Described in Homer’s Iliad and called by a succession of names ever since—from mere “exhaustion” to “shell shock” and “battle fatigue”—the distinctive condition that often afflicts soldiers after stressful wartime experiences, known as post-traumatic stress disorder (PTSD), still carries a strong social stigma. And scientists still have much to learn about its psychological and physiological underpinnings.

Though the investment firm headed by Yale College alumnus Glenn H. Greenberg, M.A., M.B.A., is known as Brave Warrior Advisors, Greenberg knew little about PTSD until he began hearing that increasing numbers of veterans of the wars in Iraq and Afghanistan had returned home with deep psychological scars left by those conflicts. For Greenberg’s wife, Linda Vester, who had worked for years as a war-zone correspondent for NBC News, the cluster of symptoms that make up PTSD were all too familiar. “She also came back with stress disorder,” Greenberg says, “and she told me how debilitating it was, such that when there was a thunderstorm she’d dive under the dining room table—literally, with her family there.”

The School of Medicine, in partnership with the VA Connecticut Healthcare System (VACHS), has been in the vanguard of PTSD research and treatment for decades. When Greenberg, a member of the Class of 1968, contacted his alma mater to find out about Yale cell biology experiments that have revealed the molecular machinery of membrane trafficking in fine detail. Much of this work was done using a “cell-free” approach, in which Rothman sidestepped the complexities of working with complete cells by isolating the intracellular components crucial to membrane trafficking. This strategy allowed him to propose that complexes of membrane-associated proteins known as SNAPs are required for vesicles to fuse with membranes.

Rothman shares the Kavli Prize with Thomas Sudhof, Ph.D., of the Stanford School of Medicine, and Ruslan Medzhitov, Ph.D., of the Innate immunityinnovator joins National Academy

In April, Yale immunobiologist Ruslan Medzhitov, Ph.D., received one of the highest honors bestowed on American scientists when he was elected to the National Academy of Sciences (NAS), the elite corps of researchers from the nation’s top scientific institutions.

The David W. Wallace Professor of Immunobiology and a Howard Hughes Medical Institute investigator, Medzhitov has done pioneering research on the innate immune system, an evolutionarily ancient physiological system that launches rapid first-line defenses against bacteria and viruses.

“There are all delighted by Ruslan’s election to the NAS, which honors his seminal research on innate immunity,” says Carolyn W. Slayman, Ph.D., //Medzhitov (page 8)

The David W. Wallace Professor

On June 3, James E. Rothman, Ph.D., the Fergus F. Wallace Professor of Biomedical Sciences and chair of the medical school’s Department of Cell Biology, was named a recipient of the 2010 Kavli Prize in Neuroscience. The biennial $1 million award, which has become one of the most prestigious in science, was established in 2008 by a partnership of the Norwegian Association of Science and Letters, the U.S.-based Kavli Foundation, and the Norwegian Ministry of Education and Research.

Rothman is one of the world’s foremost experts on membrane trafficking, the means by which proteins and other materials are transported within and between cells. The Kavli Prize highlights his contributions to the understanding of exocytosis, a form of trafficking in which spherical sacs called vesicles fuse with cell membranes to deliver their contents outside the cell.

This process is ubiquitous in biology—it is essential to cell division and insulin secretion, for example—but exocytosis plays a particularly crucial role in the nervous system. In neurons, vesicles carrying neurotransmitters fuse with cell membranes at synapses, emptying their cargo to pass on the chemical messages that govern movement, perception, cognition, memory, and mood. For three decades, Rothman has performed elegant, focused biochemical and genetic studies of disturbances in stress-related hormones in soldiers with PTSD. In 1989, Yale became home to the Clinical Neurosciences Division and the Health Services Division of the VA National Center for PTSD, //Greenberg (page 4)

In the mid-1960s, after completing a residency in psychiatry at Yale, Arthur S. Blank Jr., M.D., saw the Vietnam War first hand, working in hospitals in Long Binh and Saigon. Soon after the war ended, Blank reviewed the charts of 60 veterans and concluded that many had been misdiagnosed with maladies ranging from alcoholism to schizophrenia. In 1973, Blank, now a psychiatrist in Bethesda, Md., invited those men to a therapy group at the veterans hospital in West Haven, Conn. (now the VACHS), which helped to lay the groundwork for PTSD’s eventual acceptance as an official psychiatric diagnosis in 1980. Soon after, Yale recruited Walter Reed Army Medical Center endocrinologist John W. Mason, M.D., who led the first studies of disturbances in stress-related hormones in soldiers with PTSD.

Glenn H. Greenberg, m.a., m.b.a., headed by Yale College alumnus Arthur S. Blank Jr., m.d., who led the first studies of disturbances in stress-related hormones in soldiers with PTSD. In 1989, Yale became home to the Clinical Neurosciences Division and the Health Services Division of the VA National Center for PTSD.
Leading with vision

Yale glaucoma specialist is also helping to bring eye cancers into the light

Patients go out of their way to see Yale ophthalmologist James C. Tsai, m.d., m.b.a. One traveled four-and-a-half hours from Long Island. Another takes a car service each week from Garden City, N.Y., for post-operative care. For his weekly follow-ups, a Wall Street trader journeys to New Haven each Wednesday on the Metro-North Railroad.

