Advancing Biomedical Science, Education and Health Care

Volume 2, Issue 3  September/October 2006

Top asthma researcher is new leader of internal medicine

Jack A. Elias, M.D., the Waldemar Von Zedtwitz Professor of Medicine and chief of the Section of Pulmonary and Critical Care Medicine, has been named chair of the medical school’s Department of Internal Medicine.

Elias, a leading authority on the molecular basis of asthma and other lung disorders, will lead the school’s largest department, with 351 full-time faculty and $83 million in research funding.

“Jack Elias is the perfect candidate for chair of medicine. His credentials are impeccable,” says Robert I. Alpern, M.D., dean and Ensign Professor of Medicine. “Jack is an outstanding scientist who has published his work in the best scientific journals, but in addition he is an outstanding teacher and clinician. The pulmonary division at Yale, which Jack has supervised for many years, has produced outstanding basic and clinical research, educational programs and patient care.”

After receiving undergraduate and medical degrees from the University of Pennsylvania, Elias was an intern and resident at Tufts-New England Medical Center. He returned to Penn as a senior resident, completing a fellowship in pulmonary medicine.

Elias held a series of academic appointments at Penn, and came to Yale in 1990 as professor and chief of pulmonary and critical care medicine. He is the author of more than 160 original journal articles and is co-editor of the textbook Fishman’s Pulmonary Diseases and Disorders.

Elias’s research, which is funded by several grants from the National Institutes of Health, is focused on the molecular basis of asthma and other lung disorders, will lead the school’s faculty and $83 million in research funding.

NIH selects the School of Medicine for new clinical research initiative

$57 million grant, the largest ever, to transform discoveries into therapies

Basic biomedical research, with its careful, tightly controlled experiments on cells and laboratory animals, is painstaking work. But some of the challenges of basic science pale next to the hurdles faced by clinical and translational researchers, who test laboratory discoveries in human subjects with the ultimate goal of getting safe and effective new drugs to patients who need them.

In addition to the inherent difficulties of studying people—unlike mice, humans vary widely in genetics and life histories—clinical researchers must orchestrate large, complex studies that require hospital beds, nursing services, statisticians, lab tests, medical imaging and database management, all while navigating the dense thicket of regulations that govern research involving human subjects.

“Doing clinical research is much simpler when I started,” says Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine and director of the newly formed Yale Center for Clinical Investigation (YCCI). “Because of the daunting complexities faced by researchers today, we have lost an entire generation of clinicians, many of whom have found it very difficult to sustain their research work.”

But now Sherwin has reason to celebrate. On October 3, the National Institutes of Health (NIH) announced that the School of Medicine had been awarded a five-year, $57.3 million Clinical and Translational Science Award (CTSA), part of a major national initiative that will transform how researchers move laboratory discoveries into human studies. Key participants in the grant—the largest NIH award in the medical school’s history—including the Yale School of Nursing, the Department of Epidemiology and Public Health, the Department of Biomedical Engineering and the Combined Program in the Biological and Biomedical Sciences.

According to Tesheia H. Johnson, M.B.A., M.H.S., the YCCI’s chief operating officer and associate director for clinical research at the medical school, the unprecedented grant will allow the YCCI to train a

Glaucam specialist is named chair of ophthalmology

James C. Tsai, M.D., M.B.A., an authority on glaucoma, has been named chair of the medical school’s Department of Ophthalmology and Visual Science. As chair, Tsai will be recruiting additional clinicians and basic scientists with a focus on rapidly bringing scientific discoveries made at Yale to patients in need.

In Tsai’s research on glaucoma, a leading cause of blindness in which increasing pressure inside the eyeball causes progressive damage to the optic nerve, he has searched for drugs to protect the nerve, evaluated the effectiveness of surgical treatments and developed advanced techniques for testing visual function.

Tsai comes to the School of Medicine from the Edward S. Harkness Eye Institute of the Columbia University College of Physicians and Surgeons in New York, where his laboratory has been especially active in exploring whether erythropoietin, a hormone made by the kidney that aids in red blood cell formation, can protect the optic nerve in glaucoma.

“Yale is extremely fortunate to attract Jim Tsai as our new chair of Ophthalmology,” said Dean Ensign. “Dr. Tsai’s contributions will help advance the School of Medicine’s mission to research, educate and provide patient care.”

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Jonathan S. Bogan, M.D., an associate professor of medicine who studies type 2 diabetes, which begins when 90 percent of these individuals have insulin resistance—a condition that characterizes type 2 diabetes. Bogan studies two other metabolic disorders.

fat and muscle cells become resistant to insulin and fail to utilize glucose effectively. Understanding this process at the molecular level could lead to improved treatments for diabetes and other metabolic disorders.

Because it is water-soluble, glucose cannot pass directly through the fatty membrane that forms the surface of cells. Bogan studies two proteins that help glucose to enter the cell: GLUT4, a glucose-transporting protein that appears on the cell surface in response to insulin, and elaboration of these mechanisms by which hormones control the movement of protein within cells. This research may lead to a better understanding of the insulin resistance that characterizes type 2 diabetes.

Glucose-transporting proteins appear on the surface of cells in response to insulin, and

In the hands of gastroenterologist Priya Jamidar, the ERCP scope is a versatile tool.

Crossing borders

Medicine and surgery meet to treat gallstones and other duct disorders

Priya A. Jamidar, M.B.Ch.B., has seen a great deal of the world. After a childhood spent between Kenya, India and the United States, Jamidar received his medical degree in Belfast, and completed his residency and fellowships in Connecticut, California and Indiana before settling down in Yale’s Section of Digestive Diseases in 2004.

