communication about complex diseases and disorders,” says Debbie Hili- brand, chair of the Yale Child Study Center’s Executive Council. Hili- brand’s son David has both scoliosis and autism. “Autism, for instance, is [connected with] learning disabilities and obsessive-compulsive disorder. And those may also be worked on in multiple departments.” Technologies like the RA “will help research at the university become better-integrated and more efficient.”

“We’ve had listings from a wide range of Yale scientists who are sharing data, reagents, antibodies, human samples, research projects, and more. The response has been extremely strong. We’re also about to post information on over 90,000 peptides available from the Keck Lab,” Greenberg says, referring to one of Yale’s main centers for protein analysis. “Much more is in the works.”

The RA is secure, password-protected, and free of charge for all Yale users. To learn more about using this powerful new tool for scientific collaboration, visit vccl.researchaccelerator.org.

4 www.medicinesyale.org
**An engineered tissue’s surprising development**

Christopher K. Breuer, M.D., and Toshiharu Shinkova, M.D., Ph.D., have been studying the use of tissue-engineered vascular grafts (TEVGs) to treat congenital heart defects. TEVGs—created by seeding a biodegradable scaffold with a patient’s bone marrow cells (BMSCs)—make living vessels that will grow as a child grows and could last a lifetime. Breuer and Shinkova, both associate professors of surgery and pediatrics, and Yale colleagues explored how BMSCs are transformed to vessels in TEVGs. BMSCs are stem cells, so many scientists thought that BMSCs differentiate into the endothelial and smooth-muscle cells that comprise blood vessels.

But in the March 26 issue of *Proceedings of the National Academy of Sciences*, the group reports that BMSCs were undetectable soon after TEVGs were implanted into mice. Instead, the graft appeared to initiate an inflammatory response that drew white blood cells to the scaffold, replacing the BMSCs. These cells were also soon replaced, with the mouse’s own blood cells.

This “better understanding of how TEVGs develop in vivo will lead to improved second-generation TEVGs,” the authors write.

**New pathways toward growing new arteries**

Stimulating arteriogenesis, the growth of new arteries, in adults with cardiovascular disease is a holy grail of cardiology. Many efforts have focused on vascular endothelial growth factor (VEGF), which creates new blood vessels during embryonic development. However, VEGF has shown little success in adults, especially in those with cardiovascular disease or diabetes.

A team led by Michael Simons, M.D., the Robert W. Berliner Professor of Medicine and Cell Biology, and chief of Yale’s Section of Cardiovascular Medicine, focused instead on two interacting signaling pathways, ERK1/2 and PI3K. ERK1/2 is activated in growing arteries and suppressed in quiescent vessels, so the group searched for some PI3K inhibitory factor. In the April issue of *The Journal of Clinical Investigation*, they name the culprit, a PI3K-regulated enzyme known as Akti. Suppressing Akti released the PI3K’s brake on ERK1/2 and successfully activated growth of new arteries in mice and zebrafish.

“Because we’ve located this inhibitory pathway, this opens the possibility of developing a new class of medication to grow new arteries,” Simons says. “The next step is to test this finding in a human clinical trial.”

**Lifelong friends, also joined in giving**

Two members of the Class of 1956 who fondly recall their Yale years make gifts to the medical school

Rear Admiral William M. Narva, M.C., U.S.N., and Captain Mitchell Edison, MC, U.S.N., met as members of the School of Medicine’s Class of 1956, and have remained friends throughout their adult lives. More than 50 years later, with their medical school years firmly etched in memory and their careers largely behind them, they still speak on the phone regularly.

The two met, Narva says, because “the class was an intimate class. The whole community was very close.” Narva and Edison’s first days on Cedar Street in the fall of 1952 coincided with the arrival of Dean Vernon W. Lippard, M.D. “His pitch was, ‘I’m a freshman like you are, I’m just starting like you. You’re my class—we’re going to do this together.’” Narva recalls. “Everybody at Yale was on your side.”

The two old friends have also joined together in giving back to Yale. Edison has generously contributed to the Annual Fund for years, and he added to this long record of support in 2009 by establishing the Mitchell Edison, M.D., Endowment for International Clinical Rotations. At that time, Edison was the gift chair for his 50th reunion, and discussions with Narva planted the seed for Narva making a new $250,000 bequest in honor of his and Edison’s 50th reunion this spring. In happy coincidences, this event falls at the close of the School of Medicine’s Bicentennial celebration and at the conclusion of the University’s five-year “Yale Tomorrow” fundraising campaign.