Tsai, an expert in glaucoma research and treatment, came to Yale in 2006 from Columbia University College of Physicians and Surgeons, where he was director of the Edward S. Harkness Eye Institute. Now chair and Robert R. Young Professor of Ophthalmology and Visual Science at the School of Medicine, Tsai is also chief of ophthalmology at Yale-New Haven Hospital (ynew) and director of the Yale Eye Center.

Liz Whall, one of his patients, says Tsai’s stamina is matched by his empathy. “I don’t know how he has time to take care of so many people and still stop and listen.” But for Tsai, listening is key. “You have to tailor your treatment for every patient.”

Characterized by elevated pressure of fluid inside the eye, glaucoma can damage the optic nerve and cause irreversible vision loss. But in as many as one-third of cases, low to normal pressure measurements (a thin cornea can skew test results) can leave glaucoma undiagnosed until there is significant visual damage. Whall’s undiagnosed glaucoma was affecting her ability to do basic tasks as a mother and interior designer. After a proper diagnosis, a New York surgeon performed pressure-reducing surgery on her left eye, but it yielded only short-term results. Medication to lower pressure in her right eye had severe side effects.

Whall consulted Tsai, who suggested “revising” the previous surgery on her left eye, and advised against surgery on her right eye altogether. Today, with glasses, the combined vision of Whall’s eyes is 20/20. Born in Taiwan and delivered by a Wall Street trader’s wife, Michael J. Caplan earned his m.d., Ph.D. degrees at Yale School of Medicine in 1987. He became an assistant professor in 1988 and was promoted to full professor in 1998.

In April, Caplan was named as the first recipient of Yale’s Postdoctoral Fellows Mentoring Award. He has been given numerous other honors, including the School of Medicine’s Charles W. Bohmfalk Teaching Prize, the Young Investigator Award of the American Society of Nephrology, and the Henry P. Bowditch Award Lectureship of the American Physiological Society.

Caplan has served as interim chair since the death of his colleague Steven C. Hebert, M.D., a distinguished nephrologist and kidney researcher who served as chair from 2000 to 2008.

Expert on causes of kidney disease will lead physiology department

Michael J. Caplan, M.D., Ph.D., who studies how membrane proteins find their proper location on the cell surface, and disruptions in this process that are associated with polycytic kidney disease (PKD), has been named chair of the Department of Cellular and Molecular Physiology. Caplan, the C.N.H. Long Professor of Cellular and Molecular Physiology and professor of cell biology, also serves as associate director for basic research for the School of Medicine’s M.D./Ph.D. Program.

In PKD, a common genetic disease, the normal architecture of kidney tubules is replaced by large, fluid-filled cysts. Caplan and colleagues study the cellular and molecular pathways responsible for this process. They have made the surprising discovery that many receptor and signaling proteins involved in the sense of smell are also expressed in the kidney, a finding that suggests that olfactory signaling mechanisms may play an important role in regulating kidney function in response to chemosensory cues. Caplan earned his M.D. and Ph.D. degrees at Yale School of Medicine in 1987. He became an assistant professor in 1988 and was promoted to full professor in 1998.

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VA hospital with Yale affiliation gets top marks for care

The U.S. Department of Veterans Affairs (VA) has ranked the VA Connecticut Healthcare System (VACHS) in West Haven, Conn., first in the country among the system’s tertiary facilities, for its heart care.

“We’re not one of the largest or most well-funded facilities, but we tend to be very efficient and provide outstanding care,” says Gary Desir, M.D., professor of medicine and chief of medical services at the VACHS. “The challenge is going to be that our patient population is increasing yet our funding is not, so we have to maintain the same level of care but lower resources.”

The VACHS, one of 153 VA hospitals nationwide, achieved a perfect score in performance measures in three of nine categories: acute myocardial infarction, total hip and knee screening, and heart failure. For behavioral health screening, community-acquired pneumonia, and surgical complications it achieved a rating of “exceptional.” For diabetes, ischemic heart disease, cancer, and heart disease prevention, the VACHS, which has a long-standing affiliation with the School of Medicine, also had very high ratings.

There are more than 200,000 visits to VACHS clinics each year. The hospital offers a full range of medical, surgical, and psychiatric services to veterans, with particular strengths in epilepsy, stroke, rehabilitation for the blind, post-traumatic stress disorder, alcoholism, schizophrenia, and vireology. In addition, its medical research program is the second-largest in the VA system.

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Faulty histidine gene is a factor in Tourette’s

Best known for triggering symptoms of hay fever, histamine also acts as a neurotransmitter in the brain. A new genetic study by Matthew W. State, M.D., Ph.D., the Donald J. Cohen Associate Professor of Child Psychiatry, suggests that histamine plays a role in Tourette’s syndrome.

As reported in the May 20 issue of The New England Journal of Medicine, in a rare family in which the father and all eight children, but not the mother, have Tourette’s, affected family members all carried the same mutation in HDC, a gene involved in histamine synthesis.

Normally, HDC molecules pair up in a symmetrical complex (above left) to synthesize histamine. The mutation, which truncates the hdc protein, is found only on one of two chromosomal copies of the gene, resulting in reduced or no activity of the normal copy by forming an abnormal complex (above right).

Histamine-boosting drugs reduce Tourette’s-like behaviors in mice lacking Hdc, and several are in human clinical trials for neuropsychiatric conditions, says State, also co-director of the Yale Neurogenetics Program. “This may mean that we have the opportunity to go directly from a rare genetic finding to a new approach to treatment. In our field, that would be very unusual, and very exciting,” he says.