But it is the inner world of the human body that has most captivated Jamidar, who says he aspired to a medical career as early as he can remember. An associate professor of medicine, Jamidar is an expert practitioner of endoscopic retrograde cholangiopancreatography, or ERCP, a technique in which a long, flexible tube inserted through the mouth is used to diagnosis and treat disorders of the ducts that drain the gallbladder, pancreas and liver.

In his diagnostic work, Jamidar, guided by video monitors and by lights in the ERCP scope, threads the probe through the esophagus, stomach and small intestine and injects contrast dye into ducts to make X-rays of gallstones, duct blockages or cancer. For pancreatitis or undiagnosed cases of abdominal pain, Jamidar uses the scope to insert a tiny catheter that measures pressure in the sphincter of Oddi, a muscle that controls the flow of bile and pancreatic fluid into the small intestine. If a patient has gallstones trapped in their bile ducts, Jamidar uses a basket or balloon passed through the scope to remove the stones whole, or shatters them with an electrically generated shock wave. In patients with sphincter of Oddi hypertension, he may run a probe to make a small incision to loosen the sphincter, which gives two-thirds of patients relief from their symptoms, he says.

“The therapeutic aspect of ERCP has made a lot of surgery unnecessary,” says Jamidar, and he has been spreading the word in a series of workshops for local physicians. In these sessions, doctors seated in a conference room observe actual ERCP procedures via real-time video feeds and interact with Jamidar using two-way microphones. Jamidar hopes that seeing the benefits of the technique first-hand will help physicians improve their skills and encourage them to refer their more complicated cases to the Yale Medical Group’s burgeoning ERCP practice, which now performs more than 700 ERCP procedures per year.

“ERCP has a long learning curve, and it does carry significant risks in less-experienced hands,” Jamidar says. “We strongly believe in communicating well with gastroenterologists in the community, who tend to refer cases that have either failed elsewhere or are of a level of complexity that they need to be done at a center of excellence like Yale.”

Jamidar says that “the line between medicine and surgery has become quite blurred” by techniques like ERCP. “I’ve always loved working with my hands, and I wanted to be a surgeon at one point. But I decided to practice gastroenterology instead. ERCP comes pretty close to surgery in many ways.”

During an upcoming sabbatical, Jamidar plans to move even closer to surgery under the tutelage of Paul Swain, M.D., of the Royal London Hospital, one of the leading lights in emerging subspecialty known as natural orifice transluminal endoscopic surgery, or NOTES. Swain, who gained fame as one of the inventors of the PillCam, a capsule-sized camera that patients can swallow to capture images of the digestive tract, has recently created an endoscopic sewing machine that will allow doctors like Jamidar to suture incisions made with instruments inserted through the mouth.

Jamidar looks forward to exploring the possibilities of NOTES at Yale. “In the future we’ll have people who will draw from both surgery and gastroenterology who will be able to do a lot of things for patients without going to the operating room,” he says. “I think it’s going to be for everyone’s good.”

Expert on insulin action is winner of Keck Young Scholars award

Jonathan Bogan, M.D., an assistant professor of medicine who studies how insulin triggers cells to take up glucose from the blood, has been named one of five Distinguished Young Scholars in Medical Research for 2006 by the W.M. Keck Foundation, one of the nation’s largest philanthropic organizations supporting medical research, science and engineering.

The School of Medicine will receive as much as $1 million from the foundation over the next five years to support Bogan’s work on the biochemical mechanisms by which hormones control the movement of protein within cells. This research may lead to a better understanding of the insulin resistance that characterizes type 2 diabetes.

Jonathan Bogan

Yale welcomes new leader for medical development

Jancy L. Houck, M.A., who recently led a capital campaign for the health sciences center at the University of Florida (UF) that exceeded its goal by more than $100 million, has been named associate vice president for development at Yale and director of medical development.

“I am absolutely delighted that Jancy will be joining us at Yale, says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. “She brings an ebullient personality combined with extensive experience in medical school fundraising and a strong record of working with people with an engaging personality, enormous energy and focus. I couldn’t be more delighted personally and professionally to have Jancy on our team.”

Jancy Houck
Yale launches new stem cell research program

Leading biologist joins faculty to direct effort

Stem cells, which can create copies of themselves that differentiate into many of the myriad cell types that form the body’s tissues and organs, have been much in the news as a potentially powerful treatment for diabetes, Parkinson’s disease, heart disease, spinal cord injury and other serious illnesses.

In August the School of Medicine announced that the Yale Stem Cell Program (YSCP), a new initiative to discover the basic mechanisms of stem cell division, will be headed by Haifan Lin, Ph.D., one of the country’s leading stem cell biologists.

Lin and YSCP Associate Director Diane S. Krause, M.D., Ph.D., an associate professor of laboratory medicine and pathology and an expert on bone marrow stem cells, will oversee a group of a half-dozen scientists and an administrative and technical staff devoted to research on human embryonic and adult stem cells, as well as stem cells in the mouse, fruit fly and roundworm.

The program will also provide a scientific hub for more than 30 additional faculty members across the medical school and university campuses who work on stem cell-related topics. Over the next few years, the YSCP will grow with the recruitment of four additional faculty members.