After medical school, Narva interned at the National Naval Medical Center (NNMC) in Bethesda, Md. He then completed a three-year residency in dermatology that included stints at the U.S. Naval Hospital in San Diego and Los Angeles County General Hospital. From 1966 to 1986, as a medical officer in the Navy, he was a consulting physician to the White House and the United States Congress, and in 1986 he became Attending Physician of the United States Congress. Edison, also a career Navy man, completed residencies in surgery and urology at the St. Albans Naval Hospital in New York City, where he eventually became chief of urology in 1966. Edison subsequently became chair of the Department of Urology at the NNMC, and then at Washington Hospital Center in Washington, D.C., where at 82 he still practices four days a week.

Although their military careers took them on different courses, the friends’ paths did cross. When Narva was assigned to the U.S. Naval Hospital in Oakland, Calif., Edison, having finished his residency, joined the Department of Urology there. Edison and Narva met again..."
Dermatology Foundation, Comparison of Squamous Cell Carcinoma and Keratoacanthoma; 1 year, $20,000 • Peter Krause, Tufts University, Xenoendocytosis: A New Mechanism of Cell-to-Cell Communication, 1 year, $37,569 • Harlan Krumholz, Robert Wood Johnson Foundation, Clinical Scholars Program 1 year, $93,554 • Robert Wood Johnson Foundation, Clinical Scholars Program 2 years, 1 year, $1,085,855 • Rachel Lampert, Emory University, Mechanisms Underlying Depressed Cardiac Contractility Risk, 1 year, $1,421 • Adam Lazorchak, The Leukemia & Lymphoma Society, The Role of mTOR Signaling in the Regulation of Apoptosis, 3 years, $145,500 • Chiang-Shan Li, Tourette Syndrome Association, Inc., Imaging Cognitively Motor Control in Tourette Syndrome, 1 year, $20,000 •taxonomy, Associated Medical Research Institute, Six-Mediated Ephymeata: Role of Aging and Gender, 3 years, $255,000 • Seung Lee, Rotary International District 360 Club of Korea, Thrombospondin 2 Regulation by Nitric Oxide, 3 years, $18,500 • Actin Filament Severing, 2010’s $20,000; Kristofer Mroz, American Heart Association, Inc., Critical Role of Phosphorylation of Cofilin-Induced Actin Filament Severing, 3 years, $13,659 • Structured Studies on Epsin in Cell Migration, 2010’s $99,176, 2011’s $10,000 • Stephen Strittmatter, The Schizophrenia Research Foundation, Characterization of Isl+ Cardiovascular Progenitor Cells Using Confocal Imaging Microscopy, 1 year, $200,000 • Vincenzo DeCarli, Institute for Human Genetics, Role of Aging and Genetics of Intracranial Aneurysms, $500,000 • Stephen Stack, Duke University, The Nebraska Medical Center, Improved Algorithms for Macromolecular Structure Determination with Cryo-EM, 2010’s $198,000, 2011’s $150,000 • Praveen Mannam, American Society of Cell Biology, Mechanisms of Cofilin-Induced Cell Migration and Division Are Hallmarks of the Structural Abnormalities that Compromise Renal Function in these Patients. • After Joining Palade’s cell biology lab at The Rockefeller University in 1959 as a postdoctoral fellow, Farquhar continued her work on kidney structure and function. In 1963 she discovered tight junctions, crucial sites of cell–cell interactions, and in her subsequent work at the University of California–San Francisco, Rockefeller, Yale, and UCSF she has made seminal contributions to our understanding of membrane trafficking, the process by which proteins and other materials are transported within and between cells. This diverse body of work has earned Farquhar many accolades, including the A.N. Richards Award from the International Society of Nephrology, the Howard W. Smith Award from the American Society of Nephrology, the E.B. Wilson Medal from the American Society for Cell Biology, and membership in the National Academy of Sciences and the American Association of Arts and Sciences. • In her April lecture at Yale, Farquhar crisply presented a new line of work centered on GIT1, a protein recently discovered in her lab which appears to play a role in cancer growth and metastasis. • GIT1 binds to Gai, a member of a family known as G proteins, which are usually found on cells’ outer membranes, where they act as middlemen between receptors that detect extracellular signals and effectors that induce actions inside the cell. By contrast, Farquhar’s group and others found GIT1 to be abundantly expressed in the Golgi apparatus, an intracellular structure, with no associated receptor; when Gai was localized with a red fluorescent protein, explained Farquhar, underscoring a vivid micrograph projected behind her, the Golgi “lit up like a Christmas tree.” Further studies of this peculiar protein led to the discovery that GIT1 regulates and activates Gai: when Gai is in an active state, cells tend to migrate, whereas inactive Gai prompts cells to divide. Because unregulated cell migration and division are hallmark symptoms of the metastasic and rampant proliferation seen in the inaugural George E. Palade Memorial Lecture, sponsored by the Department of Cell Biology, was delivered to a capacity crowd by Marilyn Farquhar of the University of California–San Francisco. Farquhar, a distinguished scientist whose career spanned more than 50 years, is the widow of Palade, a Nobel Prize winner whose integration of electron microscopy and biochemistry helped to launch the modern era of cell biology. Farquhar and Palade (along with James Jamieson, now director of Yale’s m.d./ph.d. program) came to the School of Medicine in 1973 to establish the Section of Cell Biology, now a full-fledged department, and were members of the Yale faculty for 17 years. The scientists’ analysis of specimens from rapidly spreading cancers versus those from localized cancers revealed that GIT1 was far more abundant in the former than the latter, findings that were replicated in pancreas, colon, and breast cancers. Taken together, the results indicate that drug compounds that target GIT1 may prevent activation of Gai may slow the metastatic progression that proves lethal in many cases of cancer, a direction now being pursued by Farquhar’s trainees. Farquhar summed up her talk with a straightforward acknowledgment of the remaining mysteries in this latest research, and with thanks to the many young scientists who have helped her probe these questions in the lab. Then, with the wisdom gained during a life in science, she elegantly tied a bow around both sentiments. “After all, these young people all need something to do,” she said. “We need to leave some questions on the table for them.”
Expert on autimmunity is appointed Paul Beeson Professor

