Reading the language of cells

Illuminating the eczema-asthma link
Class president Adewale O. Adeniran, MD 09, shares the joy of graduation with his parents, Elizabeth and Samuel Adeniran, shown here in traditional Yoruba dress, and Will R. Ross, MD, associate dean for diversity and director of the School of Medicine's Office of Diversity.

Three-month-old Gabriel, son of Anthony J. Apicelli III, MD 09, and Angela C. Hirbe, MD 09, sleeps through the pomp and circumstance while well-dressed for the occasion.

Dean Larry J. Shapiro, MD, congratulates Nicole K. Yamada, MD 09, at the School of Medicine's Commencement ceremony held on May 15, 2009. At the event, 109 medical students were honored: 80 earned the MD degree, 16 earned the MD/PhD degree and 13 earned the MD/MA degree. In other areas of the School of Medicine, 76 students earned a master's degree, 9 earned the doctor of audiology degree, 17 earned the doctor of occupational therapy degree and 76 earned the doctor of physical therapy degree.
A continuing need for scholarship support

Turn this card for the inspiring story of a generous legacy that still helps students at the School of Medicine.

Support for today's students means a future of beneficial care and scientific breakthroughs.

See page 36
His generosity lives on

"Under the will of the late Jackson Johnson, the sum of $250,000 was donated to the School of Medicine, the income of which is to be used to aid worthy and desirable students in acquiring and completing their medical education."

With this brief item in the 1930 Washington University School of Medicine Bulletin, so began the endowed Jackson Johnson Scholarship Fund.

Jackson Johnson was president of International Shoe Company, the largest shoe manufacturer in the country early in the 20th century. He was elected to the Washington University Board of Trustees in 1919 and served until his death in 1929. He endowed the Jackson Johnson Scholarship Fund in memory of his son, Jackson Johnson Jr., who lost his life in "the Service of the United States during the Great War."

Coming during the Great Depression, these resources were critical in making it possible for aspiring young students to pursue their medical educations. And for over 70 years, this scholarship fund has continued to do just that. Since its inception, more than 700 young men and women have received about $1 million in financial assistance.

To maintain its reputation for excellence, Washington University School of Medicine must continue to attract the most promising and best qualified students. Many of these exceptional students will require financial assistance, and the need for scholarship support is growing faster than available resources can sustain.

To learn more about how you can make an impact, please contact the Office of Medical Alumni and Development at (314) 935-9691.

Washington University in St. Louis
SCHOOL OF MEDICINE
Journey to Hope

Physician-scientists are exploring the common threads among neurological disorders to speed the application of basic research to treatment.

Spoken with Feeling

Emotional and heartening stories of cancer survivors and their children are captured as part of a nationwide oral history project.

Red Alert

The skin's own defense system — activated when skin is damaged — may be the link between childhood eczema and asthma.

Ken King: A Tribute

M. Kenton King's 25-year tenure as dean of Washington University School of Medicine stands as a hallmark in academic medicine.
Heavy-duty cargo

Mallinckrodt Institute donates MRI scanner to Argentine hospital

Home-computer users often have a tough time figuring out what to do with old computers made obsolete by better and faster models, but four years ago researchers at the School of Medicine's Mallinckrodt Institute of Radiology faced a much greater challenge. Scientists replaced a magnetic resonance imaging (MRI) scanner with a more capable unit. But the old scanner was far from obsolete: It was powerful, with the potential to provide useful medical information for years to come. They decided to donate the older scanner to a hospital in Argentina.

After years of planning, the scanner finally "took off" for its new home on June 12 aboard a U.S. Air Force cargo plane that originated at Scott Air Force Base in Illinois. It arrived in Buenos Aires one week later, then traveled approximately 900 miles by truck to the St. Lazarus Institute of Neurosciences in Salta, a city in northwestern Argentina.

The proposal to donate the unit came from discussions among Marcus E. Raichle, MD, professor of neurology, radiology and neurobiology, Yvette I. Sheline, MD, professor of neurology, radiology and psychiatry, and former faculty member Gabriel de Erausquin, MD, PhD, now at Harvard.

De Erausquin, a native of Argentina, has been studying schizophrenia in a group of Argentine natives known as the Kolla. Because of their limited access to modern medical care, the Kolla — who live near Salta — present a unique research opportunity.

"It's unclear to what extent changes in the shapes of brain regions associated with schizophrenia are caused by the disease and to what extent they're caused by medicines used to treat the disease," says de Erausquin. "As we diagnose and treat these patients who have never before received therapy, this MRI unit will allow us to explore this and many other important aspects of schizophrenia."

Getting the unit to Argentina has taken years due to its size, weight and sensitivity, according to Thomas E. Conturo, MD, PhD, associate professor of radiology, who has been involved in much of the planning. Initially, researchers planned to put the unit onto a truck for transport to a cargo ship in Miami. But the scanner proved to be too big for both American overpasses and U.S. container-ship regulations.

Researchers later learned of regular humanitarian aid shipments to South America via military cargo planes and were able to negotiate inclusion of the scanner.

In addition to helping de Erausquin with his research on the Kolla, the MRI unit will be available to address the medical needs of the general population in Salta and the surrounding region.
NIH grants to fund exploration of the human body's microbes

WU Genome Center receives $16 million

The National Institutes of Health (NIH) has awarded School of Medicine researchers four grants totaling $19 million to explore the trillions of microbes that inhabit the human body and determine how they contribute to good health and disease.

The grants are part of the Human Microbiome Project, an ongoing, ambitious effort to catalog the bacteria, viruses, fungi and other microorganisms that naturally coexist in or on the body. In all, the NIH has announced $42 million in grant awards to 12 U.S. institutions that expand the scope of the microbiome project.

The largest chunk — $16 million — goes to Washington University's Genome Center, which played a central role in the initial phase of the project. In the new, four-year effort, Washington University genome scientists, led by George M. Weinstock, PhD, will decode the DNA of about 400 microbes in collaboration with scientists at three other large-scale DNA sequencing centers. This information will then be used to catalog the microbes found in samples from healthy human volunteers to find out which microbes live in various ecological niches of the body.

"We can't really understand human health and disease without understanding the massive community of microorganisms we carry around with us," says Weinstock, professor of genetics and associate director of the Genome Center. "This effort will tell us which microbes are present in certain areas of the body and what they are doing there. Ultimately, this information will change how we think about and treat many illnesses."

Washington University researchers also received another $3 million for three one-year pilot demonstration projects that will investigate the link between changes in microbial communities and certain diseases.

"Washington University is becoming a leader in a field that combines a high level of expertise in genome sequencing with physicians' intimate knowledge of disease," Weinstock says. "This large-scale effort will open doors in many areas of medicine to improve our understanding of good health and the treatment and prevention of disease."

Dean's distinction

Jacquelyn L. Fleming, coordinator in the Department of Surgery, celebrates receiving the 2009 Dean's Operations Staff Award with Dean Larry J. Shapiro, MD, right, and John P. Kirby, MD, assistant professor of surgery. Also honored were Michael C. Royal, staff pharmacist in the Department of Medicine's AIDS Clinical Trials Unit, who received the 2009 Dean's Distinguished Service Award, and Mary Hoffman, RN, a clinical research nurse coordinator in the Department of Medicine, who received the 2009 Dean's Research Support Award.

Six degrees of kidney transplant

At any one time, 85,000 people in the United States are waiting for kidney transplants. Last year, surgeons transplanted just over 15,000 kidneys. To help combat this severe shortage, Washington University transplant surgeons at Barnes-Jewish Hospital recently took part in the first six-way, multi-hospital, "domino" kidney transplant.

Working with teams from The Johns Hopkins Hospital in Baltimore and Integris Baptist Medical Center in Oklahoma City, surgeons Surendra Shenoy, MD, PhD, and Martin D. Jendrisak, MD, matched a group of incompatible donor-recipient pairs with other pairs in a similar predicament. By exchanging kidneys among the six pairs, each recipient received a kidney from a stranger, enabling transplants that otherwise would not have occurred.

"A lot of people on the waiting list have donors who would like to give a kidney, but they are not compatible," Shenoy says. "This approach has a tremendous potential to increase the number of living donor transplants and could serve as a model for other transplant centers."

A surgical team at Johns Hopkins began a cross-country set of operations with five incompatible pairs. An altruistic donor and a recipient who was next on the United Network for Organ Sharing (UNOS) organ recipient list started and ended the chain. Just like falling dominoes, the altruistic donor kidney went to a recipient from one of the incompatible pairs, that recipient's donor's kidney went to a recipient from a second pair and so on. The last remaining kidney from the final incompatible pair went to the UNOS recipient.
Heuckeroth honored for research

Pediatric gastroenterologist Robert O. Heuckeroth, MD, PhD, has won a Clinical Scientist Award in Translational Research from the Burroughs Wellcome Fund.