How cold sore viruses play hide-and-seek

Cold sores, which are caused by the herpes simplex virus (HSV), usually heal fairly quickly. But because HSV cleverly conceals itself in an inactive form, the body’s immune system never completely eradicates it, and the painful sores tend to flare up again and again.

In the August issue of *Nature Immunology*, a team led by Peter Cresswell, Ph.D., Howard Hughes Medical Institute investigator and professor in the Section of Immunobiology, provide new insights into HSV’s vanishing act.

The immune system uses proteins known as CD1d molecules to detect HSV. Infection modifies these molecules, which move in a continuous loop from the interior of the cell to the cell surface. As a result, the virus can remain hidden until its next opportunity to wreak cold sore havoc.

Further studies of how HSV fools CD1d may suggest therapeutic strategies to eliminate cold sores for good.

Throwing new light on cellular networks

Biologists have made remarkable progress in understanding life at the cellular and molecular levels over the past 30 years, but they have been hobbled in moving forward by their inability to easily study how the multitude of cells in tissues and organs form complex signaling networks, as happens in the nervous and immune systems. To date, experiments aimed at exploring these cellular networks have mostly relied on limiting, invasive techniques, such as implanting electrodes in just a few cells in animals’ brains or observing how collections of isolated immune system cells behave in a dish.

“It is clear that the next big frontier is to understand not only the individual players in the orchestra,” says Gero Miesenböck, M.D., professor of molecular and cellular biology, “but the orchestra itself—that is, how multicellular life functions.”

Now, with a 3-year, $8 million grant from the M. Keck Foundation in hand, Miesenböck and Ira Mellman, Ph.D., chair and Sterling Professor of Cell Biology, are collaborating on a research program that will study cellular networks in the nervous and immune systems in a wholly new way. The research will extend groundbreaking techniques pioneered by Miesenböck that combine tools to precisely conduct the orchestras of cellular networks with the ability to record the physiological “music” these networks produce.

Over the past several years, Miesenböck has devised ways to genetically engineer specific sets of cells so that “remote controls”—flashes of light, zaps of heat, or floods of molecules—will simultaneously activate them. To determine the downstream effects of such activation on other cells in a network, he has invented molecular sensors that can be inserted into cells and emit light when those cells are activated.

In one remote-control experiment so widely reported that Jay Leno incorporated it into two comedy routines on *The Tonight Show*, Miesenböck introduced “optical actuators,” proteins engineered to be sensitive to light, into nerve cells that govern an escape behavior in the fruit fly *Drosophila*. A flash of bright light was...
July 29: The dedication of the Martin and Evelyn Gordon Conference Room at the medical school’s Harvey Cushing/John Hay Whitney Medical Library drew a large crowd. Martin E. Gordon, M.D., clinical professor of medicine and member of the School of Medicine’s Class of 1946, chairs the Board of Trustees of the Cushing/Whitney Medical Library Associates.

Nicotine’s addictive grip on the brain

Smokers find it enormously difficult to quit: of those who try, only about 10 percent successfully kick the habit each year. The stubbornness of tobacco addiction has been attributed to nicotine, which activates various neural networks in the brain by locking onto proteins known as nicotinic acetylcholine receptors, or nAChRs.

Using neuroimaging technology, Julie K. Staley, Ph.D., associate professor of psychiatry and biomedical engineering, and colleagues compared the number of nAChRs in nonsmokers and in smokers who had abstained from cigarettes for about seven days. As reported in the August 23 issue of The Journal of Neuroscience, the team observed significantly higher densities of nAChRs in the brains of the abstaining smokers than in nonsmokers.

Moreover, the smokers’ urge to light up to relieve withdrawal symptoms was closely related to the number of nAChRs seen in certain brain regions.

This paves the way for determining why some smokers, such as women and those with neuro-psychiatric disorders, have more difficulty quitting,” Staley says.

An early start on the road to reason

The cerebral cortex, a layer of cells just a few millimeters thick on the outermost surface of the brain, is largely what makes humans “noble in reason and infinite in faculties.” New Yale research shows that developing embryos generate the first neurons of the cortex only 31 days after fertilization—much earlier than previously thought.

Using precise cellular markers, Pasko Rakic, M.D., Ph.D., chair and Doris McConnell Duberg Professor of Neurobiology, and colleagues at the University of Oxford discovered “predecessor” neurons in human embryos before the neural tube, the precursor of the central nervous system, had completely closed. These precocious cells produce long extensions that may pull them to different locations as the brain develops while also acting as temporary scaffolds to guide late-blooming cortical neurons to their proper locations.

In the July issue of Nature Neuroscience, the researchers say that studying how predecessor cells help to generate and wire up the 20 billion neurons of the adult human cortex may help to shed light into how we differ from our primate ancestors and shed light on the causes of mental illness.

Keck profiling center is a crucial contributor to “post-genomic” science

The complete gene sequence of humans has been solved, but the genome is just a recipe for proteins, the building blocks that are crucial to the structure and function of every cell in our bodies. To truly understand the body in both health and disease, scientists must learn which proteins appear, disappear or become more or less abundant under different conditions. Discovering how individual proteins behave differently in cancer cells than in normal cells, for example, could lead to new diagnostic tests and more precisely targeted treatments.

Deciphering the mystery of nAChRs, which is the domain of a new field of study known as proteomics, has proved to be a much tougher proposition than sequencing the human genome. Unlike genes, which all possess the unique double-strand structure of the DNA double helix, each protein has a unique chemical makeup, and thus displays its own three-dimensional structure and quirky behavior. In addition, proteins are frequently modified during their lifespan: the 10,000 or so genes in the human genome that are active within each cell type give rise to many times that number of ever-changing protein variants. Comprehensively cataloging this diversity is an art as well as a science, requiring expensive equipment and specialized expertise far beyond the reach of most individual laboratories.