Joseph E. Craft, M.D., newly named as the Paul B. Beeson Professor of Medicine, is an internationally recognized expert on the pathogenesis of systemic autoimmune diseases, including lupus and rheumatoid arthritis.

He and his research team seek to define the mechanisms of loss of self-tolerance and activation of autoreactive T cells in systemic autoimmune diseases, and the differentiation and regulation of T cells in normal immune responses. His research has been continuously funded by the National Institutes of Health (NIH) since 1985, and he is the current recipient of an NIH MERIT Award and directs an NIH-funded center in the rheumatic diseases.

Craft joined the School of Medicine as an assistant professor in 1981 after completing an internship and residency at Yale-New Haven Hospital (VHNH) and a fellowship in rheumatology. He became a professor of medicine in 1997, a professor of immunobiology in 1999, the chief of the Section of Rheumatology since 1991, and Craft has also directed the Yale Investigative Medicine Program since 2004. He is chief of rheumatology at VHNH.

Craft won the University of Miami's Miller Institute of Medicine in 1997, a fellowship in rheumatology. He became a professor of immunobiology in 1999.

The chief of the Section of Rheumatology since 1991, Craft has also directed the Yale Investigative Medicine Program since 2004. He is chief of rheumatology at VHNH.

Craft has been a fellow of the American Association for the Advancement of Science and to the American Society for Clinical Investigation, among other professional honors.

Craft has served numerous national, regional, and international organizations, including as chair of two standing study sections at NIH and on the scientific advisory board of the Alliance for Lupus Research. He is a member of the Board of Scientific Counselors at the NIH's National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS), and he is a member of the boards of the Arthritis Foundation and the Lupus Clinical Trials Consortium. Craft is a co-founder and serves on the board of L2 Diagnostics, a biotechnology company in New Haven.

An associate editor of Arthritis & Rheumatism, Craft also serves on the editorial board of Autoimmunity. He is active in a number of community service endeavors, including serving as a volunteer for the Connecticut Chapter of the Lupus Foundation of America.

The professorship was established in 1982 by the late Elisha Akins, M.D., to honor his colleague Paul B. Beeson, M.D., a beloved clinician, researcher, and teacher who served as chair of Yale’s Department of Internal Medicine from 1942 to 1965. An expert in infectious disease, Beeson provided an ideal by which Yale medical students, residents, and faculty members have measured themselves for decades.

Upon his departure from academia in 1981, his two chief residents summarized Beeson’s legacy: “In short,” they said, “he is the kind of physician all of us aspire to be.”