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Outlook

 Washington
University in St. Louis
SCHOOL OF MEDICINE

WINTER 2009

A child's garden

St. Louis Children's Hospital
delights the senses with
spaces for the young at heart

 Washington
University in St. Louis
Physicians

... Schwartz, PH.D., M.D.

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Building health At the BJC Institute of Health at Washington University School of Medicine, construction crews put the finishing touches on a metal exterior wall — its orderly grid symbolic of the science that will be done here in pursuit of better medical cures. The 700,000-square-foot, 11-story building opens this winter. A landscaped plaza linking it to the medical center campus will be completed in summer 2010.

Architecture by the numbers:

24,000 square feet of metal panels

20,800 square feet of brick

99,000 square feet of limestone panels

75,000 square feet of glass



Outlook

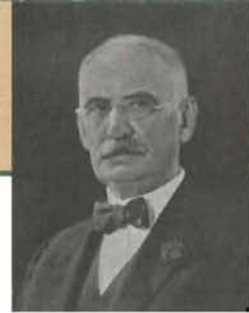
A continuing need for scholarship support

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



Jackson Johnson

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.**

Outlook

Washington University School of Medicine
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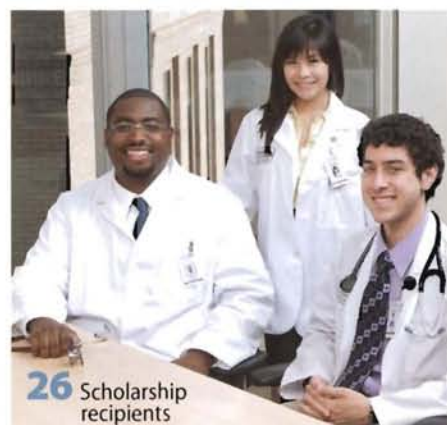
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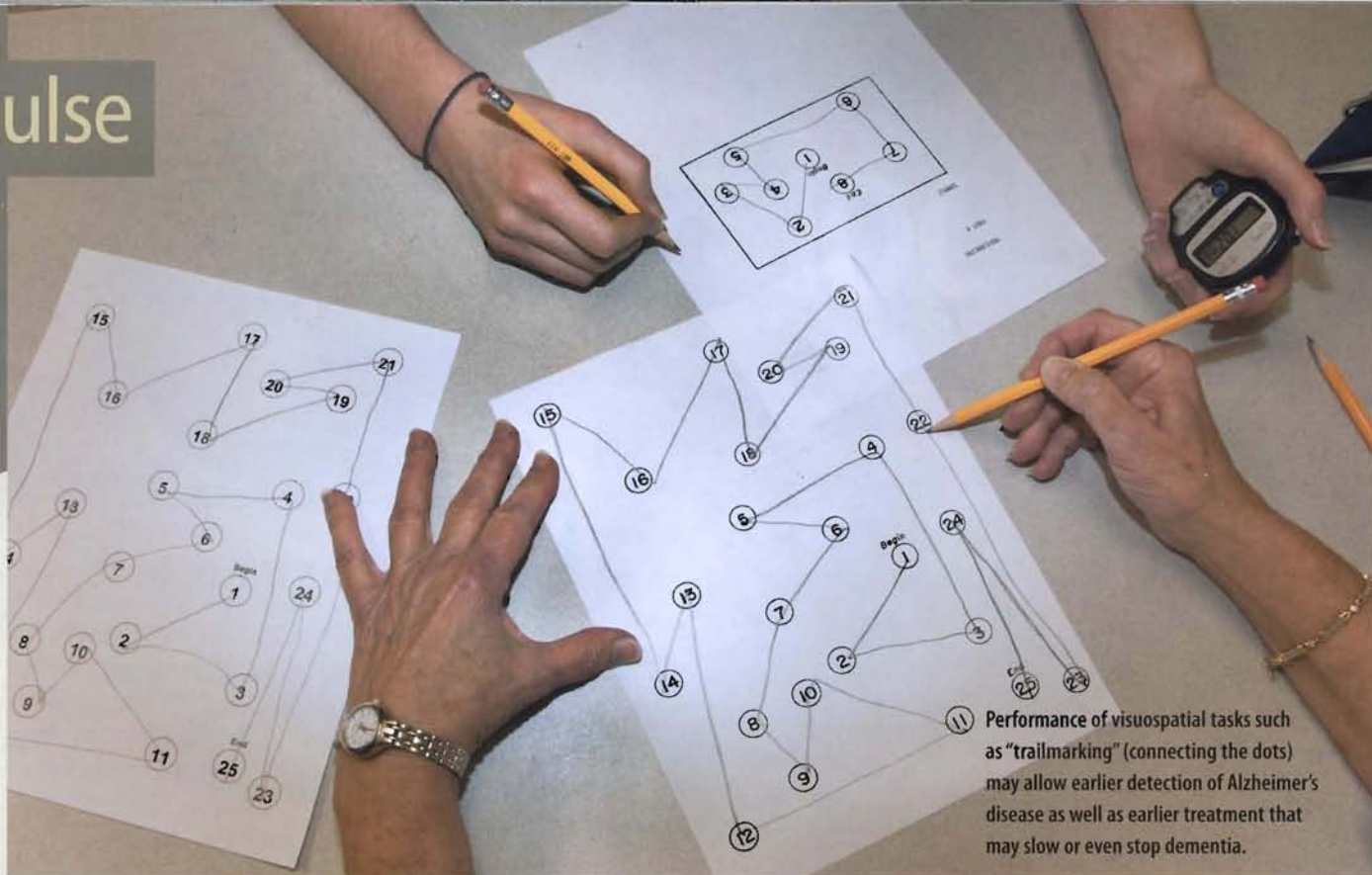
COVER Alan L. Schwartz, PhD, MD, the Harriet B. Spoehrer Professor of Pediatrics and head of the Department of Pediatrics at Washington University School of Medicine, is also pediatrician-in-chief at St. Louis Children's Hospital. Schwartz stands in front of a colorful sculpture by the artist Brother Mel Meyer, SM. For a glimpse of what makes Children's a special place for care, please turn to page 8.