Tackling the proteomics puzzle is the job of Walter J. McMurray, Ph.D., and Kathryn Stone, co-directors of the Protein Chemistry and Mass Spectrometry (PCMS) Resource, one of 12 research services in the School of Medicine’s W.M. Keck Foundation Biotechnology Resource Laboratory. Using the latest analytical techniques, McMurray, Stone and their colleagues sort, identify and quantify thousands of proteins in samples of cells, tissues and blood on behalf of researchers at Yale and around the world. The lab’s state-of-the-art equipment in the basement of 100 George Street in New Haven churns out protein profile data 24 hours a day, seven days a week, bringing researchers closer to the medical promise of the post-genomic era.

Kenneth R. Williams, Ph.D., director of the Keck Laboratory, the medical school’s outstanding and often-copied shared research resource, recognized the importance of protein profiling and the growing demand among researchers for cutting-edge proteomics techniques several years ago. What followed—a concerted effort by Williams, Stone and McMurray to bring the latest and greatest large-scale protein analysis technologies to the medical schools—paid off for Yale researchers, who have access to one of the best academically proteomics facilities anywhere in the nation.” To our knowledge,” says Williams, “no other academic core lab in the U.S. provides such a wide array of proteomic technologies.”

At the heart of protein profiling lies the analytical technique of mass spectrometry (MS), a separation and detection tool that uses high voltages and strong magnets to sort molecules, which can then be identified based on their size and electric charge. McMurray has logged more than 40 years in the field, dating from his postdoctoral work in the early days of the technique in the 1960s. He set up the first MS analyzer at Yale in 1965, and, in an example of the method’s versatility, and later used it to analyze the chemical composition of moon rocks brought back by the Apollo 11 mission. In 1984, he was named director of an MS facility launched by Alan C. Sartorelli, Ph.D., the Alfred Gilman Professor of Pharmacology, who was then director of the Yale Cancer Center.

“No other academic core lab provides such a wide array of proteomic technologies,” Walter McMurray, Keck Lab director, says.

Stone came from a completely different direction. With a brand-new bachelor’s degree in chemistry in hand, she arrived at the medical school’s fledging core research facility in 1982, intending to stay for two years. Five years later she was directing a protein chemistry facility, which eventually grew into the Keck Laboratory’s Mass Spectrometry Resource. No stranger to the vagaries of protein behavior, during her 24 years at Yale Stone has identified the “unknown” proteins in more than 5,000 samples—without making a single mistake, to her knowledge.

In 1998, Stone and McMurray merged their MS efforts into one center under the Keck umbrella. Since then, the PCMS has grown to include seven MS analyzers, and has seen the adoption of several advanced protein profiling methodologies. With names like MUDPIFF and iTRAQ, these separation and identification techniques offer researchers the chance to learn more about proteins of interest than was previously possible in a single experiment, a competitive advantage that pays off in times of tight research funding.

The excellence of the PCMS has attracted top-dollar grant support for new equipment. The latest addition, a $5.7 million high-sensitivity, high-resolution mass spectrometer—the “Cadillac of MS machines,” Stone calls it—was funded by the National Institutes of Health, as was a new supercomputer to process the massive quantities of protein profiling data the lab produces.

Funding for research projects at the center is also robust. Stone’s group does the proteomics work for large NIH-funded studies of blood vessel disease and drug addiction and provides support to the Northeast Biodefense Center, earning operating expenses by accepting samples on a fee-for-service basis from scientists around the world.

Stone and McMurray recently oversaw the resetting of the PCMS in 5,500 square feet of renovated space provided by the School of Medicine in 300 George Street, a building overlooking the medical and central campuses that is home to several bio-technology companies and medical school departments.

The result is a lab that never sleeps—as profiling techniques get better, the demand from medical school scientists continues to mount, keeping lab robots working night and day to feed the MS machines, and the staff streamlining useful data out to researchers.

Stone says the biggest challenge at the PCMS is keeping the work flowing while juggling “45 different projects for different people”—not to mention the daily phone calls from eager researchers asking, “Is it done yet?”

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cellular and molecular biology of the lungs and the mechanisms of lung injury and repair.

His research group has developed and studied genetic models of asthma, emphysema, pulmonary fibrosis and acute lung injury which have revealed potential drug targets to treat these illnesses. More than 30 scientists now working in academia and industry were trained by Elias, and he has seven patents or pending patents based on his research. Elias has been a member of the Association of American Physicians since 1998 and a councilor since 2001. He has held more than a dozen posts for the American Thoracic Society/ American Lung Association, including chairmanship of its long-range planning and scientific advisory committees and of the Scientific As

semblly on Allergy, Immunology and Inflammation. He is also a participant in strategic planning for the National Heart, Lung and Blood Institute.

Elias succeeds David L. Coleman, M.D., professor of medicine, who has served the department as interim chair since 2003. In October, Coleman assumed the chairmanship of the department of medicine at Boston University School of Medicine.

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ophthalmology and visual science,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. “His breadth of knowledge about all aspects of ophthalmology, together with outstanding leadership skills, make him an ideal choice.”

