Building upon a grant made in 2003 that established the Kavli Institute for Neuroscience at Yale, The Kavli Foundation has announced that it will contribute additional endowment funds to diversify and strengthen the institute’s interdisciplinary brain research.

Since the beginnings of neuroscience research, Yale researchers have excelled in the quest to understand the fundamental mechanisms of how the human brain develops and functions. Such findings from basic neuroscience may have profound implications for understanding brain disorders such as autism, schizophrenia, mental retardation, dyslexia, and neurodegenerative diseases. Under the direction of Pasko Rakic, M.D., Ph.D., Kavli Institute scientists have conducted influential research on the molecular, cellular, and functional organization of the cerebral cortex, the part of the brain responsible for higher brain functions such as language and reasoning.

The new commitment will enable the Kavli Institute to expand its mission to embrace Yale research on the nervous system more broadly, drawing on the expertise of the nearly 100 neuroscientists working in 20 departments across the Yale campus. “Understanding the human brain is considered the ultimate challenge of science in the 21st century,” says Rakic, chair and Dorys McConnell Nixdorff-German Professor of Neurobiology at the School of Medicine. “To achieve this laudable goal we must embrace a multidisciplinary approach, using the most advanced technologies in a variety of experimental model systems. It also requires collaboration and frequent exchange of ideas between scientists of different backgrounds. All of these will be cultivated at the Kavli Institute.” To realize this wider vision, the institute’s Steering Committee will set the institute’s research agenda, foster scientific collaborations at Yale, and build ties with researchers at Kavli Institutes elsewhere. The disciplines expected to contribute to the Yale Kavli Institute’s research range from genetics to psychology, and the institute will also foster the development of novel concepts and technologies to investigate the functional properties of the living brain.

In addition to providing research support, the new funds will provide support to top Yale graduate students in neuroscience, who will be designated as Kavli Scholars.

“We are very excited by the expanded approach to neuroscience research the Kavli Institute for Neuroscience at Yale is undertaking,” says Fred Kavli, founder and chairman of the institute.

New line of attack on a dreaded disease

In honor of a friend fighting a brain tumor, Turkish financier’s multimillion-dollar gift funds genomic analysis of deadly glioblastomas

Few diseases are as feared, or as deadly, as glioblastoma multiforme (GBM), the most aggressive and most common form of brain cancer, which accounts for about 60 percent of all brain tumors diagnosed in the United States each year. Over the past five years, improvements in radiotherapy and surgical techniques, and the advent of drugs that block blood vessel formation in tumors have significantly increased survival time in patients with GBM. But despite these advances, on average these patients live less than one year after diagnosis.

One promising avenue for transforming the prognosis faced by GBM patients is genomic research, which can identify aberrant genes present in GBM tumors and determine how such genes vary from patient to patient. Recent genomic sequencing research on GBM has already paid dividends: four new classifications of GBM based on genomic data are guiding the development of more precisely targeted therapies, as well as personalized approaches to treatment based on the genetic makeup of a given patient’s tumor.

Last year’s launch of the Yale Center for Genomic Analysis (YCGA) placed the School of Medicine at the forefront of genomic sequencing research. Now, with a $12 million, multi-year gift from Turkish financier Mehemet Kutman, M.B.A., to launch a new Yale Program in Brain Tumor Research, researchers at Yale School of Medicine will be bringing the power of the latest genomic techniques to better understand brain tumors, with a particular focus on GBM and related illnesses.

“Mehmet Kutman’s generous support for Yale’s genomic research will spur the effort to find new treatments for patients whose lives are threatened by these brain cancers,” says Yale President Richard C. Levin.

The new program will be directed by Murat Gündel, M.D., Nixdorf-German Professor of Neuroscience and Donald Baim.

In life and work, alumnus touched countless hearts

There could be no greater gratification for a physician–scientist than seeing the fruits of his or her own research become an integral part of medical practice, providing patients with a better treatment than any that had existed before.

The late Donald S. Baim, M.D., a member of the medical school’s Class of 1975 and an internationally renowned innovator in the field of interventional cardiology, had that rare privilege.

Baim, who died unexpectedly in 2009 at age 60, served as chief medical and scientific officer at Boston Scientific Corp. (BSC), a global developer, manufacturer, and marketer of medical devices, since 2006. Despite his relatively short four-year tenure, Baim was greatly beloved and admired by colleagues and patients alike.