Heuckeroth, who treats children with Hirschsprung disease and other gastrointestinal disorders at St. Louis Children's Hospital, was one of only four individuals nationwide to receive the prestigious award, which supports established, independent physician-scientists dedicated to translational research — the transfer of work from the lab to the patient's bedside.

The five-year, $750,000 award will support Heuckeroth's research into the environmental risk for Hirschsprung disease, a potentially fatal disorder in which the end of the bowel is missing the enteric nervous system, a complex network of cells that controls intestinal function, and to develop new approaches to prevent this disorder, which affects about one in every 5,000 children.

More than a decade of basic research by Heuckeroth's laboratory and other investigators has led to a sophisticated but incomplete understanding of the molecules needed for normal development of the enteric nervous system. They believe there are important gene-environment interactions that influence the occurrence of Hirschsprung disease.

Multidisciplinary effort aimed at muscle and bone disorders

Grant to focus on three research cores

A five-year, $3 million grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) will allow investigators from more than 50 laboratories at the School of Medicine to join forces in the fight against musculoskeletal disorders.

The grant funds a Core Center for Musculoskeletal Biology and Medicine. Its goal is to better understand causes and potential treatments for muscle and bone disorders, including osteoporosis, osteoarthritis and muscular dystrophy.

The center also will aid in the development of new and better ways to regenerate bone, cartilage, tendons and muscle tissue.

"Although Washington University has a long record of excellence in musculoskeletal research and clinical care, much of that research has occurred in individual laboratories that may, or may not, regularly communicate with colleagues in other departments," says center director Linda J. Sandell, PhD, the Mildred B. Simon Professor of Orthopaedic Surgery. "This effort was developed to unify and expand research in basic and translational studies that will improve the quality of life in our aging population."

Investigators will be organized into three research cores. One will study musculoskeletal structure and strength. A second will analyze the molecular structure of both healthy and sick bones, muscles and connective tissue. A third will use genetic engineering techniques to create mouse models of various muscle, bone and connective tissue diseases.

In addition to Sandell, center co-directors will be Steven L. Teitelbaum, MD, the Messing Professor of Pathology and Immunology, and Matthew J. Silva, PhD, associate professor of orthopaedic surgery. All of the investigators who will work as part of the center have grant support from the National Institutes of Health for their bone and muscle studies.

WUSM remains among nation's best

Washington University School of Medicine is No. 3 among research-oriented medical schools, tied this year with the University of Pennsylvania, according to rankings issued in the May 2009 issue of U.S. News & World Report.

The School of Medicine's internal medicine program ranks No. 6, up from No. 8 in 2008 and retaining its top 10 standing, and the pediatrics program is tied at No. 8.

The medical school was again ranked No. 1 in student selectivity — the 11th consecutive year it has been so honored. Its students' 2008 average entrance exam scores and undergraduate grade-point averages were the highest among the top 50 research-oriented medical schools.
Fooling the brain to lower BP

Some 15 million Americans have high blood pressure that can't be controlled with medication, leaving them at high risk for early death, stroke, heart disease or kidney failure.

Researchers at the School of Medicine are evaluating whether an investigational device can help these patients keep their blood pressure in check. Similar to a pacemaker, the iPod-sized device is implanted under the skin near the collarbone, with wires that carry electrical signals to nerve receptors along the carotid arteries in the neck. The signals activate the body's own system for regulating blood pressure.

"The device is designed to fool the brain into thinking a person's blood pressure is much higher than it really is," says the lead investigator of a U.S. study evaluating the device, Marcos Rothstein, MD, professor of medicine at Washington University and medical director of dialysis services at Barnes-Jewish Hospital. "The brain, as the body's central command center, responds by slowing the heart rate, relaxing the blood vessels, and filtering more salt and water from the kidneys — all of which lower blood pressure."

At the recent annual meeting of the American College of Cardiology, Rothstein presented data from a small multicenter study of 38 patients with uncontrollable high blood pressure in whom the device was implanted. On average, their blood pressure was 183/105 despite taking anti-hypertensive medications. Two to three years after the device was implanted, they had reduced their systolic blood pressure (top number) by an average of 31 points and their diastolic pressure (bottom number) by an average of 21 points.

"These are patients for whom no drugs had worked," Rothstein says. "They had no other options."

There were minimal side effects related to the device, the most common being temporary pain at the site where the device was implanted.

Rothstein, now leading a larger study, is seeking to enroll 300 U.S. patients, including 25 in St. Louis. The research is sponsored by the device's maker, CVRx Inc., of Minneapolis. To be eligible for the study, participants must be ages 18 to 75 and have blood pressure that has not responded to a combined regimen of the maximal dosages of at least two anti-hypertensives and a diuretic. Their systolic blood pressure must be consistently higher than 160 with this medication.

For more information or to enroll, please contact Lisa Murphy, RN, at (314) 747-3601 or lmurphy@DOM.wustl.edu.
Hallahan heads radiation oncology

Dennis E. Hallahan, MD, has been named new head of the Department of Radiation Oncology. He succeeds interim head Jeff M. Michalski, MD, who has held the position since April 2008.

The radiation oncology department, one of the largest in the country, is recognized as a national leader in the development and clinical implementation of major technical breakthroughs in radiation treatments for cancer patients. The department provides a rich training environment for radiation oncology health care providers. Recently, the department expanded its cancer biology, medical physics and clinical divisions and created a new division in bioinformatics and outcomes research.

“Together with Barnes-Jewish Hospital and BJC HealthCare, we will continue to advance cancer therapy technology with proton-beam therapy, image-guided therapy and a world-renowned brachytherapy center,” Hallahan says.

Hallahan conducts research to identify new molecular targets for cancer therapy and to develop drugs that improve cancer response to radiation therapy while minimizing the effects on normal tissues. He has published scientific articles about radiotherapy treatment for many types of cancers including lymphomas, brain, head and neck, lung, breast and prostate cancers, and childhood neoplasms. He has several research grants from the National Cancer Institute and from industry collaborators.

Two faculty honored with named professorships

Linda J. Sandell, PhD, has been named the Mildred B. Simon Research Professor of Orthopaedic Surgery and Mark J. Manary, MD, has been named the Helene B. Roberson Professor of Pediatrics.

The Simon professorship will help provide financial support to allow Sandell, who also is a professor of cell biology and physiology, to advance her research on the molecular mechanisms involved in cartilage development and disease. Her laboratory studies gene regulation of extracellular matrix proteins and the mechanisms related to protein expression in cartilage, bone, muscle and fat cells. She also has a long-standing interest in the cellular mechanisms associated with bone formation as well as osteoarthritis, a potentially disabling cartilage disease.

Manary has spent several years devoted to researching the effectiveness of a simple yet revolutionary peanut butter mixture with severely and moderately malnourished young children in the sub-Saharan African country of Malawi. He also is working with plant scientists at the Donald Danforth Plant Science Center to boost the nutrition in cassava, a starchy root that is a diet staple of 200 million of the poorest Africans and the third-largest source of carbohydrates for human food in the world.

Biodefense center funding extended

The National Institutes of Health (NIH) has extended funding for the Midwest Regional Center for Excellence in Biodefense and Emerging Infectious Diseases (MRCE), anchored at Washington University School of Medicine and headed by principal investigator Herbert W. "Skip" Virgin, MD, PhD, Mallinckrodt Professor and Head of Pathology and Immunology.

The center received a five-year, $37 million grant from the National Institute of Allergy and Infectious Diseases.

The MRCE is one of 11 Regional Centers of Excellence dedicated to developing new or improved ways to treat, diagnose or prevent diseases that could be used for bioterrorism, such as anthrax, or infectious diseases, like West Nile fever. The RCES also provide scientific expertise to first responders in an infectious-disease-related emergency, whether it occurs naturally or through an act of bioterrorism.
Researchers at the School of Medicine have created a line of fruit flies that may someday help shed light on the mechanisms that cause insomnia in humans. The flies, which only get a fraction of the sleep of normal flies, resemble insomniac humans in several ways.

"Insomnia is a common and debilitating disorder that results in substantial impairments in a person's quality of life, reduces productivity and increases the risk for psychiatric illness," says senior author Paul J. Shaw, PhD. "We think this model has clear potential to help us learn more about the causes of insomnia and someday develop ways to test for or treat them in the clinic.

The findings were published in the June 3, 2009 issue of The Journal of Neuroscience. Shaw's lab was the first to show that fruit flies enter a state of inactivity comparable to sleep. He also noticed that a few flies naturally slept less than others and decided to take flies with insomnia-like characteristics and breed them to amplify those qualities. The flies he bred had difficulty falling asleep in normal circumstances, and their sleep was often interrupted or fragmented. He also showed that certain flies were hyper-responsive to stimuli, and added them to the breeding pool.

After generations of breeding, Shaw's group produced a line of flies that naturally spent only an hour a day asleep — less than 10 percent of the 12 hours of sleep normal flies get. They quickly noticed an obvious and surprising behavioral change: Even though flies have six legs to balance on, the insomniac flies fell over more often. Declines in balance also have been reported in sleep-deprived humans. Shaw's flies also were slower learners and gained more fat, two indicators for fly sleep deprivation that he identified earlier. Sleep-deprived humans experience similar changes.