A Phi Beta Kappa graduate of Amherst College and an alumnus of the Stanford University School of Medicine, Tsai completed his residency in ophthalmology at the Doheny Eye Institute at the University of Southern California in Los Angeles. Following his residency, he completed glaucoma fellowships at the Bascom Palmer Eye Institute at the University of Miami and at Moorfields Eye Hospital and Institute of Ophthalmology in London. Tsai received his master’s degree in business administration from the Owen Graduate School of Management at Vanderbilt University.

Tsai has authored a wide range of scientific articles, abstracts, and book chapters in glaucoma, and has co-authored a textbook, Medical Management of Glaucoma. He is a fellow of the American Academy of Ophthalmology, the American College of Surgeons and the Royal Society of Medicine in the United Kingdom. Tsai serves as a panel consultant for the Ophthalmic Devices Panel of the U.S. Food and Drug Administration and as a committee member of the National Eye Health Education Program Planning Committee of the National Institutes of Health. He is chair of the Medical Advisory Committee of

The Glaucoma Foundation and is an elected member of the American Eye Study Club and the New York Ophthalmological Society.

As department chair, Tsai follows in the footsteps of two highly respected experts on glaucoma: Marvin L. Sears, M.D., who founded the department in 1971, and M. Bruce Shields, M.D., who has led the department since 1996.

“Dr. Tsai represents a new generation in academic ophthalmology,” says David J. Leffell, M.D., the School of Medicine’s deputy dean for clinical affairs. “We are confident and excited that he will bring the department to national and international prominence in clinical care, research, and education.”

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sufficient to activate the cell network, which caused the flies to execute their typical escape response.

When Miesenböck couples this actuator technique with his light-emitting sensors, the propagation of light-activated nerve impulses throughout a cell network can be observed over time, as downstream cells erupt in blooms of green fluorescence. “We can essentially watch information processing,” says Miesenböck.

The nervous and immune systems are quite different in organization and function. In the brain, information is conducted among nerve-cell networks that are hard-wired in place, whereas immune-system networks rely on the physical movement of various cells to specialized information transfer sites, such as lymph nodes. But Melleman and Miesenböck say that the two systems share the fundamental property of “coordinated reaction of diverse cell types to seemingly limitless numbers of inputs”—pathogens in the case of the immune system and sensory information in the case of the nervous system.

These inputs, whether a complex visual scene or a bacterial infection, begin to activate these cellular networks in our bodies to prepare us for an appropriate behavioral or immune response. In the new Keck-funded research, a beam of light (or a temperature change or some other non-invasive stimulus) will be carefully controlled and tuned in for such real-world events. Miesenböck will investigate neuronal circuits to gain insight into how the brain controls behavior, while Melleman, also professor of immunobiology, will explore how immune-system networks distinguish the body’s own cells from foreign invaders such as bacteria and viruses.

The researchers will genetically insert suites of actuators and sensors into specific classes of neurons or immune cells in mice, and they will then excise tissues containing many thousands of these cells—a chunk of the cerebral cortex, say, or a whole lymph node—for experiments in which light or another stimulus will simultaneously activate many inputs to a cellular network.

The network’s coordinated response to the stimulus, reflected in illumination patterns made by the downstream sensors, will be recorded in real time by custom-designed microscopes. Finally, this rich pool of stimulus and response data will be analyzed and interpreted using powerful computers and specialized software.

Melleman says that Miesenböck’s technology holds the potential to forever change the way that scientists study cells as systems.

“The primary goal,” Melleman explains, “is to establish the scientific and intellectual base of an essential new direction for cell biology in particular and biomedical science in general; learning how to apply reductionist approaches to understand the behavior of cells in complex tissue contexts. Unless we can do this, we will never really understand biology or have the tools to uncover the basis for complex diseases.”

Melleman, who has received numerous accolades and honors over more than two decades of research, says his new partnership with Miesenböck is a high point. “This is possibly the first time in a very long scientific career when I feel as if I am involved in something truly profound,” he says. “It is remarkably exciting.”

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new generation of interdisciplinary clinical researchers, to launch greater numbers of Phase I studies of drugs discovered at the Yale Cancer Center and to forge research partnerships with underserved populations in the community to improve public health.

The School of Medicine was the only academic medical center in New England to be awarded grants to conduct outreach programs across the nation that received CTSA, which total nearly $700 million over the next five years. The grants were inaugurated as part of the Roadmap for Medical Research, an ambitious effort to streamline translational research spearheaded by NIH Director Elias A. Zerhouni, M.D. When fully implemented in 2012, the CTSA initiative is expected to provide $500 million annually to 60 centers forming a national consortium.

According to Robert J. Alpern, M.D., dean and Ensign Professor of Medicine, the medical school is ideally positioned to fulfill the mission of the CTSA. “A strategic planning initiative completed in 2004 targeted clinical research as a priority, establishing the YCCl as a focal point,” Alpern said. “The YCCl’s structure, built on Yale’s strengths in education, basic science, and community-based research, is virtually identical to the vision put forth by the NIH in this new program.”

The educational centerpiece of the YCCl is Yale’s Investigative Medicine Program (IMP), a unique program that offers Ph.D. degrees to M.D. fellows beginning careers in translational or clinical research.

The new funding expands the IMP and opens the program to nursing, public health, biomedical engineering and biological sciences students. A new CTSA-funded YCCl outpatient facility will add to the clinical studies School of Medicine faculty have conducted at nearby Yale-New Haven Hospital for more than four decades. The YCCl will also form an Office of Community-Based Research and Engagement to build on the strong community ties of the schools of Nursing and Public Health to forge new research partnerships.