Decade-long race to make an anti-cancer compound in the lab is won by Yale chemists

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Advocate for the mentally ill backs young scientists

In January, the National Alliance for Research on Schizophrenia and Depression (NARSAD), the leading charity providing funds for research on psychiatric illness, announced that its School of Medicine scientists had won NARSAD Young Investigator Awards. The awards—which provide up to $60,000 over two years to “the most promising young scientists conducting neurobiological research” relevant to understanding mental illnesses including schizophrenia, mood disorders, bipolar disorder, autism, and anxiety disorders such as obsessive-compulsive disorder and post-traumatic stress disorder—went to:

Jessica A. Cardin, Ph.D.
Assistant professor of neurobiology

Sukia Corbetta, Ph.D.
Postdoctoral associate in psychiatry

Douglas J. Guarneri, Ph.D.
Associate research scientist in psychiatry

Jason K. Johannesen, Ph.D.
Assistant professor of psychiatry

Roger J. Jou, M.D., M.P.H.
Clinical Fellow in the Child Study Center

Janghoo Lim, Ph.D.
Assistant professor of genetics

Ruth Sharf, Ph.D.
Postdoctoral associate in psychiatry

Megan V. Smith, Ph.D., M.P.H.
Assistant professor of psychiatry

Bao-Zhu Yang, Ph.D.
Assistant professor of psychiatry

Lingjun Zuo, M.D., Ph.D.
Associate research scientist in psychiatry

In 2011, NARSAD will distribute $1.2 million in Young Investigator awards to 214 scientists around the world. Since 1987, the group has awarded more than $247 million in such grants, which can enable young scientists to pursue studies that will affect mental health through federal agencies or the private sector. On average, Young Investigators have gained sufficient leverage from their grants to raise 19 times the amount of their original NARSAD grant.

Three of Carolyn Slaysman’s grandparents, and both parents, were teachers, an influence that shaped her toward academics. After earning her Ph.D. in the Rockefeller University lab of Nobel Prize winner Edward Tatum, a postdoctoral stint at Cambridge University, and a brief tenure at Case Western University, Slaysman joined the School of Medicine faculty in 1985, rising through the ranks to the medical school’s first female department chair, and the first woman to be named a deputy dean.

In 1995, Slaysman became the first woman appointed as a deputy dean at the medical school, and she came well-prepared, having also been the first woman to head a department when she was named chair of the Department of Human Genetics (now Genetics) in 1984. Slaysman has witnessed a sea change in the status of women in science and medicine since the late 1950s, when she enrolled at The Rockefeller University for doctoral studies. In those days, each entering class at Rockefeller, hand-picked by Detlev Bronk, Ph.D., the university’s president, had 15 men and one woman. When asked at a question-and-answer session for new students why this 14.1 ratio persisted, Bronk coolly replied, “Because that’s the right number.” At Yale today, women make up a third of the total medical faculty, and since 1998, there have been more women than men in each entering medical school class.

The changes in biomedical science have been no less dramatic. Having graduated from Swarthmore College just five years after Watson and Crick’s landmark paper on the structure of DNA, Slaysman, also Sterling Professor of Genetics and professor of cellular and molecular physiology, has enjoyed helping to create a gene-sequencing facility at Yale’s West Campus that can generate the equivalent of 300 complete human genomes per month, “opening up thinking in ways people couldn’t have begun to imagine even a few years ago.” Imaging techniques, from microscopes that bring a cell’s individual proteins into view to scanners that map out functions in the living human brain, have transformed the scientific landscape. And through it all, once-impenetrable walls between fields and departments have tumbled down, as research became an increasingly multidisciplinary endeavor, “driven,” Slaysman emphasizes, “by the science itself, not declared from above.”

But for all the momentum toward “big science,” Slaysman believes that scientists will always form working units on a human scale, never relinquishing “the ability to talk around a table.” She sees her role as one of “balancing resources and possibilities,” providing individual teams with the wherewithal to succeed while also playing matchmaker, urging researchers to “reach out, interact, communicate, collaborate,” to make an academic whole bigger than the sum of its parts.

“There are 1,121 really smart people on our faculty doing important things, so there are bound to be problems,” Slaysman says. “But there’s also a constant, positive ferment—good things coming from all directions.”
A cellular doorkeeper’s role in hypertension

From their perch atop the kidneys, the adrenal glands help to control blood pressure by secreting the hormone aldosterone. In aldosteronism, often caused by adrenal tumors called adenomas, excessive levels of this hormone cause severe hypertension, but the mechanisms of tumor-induced aldosteronism have been poorly understood.

In the February 11 issue of Science, a team led by Richard P. Lipton, M.D., Ph.D., chair and Sterling Professor of Genetics, reports that many adenomas carry mutations in the gene KCNJ5, which encodes channels that selectively allow potassium ions through cell membranes. The mutated channels are less selective, allowing sodium to enter and unbalancing signaling cascades that cause adenoma cells to secrete aldosterone and to overproliferate. A KCNJ5 mutation was also found in a family with aldosteronism not caused by adenomas, suggesting that these mutations can also cause noncancerous adrenal cells to overproliferate and secrete too much aldosterone.