PHOTO BY ROBERT BOSTON

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26 Scholarship recipients



Performance of visuospatial tasks such as "trailmaking" (connecting the dots) may allow earlier detection of Alzheimer's disease as well as earlier treatment that may slow or even stop dementia.

ROBERT HUSTON

Connecting dots

Simple skills tests may help with earlier detection of Alzheimer's

A new study of mental decline in the years prior to diagnosis of Alzheimer's disease suggests that changing the focus of testing may allow earlier detection of the disease.

Current cognitive testing focuses on episodic memory, the ability to remember things like word lists or information from a reading. But scientists at the School of Medicine have found that another class of mental abilities, visuospatial skills, begins to deteriorate up to three years prior to diagnosis. These skills are tested with tasks such as connecting the dots or using a guide to build a structure with blocks.

"We may need to rethink what we look for as the earliest signs of mental change associated with Alzheimer's disease," says senior author James E. Galvin, MD, MS, a Washington University neurologist who is also on staff at Barnes-Jewish Hospital. "If we can better recognize the first signs of disease, we can start treating patients earlier, and hopefully with new treatments we can slow or perhaps even stop their progress into dementia."

The study results were published in the October 2009 issue of *Archives of Neurology*.

Galvin and his coauthors analyzed long-term data from volunteers with the Memory and Aging Project at Washington University's Alzheimer's Disease Research Center (ADRC). For three decades, ADRC researchers have conducted extensive testing of volunteers to uncover factors associated with the normal, healthy retention of mental function in seniors. The new study analyzes data on 444 volunteers ages 60 to 101 that were gathered between 1979 and 2006.

Scientists categorized the new study's results into a global measure of cognitive abilities as well as three specific types of

mental skills: episodic memory, visuospatial skills and working memory — the ability to manipulate facts from memory, such as repeating a list of numbers backwards.

Declines in episodic and working memory were discernible a year before diagnosis with Alzheimer's. Losses in the composite assessment of cognitive abilities were detectable two years prior to diagnosis, and visuospatial skills began to decline three years earlier.

The new perspective may allow doctors to detect signs of Alzheimer's earlier, but more information will be needed to make a firm diagnosis. To make that possible, ADRC researchers are correlating information from the new study with biomarkers, the physical changes associated with preclinical Alzheimer's disease. These include scanning the brain for amyloid plaques, a primary characteristic of Alzheimer's that can begin building in patients 10 years or more before clinical symptoms become apparent, or analyzing protein levels in the cerebrospinal fluid.

"The new findings raise the question of what changes are occurring in the brain during the one- to three-year period prior to diagnosis," Galvin says. "Patients have had plaques in their brain for years, and suddenly their cognitive abilities begin to deteriorate. Is a threshold being crossed where brain cell death begins to occur or really starts to pick up speed?"



Psychometrician Molly Aeschlemann, left, conducts a trailmaking test with study volunteer Jan Bunch.

Federal recovery act a boon for research across multiple fields

WUSTL among top 10 for NIH funds

Washington University in St. Louis has been awarded nearly \$80 million in funding from the 2009 American Recovery and Reinvestment Act (ARRA) to support research across a broad range of projects, including cancer, Alzheimer's disease, renewable energy, diabetes and climate change.

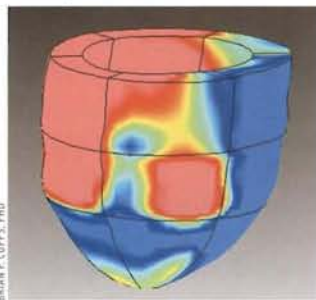
As of September 30, the end of the federal fiscal year, 175 university faculty members had received 207 awards. Some \$73 million came from the National Institutes of Health (NIH); other awards came from the National Science Foundation and the Department of Energy.