A new sort of stem cell is aimed at Parkinson’s

Parkinson’s disease, which degenerates motor function and speech, results from a loss of dopamine-producing brain cells. Drug treatments cannot always relieve the symptoms and loss of balance caused by the disorder.

Embryonic stem cells (ESC) have shown promise as a means of regenerating the lost cells, but scientists have been on the lookout for alternatives to ESCs that can be easily obtained from adult patients.

In experiments reported online in the April issue of the Journal of Molecular and Cellular Medicine, Yale researchers led by Hugh Taylor, M.D., professor of obstetrics, gynecology, and reproductive sciences, explored the therapeutic potential of cells from the lining of the uterus, or endometrium. Regularly regenerat ed after menstruation, this tissue is rich in stem cells that can be easily obtained from adult patients.

In a mouse model of Parkinson’s, transplanted endometrial cells migrated to damaged brain tissue and differentiated into dopamine-producing neurons, significantly raising dopamine levels. In typical ESCs, the process to differentiate into dopaminergic neurons is probably the safest, most easily attainable source of stem cells currently available,” says Taylor. “I think this is just the tip of the iceberg for what we will be able to do with these cells.”

Lively, hardy, and expensive, the zebra-fish is a popular species for beginning tropical-fish hobbyists. An attractive small fish native to the Ganges River and other freshwater sites in South Asia, it is also a dazzling of developmental biologists because, in addition to being easy to maintain in large numbers, zebrafish develop rapidly—their major organ systems undergo substantial development in just 24 hours—a phenomenon made all the more remarkable by the transparency of the fish’s embryos. Through a microscopic scope, says zebrafish specialist Antonio J. Giráldez, Ph.D., scientists have an intimate, clear view as the fish’s adult form swiftly unfolds.

Some basic principles of molecular biology have lately seemed to change just as dramatically. The wholly unexpected discovery about 20 years ago that short stretches of genetic material called microRNAs (miRNAs) exert profound and pervasive control of gene expression is a case in point. The study of miRNAs has since become one of the fastest-growing areas in biology, and now, by taking advantage of the zebrafish’s unique qualities, researchers in the laboratory of Giráldez, assistant professor of genetics and the Lois and Franklin H. Top, Jr. Yale Scholar (see box below), is prompting scientists to rethink strongly held ideas on how miRNAs are formed.

Until the early 1990s, it was thought that, for the most part, genes are activated or suppressed by transcription factors, which bind to DNA to promote or inhibit transcription of genes into messenger RNA (mRNA), and hence determine which genes are ultimately translated into proteins. But while studying the development of the microscopic roundworm Caenorhabditis elegans (another handily transparent organism), Victor Ambros, Ph.D., then at Harvard University, made the startling discovery that a tiny stretch of RNA, only 22 genetic letters long, switched off a crucial gene that orchestrates the timing of developmental events in C. elegans.

Over the next 10 years, scientists determined that small RNAs like that discovered by Ambros are a ubiquitous, fundamental regulator of gene expression throughout the plant and animal kingdoms. More than 700 miRNA molecules have been identified in humans, each of which may regulate hundreds (or even thousands) of genes; with such wide reach, miRNAs may interact with more than 60 percent of our genome. These findings have led to the hypothesis that miRNAs have implications not only in how humans and animals are made, but in the development of human diseases,” says Giráldez, also a member of the Yale Stem Cell Center. In 2006, the Nobel Prize in Physiology or Medicine was awarded to two American scientists for elucidating one of the main mechanisms by which miRNAs silence genes, an extraordinary turn of events considering that just 15 years earlier miRNAs were not even known to exist.

Scientists have revised many of their ideas over the past 20 years regarding how miRNAs work and how they are formed, but one character in the mosaic story has remained unchanged: Dicer, an enzyme that, as its name implies, snips complex precursors into the 21- to 23-nucleotide length that characterizes functional miRNAs. In addition to the zebra-fish’s other attributes, the species is also amenable to precise genetic manipulations. In recent work with zebrafish mutants, Giráldez has confirmed Dicer’s central role, showing that fish develop normally in the absence of this enzyme, unless some other pathway was at work.

In typical miRNA processing, once Dicer has cut miRNA precursor strands to a proper-length miRNA, the strands are loaded into a molecule known as the RNA-Induced Silencing Complex (RISC), where the business of gene-silencing actually takes place. Inside RISC, a second enzyme called Argonaute 2 (Ago2) slices up any mRNA strand containing a sequence that exactly matches the loaded miRNA.

miRNA processing was so firmly established, he and his team found this result “extremely weird, and in fact it took us almost two years to believe it,” during which time the group conducted every imaginable experiment until they were satisfied that the finding held up.

Eventually, they concentrated on one Dicer-independent miRNA called miR-451, because it is present in many species (in March, for example, researchers at Ohio State University proposed that miR-451 may regulate the growth of brain tumors in humans), and because its distinctive configuration is a bad structural match for Dicer processing, which suggested that some other pathway was at work. In typical miRNA processing, once Dicer has cut miRNA precursor strands to a proper-length miRNA, the strands are loaded into a molecule known as the RNA-Induced Silencing Complex (RISC), where the business of gene-silencing actually takes place. Inside RISC, a second enzyme called Argonaute 2 (Ago2) slices up any mRNA strand containing a sequence that exactly matches the loaded miRNA.