“This gene was not on anybody’s list to sequence in an investigation of this disease,” Lipton says. “We really hit the jackpot.”

Uncovering genes that orient organs

Our bodies exhibit symmetry—two eyes, ears, arms, legs, and so on. But internal organs such as the heart, liver, and stomach must develop asymmetrically to function properly. For example, let’s say that you were born with heterotaxy (Htx), a rare and potentially deadly birth defect, left–right asymmetry is disrupted, causing organs to be malformed or in the wrong position.

In a new genomic study published online January 31 in Proceedings of the National Academy of Sciences, Htx patients were found to be twice as likely as control subjects to harbor copy number variations (CNVs), stretches of duplications, deletions, or missing genetic material. Many genes disrupted by these CNVs have counterparts in the frog Xenopus tropicalis, and when the authors knocked out Xenopus genes they thought might be involved in left-right patterning, they identified five that are essential for proper development, none of which had previously been tied to asymmetry.

“Combining human genetics with model systems such as the frog will allow us to identify key genes that affect embryonic development and better understand the causes of these childhood disorders,” says co-author Mustafa K. Khokha, M.D., associate professor of pediatrics and genetics.

A big birthday for Child Study Center

A century of child development research and compassionate care for children with disorders is marked by world-renowned Yale department

As the School of Medicine’s bicentennial year draws to a close, Yale’s venerable Child Study Center (csc) has begun celebrating a milestone of its own—its 100th anniversary. One of the School of Medicine’s 28 departments, the csc was born in 1911 when Wisconsin native Arnold Gesell, Ph.D., M.D., a young assistant professor in Yale University’s new graduate Department of Education, persuaded medical school Dean George Blumer, M.D., to give him a single room in the New Haven Dispensary (a community clinic at the medical school founded in the late 19th century) for use in a study of mentally retarded children. From these humble beginnings, the csc has become a world-renowned center for the study and treatment of developmental disorders and other psychological conditions affecting children.

In 1921, Gesell was named to lead an expanded Clinic of Child Development, where his work profoundly influenced a burgeoning field. As one of the first researchers to attempt a quantitative study of development by measuring the responses of infants and children to different stimuli, Gesell used the relatively new medium of film to record and study behavioral patterns, eventually filming about 12,000 children. He concluded that mental development occurs in identifiable stages, similar to those seen in physical development. Although some of his views have since fallen out of favor, Gesell’s overall influence on American psychology, as well as on child-rearing practices, has been a lasting one.

Following Gesell’s retirement, Milton J.E. Senn, M.D., was recruited in 1948 to serve as both chairman of the Department of Pediatrics and director of the renamed and reorganized csc. The designation as a center reflected the University’s desire for a multidisciplinary approach to the study of children and child development. An innovator in pediatrics, Senn was a pioneer in bringing mental health principles into pediatric practice, and as the csc’s new leader he welcomed the insights of social workers, early childhood educators, and other nonmedical child specialists.

Senn was succeeded in 1966 by Albert J. Solnit, M.D., who had been the first resident in child psychiatry at Yale. Solnit was a child psychiatrist, pediatrician, and psychoanalyst who pioneered work on social policy and child custody. He built even more interdisciplinary connections, fostering collaborations with Yale Law School and overseeing the formal establishment of the csc as a department of both the medical school and Yale-New Haven Hospital.

The csc also was deeply influenced by its fourth director, the late Donal J. Cohen, M.D., one of the most influential American child psychiatrists of his generation. Cohen updated tradition, rejecting conventional notions that development can be explained in either environmental or genetic terms and seeking to bridge these two viewpoints. In Cohen’s studies of autism, for example, he blended the latest research findings, and he came to view the disorder as both genetically and neurologically based—a break from the then-common belief that autism resulted from flawed parenting.

In the difficult period following Cohen’s death in 2001, John E. Schwalter, M.D., now professor emeritus in the csc, filled in as interim director until 2002, when Alan E. Kazdin, Ph.D., now John M. Musser Professor of Psychology at Yale and a leader in the development of evidence-based treatments for mental disorders in children, was named the csc’s fifth director. The current director, Fred R. Volkman, M.D., the Irving B. Harris Professor of Child Psychiatry, Pediatrics, and Psychiatry, was inspired by Cohen’s work, and initially came to the csc in 1999 while Volkman was on leave to become a leading scholar in autism and related disorders.