The largest chunk — \$10 million — went to the Genome Center for a project to generate comprehensive genetic maps of mutations that underlie 20 types of cancer. Over time, the project is expected to lead to new ways to diagnose, treat or even prevent cancer. Other awards to School of Medicine

researchers will support:

- Testing an MRI-based heart-imaging technique that has the potential to determine whether heart muscle is alive or dead more accurately than currently available tests. The technique offers unprecedented precision and may help to improve the effectiveness of cardiac surgery.

- Investigating ways to



Advanced heart imaging detects functional anomalies (red and yellow)

diagnose Alzheimer's disease before the onset of dementia by combining information from brain scans that image amyloid plaques — a key feature of Alzheimer's — with an analysis of key proteins in spinal fluid. Earlier diagnosis could allow patients to receive new treatments before the disease causes irreversible brain changes that lead to memory loss.

- Establishing a program that helps guide women in poor, minority communities in north St. Louis County through breast cancer screening and follow-up treatment, if needed.

The awards have a significant economic impact in the St. Louis region. A recent survey by Families USA Foundation showed that every dollar of NIH funding to Missouri in 2007 generated \$2.09 of economic activity in the community that received the award.

“By this estimate, recent stimulus funding to Washington University will generate well over \$200 million in goods and services in our region,” says Evan D. Kharasch, MD, PhD, the university's interim vice chancellor of research. “Moreover, research conducted with stimulus funds furthers our efforts to improve the lives of all people.”



Problem solvers Bringing together faculty from various disciplines to solve formerly “unsolvable” problems is the goal of the Center for Innovation in Neuroscience and Technology (CINT), an initiative supported by the School of Medicine's Department of Neurosurgery and the university's School of Engineering & Applied Science. At an open house held on October 12, CINT director Eric C. Leuthardt, MD, assistant professor of neurosurgery, and others showcased technologies developed during the center's first two years.

Solnica-Krezel new department head

Lilianna Solnica-Krezel, PhD, has been chosen to head the Department of Developmental Biology. She succeeds interim head David M. Ornitz, MD, PhD, who has returned to full-time research and teaching responsibilities after holding the position since October 2004.

Solnica-Krezel comes to St. Louis from Vanderbilt University, where she was the University Professor and the Martha Rivers Ingram Professor of Developmental Genetics. She also is a professor of biological sciences, pediatrics, cell biology and physiology, and developmental biology.

In 2007, the Department of Molecular Biology and Pharmacology became the Department of Developmental Biology, reflecting a shift in research focus. During the past 15 years, the department has recruited researchers interested in embryonic development, aging, regenerative biology and physiology. Its focus now encompasses an organism's development through life.

Solnica-Krezel studies molecular and genetic mechanisms that control the early development of vertebrate animals. She has studied this process in zebrafish, using a combination of genetic analysis with embryological and molecular methods. She has received multiple research grants from the National Institutes of Health, March of Dimes Birth Defects Foundation and Human Frontier Science Program.



Lilianna Solnica-Krezel, PhD



ROBERT BOYD

With honors Leslie E. Kahl, MD, associate dean for student affairs, with third-year medical students Matthew S. Painschab, left, and Travis L. Shiba. The two were among 35 students recognized at the annual Student Awards Luncheon held on November 13. Painschab was honored for his community service and student group activities during the first two years of medical school; Shiba was the recipient of the Medical Center Alumni Scholarship Fund Prize, given annually to a student who has shown excellence during the preceding year.

Institute of Medicine elects DeBaun

Michael R. DeBaun, MD, has been elected to the Institute of Medicine of the National Academy of Sciences, one of the highest honors that U.S. medical scientists can receive.

DeBaun, who holds the Ferring Family Chair in Pediatric Cancer and Related Disorders and is a professor of pediatrics, biostatistics and neurology, was recognized for his major contributions to the advancement of the medical sciences, health care and public health.

He has established an internationally renowned program for treatment, education and research into the complications of sickle cell disease. Under his leadership, a team of investigators received funding for the first NIH-sponsored international clinical trial in sickle cell disease. His research also has focused on determining the epidemiology, clinical significance and genetic basis for asthma and pain in children with sickle cell disease.

DeBaun, who also is a pediatrician at St. Louis Children's Hospital, has initiated many community-based activities to improve the quality of life for individuals with sickle cell disease. These include a camp for children with the disease; the Charles Drew program, a cooperative effort with the American Red Cross to increase the number of African-American blood donors; and Sickle Cell Sabbath, a faith-based educational program about sickle cell disease.



Michael R. DeBaun, MD

Treatments improve outlook for pancreatic cancer patients

Clinical trials examine drug reactions

A team of surgeons and oncologists at the Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital is aggressively tackling pancreatic cancer — one of the deadliest forms of the disease — and conducting clinical trials of innovative treatment regimens.

“The perception of many people is that once you receive a diagnosis of

video feature at:
mednews.wustl.edu

pancreatic cancer there's not much that can be done, but that's not true,” says David C. Linehan, MD, associate professor of surgery. “We're attacking this very difficult disease from multiple angles; it's a team effort. One of our areas of focus is ways to manipulate the immune system so that it can fight the tumor.”