Surprisingly, although 70 hours of sleep deprivation will kill a normal fly, the insomniac flies can spontaneously go up to 240 hours without sleep and still survive.

"Overall, the flies are able to perform better than they should, given how much sleep they miss," says former postdoctoral student and lead author Laurent Seugnet, PhD. "That makes it tempting to speculate that insomnia is like drug addiction: As it increases the body's overall vulnerability and risk of collapse, it also seems to boost certain factors that help resist collapse.

When researchers tested the insomniac flies for changes in gene activity levels, they found altered activity in genes involved in metabolism, nerve cell activity and sensory perception. Moreover, they found that activity levels of at least two of the genes are changed in sleep-deprived humans.

Researchers speculate that some genes altered by insomnia and sleep deprivation may simultaneously contribute to both detrimental and temporarily advantageous effects. Shaw has conducted follow-up studies of the altered genes and how restoring normal genetic activity levels affects insomnia and its symptoms.
Robert Willson, who has amyotrophic lateral sclerosis, talks with neurologist Timothy M. Miller, MD, PhD, assistant professor of neurology, at the Center for Advanced Medicine.

JOURNEY TO HOPE

The Hope Center for Neurological Disorders helps ensure forward motion through groundbreaking research and treatments

BY JUDY H. WATTS
HE WASTED MUSCLES AND SLURRED SPEECH of advancing ALS (amyotrophic lateral sclerosis), the tremors and movement difficulties of Parkinson's disease, the slow melting of minds beset by Alzheimer's disease — such bundled symptoms are so striking that most people assume that the neurological afflictions they signal are unrelated. Not so, says Mark P. Goldberg, MD, director of the Hope Center for Neurological Disorders. "Patients with brain or spinal disease should of course seek treatment from clinicians specializing in their disorder, but researching specific diseases is not the fast path to a cure. Research shows that diseases of the brain, spinal cord and nerves have common threads that can only be discovered on a fundamental level. When we understand these shared disease pathways, we can begin to find cures. That is the work of the Hope Center."

Center without walls
Given the complexity of the central nervous system itself — a dynamic, multiscaled and sensitive array of profoundly integrated structures and processes — the Hope Center mandates research input from many disciplines. It includes geneticists, molecular, cell and developmental biologists, pathologists, engineers, biochemists and clinician-scientists such as neurosurgeons, pediatricians, internists, psychiatrists, radiologists and anesthesiologists.

In every sense "a center without walls," the Hope Center facilitates research by 70 scientists on Washington University's medical and Danforth campuses. The Hope Center's administrative core is in the Biotechnology Building, and its Program on Protein Folding and Neurodegeneration will be situated in the new BJC Institute of Health at Washington University, located at the heart of the medical campus.

The Hope Center supports innovative research programs through seed grants that effectively leverage traditional grants and contracts as well as private funding. (To learn more, see Advancing Hope, an article about the Danforth Foundation challenge, on page 26.) Basic research and scholarly publication, while thriving, are only the beginning of the process. The Hope Center's guiding principle is translational research: supporting the creation of new knowledge about the brain and nervous system and then enabling its rapid translation into cures, new treatments and diagnostic tools for clinicians and patients.

"When scientists with different perspectives and training focus on a problem together, the translational process accelerates," says Goldberg, who is professor of neurology, anatomy and neurobiology, and biomedical engineering.

Hopeful response to the times
The Hope Center developed at an intersection of influences. One was Hope Happens, a foundation the late Christopher Wells Hobler established in 2002 to quickly find a cure for ALS patients like himself. Another was the Center for the Study of Nervous System Injury, established in 1991 by former Washington University faculty member Dennis W. Choi, MD, PhD.

At the same time, Goldberg and colleagues like David M. Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology, had been impressed with how much progress resulted from collaborative work across disciplines — an approach that Washington University had encouraged for decades. They wanted to implement such a system to solve the staggeringly difficult questions about brain disease. CONTINUES PAGE 12
Tracking gene mutation to treat its effects

Robert H. Baloh, MD, PhD  Assistant Professor of Neurology
Hope Center Program in Mitochondria and Bioenergetics

Robert H. Baloh, MD, PhD, deciphers the molecular mechanics of neurodegenerative disease. Two of his research focuses are amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, and Charcot-Marie-Tooth disease (CMT). As neurons die in the motor pathways of an ALS patient’s brain and spinal cord, muscles atrophy. The patient becomes profoundly weak, unable to speak or swallow, and eventually dies from respiratory failure three to five years after diagnosis. In contrast, though CMT involves degeneration of similar motor pathways, it progresses slowly over a patient's lifetime, typically causing foot drop, foot deformities, falls and hand weakness as peripheral nerves deteriorate.

Baloh's lab is investigating a gene known as TDP-43, a key regulator of messenger RNA splicing, which edits protein-building instructions from DNA to allow proper protein assembly. Abnormalities can radically alter cellular function.

During collaborative research published in *Annals of Neurology* in February 2008, Baloh and Hope Center colleagues, including Nigel J. Cairns, PhD, research associate professor of neurology and of pathology and immunology, and Alison Goate, PhD, professor of neurology and of genetics, linked a mutation in TDP-43 to an inherited form of ALS and are now creating a mouse model for the disease. They will then compare animal models, cultured neurons and cell lines to existing models of ALS based on mutations in the SOD1 gene.

"Our expectation," Baloh says, "is that understanding how disease mutations in TDP-43 and SOD1 cause neurodegeneration will allow us to identify effective treatments."

In pursuit of brain and spinal cord repair

Valeria Cavalli, PhD  Assistant Professor of Neurobiology
Hope Center Program in Axon Injury and Neurodegeneration

Valeria Cavalli, PhD, a specialist in neuronal cell biology and axon injury, is engaged with one of medicine's great challenges: to reverse paralysis and restore nerve function when the central nervous system (CNS) has been severely damaged by stroke, spinal-cord injury or disease. Whereas peripheral nerves, like most of the body's tissues, can usually repair themselves, damaged neuronal axons in the CNS that normally deliver essential electrochemical payloads cannot spontaneously regenerate. When axon damage interrupts transport — of mitochondria, cytoskeletal polymers, neurotransmitters — the delicate conduit degenerates and mental and physical functioning follow suit.

Cavalli wants to know how neurons in the peripheral nervous system manage to regenerate and learn what is different about them and their response to injury. She aims to determine whether they somehow sense injury and their counterparts in the CNS do not—or whether neurons in each system "sense" but only one responds in a particular way.

After dissecting the molecular events from the point of peripheral nerve damage to self-repair, Cavalli intends to determine which steps in CNS response sequences are deficient and devise ways to assist, perhaps by bypassing or stimulating the appropriate mechanism.

"My findings will apply to many neurodegenerative diseases, in which axon damage is due not to traumatic injury but to the effects of protein aggregation or impaired function, which then cause degeneration."

Neural function research: sciatic nerve of a mouse
Tracing molecular missteps

Rohit V. Pappu, PhD  Associate Professor of Biomedical Engineering
Hope Center Program on Protein Folding and Neurodegeneration

Part of the work of biophysicist Rohit V. Pappu, PhD, concentrates on how proteins clump together.

This research is relevant to Huntington’s disease — which affects balance, speech and muscle strength, and typically causes death within 20 years — as well as eight other inherited neurodegenerative diseases. All are technically termed polyglutamine expansion disorders, and that means that the affected person produces a protein with an abnormal stretch containing many units of the amino acid glutamine.

In research that answered a long-standing question about why proteins rich in polyglutamine should aggregate, Pappu and coworkers showed that despite the purported “water-loving” nature of glutamine, polyglutamine molecules behave like readily aggregating “greasy” molecules. These findings were made using novel fluorescence measurements coupled with polymer theory and computer simulations.

Further work showed that this aggregation depends on the length of the polyglutamine stretch. “We showed that the inability of individual polyglutamine molecules to fold into well-defined three dimensional structures promotes aggregation,” Pappu says. “By aggregating, the polyglutamine molecules interact to achieve structures that individual polyglutamine molecules cannot achieve on their own.”

Pappu is also part of a project led by Jin-Moo Lee, MD, PhD, associate professor of neurology, and Carl Frieden, PhD, professor of biochemistry and molecular biophysics. The study showed that cells take up small amounts of amyloid beta (Abeta) — peptides that make up extracellular plaques in brains of people with Alzheimer’s disease. Using neuroblastoma cells — malignant but easy-to-work-with cells representative of neurons — the researchers administered Abeta to cells in small, physiologically relevant amounts. They found that the cells took up Abeta and packed it into lysosomes, specialized acidic pouches within cells that digest unwanted proteins. However, the acidic conditions and confined space within lysosomes provide conditions that are conducive to Abeta aggregation, whereby “nature’s protection appears to end up becoming a problem.”
“In 2004, Hope Happens approached us about working together,” Goldberg recalls. “It was good timing for both groups. We had a plan in place, and it was just what they were looking for. Neurological science was advancing so rapidly that it was time to begin thinking hard about moving quickly to treatments.”