Over the last 100 years the csc has been home to generations of faculty and trainees who have shaped both the science and social policy surrounding childhood development and mental health issues. The Center now includes the Edward Zigler Center in Child Development and Social Policy, named for Edward F. Zigler, Ph.D., Sterling Professor Emeritus of Psychology and chief architect of the Head Start and Early Head Start programs. The Zigler Center has dramatically changed the landscape of services for children and families locally, regionally, and globally. James P. Comer, M.D., M.P.H., the Maurice Falk Professor of Child Psychiatry in the csc and associate dean for student progress at the School of Medicine, began developing a plan to improve low-achieving elementary schools in New Haven in 1968. Modeled on the children and adolescents development and learning research is increas-ingly linked, that program, now known as the School Development Program, or SDP, informs state and national education policy and practice and has been implemented in hundreds of schools around the world.

Today the csc remains at the forefront of the field of child development. Researchers at the Center are making significant strides in many areas, using brain-wave technology, genomics, and neuroimaging, and conducting clinical trials to study such diverse phenomena as the lasting effects of stress and trauma during early brain development; accurate diagnosis of autism in infancy; psychosocial care for children diagnosed with cancer; the genetic and neural bases of Tourette’s syndrome, and other developmental disorders; and the efficacy of drugs in treating childhood disorders.

The Albert J. Solnit Training Program, established in 2004 as a lasting tribute to the former csc director, perpetuates Solnit’s dedication to clinical excellence and superior education. This six-year, combined clinical and research program admits only two students per year, qualifying graduates for both the adult and child psychiatry board exams and preparing them to help children and families who face the potential disruptions and devastations of a diagnosis of a mental health disorder.

Volkman credits the center’s broad, multifaceted approach for its continued success. “Because there’s so much going on here, it means there’s more potential for cross-disciplinary work,” he says, a model that will guide the csc through its second century of achievement.

The next century of progress

According to recent data from the National Health and Nutrition Examination Survey, approximately one in five children in the U.S. will meet the diagnostic criteria for a mental health disorder such as Tourette’s syndrome, autism, anxiety, bipolar disorder, or depression. For 100 years, researchers and physicians at the Yale Child Study Center (csc) have provided compassionate care for children and adolescents, rapidly translating scientific discoveries into practical treatments in the clinic, the home, and the com-munity. Your gifts to these csc programs will sustain this legacy into the next century.

The Albert J. Solnit Integrated Training Program (up to $15 million) A highly selective six-year program (see story above) that gives future clinicians intensive training to provide crucial treatment and support to children with mental disorders, and their families.

Clinical Excellence Fund ($250,000–$5 million) Enables the translation of scientific research to innovative therapies in the Child Study Center’s general and specialty clinics (autism, Tourette’s syndrome/ocd, trauma, and anxiety disorders).

Community Program Fund ($100,000) Provides support for international programs that work with governments and organi-zations around the world to improve children’s mental health.

For more details, contact Zsuzsanna Somogyi at (203) 436-8559.
January 11  Yale’s Child Study Center (CSC) kicked off its 100th year with a Centennial Series Symposium on infant mental health in honor of Arnold Gesell, M.D., the CSC’s founder (see related story, p. 3). From left: Linda Mayes, M.D., Arnold Gesell Professor of Child Psychiatry; Helen Egger, M.D., visiting assistant professor in the CSC; (back row) Fred R. Volkmar, M.D., director of the CSC and the Irving B. Harris Professor of Child Psychiatry, Pediatrics, and Psychiatry; Katarzyna Chawarska, Ph.D., associate professor in the CSC; and Walter S. Gilliam, Ph.D., associate professor in the CSC and director of The Edward Zigler Center in Child Development and Social Policy.

February 18  A Reception Honoring Flora M. Vaccaro, M.D., who was named Harris Professor of Child Psychiatry in October, was held in the School of Medicine’s Beaumont Room. Carolyn M. Mazure, Ph.D., associate dean for faculty affairs, professor of psychiatry and psychology, and director of Women’s Health Research at Yale (left), celebrates with the honoree, who recently founded the Program in Neurodevelopment and Regeneration, an interdepartmental initiative that will use induced pluripotent stem cells as a research tool to understand neuronal development in individuals with specific neuropsychiatric disorders.
In 11 steps, chemists make a giant leap

The ‘blood, sweat, and tears’ of Yale researchers push them over the top to crack the daunting, decade-old puzzle of a potent anticancer agent

In the latest chapter of a 15-year scientific story spanning the globe from the South Pacific to New Haven, a team of scientists in Yale’s Department of Chemistry has achieved the first synthesis of an elusive chemical compound, opening the door to the development of a new class of molecules to target and destroy cancer stem cells. Many researchers believe that these cells are a root cause of some of cancer’s deadliest characteristics, including resistance to chemotherapy, tumor relapse, and metastasis.