A new pathway found for microRNAs, powerful and versatile regulators

New pathway found for microRNAs, powerful and versatile regulators

ADVANCES

Health & Science News

New pathway found for microRNAs, powerful and versatile regulators

Yale Scholars: a gift that yields scientific dividends

In 2007, medical school alumnus Frank Top, M.D., and his wife, Lois (right), made a $2.5 million gift to the School of Medicine to establish a Yale Scholar endowment, a fund that smooths the way for a promising young scientist beginning his or her career. Yale Scholars receive four years of research funding; by year five, when a researcher generally has independent grant funding, the award passes on to another top recruit. Exciting new work by Antonio Giráldez, the Lois and Franklin J. Top, Jr. Yale Scholar, is described on this page. “To take talent that’s already been recognized in a postdoctoral program and let that person run with it makes an awful lot of sense,” says Frank, and Lois agrees. “It’s really time-consuming to pursue a research career,” she says, “and you can use all the help you can get.”

A named Yale Scholar position can be endowed with a gift of $2.5 million, which is matched dollar for dollar by Yale University, creating a $5 million endowment. Donors receive Yale Tomorrow campaign and reunion credit for the full amount. For more information, contact Janey Houch at (203) 436-8560.

Antonio Giráldez (center), leader of a study that revealed a new pathway for microRNA processing, in the medical school’s zebrafish facility with co-authors (from left) Heather Patnode (research assistant), Daniel Cifuentes (postdoctoral fellow), Huiling Xue (postdoctoral fellow), and David Taylor (graduate student in molecular biophysics and biochemistry).
A familiar voice speaks up for Alzheimer’s patients, research

It began with a sweatshirt. In December 2007, when Tony- and Emmy- Award-winning actor David Hyde Pierce appeared on the Today show to promote Cartman, the Broadway comedy in which he was then appearing, an alert viewer in New Haven noticed that Hyde Pierce was wearing a Yale College sweatshirt bearing the name of an Important Medical School That Is Not Yale.

A package was soon delivered to Hyde Pierce’s dressing room at the Al Hirschfeld Theater with a tongue-in-cheek note from Dean Robert J. Alpern, M.D., that read, in part, “I have been remiss in not providing you with the relevant clothing associated with your alma mater . . . and am enclosing a Yale School of Medicine sweatshirt, hat, and scarf.” The hat, a baseball cap, was a hit: Hyde Pierce, best-known for his portrayal of the cultured, persnickety Niles Crane, M.D., Ph.D., in the long-running CBS sitcom Frasier, says he wears the cap “religiously.” (The fictional Crane earned his undergraduate, M.D., and Ph.D. degrees at Yale.)

But Alpern’s letter also had a serious purpose. During his career, Hyde Pierce has lent his voice to animated characters as various as The Simpsons’ Cecil Terwilliger and Slim the stick-insect in A Bug’s Life. But for 15 years, he has been one of the most visible and articulate spokesmen for The Alzheimer’s Association, raising awareness of the urgent need for better diagnostic tools and effective treatments for Alzheimer’s disease (AD). Because Alzheimer’s has made the expansion of research on neurodegenerative diseases a touchstone of his tenure as dean, he invited Hyde Pierce to visit the School of Medicine to learn about the school’s diverse research efforts in AD.

“Statistically, this is a disease that’s going to affect everybody in one way or another,” Hyde Pierce says, and this trend has been borne out in his own life. The disease killed his beloved grandfather, and advancing dementia would likely have claimed his father but for a fatal bout with pneumonia. “When he died, he still knew us,” says the actor, a former national board member (now an honorary member) of the Alzheimer’s Association.

Hyde Pierce took up his offer to visit New Haven, and met with scientists exploring AD on every front in the search for new treatments. “When you see these bustling intellectuals working on this thing, and how much has been done,” Hyde Pierce says, “it gives you hope.” He was “pleased and proud, having gone to Yale, to find out about the medical school’s vibrant neurodegenerative research community,” and this past March he joined Alpern and a group of School of Medicine scientists at the Yale Club of New York for a presentation of the School of Medicine’s Alzheimer’s disease research.

The session was moderated by John H. Krystal, M.D., the Robert McNeil Professor of Translational Research, chair of the Department of Psychiatry, and an authority on neuropsychiatric disease. To lead off the talks, Associate Professor of Pharmacology Ya Ha, Ph.D., whose team published the first-ever crystal structure of an enzyme that acts inside cell membranes in 2007, discussed how his work relates to human gamma-secretase, the enzyme that creates the amyloid fragments involved in AD. Stephen M. Strittmatter, M.D., Ph.D., the Vincent Coates Professor of Neurology and co-director of the Yale Program in Cellular Neuroscience, Neurodegeneration, and Repair, then presented his surprising recent findings on how the amyloid-beta (Aβ) protein that comprises the “plaques” found in AD patients’ brains may begin the destructive cascade that eventually erases memories (see related story, p. 3). Finally, Christopher H. van Dyck, M.D., professor of psychiatry and neurobiology and director of Yale’s Alzheimer’s Disease Research Unit, reported on progress using imaging techniques such as positron emission tomography (PET) to measure brain levels of Aβ, which may soon achieve the elusive goal of early AD diagnosis, providing doctors with enough time for treatments to make a difference.

In his own remarks, Hyde Pierce navigated “the twin horns of the Alzheimer’s dilemma” that he says frame most of his talks on the subject. It is essential, he says, to “keep hope alive and let people know there’s progress,” but also to drive home the urgency of the current situation. “We have no treatments, and we need to be candid about this disease.”