Organizing the science

To that end, the Hope Center set out to explore neurological diseases’ common mechanisms and effects on brain cells at the level of genes and molecules. Two basic research themes developed. The first, the Hope Center Program on Protein Misfolding and Neurodegeneration, is based on the idea that in neurodegenerative diseases, proteins somehow fold incorrectly after they are formed and then create problems as they aggregate. The program will be one of five Interdisciplinary Research Centers (IRCs) formed under BioMed 21, the university’s translational research initiative. Led by Holtzman and Alison Goate, PhD, the Samuel and Mae S. Ludwig Professor of Genetics in Psychiatry, the IRC involves 25 researchers whose teams will occupy five laboratories in the new BJC Institute for Health building — the hub for BioMed 21 — when the School of Medicine and Barnes-Jewish Hospital open its doors in January 2010.

Among numerous researchers who have made notable discoveries is Timothy M. Miller, MD, PhD, assistant professor of neurology and director of the Hope Center’s Christopher Hobler Laboratory. Miller’s innovative therapy for ALS that targets the mechanism of protein misfolding has advanced to human trials.

The second major research thrust at the Hope Center is the Program in Axon Injury and Repair. Investigators are seeking to understand how neuronal axons degenerate — with the new realization that when an axon is damaged, the fiber itself triggers a new pathway of active degeneration that could be interrupted with an entirely new kind of treatment. Jeffrey D. Milbrandt, MD, PhD, the David Clayson Professor of Neurology, found that a particular molecule arrests the process and then described the pathway; therapies have since been licensed for clinical development. And in April 2009 — in another example among many — Aaron DiAntonio, MD, PhD, associate professor of developmental biology, discovered a complementary second pathway leading to axon degeneration, suggesting treatments with powerful potential.

“We’re getting so close to truly understanding neurodegenerative disorders and are making headway with new therapies,” says Holtzman, who credits the Hope Center’s infrastructure for its success in both research and funding. He chairs a steering committee of senior scientists (Goate, Goldberg, Milbrandt and Eugene M. Johnson Jr., PhD, professor of neurology and of molecular biology and pharmacology) to evaluate progress, with oversight from the Hope Center’s executive committee. Matthew J. Stowe, JD, administrative director, coordinates the overall team effort.

Eliminating barriers

Still another way the Hope Center ensures progress is by knocking down conventional barriers, creating smoother, faster pathways to translation. In addition to putting the right minds together to solve complicated problems — such as matching basic scientists with clinicians — administrators have provided core facilities for animal models, amyloid-beta microdialysis, neuroimaging and transgenic and viral vectors. New facilities, equipment and instrumentation — most recently, the medical school’s first atomic force microscope — are added, funding permitting, in response to investigators’ needs. And a new collaboration with the Office of Technology Management recently has been implemented to help scientists disclose and patent inventions and to ready their ideas for biotechnology or drug company licensing.

“In one sense, it’s good that our researchers are distributed across the campuses,” says Goldberg. “They can work near their home departments without changing affiliations and neighbors. The only downside is that while we gather regularly, we don’t interact every day. Bumping into people in a hallway can be at the heart of science. Finding new ways to bring scientists together — now, there is a challenge!”

A Danforth Foundation challenge strengthens the Hope Center’s promise for developing better treatments: Please see page 26.
Cancer is a difficult diagnosis to acknowledge — especially what a parent with cancer must explain.

A StoryCorps project to capture the emotional stories of survivors may help others say what must be said.

BY HOLLY EDMISTON
Kathy Ferrara knows how difficult it can be to tell children about one's own cancer diagnosis. Two years ago, Ferrara, then 42, was diagnosed with Stage II colon cancer. At the time, her three children were ages 18, 16 and 13. Having lost their dad just six years earlier, it was all the harder.

"When their father died, it was like a freight train hitting all of us," Ferrara says. "So I really had to think through how I was going to break this news to them." She ended up taking a positive, yet no-nonsense approach, telling her kids the facts about each step of her treatment: surgery, participation in a clinical trial, and chemotherapy. Today, Ferrara is cancer-free and feels great.

Yet when she reflects, Ferrara remembers how complicated the experience was. When StoryCorps, a national oral history project, visited Siteman Cancer Center locations in the St. Louis area earlier this year, Ferrara hoped her story could help other parents face this daunting challenge.

Brandi Brown, left, and her mother, Kathie Bryson, prepare for a StoryCorps session, assisted by facilitator Naomi Green.

While in St. Louis, StoryCorps researchers asked parents to relate how they had shared their cancer diagnoses with their children. By collecting these personal stories, they intend to identify the most effective ways for parents to tell their children about this disease.

"Most parents diagnosed with cancer aren't sure how to talk to their kids about it, and there aren't many resources available to help them," says Matthew W. Kreuter, PhD, an adviser on the StoryCorps project and director of the Health Communication Research Laboratory at Washington University's Brown School of Social Work. "This project will help future cancer patients prepare for and make the most of these conversations."

That's why Ferrara agreed to participate, along with her now 19-year-old middle daughter, Natalie. "Once I learned about StoryCorps and heard some of the testimonies, I thought it was amazing," Ferrara says.

Two years ago, Ferrara hardly had time to process the news of her cancer diagnosis herself before she had to talk with her kids. She had minor symptoms, so her doctor prescribed a colonoscopy. As soon as the procedure was finished, she got the abrupt news that she had colon cancer and would need surgery the next day.

"My kids didn't even know I was going in for the colonoscopy," says Ferrara. "When I finally had the opportunity to talk to them at the hospital later that day, I'd had some time to think about how I was going to move forward, without making..."
it any worse than it was. So I just told them: 'Here's what we know. Here's the prognosis, which is very good. I'm in very capable hands.'

Her children seemingly took the news well. “My mother is very matter of fact,” says Natalie. “I’m used to that. When she told us, I knew it was a big deal, but I didn’t really grasp exactly what was happening until my sister called and was very upset. It was the ‘what ifs’ that freaked me out.”

Though she remained nervous, her mother’s pragmatic approach to treatment and the support of family and friends was of great comfort to Natalie and her siblings.

Later, through StoryCorps, Ferrara learned in more detail what her children had actually been thinking at that time, and she also shared some of her own fears. “I think I said a few things that Natalie hadn’t heard or that I hadn’t actually said before about being scared, having to let go, and understanding truly what faith means,” says Ferrara.

For the StoryCorps session, mother and daughter were seated in a comfortable area with a microphone for each. For nearly an hour, they discussed their experience. A moderator was present to ask questions and guide the interview.

Natalie says StoryCorps helped her to find closure. “My mom, brother, sister and I hadn’t really talked about it a lot,” she says. “We just kind of went through it. It was great to sit down and talk — to see what we were thinking at the time.”

There were some surprises. Ferrara had not known that Natalie felt she should have taken better care of her mom during her treatment. “In my mind,” says Ferrara, “all the kids were there for me and we were so understanding. They took great care of me!”

Natalie’s most vivid recollection from the StoryCorps dialogue was learning that the first words her mother heard upon waking up from her colonoscopy were: “You’re in trouble.”

“I will never forget that,” says Natalie. “I thought that was a horrible way to say it.”

Natalie and her mom both hope that their participation in StoryCorps will help others. “Learning that bad things can and do happen to everyone has made me stronger,” says Natalie. “I hope our story can make a difference for other people facing similar experiences.”

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Straight talk

Siteman Cancer Center offers a range of resources for families who must discuss, prepare for, and cope with cancer

From disease-specific support groups to therapeutic programs such as "Arts as Healing," Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine has long provided support, education and hope to cancer patients and their families.

Now Siteman has partnered with The Wellness Community of Greater St. Louis to provide access to even more programs. Together, they are dedicated to helping people affected by cancer learn vital skills that will enable them to regain control, reduce isolation and restore hope, regardless of the stage of their disease. The Wellness Community offers classes such as Music for Recovery, Ask an Attorney and Gentle Yoga, all free of charge to patients, and provides a homelike setting for people fighting cancer to connect with and learn from each other.

“The Wellness Community does an outstanding job of helping those diagnosed with cancer work through difficult times,” says Teresa L. Deshields, PhD, Siteman’s manager of psychosocial oncology services. “With this partnership, Siteman can offer patients a truly comprehensive program that not only helps them better understand cancer, but also makes fighting the disease an easier process.”

The new partnership will offer programs at Siteman’s main location at Washington University Medical Center in St. Louis’ Central West End and at its Barnes-Jewish West County Hospital location in Creve Coeur, Missouri.

To learn more about the cancer-related programs of Barnes-Jewish Hospital and Washington University School of Medicine at Siteman Cancer Center, please visit siteman.wustl.edu.
Why do children with eczema so often get asthma?