Yale’s research “cores,” which give scientists access to state-of-the-art biomedical technologies, are also instrumental to the new effort. The CTSA funding will create a new Office of Research Services within YCCl that will provide clinical investigators with “one-stop shopping” for regulatory, bioinformatics, and patient recruitment services.

“The development of this consortium represents the first systematic change in our approach to clinical research in 50 years,” Zerhouni said in announcing the award. “By working together, these sites will serve as discovery engines that will improve medical care by applying new scientific advances to real-world practice. We expect to see new approaches reach underserved populations, local community organizations and health care providers to ensure that medical advances are reaching the people who need them.”
An eye for science

The tax Gallery, located in the School of Medicine’s Anlyan Center, showcases scientific images created in medical school laboratories. Co-directed by Lorraine F. Rosenman, operations manager and customer advocate in the medical school’s Office of Facilities, and Terry Dagradi, image specialist in the ITS-Med Media Group, the gallery was made possible by the Facilities Operations group.

Confocal micrograph of a tick from the family loaders, the vector for Lyme disease. Ruth R. Montgomery, Ph.D., senior research scientist in the Department of Internal Medicine’s Section of Rheumatology, and Utpal Pal, Ph.D., now an assistant professor at the Virginia-Maryland Regional College of Veterinary Medicine, imaged living ticks 24 hours after injecting them with fluorescent dyes to label surface structures and cells in the midgut.

Scanning electron micrograph by Daniel Ehrenkranz, Ph.D., assistant professor of medicine, of a glomerulus in the kidney of the two-toed amphisbaena (Amphisbaena means), a salamander found in the southeastern United States. Glomeruli are found in the nephron, the basic structural and functional unit of all vertebrate kidneys. They are composed of capillaries and an epithelium that filters the blood. Here, epithelial cells (round and oval structures) are seen sending out extensions to surround the capillaries (hubular structures) beneath.

A section of rectal mucosa tissue from a macaque monkey stained with fluorescent antibodies to DC-sign (green) and cc55 (red) and imaged with confocal microscopy by Akiko Iwasaki, Ph.D., associate professor of immunobiology. DC-sign binds to the human immuno-deficiency virus (hiv-1) and cc55 is a co-receptor for hiv-1. Cell nuclei are seen in blue.

Grants and contracts awarded to Yale School of Medicine March/April 2006

Federal

Frederick Altice, NIH, Improving Health Outcomes for Relaxed HIV+ Prisone rs, 2 years, $413,139; Lynn Cooley, NIH, Odyssey IV: Confocal System, 1 year, $32,627; Richard Ehrenkranz, NIH, UNC-Chapel Hill Biotechnology Cooperative Multi-Center Neuronal Research Network, 5 years, $1,485,696; Emil Fikrig, NIH, Trans-Specific Borellia Gene Expression, 5 years, $1,443,290; Elena Grigorenko, NIH, Genetic Basis of Developmental Disabilities, 5 years, $1,210,894; Stephanie Halene, NIH, Role of CR2/Ep in Myeloid Differentiation, 5 years, $1,608,322; Lyndsay Harris, U.S. Department of Defense, Molecular Classification of Response to Therapy in HER2-Positive, Early Stage Breast Cancer, 2 years, $999,427; Christina Herrick, NIH, The Response in the Citalo- minus Environment, 5 years, $1,239,255; Leon ard Kacsmar cse, NIH, Expression of Ion Channels in the Nervous System, 5 years, $1,272,500; Arie Kaffman, NIH, Effect of Maternal Care on Neurogenesis and Behavior, 5 years, $913,457; Anthony Koleske, NIH, A Biochemical Screen for Novel Regulators of Neuronal Morphogenesis, 2 years, $198,987; William Koningsberg, NIH, Molecular Biology and Structure of 70s Replicase, 4 years, $1,329,349; James Leckman, NIH, Treatment of Tourette Syndrome and Obsessive-Compulsive Disorder, 5 years, $645,320; Luis Macenon, NIH, Mediated Inactivation of Neurotransmitter, 3 years, $495,103; Ruth Montgomery, NIH, Mechanism of Vector Sialic Acid Inhibition of Insect Immunity, 2 years, $449,632; Peter Moore, NIH, Program in Macromolecular Structure, Molism, Control, 3 years, $463,015; Xanophon Papanikolaou, NIH, Biomage Suite: A Structural, Functional, and Metabolic Image Analysis Platform, 4 years, $1,466,357; David Rothstein, NIH, Immune Tolerance to Transplanted Myoblasts, 5 years, $1,441,450; Jody Sinclaire, NIH, Work Life, Health Habits, and Health: Longitudinal Analysis, 4 years, $1,173,250; Scott Strobel, NSF, Ribonovitch Structure Function Analysis, 1 year, $154,886; Joan Sweasy, NIH, Characterization of a Dna Polymerase Beta–Deficient Mouse, 1 year, $1,456,065; Benjamin Turk, U.S. Department of Agriculture, Identification of Substrates and Inhibitors of the Anthrax Lethal Factor, 1 year, $219,928

Non-Federal

Hervé Agassiz, Edward Mallinckrodt, Jr. Foundation, Identification of Host Factors Involved in Intracellular Pathogen Infection, 1 year, $60,000