The prolific Hyde Pierce has received many accolades since he graduated from Yale College in 1981, including a Tony Award in 2007 for his work in Cartman, and four Emmys for Frasier. But earlier this year he brought home a different sort of prize, one that is particularly apropos for a man who has made his name as both actor and advocate: the Tony Awards’ 2010 Isabelle Stevenson Award, which honors his “substantial contribution” to the Alzheimer’s Association.

OUT & ABOUT

April 15 During their annual visit to the medical school’s Center for Neuroscience and Regeneration Research (cnrr), members of the Paralyzed Veterans of America (pva) had dinner with cnrr scientists in Branford College’s Common Room and received scientific updates at cnrr labs the following day. From left: Yale University President Richard C. Levin accepts a pva donation of $300,000 from Gene A. Cèrentino, national president of pva, joined by Stephen G. Waxman, M.D., Ph.D., cnrr director, and Bridget Marie Flaherty Professor of Neurology, Neurobiology, and Pharmacology pva has been a steadfast supporter of the cnrr for over 20 years, and has made donations totaling millions of dollars to fund the center’s research.

May 11 At the School of Medicine’s annual Student Research Day, held in the atrium of the Anlyan Center, M.D./Ph.D. student Daniel Balkin, one of 71 students who presented original research, discussed his work with Associate Research Scientists Zhi-Jia Ye, Ph.D., and Associate Professor of Medicine Arya Mani, M.D. The Farr Lecture, the culminating event of Student Research Day, was delivered by Lewis Landsberg, M.D., Irving S. Cutter Professor of Medicine and dean emeritus of the School of Medicine.

May 14 The members of the Class of 2010 launched their careers as physicians at this year’s Commencement ceremonies. Graduate David Myles ’10, who will join the Pediatric Residency Program at Johns Hopkins Children’s Center, celebrated with his family this year’s Commencement address was given by Donald M. Berwick, M.D., M.P.P., professor at the Harvard School of Public Health, newly appointed by President Obama to head the Centers for Medicare and Medicaid Services. Many students graduated with joint degrees at this year’s Commencement: 15 received M.D./Ph.D. degrees, 22 received M.D./M.S. degrees, one received an M.D./M.I.A., and one received an M.D./I.M.P.H.

June 3–5 Medical school alumni turned out in droves for Alumni Weekend, which featured symposia on “Doctor as Patient” and “When Illness Strikes the Leader”, an academic review of the legacy of pioneering neurosurgeon Harvey Cushing, M.D., and guided tours of the Medical Library, campus improvements, the new Smilow Cancer Hospital, and the 154-acre West Campus. Saturday marked the dedication of the new Harvey Cushing Center, which includes a dramatic display of Cushing’s whole-brain specimens, clinical drawings and photographs, and memorabilia. Class Dinners, including one in honor of the Class of 1960’s 50th reunion, took place at New Haven–area restaurants. Members of the Class of 2000, including (from left) Carl J. Seashore, M.D., Daniel Jacoby, M.D., Linda Maxwell, M.D., John D. Mahoney, M.D., Darren L. Lish, M.D., and Felix Adler, M.D., celebrated their 10th reunion.

Zhi-Jia Ye, Ph.D., and Associate Professor of Medicine Arya Mani, M.D. The Farr Lecture, the culminating event of Student Research Day, was delivered by Lewis Landsberg, M.D., Irving S. Cutter Professor of Medicine and dean emeritus of the School of Medicine.
Advances in Neurodegeneration, and Repair.

Strittmatter, the Vincent Coates Professor of Neuroscience at Yale's Interdepartmental Neuroscience Program, is a winner of the 2010 Harold M. Weintraub Graduate Student Award. The award, sponsored by the Basic Sciences Division of the Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, Wash., recognizes outstanding achievement by graduate students in the biological sciences. Carey is one of 13 graduate students in North America to receive the award this year. The awardees participated in a scientific symposium on May 7 at the FHCR.

Carey, who received her M.D. in 2009 and her Ph.D. at Commencement this past June, has focused her research at Yale on olfactory receptors in the mosquito Anopheles gambiae, the primary carrier of malaria in sub-Saharan Africa. Carey will soon begin a postdoctoral fellowship at the Institut Pasteur in Paris, France.

In the February 3 issue of Nature, Carey and colleagues, including her advisor John R. Carlson, Ph.D., the Eugene Higgins Professor of Molecular, Cellular, and Developmental Biology, identified A. gambiae odorant receptors that are precisely tuned and highly sensitive to components of human body odors, which may help them to locate and infect the hundreds of millions of people afflicted with malaria each year. In this research, which formed the basis of her Ph.D. thesis, Carey recorded over 27,000 responses to 110 different odors from a variety of A. gambiae receptors expressed in the antennae of mutant fruit flies. This work "was of epic proportion," Carlson says. "It required an enormous amount of effort, a high level of skill, and a great deal of creativity. Allison was also a wonderful colleague."

A major goal of the Carlsom lab is to apply knowledge of the molecular basis of A. gambiae olfaction to reduce the mosquitoes’ attraction to human odors or to lure them into traps, strategies that may slow the transmission of malaria.

The Weintraub Award, established in 2000, honors the late Harold M. Weintraub, Ph.D., a founding member of the FHCR's Basic Sciences Division and a leading researcher in developmental biology. Carey is one of two students in Carlson's lab to win the award recently—Elissa Hallem, Ph.D., was an awardee in 2009.