Their latest clinical endeavor yielded promising results by including the immune-system stimulator interferon along with chemotherapy and radiation in patients who had their pancreatic tumors surgically removed. In a study published in the *Annals of Surgery*, the team reported that the three-year survival rate was 41 percent for patients on this regimen. In comparison, typical three-year survival rates are about 30 percent.

Linehan and colleagues are part of the largest regional surgical referral center for disorders of the liver, gallbladder, pancreas and GI tract. Many of their patients have survived five or more years after diagnosis. The team is continuing to initiate new trials for pancreatic cancer and plans to start a second trial of interferon-based therapy to attempt to reduce adverse reactions by altering time and dosage.

Becker honored for leadership role

Bernard Becker, MD, who headed the School of Medicine's Department of Ophthalmology and Visual Sciences from 1953 to 1988, is this year's recipient of the American Academy of Ophthalmology's highest honor: the 2009 Laureate Recognition Award.

Becker, lecturer and professor emeritus, was recognized for his pioneering efforts in research, clinical care and education.

Under his tenure, the department became internationally recognized for exceptional research and teaching. Many residents who trained with Becker now serve as department heads or hold other prominent positions in academic ophthalmology throughout the world.



Bernard Becker, MD



A slice of heaven

Medical students await the verdict as faculty judges, from left, Glenn C. Conroy, PhD, Krikor T. Dikranian, MD, PhD, Koong-Nah Chung, PhD, Paul C. Bridgman, PhD, and Robert J. Rothbaum, MD, not shown, judge the first annual Fall Fest Pie Contest. The event, held October 21 at the School of Medicine's Farrell Learning and Teaching Center, featured a variety of flavors, but top honors went to second-year medical student Katherine M. Holzem for her key lime pie. Second-year medical student Amelia G. Drace took second place with turtle cheesecake; third place went to first-year medical student Elizabeth A. Germino, who created a mixed-berry pie.



A berry good try, but will this slice make the grade?

OPHTHALMOLOGY AND VISUAL SCIENCES

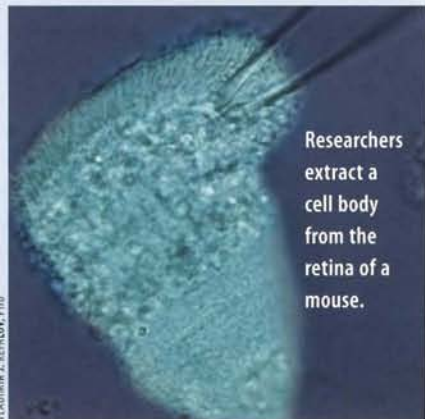
Out of the darkness and into the light

Ever wonder how your eyes adjust during a blackout? When we go from light to near total darkness, cells in the retina must quickly adjust. Vision scientists at the School of Medicine have identified an intricate process that allows the human eye to adapt to darkness. The same process also allows the eye to function in bright light.

The discovery could contribute to better understanding of human diseases that affect the retina, including age-related macular degeneration. That's because the disease and the pathway that researchers identified involve the same cells called cone cells.

"Age-related macular degeneration may be modulated, perhaps, through this pathway we've identified in the retina," says principal investigator Vladimir J. Kefalov, PhD. "Deficiencies in this pathway affect cone cells, and so does macular degeneration, so it's possible that if we could enhance activity in this pathway, we could prevent or reverse some of that damage to cone cells."

The retina's main light-sensing cells are called rods and cones. Previous animal studies showed that cones rely on light-sensing molecules that bind together to make up visual pigments. The pigments are destroyed when they absorb light and must be rebuilt, or recycled, for the cone cells to continue sensing light. When this recycling was prevented, the rods no longer worked, but the cones continued to function. This



Researchers extract a cell body from the retina of a mouse.

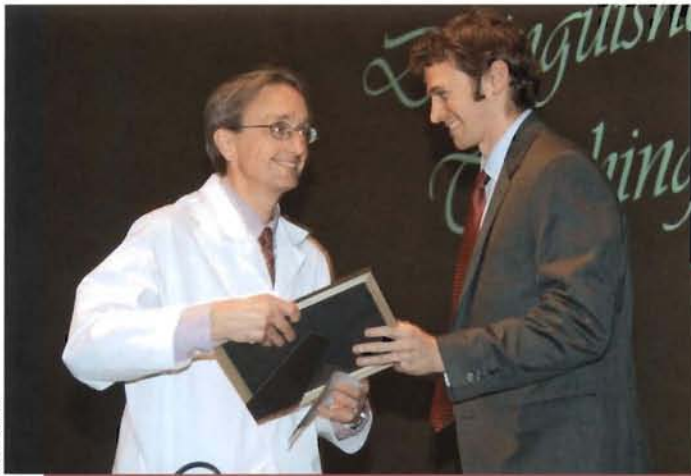
VLADIMIR J. KEFALOV, PH.D.

made it clear to the researchers that a second pathway was involved.