The story begins in 1996, when a team of scientists from Wyeth-Ayerst Research (now part of Pfizer) and the University of Utah were analyzing marine organisms they had collected in Fiji in the hopes of finding useful chemicals for drug development. From a bright orange sea squirt retrieved from the seabed, the group isolated a chemical known as lomaiviticin. Scientists in Yale’s Department of Chemistry has achieved the first synthesis of an elusive chemical compound, which they called lomaiviticin. The structure of the compound suggested that it might have a bacterial origin itself, and after five years of subsequent analysis the team discovered a previously unknown species of symbiotic bacterium living on the sea squirt that produced yet another chemical with impressive anticancer and antibacterial properties, which they called lomaiviticin.

But the bacterium that produces lomaiviticin is extremely rare, and it cannot be easily coaxed into creating the molecule in the laboratory. For the past decade, chemists worldwide have been striving without success to synthesize lomaiviticin to obtain sufficient quantities for exploring its anticancer properties more deeply. Now, as reported online January 31 in the Journal of the American Chemical Society, a team at Yale, led by Seth Herzon, Ph.D., has managed to synthesize a form of the compound known as lomaiviticin aglycone for the first time.

"About three quarters of anticancer agents are derived from natural products, so there’s been lots of work in this area," says Herzon, assistant professor of chemistry. "But this compound is structurally very different from other natural products, which made it extremely difficult to synthesize in the lab." Herzon’s team, which managed to synthesize the molecule in just 11 steps starting from basic chemical building blocks, has been working on the problem since 2008 and spent more than a year and a quarter on just one step of the process involving the creation of a carbon-carbon bond. It was an achievement that many researchers deemed impossible, trying to work around it using other techniques, but the Herzon team’s persistence paid off.

"A lot of blood, sweat, and tears went into creating that bond," Herzon says. "After that, the rest of the process was relatively easy." // Herzon (page 4)

Surgeons-turned-detectives explore the dawn of chemotherapy

Thanks to the unearthing of long-lost medical records by two dogged surgeons, the full story of the first use of intravenous chemotherapy for cancer, which occurred at Yale in the early 1940s, can now be told.

The general outlines of this event—that a lymphoma patient, known only as "J.D." in the medical literature, received the first known chemotherapy at New Haven Hospital (now Yale-New Haven Hospital) in 1942—have been recounted by historians based on the recollections of those involved in the case, but the specifics have until now remained a mystery.

Two years ago, Clinical Professor of Surgery John E. Fenn, M.D. and Robert Udelsman, M.D., M.B.A., chair and William H. Carmalt Professor of Surgery, became fascinated by J.D.’s case and determined to try to locate his medical records. The problem was that they had no name, date of birth, medical record number, or precise dates of treatment—only the patient’s initials.

For months the two pursued records from that era, including pathology reports, of every "J.D." they could find. Michael Kashgarian, M.D., professor emeritus and senior research scientist in the Department of Pathology, whom they enlisted to help, finally found a report that looked promising, but the medical record number contained errors. Thanks to the help of a persistent archivist, they eventually narrowed the possibilities down to one patient. In a moment of triumph, Fenn sent Udelsman an one-word e-mail: FOUND!

The records revealed that an immigrant from Poland first came to New Haven Hospital in 1941 for treatment of massive tumors in and around his neck that had diminished his ability to eat, sleep, breathe, and turn his head. Radiation treatments were quite effective at first, but by August of the following year the tumors had recurred and had developed resistance to treatment with X-rays. As no other therapeutic options for cancer had yet been developed, doctors had nowhere else to turn.

Surgeons-turned-detectives explore the dawn of chemotherapy

Now? Later? Brain cells help us make the call

Sorting out the steps in Salmonella infection

Salmonella bacteria invade the gut by piercing a needle-like structure through the intestinal lining to inject their own proteins into cells. First the needle complex moves into place, and then, in sequence, proteins called translocases and effectors queue up translocases and effectors. How do they act as a sorting platform, underlying this step-by-step process. Analyzed the molecular choreography of this region in decision-making.

We all prefer receiving large rewards instantly or a larger quantity provided a tiny amount of apple juice delivered right away, but we typically must choose between small, quick payoffs and bigger ones that occur later. Neuroscientists have determined that a brain region called the basal ganglia is crucial in helping us evaluate the size and timing of such incentives. As reported in the January 13 issue of Neuron, a team led by Daeyeol Lee, Ph.D., associate professor of neurobiology and psychology, determined which basal ganglia structures govern these choices. Lee and colleagues recorded the activity of neurons in the caudate nucleus and ventral striatum of the basal ganglia in monkeys that shifted their gaze toward different patterns on a computer screen to receive either a tiny amount of apple juice delivered instantly or a larger quantity provided seconds later. The team found that the caudate nucleus contributed more to these judgments than did the ventral striatum. Neurons in the caudate seemed to compare the values of the treats based on their delay and magnitude, revealing a new role of this brain region in decision-making.