Experts in cellular signaling discovered how skin cells in danger might sound a body-wide alert.

But lung cells in turn make an unfortunate response.

The rawness, itching and oozing of eczema, a chronic skin rash, and the coughing, wheezing and breathlessness of asthma have something in common — something besides their unpleasantness, that is. Both are frequent in young children, and often a child will contract both disorders, first eczema, then asthma.

It sounds coincidental, but it’s not always. Asthma follows eczema so often that doctors use the faintly martial phrase, atopic march, to describe the progression. About one-fifth of children get eczema, also called atopic dermatitis, and asthma occurs in one-half to two-thirds of those with moderate to severe eczema.

Immunologists, dermatologists and lung specialists have debated and studied atopic march for years without agreeing on a definitive cause for the mysterious phenomenon. But sometimes a new perspective on a stubborn problem reveals an answer; that’s what happened in the laboratory of Raphael Kopan, PhD, professor of developmental biology and of dermatology.

Although the scientists didn’t set out to investigate asthma, they believe they have pinned down the source of atopic march — a compound called TSLP, which the skin secretes when it’s damaged or defective. They have demonstrated that TSLP can travel from the skin to the lungs and instigate asthmatic symptoms in laboratory mice with a skin disorder.

“We’ve shown that instead of wondering about the role of myriad immune factors — T helper cells, B cells, myeloid cells — we can narrow atopic march down to one molecule,” Kopan says. “Now the question might be, how can doctors prevent eczemic skin from making TSLP? If that can be done, kids who have eczema may no longer have to worry about it leading to asthma.”

By Gwen Ericson
What happened next began with a survey of similar research. Many papers connected eczema with TSLP. Still others connected asthma with TSLP. But no one before Kopan and his colleagues had made the seemingly obvious connection. So they devised experiments to test this idea, which showed that TSLP is the probable catalyst of atopic march.

Mice with a skin disorder were dying; the question was why. They were found to have a profusion of white blood cells—a sign of a very active immune system. Researchers discovered the cause was a substance called TSLP. In mice and people, TSLP alerts the immune system to skin damage. But in the mice with eczema, TSLP was so overproduced that it was like repeatedly dialing 911: Their immune systems went into overdrive, with body-wide consequences.

While investigating cellular signaling, Raphael Kopan, PhD, and colleagues discovered a process that could explain atopic march—the progression from childhood eczema to asthma.
Healthy skin

Borderline communications: Sounding the alarm

The skin and the lung's airways exist at the border; the skin and the lungs are the body's barriers against the external world. Cells that form these barrier organs and other tissues integrate their functions through biochemical signaling throughout the body.

In mice, eczemic skin appears to send a warning signal: TSLP. The lungs respond to it as a red alert, and the result is asthma. If this is indeed the mechanism in people, then it should be possible to develop treatments that block the systemic alarm that leads from eczema to asthma.
Finding the key to atopic march has unlocked new doors for Kopan and his team. These basic research scientists are now entering into a collaboration on studies involving human patients. They will test the amount of TSLP in the blood of people with eczema and determine whether higher levels lead to more propensity to asthma.

This research could soon uncover ways to prevent excess TSLP production in eczemic skin and thereby break the link to asthma. And further down the road, other research might reveal how to inhibit TSLP production in the lungs to stop asthma even in cases that aren’t associated with eczema.

Kopan says this work is a prime example of why medical schools maintain basic research laboratories. "We backed into this discovery because we are allowed to play to a degree, to start with an observation and follow through without necessarily having a medical application in mind."

Labs like Kopan’s are also adding to the knowledge physicians need to do their jobs. "Look at it this way: doctors are like repairmen for a very complicated machine; even with a lot of experience, something can go wrong that the repairmen don’t understand," says Kopan. "Then they need to consult the manufacturer’s manual (present in our DNA). You might say we’re translating this manual to improve our understanding of the body’s manufacturing process and its functions as an integrated system.”
The celebrated deanship of M. Kenton King, MD, remains among the longest "reigns" in higher education. And his influential tenure is still being honored.

BY CANDACE O'CONNOR
Before accepting the position of Dean of the School of Medicine, King was reassured: “You'll only need to be in the office 30 minutes a day.”

“What they would do if they disagreed with him was simply remain silent.”

On this day, Cori paced restlessly up and down and then issued a terse request from the search committee that he chaired. “We have decided we want you to be the dean. Will you accept?”

In case King felt any qualms about the workload or about succeeding Edward Dempsey, MD, who had left abruptly after a contentious tenure, Cori added some reassurance: “You’ll only need to be in the office 30 minutes a day.”

So the 39-year-old King — until a few months earlier an associate dean and internist, with only hazy administrative ambitions — took on this huge, complex and decidedly full-time task. When he retired in 1989, after 25 years of service, he had become one of the longest-serving medical deans in the United States, as well as one of the most successful.

A quiet leader: M. Kenton King says that he “just wanted to do a good job.”

Academic hero

“Ken King is one of my heroes,” says Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the medical school. “In his quiet and unassuming way, he played a key role in shaping the current Washington University School of Medicine. He led with integrity and had the respect and confidence of faculty, students and staff. He has served the School long and well and has left an enduring mark.”

Letters from colleagues, written at the time of King’s retirement, speak eloquently to his decency and fairness, kindness and wisdom, patience and honesty. “You have the wonderful ability to recognize foibles and defects in people without becoming cynical or disdainful about them,” wrote Samuel B. Guze, MD, chairman of the Department of Psychiatry. “As you know, I believe you would have made a superb psychiatrist.”

Said Harvey R. Colten, MD, chairman of the Department of Pediatrics: “Casey Stengel said, ‘The secret of managing a ball club is to keep the five guys who hate you away from the five who are undecided.’ You would have done this but for you, in a sense, the task has been easier. Who could ever find the five guys who hate you?”
Or as neurology head William M. Landau, MD, wrote: “Whatever has been accomplished in this department or this medical school in the last quarter century includes more than a fair share of Ken King’s blood, sweat and tears. Your quiet leadership has launched us into our world-class role… “I am glad that you will hang around to remind our successors from time to time that consistently thoughtful consideration works miracles.”

Childhood and education

Born and raised in Oklahoma City, M. Kenton King (M for “Morris”) was the son of C. Willard King (C for “Cassius”), a dry goods salesman from a tiny Kansas town where it was the custom to give children an honorary first name. No one in King’s family was a doctor, but after serving in the U.S. Navy during World War II and graduating from the University of Oklahoma in 1947, he decided to attend Vanderbilt University’s medical school on the G.I. bill.

By the time he had finished, he was seventh in his class. “Many medical students were married and a few had children,” he says with self-deprecating humor. “I had nothing else to do at night but study.”

For his internship, he was accepted into the demanding program at Barnes Hospital, and then stayed for residency training in internal medicine, serving as chief resident in 1955. Among this faculty of outstanding physicians, he most admired internal medicine head W. Barry Wood, MD, a star scholar and athlete. When Wood left for Johns Hopkins University in 1955, King went along to do a fellowship in microbiology and become a junior faculty member.

In 1957, he returned to Washington University to join the preventive medicine faculty and head the Student Health Service, becoming associate dean five years later. By then he had a wife — June Greenfield King, a 1951 graduate of the Washington University School of Nursing and formerly head nurse on a Barnes Hospital medical and surgical ward — along with a growing family. Asked in 1965 about his hobbies, he said: “I’ve got four boys at home. All are under seven years old. Need I say more?” Their workload increased when a fifth son was born the following year.

Highlights of the King years

With his surprise accession to the deanship, he began work on several fronts. Early on, he made a key appointment, naming pediatrician John C. Herweg, MD, as associate dean of the medical school with responsibility for admissions. “I thought that was one of the best decisions I ever made,” he says now.

As vacancies occurred, he chaired committees that eventually recruited new heads in all 17 departments, thus reshaping the Executive Faculty. Among the external choices he names with great satisfaction are P. Roy Vagelos, MD, replacing Cori in biochemistry, Philip R. Dodge, MD, in pediatrics, and Gerald D. Fischbach, MD, in anatomy.

At the same time, he championed a dramatic change in the composition of the student body, favoring more minority and women students. In 1964 he told the St. Louis Post-Dispatch: “There is simply no basis for skepticism about women doctors any more…. [W]omen have distinguished themselves beyond doubt in every field and function of medicine.”

By the end of his tenure, the campus looked vastly different, with more than 30 buildings spread over 50 acres. Among the additions were the McDonnell Medical Sciences Building, the Clinical Sciences Research Building, a renovated East Building and the new Becker Medical Library. In other areas, King worked to strengthen the amount and quality of medical research and to bolster alumni relations.

Today, he remains keenly interested in the School’s welfare, while enjoying his family, which now includes eight grandchildren. Last October, he and his wife faced a tragic loss when their son, University City Police Sgt. Michael King, AB ’80, was killed while on duty in the Delmar Loop.