To determine what made this possible, Kefalov's team focused on Müller cells, a particular cell type in the retina that supports and interacts with rods and cones. They destroyed the Müller cells in animal models, then exposed the retina to bright light, followed by darkness. "When we did this, the retinal visual pathway could not function because cones ran out of photopigment and could not adapt to dark."

The results, published in the October 13, 2009 issue of *Current Biology*, suggest that Müller cells are key to this pathway in mammals, including humans. When those cells function properly, cones are able to function in bright light and adapt to darkness, independently of the pigment epithelium.

This discovery means it may one day be possible to manipulate this pathway in the retina to improve vision when the other pathway, involving pigment epithelium, has been interrupted by injury or disease.



ROBERT BOSTON

Extraordinary teachers Clay F. Semenkovich, MD, the Herbert S. Gasser Professor of Medicine and professor of cell biology and physiology, accepts congratulations from Class of 2012 President Ryan E. Anderson at the annual Distinguished Service Teaching Awards ceremony held on November 2 at the Eric P. Newman Education Center. Semenkovich, who received the Humanism in Medicine Award for being a caring and compassionate mentor in the teaching and advising of medical students, was one of more than 50 School of Medicine faculty honored at the event.

Milbrandt named genetics head

Jeffrey D. Milbrandt, MD, PhD, has been named head of the Department of Genetics and the James S. McDonnell Professor. He succeeds interim head Susan K. Dutcher, PhD, who had held the position since June 2006.

Milbrandt, who joined the School of Medicine faculty in 1983, brings a strength in basic and translational science to the position and an appreciation of the expanding role of genetics in the diagnosis, prognosis and treatment of disease. As head of genetics, he hopes to bolster faculty collaborations

with researchers in clinical and preclinical departments and encourage investigations that utilize genetic analysis to understand basic mechanisms of disease.

The department is widely recognized for its study of fundamental genetic mechanisms that underlie biological processes. The department also includes the world-renowned Genome Center, whose scientists played a leading role in the Human Genome Project. More recently, these scientists have pioneered the decod-

ing of cancer patients' genomes to identify genetic changes at the root of the disease. Computational biologists in the department are highly regarded for their study of complex genetic networks and the statistical analysis of genetic data.

Milbrandt's own research has focused on neuronal signaling cascades stimulated by neurotrophic factors and on understanding how glial cells contribute to axonal regeneration after nerve injury.

Multinational effort to study Hispanic health and disease

Mortality, economic impact are focus

The Prevention Research Center (PRC) in St. Louis is launching a multinational research project focused on preventing the leading causes of death in Hispanics in the United States and Latin America. The project is funded by the Centers for Disease Control and Prevention's National Center for Chronic Disease Prevention and Health Promotion.

The PRC in St. Louis, a collaboration between Washington University and Saint Louis University, will conduct a four-year, \$2.8 million effort to apply and adapt evidence-based strategies for preventing heart disease, cancer, diabetes and obesity in the United States, Mexico and Brazil.

"By understanding strategies for physical activity promotion that work in Latin America, we will be better able to address the needs and preferences of Hispanic populations in the United States," says Ross C. Brownson, PhD, project director and professor at the university's School of Medicine and the George Warren Brown School of Social Work.

Chronic diseases are a growing challenge for public health in Latin America and globally. In Brazil, chronic diseases such as heart attack and stroke are leading causes of mortality, generating premature deaths and economic burden.

In a previous phase of this project, PRC researchers evaluated evidence from physical activity interventions carried out in community settings in Recife, Brazil. Physical education instructors there taught free calisthenic and dance classes in public spaces, led walking groups and provided nutrition information. Scientists determined that the project greatly increased physical activity among community members.

In the project's current phase, researchers will disseminate results from the previous study to communities, institutions and public health professionals in Brazil and across Latin America. They also may teach school administrators and public health and medical professionals the latest approaches to physical activity as well as evaluate innovative exercise programs in schools and parks in Brazil.

"We hope this new program will build on what we have already learned," says Brownson, also a faculty scholar of Washington University's Institute for Public Health. "Coupled with healthy eating, physical activity can help prevent and control diabetes, hypertension and heart disease, resulting in improved quality of life and health."



MARCIA MUNK

Physical education taught in public spaces improves community health.



Jeffrey D. Milbrandt, MD, PhD



A micrograph of muscle fibers shows that a new mouse model of ALS loses muscle mass just like humans afflicted by the paralyzing disorder. Scientists hope the model will help them more effectively screen potential new treatments for ALS.

SCIENCE IMAGE COURTESY ROBERT H. BALOH, MD, PhD, MIRROR: PHOTOS.COM; PHOTO ILLUSTRATION BY ERIC COOING

NEUROLOGY

ALS model mirrors human disorder

A new mouse model of amyotrophic lateral sclerosis (ALS) closely resembles the paralyzing disorder in humans, researchers at the School of Medicine reported in the November 3, 2009 issue of *Proceedings of the National Academy of Sciences*.