The work may help to explain psychiatric conditions characterized by a bias toward immediate gratification. "We don’t know the anatomical basis of… problem gambling or impulsive behavior," Lee says. "Now we are starting to pinpoint those areas, even down to individual neurons."
The United States faces a severe shortage of physicians in the coming decades. As the health care needs of the aging Baby Boom generation grow, the number of medical school students electing to enter the field of primary care is in sharp decline. According to the National Resident Matching Program, students choosing residency training in general internal medicine fell from 375 in 1999 to 264 in 2018.

One of the factors that has been found to influence students’ views of general internal medicine as a career choice is the quality of the education-al experience in internal medicine. The VA Connecticut Healthcare System (VACHS) is now poised to address that issue with a new $5 million grant from the Department of Veterans Affairs to establish a Center of Excellence in Primary Care Education. The Yale-affiliated VACHS is one of only five facilities in the country to receive the five-year grants, which will support a new approach to training internists and other health care profes-sionals. Traditionally, internal medici-nists have spent most of their time training in inpatient settings, but the majority of patients are now treated in outpatient settings. “Training hasn’t really kept up with the reality of how internists prac-tice,” says the School of Medicine’s Patrick G. O’Connor, M.P.H., professor of medicine and sec-tion chief of general medicine.

Under the existing system, resi-dents spent just one half-day a week at the VACHS, but they will now go there for training every day for two months at a time, a total of 10 months of intensive training over the three years of residency. Interns and first-year residents will continue to spend a half day per week at the VA in between the two-month intensive blocks. “Restruc-turing their schedule will allow them to really learn what a primary care doctor actually does, which is to be there every day for their patients and have long-ti-meshed relationships,” says Assistant Professor of Medicine Rebecca Brienza, M.D., M.P.H., who will serve as director of the new center.

The center will also establish a one-year post-graduate program in primary care for nurse practi-tioners, becoming the first program in the country to do so under a separate grant. Residents and nurse practitioners will train in teams, taking care of patients together for a 12-month period, with the nurse practitioners providing continuity of care during the time residents are training at other locations between their two-month stints.

“The current way we train post-graduate M.D.s and nurse practitioners is really a ‘silos’ model, where there’s no cross-utilization or transfer of knowledge,” says Brienza. “We’ve learned that caring for patients in multidisciplinary care teams is a better approach, with better outcomes for patients.” The cen-ter will provide training in interpro-fessional collaboration to residents and nurse practitioners, as well as students in medical school, undergraduate nursing programs, pharmacy, and health psychology. They will learn how to work effectively as members of a team, how to appreciate the input of other disciplines, and how to effectively communicate with patients, and conflict manage-ment. “All those things with regard to teamwork that are assumed that health professionals know but that there’s actually no real training for,” says O’Connor.

The new training model fits well with changes brought about by the re-cent health care reform legislation, with its concept of a “medical home,” an outpatient-based primary care practice through which care is coordinated. The program is itself a collabora-tion between the VA, Yale School of Medicine, Yale School of Nursing, University of Connecticut School of Medicine, and Fairleigh Dickinson University School of Nursing. The five institu-tions will contribute a total of over 200 trainees over a five-year period. “Training programs need to prepare physicians not only for the present, but also for the future, when they’ll have more responsibility for team care and organization of services for patients,” says O’Connor.
The gift, which was announced at a February 17 ceremony at Yale’s Woodbridge Hall, was made by Kutman in honor of a close friend and fellow board member at Istanbul-based Global Investment Holdings, a merchant bank with diverse interests in Turkish seaports, real estate, energy generation and distribution, and financial institutions. Kutman’s colleague is currently being treated for gbm.

“I have a great deal of confidence in both Dr. Günel and Yale School of Medicine,” says Kutman. “We hope very much to break new ground in gbm-related research in the near future.”

Based on this agreement, some 400 samples of brain tumors from Turkish hospitals will be delivered to Yale, a valuable research resource that will supplement the many pathological specimens already on hand at the medical school.

“In spite of much research and the application of the latest in technology, the prognosis for survival of patients with gbm is unacceptably short,” says Robert J. Alpern, M.D., Dean and Ensign Professor of Medicine. “Basic research leading to an understanding of the biology of these tumors is essential. The generous gift of Mr. Kutman will permit Murat Günel to use state-of-the-art genomics to study the molecular mechanisms responsible, thus paving the way for new treatments.”

Günel says that sequencing of gbm tumors so far, while quite productive, is incomplete. “As we work to contribute to a complete catalog of the mutations present in brain tumors, we will be able to understand individual tumors and come up with better therapies,” he says.