Yale-designed iPhone application provides Lyme disease information, employs user's location to assess risk

Thanks to faculty and students at the Yale School of Public Health (YSPH), users of Apple's popular iPhone can better protect themselves against Lyme disease, the most prevalent insect-borne disease in the United States.

The new application presents data on the abundance of infected ticks at the location of the user anywhere within the U.S., based on information from the phone's Global Positioning System (GPS) hardware. If ticks are determined to be present, the user is given a list of precautions to avoid bites. A chart with life-size photos is provided to aid in the identification of black-legged ticks (Ixodes scapularis, also known as deer ticks) at each life stage, useful information because these ticks cannot transmit Lyme disease during some stages.

If the user has been bitten, the program provides instructions on how to properly remove a tick, along with a narrated video.

"This is the first health application for smartphones that could have an immediate impact on a major disease," said Durland Fish, Ph.D., professor of epidemiology at YSPH, who oversaw the development of the application.

Lyme disease can be transmitted through bites of feeding an infected tick, and most physicians will treat patients who experience such bites with a short course of antibiotics to prevent the disease. To help users determine when they were bitten, the application depicts ticks at various stages of blood engorgement and advises patients to seek medical attention if the photos suggest that a removed tick had been attached for 48 hours or longer. A panel of photos of skin rashes characterizes Lyme disease at 4 stages, with a list of other symptoms also prompts users to seek immediate medical attention if they believe they are infected. To help users obtain medical care in unfamiliar locations, a GPS-based physician locator finds nearby doctors and provides the phone number and directions to each physician's office.

"You can only get Lyme disease in certain areas, only by certain ticks, and only after a tick has remained attached for a certain amount of time," says Fish. "Information provided by this app should help many people prevent Lyme disease."

Content for the application is provided by Lyme disease researchers at the School of Medicine—where Lyme disease was first identified—in cooperation with the U.S. Centers for Disease Control and Prevention, the American Lyme Disease Foundation, and IntuApp, an applications development company in New York City. It is available through the Apple iTunes Store for $1.99, with proceeds supporting the research and education mission of the American Lyme Disease Foundation based in Lyme, Conn.

Grad student lauded for malaria mosquito research

Allison Carey, M.D., Ph.D., who just completed her doctoral studies in Yale's Interdepartmental Neuroscience Program, is a winner of the 2010 Harold M. Weintraub Graduate Student Award. The award, sponsored by the Basic Sciences Division of the Fred Hutchinson Cancer Research Center (FHCR) in Seattle, Wash., recognizes outstanding achievement by graduate students in the biological sciences.

Carey is one of 13 graduate students in North America to receive the award this year. The awardees were selected from a pool of 30 applicants and participated in a scientific symposium on May 7 at the FHCR. Carey, who received her M.D. in 2009 and her Ph.D. at Commencement this past June, has focused her research at Yale on olfactory receptors in the mosquito Anopheles gambiae, the primary carrier of malaria in sub-Saharan Africa. Carey will soon begin a postdoctoral fellowship at the Institut Pasteur in Paris, France.

In the February 3 issue of Nature, Carey and colleagues, including her advisor John R. Carlson, Ph.D., the Eugene Higgins Professor of Molecular, Cellular, and Developmental Biology, identified A. gambiae odorant receptors that are precisely tuned and highly sensitive to components of human body odors, which may help them to locate and infect the hundreds of millions of people afflicted with malaria each year. In this research, which formed the basis of her Ph.D. thesis, Carey recorded over 27,000 responses to 110 different odors from a variety of A. gambiae receptors expressed in the antennae of mutant fruit flies. This work "was of epic proportion," Carlson says. "It required an enormous amount of effort, a high level of skill, and a great deal of creativity. Allison was also a wonderful colleague."

A major goal of the Carlson lab is to apply knowledge of the molecular basis of A. gambiae olfaction to reduce the mosquitoes' attraction to human odors or to lure them into traps, strategies that may slow the transmission of malaria.

The Weintraub Award, established in 2000, honors the late Harold M. Weintraub, Ph.D., a founding member of the FHCR's Basic Sciences Division and a leading researcher in developmental biology. Carey is one of two students in Carlson's lab to win the award recently—Elissa Hallem, Ph.D., was an awardee in 2009.

Yale-designed iPhone application provides Lyme disease information, employs user’s location to assess risk

Thanks to faculty and students at the Yale School of Public Health (YSPH), users of Apple’s popular iPhone can better protect themselves against Lyme disease, the most prevalent insect-borne disease in the United States.

The new application presents data on the abundance of infected ticks at the location of the user anywhere within the U.S., based on information from the phone’s Global Positioning System (GPS) hardware. If ticks are determined to be present, the user is given a list of precautions to avoid bites. A chart with life-size photos is provided to aid in the identification of black-legged ticks (Ixodes scapularis, also known as deer ticks) at each life stage, useful information because these ticks cannot transmit Lyme disease during some stages. If the user has been bitten, the program provides instructions on how to properly remove a tick, along with a narrated video.

“This is the first health application for smartphones that could have an immediate impact on a major disease,” said Durland Fish, Ph.D., professor of epidemiology at YSPH, who oversaw the development of the application.