Reflecting on his tenure, King is characteristically modest. “Many of the deans in the country were chosen for some other feature, such as their research,” he says. “I had an attitude that some of the other deans did not possess: that is, I just wanted to do a good job as dean.”

And while he might never admit it, he succeeded. His successor as dean, William A. Peck, MD, wrote in his laudatory 1989 retirement letter: “You have established a new benchmark for dedication to our institution.” Or as William H. Danforth, who served alongside King as medical school vice chancellor before becoming university chancellor, put it in his 1989 retirement letter: “The King quarter-century has been a golden age. It has been an honor to have been a part of it.”

Before he was Dean: King, standing, in the late 1950s, in the bacteriology lab with Carl Harford, MD, and an unknown female colleague.
Results are in!

MATCH DAY WAS HELD MARCH 19, 2009, and 114 medical students took part in the National Resident Matching Program. During the annual ceremony, senior medical students in the United States learn which residency programs they will enter. School of Medicine graduates are highly successful in obtaining competitive training programs. In 2009, 27 percent of the graduating class selected a primary care field and 34 percent matched into highly competitive fields including ophthalmology, neurosurgery, urology, orthopaedic surgery, plastic surgery, otolaryngology, dermatology and diagnostic radiology.

ARIZONA
Tucson
University of Arizona
AFFILIATED HOSPITALS
EMERGENCY MEDICINE
Suzanne Michelle Rhodes

COLORADO
Denver
University of Colorado
School of Medicine
INTERNAL MEDICINE
Syd Quang Dao

CALIFORNIA
Los Angeles
Children's Hospital
PEDIATRICS
Holly Brianne Lindsay

San Diego
University of California, San Diego Medical Center
EMERGENCY MEDICINE
Theodore Nader Armstrong
PEDIATRICS
Nicole Keiko Yamada

Stanford
Stanford University
OTOLARYNGOLOGY
Dong Hoon Lee
PEDIATRICS
Mitsuki Jane Seppa

CONNECTICUT
New Haven
Yale-New Haven Hospital
ORTHOPAEDIC SURGERY
Luis Alberto Vega

DISTRICT OF COLUMBIA
Washington
George Washington University
OPHTHALMOLOGY
Joshua Arthur

INDIANA
Indianapolis
Indiana University
School of Medicine
OPHTHALMOLOGY
Joshua Honghan Hou

ILLINOIS
Chicago
Cook County Hospital
EMERGENCY MEDICINE
Ghazal Shafei

LOUISIANA
New Orleans
Tulane University
School of Medicine
ORTHOPAEDIC SURGERY
Mae Ewing Young

MARYLAND
Baltimore
Johns Hopkins University-Bayview Medical Center
INTERNAL MEDICINE
Hamid Majid Karbgo

NEOLOGY
Robert Mestayer Mallery
PATHOLOGY
Jason Michael Baron

Worcester
University of Massachusetts Medical School
SURGERY-PRELIMINARY
James Robert Wade

MICHIGAN
Ann Arbor
University of Michigan
OPHTHALMOLOGY
Sharmini Ash Balakrishnan

MINNESOTA
Minneapolis
University of Minnesota Medical School
INTERNAL MEDICINE
Sara Marie Champlin

ORTHOPAEDIC SURGERY
David Micah Brogan

ROCHESTER
Mayo School of Graduate Medical Education
ORTHOPAEDIC SURGERY
David Micah Brogan

MISSOURI
Kansas City
University of Missouri
OPHTHALMOLOGY
Ronald Luke Rebenitsch

Good news:
Neil S. Sachanandani, MD 09

Staying in St. Louis: Timothy T. and Molly K. Tran are among 26 members of the Class of 2009 who secured residencies at Barnes-Jewish Hospital and Washington University School of Medicine.

Ta-da! Fang Bu, MD 09, and two classmates will complete pediatric residencies at St. Louis Children's Hospital.
Advancing hope

The Danforth Foundation challenge: promise for Hope Center patients and their families

About 3,000 Americans are diagnosed with neurological disorders every day. As life expectancy increases, this figure is projected to double in the next 30 years. The current financial and emotional costs of these disorders are staggering. In years to come, such costs will increase exponentially.

Hearing a diagnosis of conditions such as Huntington’s disease, amyotrophic lateral sclerosis (ALS), stroke or multiple sclerosis (MS) can be devastating for both patients and their families. For many of these diseases, there are limited treatments and no cures.

“It’s very exciting to know there’s something as outstanding as the Hope Center in my backyard,” says Jessica Spear, 3-year-old Brendon’s mom. The two were photographed during a recent visit to St. Louis Children’s Hospital.

To learn more about Brendon and pediatric stroke, visit BrendonsSmile.org.

The Hope Center for Neurological Disorders, a research center dedicated to fast-tracking the process of finding causes and cures for these and other neurological disorders, is actively working to change that. Its researchers believe that fundamental discoveries made in one disease can lead to more effective treatments and diagnoses in many others.

The Hope Center received a significant boost through a $10 million gift from the Danforth Foundation, which will create an endowment to support innovative research and will be named for the late Donald Danforth Jr., a 1955 graduate of the Olin Business School at Washington University and executive vice president ofRalston Purina Co.

Now the university and Hope Happens, an initiative begun by Christopher Wells Hobler, who lost his life to ALS in 2005, have committed to raise matching endowed funds of $10 million by December 2013.

The tremendous excitement of this catalyst for the research effort is best described by patients and their families — those who will directly benefit from its results.

Helping the youngest patients

When toddler Brendon Spear began making attempts to walk, his mother noticed that he dragged his right foot and favored his left arm.

“It reminded me of someone who had suffered a stroke,” recalls Jessica Spear, who had previously cared for stroke patients at a nursing home. “But then I would tell myself, ‘Babies don’t have strokes.’”

Brendon’s pediatrician and a pediatric orthopedist both dismissed Spear’s concerns about her son’s gait, telling her Brendon would outgrow these problems. He was almost 2 years old when a neurologist determined that he had suffered a stroke in utero and had cerebral palsy as a result.

Brendon, now 3, loves to race cars and chase his cat, Ruthie. But he wears braces on both feet and a splint on his right arm. He also...
stutters and becomes frustrated trying to find the words to express what he’s thinking.

Since being referred to Bradley L. Schlaggar, MD, PhD, associate professor of pediatric neurology, and beginning therapy, Brendon can run faster, jump higher and climb stairs using alternate feet. His speech also has improved.

“Our goal is to increase awareness of pediatric stroke and encourage much needed research in this area,” says Spear. “You feel like you’re in a race against time when you have a child with these needs.”

**Ongoing care, support — and optimism**

As a 24-year-old newlywed, Carole Wilson was told she had multiple sclerosis (MS), a condition in which the immune system attacks the central nervous system. An avid runner and walker, Wilson had made an appointment with her doctor because she thought a pinched nerve was causing numbness in her left leg.

“I was shocked,” Wilson says of her diagnosis. “I asked if I could still have children.”

Five years later, Wilson gave birth to a son. She felt fine during her pregnancy, but had her first flare-up when her new baby was just 6 months old.

MS has mainly affected Wilson's legs. When her son was 4 years old, she began using a cane. Today, at 45, she needs a walker for everyday life and uses a wheelchair at the mall or a baseball game.

Wilson came to Washington University years ago after reading an article about neuroimmunologist John L. Trotter, MD. When he died suddenly in 2001, she became a patient of Becky R. Parks, MD, assistant professor of neurology.

“I feel like I’m in the loop and am getting the best care available,” says Wilson, who serves on the Hope Center’s advisory board. “When I toured the Hope Center, just seeing all the research being done was so exciting.”

Wilson has met many of the Hope Center physicians, and she's inspired by their dedication.

“I think the Hope Center has exceptional leadership and a great group of doctors,” she says. “If anyone can find a link between these neurodegenerative diseases, they can.”

**Partnering for a good outcome**

In 2007 and 2008, Zoe Cooper participated in clinical trials of the drug Rituxan for the treatment of MS. Before beginning the first trial, she suffered a seizure. She also had experienced numbness, balance problems and trouble driving. An MRI revealed she had 13 lesions on her brain.

Cooper received an IV of Rituxan once a week for one month during the trials. A follow-up MRI after her last treatment showed that the lesions had disappeared.

“It was like living a miracle,” says Cooper, a 51-year-old registered nurse who was first diagnosed with MS in 2001. “I’m getting goose bumps just talking about it. I felt like my old self again.”

It was Cooper’s physician, Anne Cross, MD, professor of neurology, who referred her to the trials. “I can’t express how excited and grateful I am that I was in a place with a group of doctors where this was available,” Cooper says. “I know if I get sick again, there is something that works for me.”