School of Medicine researchers at the YCGLA led by Günel’s longtime mentor and colleague Richard P. Lipton, M.D., Ph.D., chair and Sterling Professor of Genetics and Howard Hughes Medical Institute investigator, have pioneered a speedy and inexpensive genomic technique known as exome sequencing, in which only those parts of the genome containing protein-coding genes are sequenced. This approach will be valuable for studying a variety of brain tumors, says Günel, because the genomic research on other brain tumors completed by scientists so far suggests that some genes may have a major effect, and that even a single gene mutation could play a role in a large percentage of tumors. However, Günel says, it will be important to compare data from exome scans with those of the entire genome, because non-coding genomic regions are believed to play an important role in tumor formation in the brain.

Though the Yale Program in Brain Tumor Research has just been established, research on the genetic roots of gbm is already up and running at the School of Medicine, says Günel. “We’re sequencing brain tumors right now,” he says. “There’s no time. A cure cannot wait.”

From left: Miyoung Chung, vice president for scientific programs at the Kavli Foundation, and Robert W. Conn, Kavli Foundation president, joined Yale President Richard C. Levin and Pasko Rakic, director of the Kavli Center for Neuroscience at Yale, to mark the foundation’s renewed support for the center, which will expand its reach to embrace a broader range of neuroscience research at Yale.

// Kavli (from page 1) // // GBM // // Bairn // // Cornell College
Tamas L. Horvat, d.v.m., ph.d., pro-

Wallace Professor of Biomedical Research
studies role of brain circuits in metabolism

Tamas L. Horvat, d.v.m., ph.d., pro-

and genetic techniques to better un-
derstand biological events at the level of the organism. Horvat, also a professor of neu-
robiology and of obstetrics, gynecolo-
gy, and reproductive sciences, is the
founding director of the Yale Program in Integrative Cell Signaling and Neu-
robiology of Metabolism, which was
launched in 2009.

A winner of the National Institutes
of Health Director’s Pioneer Award in
2010, Horvat has also been honored
with an Alexander von Humboldt
Professorship by the Republic of Ger-
many’s Ministry of Science.

The Wallace Professorship in Bio-
medical Research was established in
August 2010 by philanthropists Jean
and David W. Wallace of Greenwich,
Conn. The endowed chair supports
the academic, research, and teach-
ing activities of a School of Medicine
faculty member whose work advances
the school’s strategic vision and who is
recognized as among its most promis-
ning and productive researchers.

// Herzon (from page 5)

In 2010, Herzon was named a Se-
arl Scholar, an award granted each year to 15
“exceptional young faculty in the biomed-
cal sciences and chemistry,” according to the program’s website.

In addition to lomavitcin aglycon,
Herzon’s team has also created smaller,
similar molecules that have proven
potentially effective against ovarian
stem cells, says Gil Mor, m.d., ph.d.,
a researcher at the School of Medicine
and Yale Cancer Center who is collabo-
rating with Herzon to test the new class
of molecules as cancer therapies.

“Ovarian cancer has a high rate of
recurrence, and after using chemother-
apy to fight the tumor the first time,
you’re left with resistant tumor cells
that tend to keep coming back,” Mor
explains. “If you can kill the stem cells
before they have the chance to form a
tumor, the patient will have a much
better chance of survival—and there aren’t many potential therapies out there
that target cancer stem cells right now.”

Cancer stem cells are thought to be pre-
cursors to tumors, the -different of other
cancers as well, including in the brain,
lung, and prostate, and in leukemia.

Herzon, Mor, and colleagues will
continue to analyze lomavitcin agly-
con to better understand its actions
on cancer stem cells at the molecular
level, and they hope to begin testing the
compounds in animals shortly.

“This is a great example of the
synergy between basic chemistry and
the applied sciences,” Herzon says.
“Our original goal of synthesizing this
natural product has led us into entirely
new directions that could have broad
impacts in human medicine.”

Expert on prevention of falls in the elderly is honored for a pioneering body of research

The American Geriatrics Society (AGS) has awarded Mary E. Tinetti, m.d.,
the Edward Henderson Award, which
recognizes a distin-
guished clinician,
educator, or research-
er who has made
significant contribu-
tions to the field.

The AGS is honoring
Tinetti for her pioneering
work on falling in the elderly and its prevention.
Tinetti will receive the award and will pres-
ten the Henderson State-of-the-Art Lecture at the AGS’s 2011 Annual
Scientific Meeting in Washington, D.C., in May.

Tinetti is the Gladys Phillips
Crofoot Professor of Medicine and
Epidemiology and Public Health, and
director of the Yale Program on Aging
at the School of Medicine.