Like humans with ALS, the mice studied develop progressive paralysis; lose muscle mass and specific types of motor neurons, which are nerve cells that control muscles; and die of the disorder, which is currently fatal in humans.

"As far as we know, this is the first mouse model that recapitulates 'typical' ALS to be produced in more than a decade," says senior author Robert H. Baloh, MD, PhD, assistant professor of neurology. "That could make it very helpful for our efforts to better understand and identify treatments for this terrible disorder."

The mice have a point mutation or single letter of erroneous DNA code in the gene for a protein called TDP-43.

Washington University scientists Nigel J. Cairns, PhD, and Alison Goate, PhD, sequenced a point mutation in the TDP-43 gene of a St. Louis family with an inherited form of ALS, and Baloh's lab created a mouse line with the family's mutation.

"TDP-43 is only the second gene to be linked to an inherited form of ALS that appears clinically identical to sporadic ALS, and it's very promising that this similarity

The utility of this model to mirror human ALS should aid development of better treatments.

allows the symptoms of sporadic ALS to be accurately modeled in mice," Baloh says.

While mice typically live more than two years, mice with the TDP-43 mutation live only five months. Like humans, the mice develop problems with walking, lose muscle mass and eventually become paralyzed.

In addition to helping researchers understand what causes some forms of ALS, the new mouse model may provide an important tool for screening new drugs. Scientists already have another mouse model of ALS with a mutation in SOD1, the first gene to be linked to an inherited form of ALS with typical symptoms. However, according to Baloh, it hasn't always been the best tool for predicting whether treatments will work in humans.

"If we use the two models together to test potential treatments, that might provide us with a much finer screen," says Baloh. "This could help relieve some frustration in the field, because there are a number of new drugs ready to be tested in humans, and we urgently need ways to determine which should be tried first."

The TDP-43 mice also have brain damage similar to patients with frontotemporal dementia, a disorder sometimes associated with ALS. Baloh and colleagues will use the mice to explore the potential connection.



The cafeteria is a colorful destination.



Arianna Dougan takes a break in the Olson Family Garden at St. Louis Children's Hospital.

No children want to be in a hospital. They'd *rather* be in Children's

OASIS



ST. LOUIS CHILDREN'S HOSPITAL AT WASHINGTON UNIVERSITY MEDICAL CENTER
A PHOTO ESSAY BY ROBERT BOSTON



Excellence in patient care, inviting architecture and attractive landscaping — all served with a playful sense of whimsy — are hallmarks of the internationally renowned St. Louis Children's Hospital, consistently ranked among the United States' best pediatric hospitals by *Parents* and *U.S. News & World Report* magazines.

The hospital celebrates 130 years
www.stlouischildrens.org

The hospital's look and feel help make hospital stays less stressful for children and their families. Staffing agency Soliant Health rated St. Louis Children's Hospital No. 6 among the nation's 20 most beautiful hospitals, citing its "rooftop garden that sports an acre of landscaped splendour, including water features and sculpture-art that kids can actually play with."



Dana R. Abendschein, PhD, clowns around with patient Brionna Wilson.



"I truly believe that this special place enhances outcomes for the quality care provided by our physicians. In pediatric medicine, offering a warm, friendly, and even playful environment helps lower the stress levels of patients and their families. St. Louis Children's Hospital becomes a home away from home for them."

Dept. of Pediatrics celebrates 100 years
peds.wustl.edu

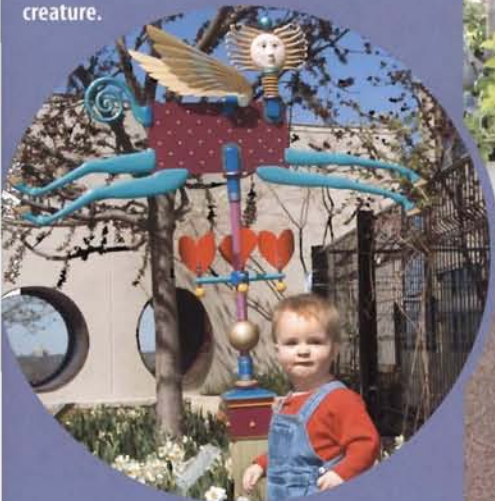
Alan L. Schwartz, PhD, MD

Harriet B. Spoehrer Professor of Pediatrics and head of the Department of Pediatrics at Washington University School of Medicine, pediatrician-in-chief at St. Louis Children's Hospital

Patients and their siblings have many ways to stay occupied while waiting for appointments. Here, two young boys are transfixed by a kinetic sculpture.



Tyler Armbrecht poses beneath a magical creature.



Spectacular roof-top garden flora.



A kaleidoscope encircles plants and scrambles their colors.





Bobby Macintosh travels down a brightly colored hallway.

From the rooftop garden, visitors can gaze upon Forest Park, located just across Kingshighway Boulevard and home of the world-famous St. Louis Zoo, Science Center and Art Museum.



Kaley Holbert marvels at a turtle sculpture, one of many inanimate creatures who call the garden home.

Regular visits by support dogs and their owners bring joy to patients and their families.