Cooper’s dream is that Hope Center researchers will be able to find similarly effective treatments for other patients with neurodegenerative disorders. "I wish," she says, "that other people could have the same results."
MD Reunion 2009 brought together a community of medical alumni to celebrate and learn. This gathering of physicians, scholars and longtime friends featured educational programs, medical center tours, dressed-up dinners and casual fun. From the class of 1999 starting the reunion tradition with their 10th to the Class of 1944 proudly feting their 65th, at the School of Medicine, everyone was home again.

Photos by Robert Boston and Mark Beaven

Kenneth Gilbertson, MD, and current medical students discuss SPOTS, a student-initiated project
Alumni Achievement Award honoree David Hussey, MD 64, with his wife, Mariam Hussey.

Lisa Wichterman and Keith Wichterman, MD 74, await the next CME session.

Trang Le-MacKenzie and Thomas MacKenzie, MD 89.

Class of 1959 Reunion Co-Chair Ann Flipse, MD 59, and her three children, Tom, Annie and Jay.

25th Reunion celebrants gather at the awards banquet. From left: Ronald Wainz, MD 84, Bobbie Loeffler, MD 84, Jennifer Wray Cole, MD 84, and Jon Friedman, MD 84.

James Lindsey, MD 69, George Randall, MD 69, Rick Jacobs, MD 69, and Bill (Larry) Adams, MD 69.

Barry Siegel, MD 69, and his wife, Marilyn Siegel, MD, celebrate his 40th reunion at the Class of 1969 dinner.
Distinguished Service Award recipient William Shearer, MD 70, and CME presenter Morey Haymond, MD 69

Chancellor Mark Wrighton, Nobuko Kuhn, MD 69, and Risa Zwerling Wrighton at the Alumni Awards Banquet

Celebrating their 25th reunion, from left: Will Ross, MD 84, Joseph Awad, MD 84, Susan Rollins, MD 84, Ethan Cruvant, MD 84, David Wilson, MD 84, Edward Rollins, MD 84, Joseph Kent, MD 84, Christopher Gallagher, MD 84, and George Hvostik, MD 84

A family tradition! Robert H. Lund, MD 49, Herluf G. Lund Jr., MD 85, and Herluf G. Lund Sr., MD 49, gather at the Awards Banquet

Amy Ronner and Michael Pacin, MD 69

Karen Wright, Jeffrey Wright, MD 79, and Mary Anne Rudloff, MD 79, catch up during the Class of 1979 dinner

Ted Kuczmar, MD 79, and his wife, Debra, at the Class of 1979 dinner

Class of 1959 Reunion Co-Chair Charles Norland, MD 59, and wife Dorothy Norland
The School of Medicine honored five exceptional alumni and faculty at the annual Awards Banquet.

From left: Michael Georgieff, MD 79 (Alumni Achievement Award), Will Ross, MD 84 (Alumni/Faculty Award), David Hussey MD 64 (Alumni Achievement Award), William Shearer, MD 70, PhD (Distinguished Service Award). Not pictured: Emily Smith, MD 68 (Alumni/Faculty Award).

50th Reunion celebrants Joy Severin, Allen Parelman, MD 59, Jean Lee Parelman and Sanford Severin, MD 59, enjoyed reminiscing about their days as students.

James Lindsey, MD 69, his wife, Maggie Lindsey, and Garry Fathman, MD 69, enjoy a laugh.

Joseph Awad, MD 84, and Jane Gilliam with their son, Thomas.

Current medical students and alumni chat about student life while enjoying the view from the Olson Family Garden at St. Louis Children's Hospital.

Sarah Brent and Jeffrey Brent, MD 99.

Class of 1974 celebrants Bettye Thomas, Leyland Thomas, MD 74, and Robert Weiss, MD 74.

Where you belong!

Save the dates for the 2010 MD Reunion • April 29–May 1
New WUMCAA leadership elected

Incoming president Herluf G. Lund Jr., MD 85, was introduced to the Washington University Medical Center Alumni Association (WUMCAA) by Jennifer Wray Cole, MD 84, a member of the 25th medical reunion class and outgoing president, during the 2009 Alumni Awards Banquet.

WUMCAA encourages a spirit of fellowship among alumni, promotes the interests and reputation of the School of Medicine and the medical center, and works to advance medical and allied sciences.

MD Reunion Challenge Honor Roll

William L. Adams, MD 69  
Ann M. Ainsworth, MD 69  
Carl Frederick Bigler, MD 84  
Richard John Boos, MD 84  
John Anthony Burton, MD 89  
Leonard Caladney, MD 69  
Delphine L. Chen, MD 99  
Jennifer Wray Cole, MD 84  
Neil W. Culp, MD 59  
Larry Di Fabrizio, MD 84  
Michael C. Edelstein, MD 84  
Max L. Elliott, MD 64  
Lewis C. Fischbein, MD 74  
Ann Randolph Flipse, MD 59  
John Raymond Frame, MD 79  
Pearl E. Grimes, MD 74  
Thomas B. Hall III, MD 69  
Robert E. Herold, MD 74  
David Chung Kuen Hu, MD 79  
Mary Ann Fletcher Hurley, MD 69  
David H. Hussey, MD 64  
Mark Howard Jaffe, MD 74  
Joseph H. Kent, MD 84  
E. Lee Knuteson, MD 69  
Nobuko O. Kuhn, MD 59  
Irving Kushner, MD 59  
Daniel K. Lane, MD 59  
Eunice J. Larson, MD 64  
Patty Lee, MD 89  
Wenzel A. Leff, MD 59  
Armond Leon Levy, MD 94  
David Alan Lubarsky, MD 84  
Robert R. Lyle, MD 49  
Robert McMahon, MD 89  
Edward Charles Miller, MD 79  
Marek Alexander Mirkik, MD 84  
William E. Muntz, MD 59  
William N. Neubauer, MD 69  
Lenore Tomoye Nii, MD 84  
Charles C. Norland, MD 59  
James Wilson Owen III, MD 79  
Gerald F. Peppers, MD 59  
Kristin Leslie Ratliff, MD 99  
Alexandra Ilma Reichman, MD 84  
Albert L. Rhoton Jr., MD 59  
William Bradford Rockwell, MD 84  
Edward Sterling Rollins, MD 84  
Susan D. Rollins, MD 84  
Mary Anne Rudloff, MD 79  
Raymond G. Schultz, MD 59  
Barry A. Siegel, MD 69  
David Sperling, MD 59  
Richard Srebro, MD 59  
Clifford R. Talbert Jr., MD 59  
Thomas E. Vaughan, MD 89  
Theresa Gay Vircoy, MD 84  
James Barry Weinstein, MD 79  
John R. West, MD 59  
David Joshua Whellan, MD 94  
Thomas Seth Winokur, MD 79  
David L. Younger, MD 69

MD Reunion gift effort a success

MD alumni celebrating reunions were extraordinarily generous in supporting their class gifts. These gifts included enthusiastic work by the 25th and 50th reunion classes to establish endowed scholarships (70 percent of the Class of 1959 participated), as well as other individual gifts.

Spurring strong Reunion giving was the MD Reunion 2009 Eliot Society Challenge. This challenge was sponsored by Robert E. Connor, MD 79, and it was fully subscribed by his fellow Reunion alumni before they arrived to celebrate Reunion weekend in May. The challenge grant, which was made in honor of the MD Class of 1979 30th Reunion, resulted in 62 qualifying gifts totaling more than $137,000. Through his gift, Connor encouraged reunion-year MD alumni to mark the occasion by either joining the Eliot Society, or if already members, upgrading to a higher level.

Washington University School of Medicine would like to thank Dr. Connor and all the individuals (in box, at left) who responded to the MD Reunion Challenge.
1930s

Howard R. Bierman, MD 39
Bierman served as a U.S. Navy flight surgeon during World War II, during which time he was fondly referred to as “Doc.” From 1946 to 1953 he was the principal clinical investigator for the National Cancer Institute. He then became the first medical director of the City of Hope, an NCI-designated Comprehensive Cancer Center in Los Angeles. He held that position from 1953 to 1959.

1940s

Llwellyn Sale Jr., MD 40
Sale recently moved from the home he lived in for 52 years to a facility for senior citizens in Clayton MO. The transition has been a challenge, but he feels time will help. He was able to attend the 2008 Reunion Banquet and was happy to see familiar faces in the crowd.

Donald Moore, MD 42
Moore and his wife, Barbara, recently moved to Sunrise Independent Living in Salt Lake City UT. After retiring at age 74, Moore continued to volunteer at the John M. Browning Firearms Museum in Ogden UT until he was 90 years old.

John L. Cockrell, MD 43
After an internship at San Francisco General Hospital, Cockrell served in the U.S. Army with the 103rd General Hospital in England. In 1951, he joined the Women’s and Children’s Clinic in Eugene OR. He retired in August 1986.

David Stadtner, MD 43
Stadtner and his wife have been retired for more than 20 years. After retirement, he continued to operate the allergy clinic at the local county hospital. Every year as retirees, Stadtner and his wife have led a rather active life, making Elderhostel journeys annually as well as trips to the Shakespeare Festival in Cedar City UT. The couple lives in Stockton CA.