Lyme disease can be transmitted through bites of feeding an infected tick, and most physicians will treat patients who experience such bites with a short course of antibiotics to prevent the disease. To help users determine when they were bitten, the application depicts ticks at various stages of blood engorgement and advises patients to seek medical attention if the photos suggest that a removed tick had been attached for 48 hours or longer. A panel of photos of skin rashes characterizes Lyme disease at 4 stages, with a list of other symptoms also prompts users to seek immediate medical attention if they believe they are infected. To help users obtain medical care in unfamiliar locations, a GPS-based physician locator finds nearby doctors and provides the phone number and directions to each physician’s office.

“You can only get Lyme disease in certain areas, only by certain ticks, and only after a tick has remained attached for a certain amount of time,” says Fish. “Information provided by this app should help many people prevent Lyme disease.”

Content for the application is provided by Lyme disease researchers at the School of Medicine—where Lyme disease was first identified—in cooperation with the U.S. Centers for Disease Control and Prevention, the American Lyme Disease Foundation, and IntuApp, an applications development company in New York City. It is available through the Apple iTunes Store for $1.99, with proceeds supporting the research and education mission of the American Lyme Disease Foundation based in Lyme, Conn.

Grad student lauded for malaria mosquito research

Allison Carey, M.D., Ph.D., who just completed her doctoral studies in Yale’s Interdepartmental Neuroscience Program, is a winner of the 2010 Harold M. Weintraub Graduate Student Award. The award, sponsored by the Basic Sciences Division of the Fred Hutchinson Cancer Research Center (FHCR) in Seattle, Wash., recognizes outstanding achievement by graduate students in the biological sciences. Carey is one of 13 graduate students in North America to receive the award this year. The awardees participated in a scientific symposium on May 7 at the FHCR.

Carey, who received her M.D. in 2009 and her Ph.D. at Commencement this past June, has focused her research at Yale on olfactory receptors in the mosquito Anopheles gambiae, the primary carrier of malaria in sub-Saharan Africa. Carey will soon begin a postdoctoral fellowship at the Institut Pasteur in Paris, France.

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With funding from the National Institutes of Health, Linda Mayes (left) and associate research scientist Michael Crowley (right) use dense-array electroencephalography (EEG) to measure changes in brain function that result from childhood stress, whether caused by prenatal exposure to cocaine or broader, more encompassing stresses such as poverty and violence.

Crowley’s daughter, Lia, is wearing a net containing dozens of electrodes, which detect the differences in electrical potentials across the surface of the brain.
When Annie Marie Le, an idealistic and ambitious doctoral student in Yale’s Combined Program in the Biological and Biomedical Sciences (BBS) at the time she died in September, the Yale community—and the world—reacted with grief and dismay.

In the wake of Le’s death, members of many parts of the Yale community came together to forge a scholarship fund that would commemorate her life and exemplary spirit in a lasting way by supporting the work of current graduate students. Soon after, the Yale Corporation established the Annie Le Fellowship to provide assistance to doctoral candidates in the BBS program “whose demonstrated commitment to bettering the world around them and outstanding record and research exemplify the qualities represented in the life and career of Annie Le.”

Two graduate students in the BBS program—Julie Button, a fifth-year graduate student in microbiology; and Jason Wallace, a fourth-year gradu- ate student in molecular, cellular, and developmental biology—have been named the inaugural Annie Le Fel- lowships and will receive funding for the 2010–2011 academic year.

Button, who works in the laboratory of Salvatore profile who focuses on the Type III Secretion System and an engineered E. coli strain that produces Gram-negative bacteria to help them infect a host’s cells by moving factors into those cells that promote the bacte- ria’s survival and replication, Wallace, a doctoral student in the lab of Ronald R. Breaker, Ph.D., the Henry Ford II Professor of Molecular, Cellular, and Developmental Biology and Howard Hughes Medical Institute Investiga- tor, studies large, non-coding RNAs that were recently discovered in several species of bacteria, which appear to be important for helping the bacteria survive extreme stress.

In addition to their academic work, both fellows are public-spirited. Button participates in the Hill Neighborhood Mentoring Program, has served on the Graduate Student Assembly for two years, and has sung with the Academia Nuts, the graduate school’s all-female a cappella group. Wallace provides Spanish-English translation for his church and has served as a career mentor for the Boy Scouts of America.

“Annie Le was an exemplary stu- dent, and someone who was concerned about the community in which she lived. And so we thought that the fellow- ship really would emphasize those two qualities—that is, the capacity of someone to really be an absolutely outstanding student, who is also concerned about the larger world in which she he she lives. We thought it was a really appropriate way to com- memorate her life and her time at Yale,” says Jon Butler, Ph.D., the Howard R. Lamar Professor of American Studies, History, and Religious Studies. Butler was dean of Yale’s Graduate School of Arts and Sciences when Le died, and he oversaw the implementation of the new fellowship.

“Annie came to Yale to study and train as a biomedical scientist,” says Elias Lisol, Ph.D., associate profes- sor of pharmacology and Le’s former doctoral supervisor. “She also cared about people and treated everyone with respect. It is for these reasons that Yale University established this fellowship in her memory."

An initial $500,000 endowment from the Yale Corporation has been in- creased by additional gifts from friends and members of the Yale community. In April, the Association of Asian American Yale Alumni, the Association of Yale Alumni, the Yale Alumni Asso- ciation of Metropolitan New York, the Yale Life Sciences Alumni Association, and several other groups collaboratively organized a benefit concert for the fund in New York City.

After earning her undergraduate degree in cell and developmental biology at the University of Rochester, Le came to Yale for graduate work in 2007. Working in the laboratory of her advisor, Adam M. Bennett, Ph.D., associate professor of pharma- cology, Le was exploring the effects of metabolic stresses on an enzyme connected with mitochondrial func- tion in muscle cells. She planned to devote her life to biomedical research, and had dreamed of having a scien- tific career at the National Institutes of Health.