Artists



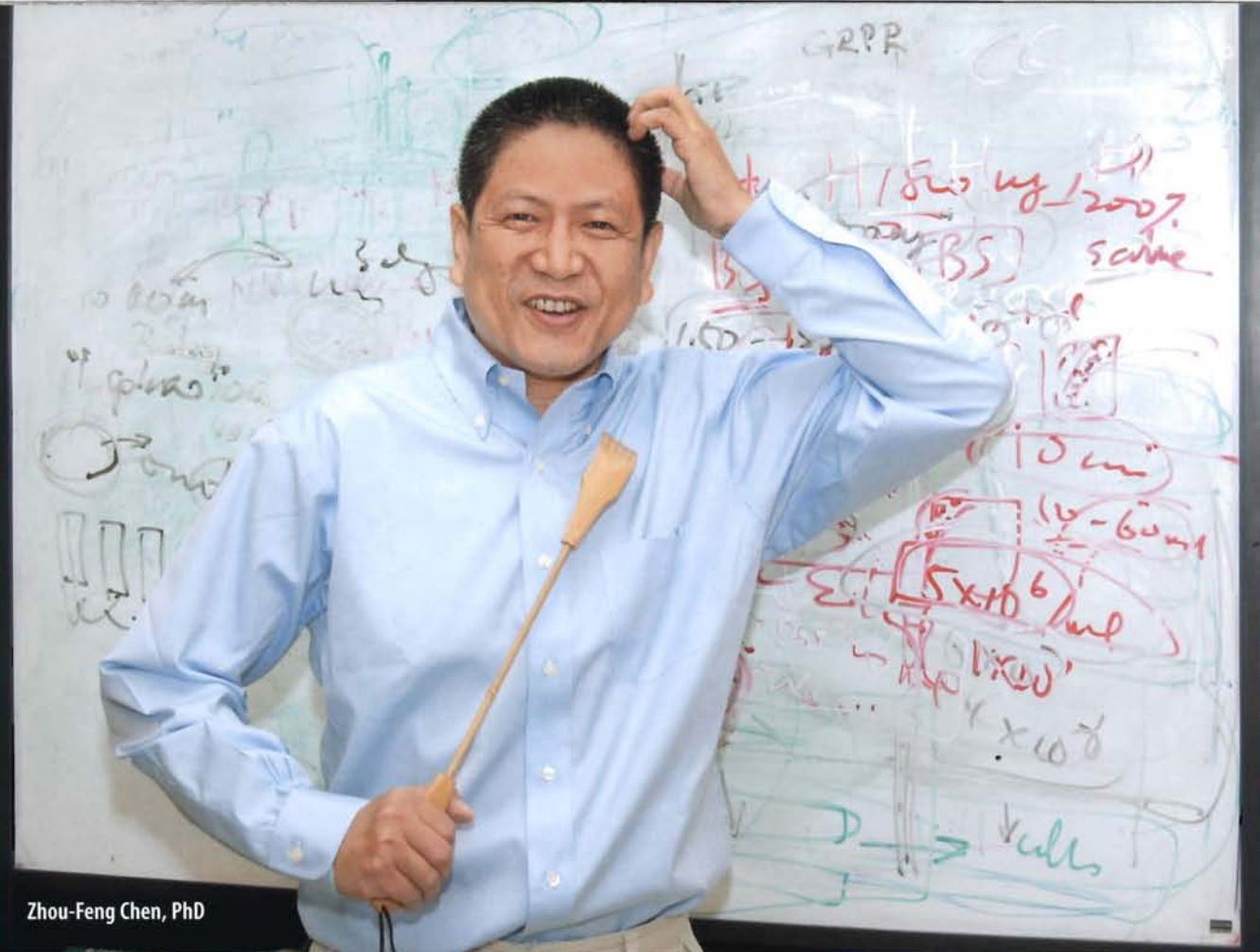
He worked with staff horticulturist Gary Wangler to make a gift for his mother.



Grace and Beckham Lee play with the sculpture ball.



The rooftop garden offers natural beauty and quiet spaces for contemplation.



Zhou-Feng Chen, PhD

Scratching the surface

While studying a specific gene for pain, researchers happened upon an explanation for itch that could lead to better chronic itch management

BY JIM DRYDEN

As native St. Louisan and baseball philosopher Yogi Berra once said: "You can observe a lot just by watching." Although he never heard Berra's famous "Yogi-isms" while growing up in China, Zhou-Feng Chen, PhD, has followed the former catcher's sage advice anyway.

Chen decided that if he wanted to learn whether an animal is itchy, an easy way to find out would be to watch and see whether the animal scratches. So for the last couple of years, Chen and others in his laboratory have spent a good deal of time watching mice scratch.

It all began when Chen, an associate professor of anesthesiology, psychiatry and developmental biology was trying to learn more about pain sensation. His laboratory was looking for genes in the spinal cord that might be related to the pain response. Itch also was involved because historically, scientists had thought of the itch response as being a slightly less intense version of pain and that both sensations were transmitted through the same neural pathway.