1950s

John W. Ubben, MD 45
Ubben and his wife, Dorothy, live in a new villa at the Lake of the Ozarks in Missouri. They enjoy attending educational events at the state-of-the-art, joint commission-accredited hospital near their home. Living in a resort area offers them the chance to participate in many activities such as fishing, boating and other water sports.

1960s

Steven Teitelbaum, MD 64
Teitelbaum lives in St. Louis. His son, Aaron, owns two restaurants in the area: Monarch in Maplewood and Herbie’s (the old Balaban’s) in the Central West End. He looks forward to his next reunion.

1970s

John E. Finch, MD 59
Finch is enjoying retirement. After being a widower for years, he married Linda Angell, MD, on Oct. 12, 2008. Linda trained in Iowa and Boston. She recently retired from a very successful pediatric ophthalmology and eye surgery practice in Michigan. Both Finch and his wife are talented competitive ballroom dancers. In the last few years they have traveled to Africa, Russia, Ukraine and France. The couple resides in Sarasota FL.

Stanley G. Nathenson, MD 59
Nathenson received the Horwitz Prize for Outstanding Research in January 2008. He also was honored at the Symposium on Immunology in June 2008 by the Albert Einstein College of Medicine in Bronx NY.

Allen G. Parelman, MD 59
Parelman retired from a practice in ophthalmology in Kansas City MO in 1999. His son joined the practice in 1989, and the elder Parelman enjoyed the 10 years they were able to work together. Today Parelman spends summers and winters in Aspen CO biking, skiing and participating in the wonderful cultural activities that abound in the area. He has children and grandchildren scattered from east to west and spends much of his time visiting them and touring the world. For the past 10 years, he has done volunteer work in Eastern Europe for one week each year.

1980s

Susan J. Berres, OT 83, PT 85
Berres, who lives in Charlottesville VA, was recently named an Outstanding Contributor in the University of Virginia Health System, the highest award given to its employees. She has been part of the pediatric occupational therapy team in acute care and inpatient rehabilitation since 1991. On the civic front, she currently heads up a project to publish student poetry on all city buses, edits the local Peace and Justice Center e-mail...
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Steven Fabian, MD 99
Fabian and his family moved to Boston MA in June of last year, where he began a renal fellowship through Brigham and Women’s Hospital joint program. He and his wife run into many Washington University alumni there. They have two children: Sophia, 3, and Alexis, 1.

Amanda Heidemann, MD 99
Heidemann is still with BJC Medical Group in St. Louis as a medical director. She is working on the electronic medical records project. She is pleased that all the practices are now live, and she has just launched the Community Health Connection, an electronic data-sharing portal covering the St. Louis metropolitan area. Eventually, she hopes to have all the health systems in the area sharing patient records to improve safety and quality of care. In addition, Heidemann does some work in urgent care at BJC Health Care facilities. She enjoys spending time with her boys, Adam and Eric.

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2000s
Matthew and M. Laurin Council, MD 04
The Councils welcomed their second baby girl, Sophie Anne, in March 2009. Both remain at Washington University School of Medicine. Matt currently serves as chief resident in the Department of Ophthalmology, while Laurin continues her residency in dermatology.

Percy F. Morales, MD 04
Morales finished his internal medicine residency in June 2008. He has been accepted to do a cardiology fellowship at Baylor University. This will allow him to stay in Houston TX, where he enjoys the warm weather.

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IN MEMORY
Robert M. Bond, MD 45
Bond died on Oct. 13, 2008. After graduating from Washington University School of Medicine, he completed a residency at Virginia Mason Hospital in Seattle WA. He then spent three years in the Medical Corps of the U.S. Navy. On discharge from the service, he set up a medical practice in Pomeroy WA as a general practitioner. During the eight years he was there, he also served as the county health officer for Garfield County WA.

James A. Jernigan, MD 49
Jernigan died April 26, 2009. After graduating from Washington University School of Medicine, Jernigan achieved the rank of lieutenant colonel with the U.S. Air Force. Following his military service, he was in private practice from 1960 until 1971. He then joined the Department of Community Medicine and Family Health at the University of Florida in Gainesville FL.

Ellis J. Van Slyck, HS 49
Van Slyck died on Dec. 20, 2008, after a long and courageous battle with cancer. He was chief of hematology at Henry Ford Hospital in Detroit MI for many years, and his life was full of good works and compassionately skilled service to his patients.

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* Mail to: Washington University in St. Louis • Office of Medical Alumni and Development • Campus Box 1247, 7425 Forsyth Ave., Suite 2100, St. Louis, MO 63105-2161 • Phone (314) 935-5373 • E-mail alumni@medicine.wustl.edu • Update online: medicalalumni.wustl.edu

Summer 2008
Shirley J. Peterson, MD 49

Peterson died on Jan. 17, 2009, after a brief illness. She was 86. She practiced pediatrics for 32 years. Following her internship at St. Francis Hospital in Evanston IL, Peterson served two years in the U.S. Navy Reserve as a lieutenant at the Pawtuxet Naval Air Station in Maryland. She was the first female doctor on staff. After Navy service, she returned to Washington University to obtain a pediatric certification. She then served at the Municipal Contagious Disease Hospital in Chicago IL, St. Louis Children’s Hospital, and Children’s Memorial Hospital in Chicago. In 1955, she opened an office in her home, providing infant and child care for several generations of families in the Barrington IL area.

Marvin Stein, MD 49

Stein, a leader in the field of academic psychiatry, died on May 16, 2009, at the age of 85. A St. Louis native, he received his undergraduate and medical degrees from Washington University, where he also completed an internship and a residency in psychiatry. Despite moving to New York early in his career, he remained a lifelong fan of the St. Louis Cardinals. At the time of his death, Stein was the Esther and Joseph Klingenstein Professor Emeritus of Psychiatry at the Mount Sinai Medical Center in New York NY, one of several titles he held during his more than 20 years there. Known primarily as a pioneer in understanding the relationship between stress and the body’s immune system, he also was proud to have mentored many young clinicians and scientists. Throughout his career, Stein held many influential positions with various medical associations, and he served on several National Institute of Health committees and editorial boards. A distinguished author, he wrote extensively about psychosomatic medicine and edited two books on the intersection of psychiatry and the immune system. At the time of his death, he was working on a book about the history of psychiatry. He is survived by his wife of 59 years, Ann; two daughters, Leslie Stein, PhD, and Lisa Bickford; a son, David Stein, PhD; and four grandchildren. His family requests that memorial contributions be directed to Washington University School of Medicine, 7425 Forsyth Ave., Campus Box 1247, St. Louis, MO 63105-2161.

William C. Weaver, MD 51

Weaver, a resident of Leavenworth CA, died on Feb. 21, 2009. He had lived in Leavenworth for 13 years and was a retired medical doctor from Redondo Beach Medical Center in California.

Robert E. Martin, MD 54

Martin died on April 2, 2009, at Oak Crest Care Center in Parville MD after a short illness. After graduation from Washington University School of Medicine, Martin completed his internship and surgical residency at Union Memorial Hospital in Baltimore MD. In 1959, he started a private practice with privileges at both Union Memorial Hospital and Greater Baltimore Medical Center. Throughout his career, he authored many articles published in medical journals and was affiliated with many professional organizations. He also served as a consultant and an academic instructor and, from 1972 to 1975, as chief of staff at Union Memorial. Upon retirement at age 69, after 40 years in practice, Martin’s interest turned to his rose and vegetable gardens, which he tended to with meticulous care. He was also an avid sailor of the Chesapeake Bay and the East Coast.

Kent Smith, MD 62

Smith died on Feb. 17, 2009. He grew up in Sherman TX, graduating as valedictorian of his Sherman High School class. Following three years at the University of Texas in Austin, he entered Washington University School of Medicine. After graduating from medical school, he completed a residency in pathology at Baylor University Medical Center in Dallas. He then spent the next two years as a major in the U.S. Army Medical Corps, the first year in Fort Mead MD, and the second year in Vietnam, where he received the Bronze Star.
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Touching a nerve Researchers at the School of Medicine are working across disciplines to study the fundamental connections among neurological diseases. This image from the laboratory of Valeria Cavalli, PhD, shows nerve cells from a mouse embryo spinal cord (red) and corresponding nuclei (blue). Cavalli, a specialist in neuronal cell biology and axon injury, is one of 70 physician-scientists conducting translational research on the brain and nervous system via the university’s Hope Center for Neurological Disorders. To learn more, please turn to page 8.
From the WUSM scrapbook

When M. Kenton King assumed the deanship in 1964, no one could have foreseen the long-term significance of his appointment. This quiet, modest man helped set ambitious goals for the School of Medicine during his 25-year tenure. King and the colleagues he inspired reflect on his contributions in a story beginning on page 21.

News of King's appointment in 1964, and the cover of Outlook honoring his career when he retired in 1989.