“One of the many tragic aspects about losing Annie was that it was only after her death that the Yale commu- nity at large learned about her and her wonderful qualities,” says John D. Al- varo, Ph.D., administrative director of BBS. “The fellowship in her name now enables us to identify and celebrate other talented and selfless students, some of the hidden gems among the student body.”

The Annie Le Fellowship will be awarded each year by the Graduate School of Arts and Sciences, at the recommendation of faculty in the biological and biomedical sciences. To contribute to the fellowship fund, contact Wesley Poling, Ph.D., at wesley.poling@yale.edu or (203) 432-7910.

\* Giraldez (2009:133)
A ‘can-do, visionary’ scientist is named graduate school dean

Thomas D. Pollard, M.D., Sterling Professor of Molecular, Cellular, and Developmental Biology, has been appointed dean of Yale’s Graduate School of Arts and Sciences, effective July 1. As an undergraduate at Pomona College in his native California in the early 1960s, Pollard, also professor of molecular biophysics and biochemistry and of cell biology, was eager to understand how cells move (cell motility) and how they divide to form daughter cells (cytokinesis), questions that have guided his research ever since.

For more than three decades of research on these topics, Pollard has won some of the most prestigious awards in biomedical science, including the E.B. Wilson Medal (2004), from the American Society for Cell Biology; the Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Science (2006, with James A. Spudich, Ph.D., of Stanford School of Medicine); and the Gairdner International Award (2006, with Alan Hall, Ph.D., of Memorial Sloan-Kettering Cancer Center).

Pollard's research has mapped out the interactions of synaptic vesicles with the cell membrane. Because these processes drive cancer's spread and the growth of tumors, research in Pollard’s laboratory, which has combined techniques from biochemistry, biophysics, cell biology, and genetics, has focused on actin filaments—long, thin protein fibers that are a basic component of the cytoskeleton, the intracellular framework that lends strength to cells and gives them their shape. Actin filaments generate force for locomotion in white blood cells and cancer cells, and form the ‘purse string’ that pinches a cell into two daughter cells during cell division, a process that is also important in wound healing.

“As always a scientist at heart,” as he was described by Yale President Richard C. Levin upon his appointment, Pollard has nonethe- less gravitated to leadership roles throughout his career. He is served as director of the Salk Institute for Biological Studies, of the Biophysical Society, and of the ASCB, which has called him the ‘personification of [the society’s] can-do, visionary spirit.’ He was associate editor of the Journal of Cell Biology for seven years.

With bachelor’s degrees in chemistry and zoology from Pomona, Pollard earned his M.D., cum laude, at Harvard Medical School, where he was later a professor. He joined the Yale faculty as Eugene Higgins Professor of Molecular, Cellular, and Developmental Biology in 2001.

Pollard is a member of the National Academy of Sciences and the Institute of Medicine, and a fellow of the American Academy of Arts and Sciences, the Biophysical Society, and the American Association for the Advancement of Science, for which he now serves as president. Married to his wife, Patty, since 1964 (she has been president of the Yale University Women's Organiza- tion for the past 4 years), Pollard passed on a love of science to his chil- dren, Katie and Dan, both of whom are computational biologists. In a 1992 ASCB profile, he said of his fam- ily, “We all like to see things work!”

Expert on disability in elderly elected to venerable medical society

Thom M. Gill, M.D., an authority on the epidemiology and prevention of disability among older persons, has been elected to the Association of American Physicians (A.A.P.).

The Indiana Professor of Ge- netic Medicine and professor of medicine and pediatrics, Gill seeks to understand the mechanisms underlying physical decline in community-living older people and to develop means of preventing such decline.

Since 1997, Gill has been principal investigator on the Preparing Events Project (PEP), which has revolution- ized our understanding of disability in older persons. Through monthly phone interviews and regular home visits, PEP researchers have learned that, contrary to a widely held belief that disability is irreversible, older people often recover quickly from disabling events. In 2006, the National Institute on Aging backed PEP with a $2.5 million Merit Award, allowing Gill to continue the 12-year study for several more years.

More recently, Gill, co-director of both the Yale Program on Aging and the Claude D. Pepper Older Americans Independence Center, has embarked on studies of the potential benefits of testosterone treatment in symptom- atic older men and the effectiveness of exercise interventions in preventing disability, and has explored strategies to promote independent bathing in community-living older people.

Gill, also director of the Yale Center for Disability and Disabling Disorders, has received many accolades, including the Paul Bessler Developmental Scholar Awards in Aging Research Award, and the Outstanding Scientific Achieve- ment for Clinical Investigation Award from the American Geriatrics Society, and the Ewald W. Boese Research Award in the Biomedical Sciences.

After completing his M.D. at the University of Chicago in 1987, Gill came to Yale as a Robert Wood Johnson Clinical Scholar for research training in clinical epidemiology. After a year as a postdoctoral fellow, Gill joined the PEP faculty in 1994. Gill oversees the Yale Research Fellowship in Geriatric Medi- cine and Clinical Epidemiology, and is director of the Pepper Center’s Research Career Development Awards.

Founded in 1884 by seven physi- cians (including legendary physician Sir William Osler, M.D.) the AAP elects members who make “outstanding con- tributions to the advancement of science and medicine.”