Fengwei Bai, Health Research Inc., Lentivirus Mediated Delivery of West Nile Virus RNA Therapeutics, 1 year, $35,000; Nancy Berliner, Robert Lee and Carla Guthrie Patterson Trust, Disruption of Myopathy due to Human Anaphylaxis Infection, 1 year, $62,000; Michael Bracken, University of Vermont, Cystic Fibrosis National Review Group (CFNRG), 5 years, $422,847; Kathleen Carroll, University of California—Los Angeles, Starting Treatment with Agonist Replacement (START), 17 months, $1,388,000; Marie Egan, Cytoxic Fibrosis Foundation, Bone Marrow—Derived Stem Cells: Potential Use in CF, 2 years, $954,400; Brian Elbel, Russell Sage Foundation, Choice Sets and Consumer Selection of Health Plans, 1 year, $4,679; Lyndsay Harris, CALGB Foundation, rna Profiling from Paraffin in CALGB 93242d45, 1 year, $303,937; Josephine Hohl, Virto Institute, LLC, Genome-Wide Linkage Dissection Mapping for Carcinoid Susceptibility, 2 years, $34,000; Marci Allen, Masculine Vision Foundation, Age-Related Macular Degeneration Susceptibility Genes, 3 years, $240,000; Peter Jatlow, University of Connecticut Health Center, Urine Catecholamine Testing, 1 year, $99,420; Harriet Kluger, Novogen Limited, Assessing the Activity and Mechanism of Action of NY-451 and NY-496 in Malignoma, 1 year, $37,245; Charles Lockwood, March of Dimes, Abruptly-Induced Petterm Delivery Effects Functional Endometrial Progestrogen Withdrawal, 3 years, $89,101; Linda Marc, Connecticut Health Foundation, Recruiting, Retaining, and Promoting CRM Faculty at TVIP, 18 months, $50,000; Angus Nairn, Rockefeller University, Drug of Abuse—Role of Protein Phosphorylation: Three Striatum Protein Kinases and Actions of Psycho-stimulants, 5 years, $364,444; Laura Niklasson, Columbia University, Engineering Vascularized cardiac Muscle, 6 months, $255,000; Errol Norwitz, March of Dimes, Progestosterone Receptor Dysregulation and Preterm Birth, 3 years, $573,688; Scott Rickes, IS Genetics, Newborn Screening for Sex Chromosome Disorders, 1 year, $50,138; Susumu Tomita, Edward Mallinck- rodt, Jr. Foundation, Molecular Mechanism for Excitatory Synaptic Plasticity in the Brain, 1 year, $267,097; Maria Ulickas Yoord, Henry Ford Health System, The HMO Cancer Research Network (CRN), 1 year, $31,000; Flora Vaccarino, Tourette Syndrome Association, Inc., Inhibitors Intervention in Tourette’s Syn- drome, 1 year, $73,345; Hong Wang, American Cancer Society, Inc., The Impact of the Penetration of Domestic-Made Foreign-Brand Cigarettes on Tobacco Consumption in China, 2 years, $40,000

After immunization, large numbers of B lymphocytes that are specific for the foreign compound form an aggregate of dividing cells known as a germinal center, seen here in a widefield fluorescence micrograph made by Associate Research Scientist Ann M. Haberman, Ph.D., in the laboratory of Mark R. Slomchik, M.D., Ph.D., professor of laboratory medicine and immunobiology. As the germinal center expands, non-responding B cells (green) are displaced by responding B cells (red). Contact with the fine extensions of follicular dendritic cells (red) encourages long-term survival and differentiation of germinal center B cells.
Maverick psychiatrist overturned tradition to devise lifesaving therapy

Aaron T. Beck, M.D., a 1946 graduate of the School of Medicine who created cognitive therapy and transformed the practice of psychiatry, has received the 2006 Albert Lasker Award for Clinical Medical Research. Sometimes called the "American Nobels," the Lasker Awards are the nation's highest honors for contributions to biomed-ical science.

Freudian psychoanalysis was ascendant when Beck completed his own training as an analyst in 1956, but its influence was counterbalanced by increasing calls to subject psychoana-lytic concepts to the rigorous scientific scrutiny applied in other branches of medicine.

Beginning in the late 1950s at the University of Pennsylvania, Beck began a series of studies of core psychoanalytic concepts, such as the idea that depression was caused by uncon-scious, unexpressed rage toward some individual in a patient's life. Psychoana-lysis held that the target of this anger could be revealed in dreams, and that patients could be relieved of depression through insights gained from analyzing dreams.

In the course of this work, Beck not only found that patients did not have dreams of this sort, but he iden-tified a conscious cause of depression in "automatic thoughts"—persistent, unrealistic feelings of inadequacy that bleakly colored his patients' moods and undermined their attempts to fully engage with others. Many similar findings led Beck to abandon psychoanalysis, and by 1964 he had laid the foundations of cognitive therapy, a systematic form of "talk therapy" that aimed to modify the distorted thinking patterns seen in many psychological disorders. Although cognitive therapy was fiercely resisted at first, controlled trials conducted by Beck in the 1970s revealed his techniques to be more ef-fective in treating depression than the antidepressant medications available at the time.

Cognitive therapy is now a main-stay of psychiatric practice around the world for the treatment of an array of psychiatric disorders. It has been shown to be a powerful adjunct to medication in treating these seri-ous psychological conditions, such as bipolar disorder and schizophrenia, and it has proved highly effective in preventing suicide among severely depressed patients.