She was the first investigator
to show that older adults at risk for falling and injury could be identiﬁed, that falls
were associated with a range of serious adverse outcomes, and that multifac-
tated risk-reduction strategies were both successful and cost-effective.

Her work has transformed the
prevailing view of falls as an in-
evitable consequence of aging to a
preventable event with a multidimen-
sional set of risk factors that can be identified and controlled.

Tinetti has also investigated and published extensively on functional disability and mobility impairment.
She is now involved in efforts to trans-
late these research findings into clinical and public health practice.

Most recently, Tinetti has focused her research on clinical decision-
making in the face of multiple health conditions.

Tinetti has been awarded many of the highest accolades in geriatrics.
In 2009, she received a MacArthur
Foundation Fellowship (popularly known as a “genius” award) recognizing
her contributions to the area of fall prevention in older adults.

New AAAS Fellows

Three School of Medicine faculty
members have been elected Fellows of
the American Association for the
Advancement of Science (AAAS), an
international nonprofit organiza-
tion dedicated to advancing science
around the world for the benefit of all
people. The AAAS also publishes the jour-
nal Science.

At the AAAS Annual Meeting
in Washington, D.C., in February,
503 new Fellows will receive
their exceptional contributions to
science and technology.

// Surgeons (from page 5)

At about the same
time, under the auspices of the
War Department’s Office of Scientific
Research and Development, formed
by President Franklin D. Roosevelt,
School of Medicine faculty members
were conducting highly classified re-
search projects to support the Allies’
 effort in World War II. Pharmacolo-
gists Louis S. Goodman, m.d., and
Alfred Gilman, Ph.D., were search-
ing for antidotes to mustard gas,
the chemical warfare agent that had been
used to such devastating effect in
World War I.

In studies of nitrogen mustard, a
relator of the poison gas, Goodman
and Gilman observed that lymph
cells in animals were particularly
sensitive to the compound’s toxicity,
which led them to wonder whether it
would also kill lymphoma cells.

Indeed it did: when nitrogen mustard
was administered intravenously to
mice with lymphoma, their tumors
shrank rapidly and soon disappeared,
an unexpected and unprecedented
result. However, mirroring J.D.’s
response to radiation treatment, the
mice recur, and subsequent
treatments with nitrogen mustard
were less and less effective.

To find the cause of the regres-
sion in the mice had been dramatic
and had significantly increased their
survival time. Goodman and Gilman
were eager to test nitrogen mus-

tard clinically, and they approached
Gustav E. Lindskog, m.d., then an
assistant professor (he would ulti-
mately go on to chair the Department
of Surgery), about attempting an
experimental nitrogen mustard treat-
ment of J.D.’s terminal cancer.

On August 25, 1942, J.D., recog-
nizing that he had no other alterna-
tives, consented to the treatment and
became the first patient to receive
intravenous chemotherapy for cancer.
By the end of September his tumors
had completely regressed and no can-
cer cells were detectable in a biopsy of
his lymph nodes. Unfortunately the
tumor returned by mid-October, and
just as Goodman and Gilman had ob-
served in animals, the newly emerged
tumor displayed increasing resistance
to nitrogen mustard, which was also
found to be toxic to white blood cells.
On December 1, 1942, after 96 days in
the hospital, J.D. died.

Fenn and Udelsman say that J.D.’s
case was immensely important be-
cause it revealed three aspects of che-
motherapy—tumor regression, tumor
resistance, and toxic side-effects—that
shaped the development of better
oncology drugs thereafter. Nearly
70 years later, the pair has published
a paper in the March issue of the
Journal of the American College of Surgeons that tells the story of the slouching that
uncovered J.D.’s medical record, and
also clarifies and corrects many of
the specifics of his case.

J.D.’s hospital admission re-
cord, written up by a Yale medical
student, fills in the detail that had
until now been missing by describ-

g the patient’s management,
the events that led to the use of nitrogen
mustard for treatment, the patient’s
social and psychological condition, and
how the decision to attempt chemotherapy
emerged. The student’s drawings in
the medical record are “beautiful,”
Udelsman says. “This was the birth
of medical oncology.”

Igor E. Galán, Ph.D., d.v.m.,
the Lucille P. Markey Pro-
sessor and chair of the
Section of Microbial Pathogenesis,
is renowned for his work on the
mechanisms of patho-
genesis of the intestinal
pathogens Salmonella enterica and Campy-
lobacter jejuni.

Haifan Lin, Ph.D., director of the

d of Medicine and
Professor of Biomedical Research,
has been the area leader in under-
standing the role that bits of genetic material was play in stem cell differ-
entiation and self-renewal.

Hongyu Zhao, Ph.D., profes-
sor of public health (biostatis-
tics), genetics, and statistics,
develops statistical, compu-
tational, and visualization tools for molecular biology and genetics.