The Lasker Awards were inaugu-rated in 1946 by the Albert and Mary Lasker Foundation, a philanthropic organization founded by advertising executive Albert Lasker and his wife, Mary, a leading donor of public funding for biomedical research. In announcing Beck's award, Joseph L. Goldstein, M.D., chair of the foundation's international jury and one of 71 Lasker Award winners to go on to win the Nobel Prize in physiology or medicine, said, "The development of cognitive therapy by this year's Lasker clinical awardee is one of the most important advances—if not the most important advance—in the treatment of these diseases in the last 50 years."

Two other Lasker awardees for 2006 also have Yale connections. Joseph G. Gall, Ph.D., whose distinguished 57-year career in cell bi-ology was recognized with the Albert Lasker Award for Special Achievement in Medical Science, earned his under-graduate and graduate degrees at Yale University. Now a member of the National Insti-tute of Washington, from 1963 to 1983 Gall was a member of Yale's Depart-ment of Biology, where he invented in situ hybridization, a method to local-ize specific DNA or RNA sequences in tissue samples that is still widely used in cellular and molecular biology.

One of Gall's postdoctoral stu-dents at Yale during the mid-1970s was Elizabeth Blackburn, Ph.D., now the Morris Herzstein Professor of Biology and Physiology at the Univer-sity of California—San Francisco. For her discovery of telomerase, a chromosome-repairing enzyme that plays roles in cancer and aging, Blackburn is one of three recipients of the 2006 Albert Lasker Award for Basic Research.

School of Medicine alumnus is honored with Lasker Award

Aaron Beck challenged psychoanalysis and laid the groundwork for cognitive therapy. Bogan from page 2

TUG, a tethering protein that holds GLUT4 in place inside the cell until insulin stimulation releases it to the cell surface, Bogan and his coworkers first identified TUG in 2003.

"While most research on insulin stimulation of glucose uptake has focused on the cell-surface receptor that binds insulin and begins a signal-ing process inside the cell, we have targeted the other end of the process," says Bogan.

As a Keck Young Scholar, Bogan was able to collaborate with Yale investigators in structural biology, physiology and cell biology to examine the relation-ship of these two key proteins to other molecules in the cell. After earning an undergraduate degree in electrical engineering at Yale, Bogan received his M.D. at Har-vard Medical School and completed his residency and endocrinology fellowship at Massachusetts General Hospital.

Bogan was a visiting scientist at the Whitehead Institute for Biomed-i-cal Research and a member of the medical faculty at Harvard before joining the School of Medicine's facul-ty in 2002.

Originally established in 1998 as a five-year, $25 million initiative, the Keck Young Scholars program was designed to support groundbreaking research by addressing the fundamental mechanisms of human disease. In 2003, the foundation's board renewed the program for an addi-tional five years. Mark B. Gerstein, Ph.D., Albert L. Williams Professor of Biomedical Informatics, was named a Young Scholar in 1999.

TUG, GLUT4

Awards & honors

Heping Zhang, Ph.D., professor of public health and statistics, has been named a fellow of the Institute of Math-ematical Statistics (IMS). Established in 1935, the IMS is an organization that fosters the development and dis-semination of theory and applications of statistics and probability. This year, Zhang is one of 20 IMS members selected for the honor, which has been granted to only 5 percent of the society's 4,500 active members. The IMS cited Zhang's "distinguished con-trIBUTIONS to genetic statistics, public health, and medicine."

Barry L. Zaret, M.D., Robert W. Berliner Professor of Medicine and professor of diagnostic radiology, received the Distinguished Service Award of the American Society of Nuclear Car-diology (ASNC), the highest award granted by the society, at the ASNC's annual meeting in Montreal in Sep-tember. The award, which has been given only four times previously, rec-ognized Zaret's contributions to the field of nuclear cardiology; in which radioactive tracers are used for diagnostic and therapeutic purposes, and his 10-year term as the founding editor-in-chief of the Journal of Nuclear Cardiology.

Tarek Fahmy, Ph.D., and Ervin Lavik, s.c.d., both assistant professors of biomedical engineering, have received Wallace H. Coulter Foundation Early Career Translational Research Awards in Biomedical Engineering. Fahmy was recognized for developing nanoparticle technology that can track T cells (such as those responsible for lupus) by MRI and can also deliver drugs to those cells. Lavik was honored for her development of a long-term drug-delivery technol-ogy for the treatment of glaucoma. The awards were established in 2005 in memory of the foundation's benefactor, "an engineer, inventor, and entrepre neur who believed that the results of research must be taken to the stage of a commercially viable product in order to truly benefit humanity."

Alison P. Galvani, Ph.D., assistant professor of epidemiology, and Frank J. Slack, Ph.D., assistant professor of molecular, cellular and developmental biology, have received 2005 Science Initiative Awards from the National Academy of Sciences. The awards provide up to $400,000 toward "the acquisition of new knowledge and ... the responsible application of knowl-edge for solving real-world problems." Galvani's research merges game theory, psychology, economics, epidemiol-ogy and other disciplines to develop optimal strategies for community vac-cination against human papillomavirus. Slack will explore the use of microor-gans to diagnose and treat brain cancer.

Philip E. Rubin, Ph.D., adjunct professor in the Department of Surgery and chief executive officer of Huntskin Labora-tories, is an independ-ent, Yale-affiliated research institute focusing on the science of the spoken and written word, which has been named chair of the National Academies (NA) Board on Behav-ioral, Cognitive and Sensory Sciences (BCSS). The BCSS is an advisory board that helps the National Research Council, the NA's research wing, to identify areas in which new scientific developments are creating opportuni-ties or problems for public policy.