That's what it said in the neurology textbooks, anyway. As it turns out, those textbooks were wrong.



While searching for genes related to pain, Chen's lab began studying a gene called GRPR (gastrin-releasing peptide receptor). Among the potential pain-sensing genes they identified, GRPR stood out because it was active on a relatively small number of nerve cells in the spinal cord.

To get an idea of what the gene was doing, they studied mice without the GRPR gene to learn how they were different from normal animals.

"At first, we were a little bit disappointed," Chen says, "because the mice without a GRPR gene seemed to react to painful stimuli in the same way normal mice did."

But then they injected the normal mice with a substance that stimulates GRPR, and the mice started to scratch.

"That's when we thought the gene might be related to itch sensation," Chen says. "So we began to look carefully at the itch response in mice with and without GRPR."

They studied itching by watching the mice scratch, and the researchers found that the normal mice scratched vigorously when exposed to a variety of itch-producing substances. The mice without GRPR, on the other hand, scratched less.

But when either strain of mouse was exposed to painful stimuli, such as an injection, the mice without GRPR withdrew and licked themselves just like the normal mice.

So, although they reacted very differently to itchy things, they both avoided pain and reacted to painful stimuli in identical ways. From that behavior, Chen was able to recognize that pain and itch were not two parts of the same response, but were different responses altogether.

This told the researchers that GRPR was helping to regulate itch and, because the gene was functional only on a small number of neurons, Chen's team zeroed in on those particular cells to see whether they made up an itch-specific pathway in the spinal cord.

In the September 18, 2009 issue of the journal *Science*, Chen reported that such a pathway was likely. Unlike the earlier experiments involving mice without GRPR, this time Chen's team injected the spinal cords of normal mice with a neurotoxin called bombesin-saporin. The neurotoxin binds to GRPR, and it killed the neurons that had a functional GRPR gene.

Then they looked at the mouse behavior again. When the mice injected with bombesin-saporin were exposed to things that caused itching, they didn't scratch. An appropriate dose

of the neurotoxin caused the mice to scratch 80 percent less and, in some cases, eliminated scratching altogether.

Further tests on the mice showed that other neurologic functions, such as motor control, were not affected when GRPR-expressing neurons were destroyed.

But, as with the mice without GRPR, the pain response wasn't affected. "This finding has very important implications for therapy," says Chen, who also is an investigator at Washington University's Pain Center. "We've demonstrated that GRPR functions on specific neurons that are critical for itching, but not for pain."

The ability to separate pain sensation from itch suggests that it may be possible to treat itch with drugs that don't

The ability to separate pain sensation from itch suggests that it may be possible to treat itch with drugs that don't alter the pain response.

alter the pain response, and vice versa. That's important because pain can be an important protective cue that warns of danger, says Alex S. Evers, MD, the Henry E. Mallinckrodt Professor and head of the Department of Anesthesiology. "This means that potentially we can design agents that selectively block out the pruritic side effects of pain-killing drugs, particularly opiates," says Evers. "This could be important in allowing better analgesic therapy in a variety of situations from cancer pain to labor pain."

Itching is a common side effect of painkillers like morphine, and treatment options for itchy patients have been limited. But Chen's team already has decoupled

itching induced by opiates from pain control in mice.

"If we inject a GRPR inhibitor and morphine into the spinal cord in the mouse, the drug continues to have its analgesic effect, but the mice don't scratch," Chen says. "That provides still more evidence that analgesia and itching can be separated."

Many human patients with chronic pain receive spinal perfusions of opioid drugs to control their pain. Perhaps, Chen says, one day those patients may receive the opioid drug along with a second drug that inhibits GRPR so that they can enjoy the benefit of pain relief without the side effect of itching.

Chen is now working to characterize the itch-specific neuronal pathway. He's also studying GRPR-expressing neurons in the spinal cord, looking for other genes that may be related to the itch response. Meanwhile, he continues to keep an eye on his mice because, after all, you really can observe a lot just by watching.

SEE GRAPHIC NEXT PAGE

The traditional view

For centuries, itch and pain were presumed to be no more than different degrees of sensation — a belief based on assumptions that the central nervous system performs as a single conduit of generalized sensory information. Although this simple view no longer makes sense, making finer distinctions among complex neurochemical functions still pushes the limits of human understanding — and technology.

Pain

Itch/Pain

Itch

SCALE OF SENSATION

What's the difference between



The legendary satyr Marsyas suffered a painful fate for having challenged the god Apollo. Although Marsyas is bound to his doom, the universal reaction to pain is to withdraw. This aversion can affect attitudes toward pain research, too. Unlike itching and scratching, which sometimes amuse people, there is often a visceral distaste for pain studies that are intended to help alleviate suffering.



PAIN SENSATION

- Withdrawal reflex
- Sensed within the body and in the skin
- Pain suppresses itchiness
- Pain-control drugs can have an unfortunate side effect: *itching*

Withdrawal



Fire



ITCH SENSATION

- Scratch reflex
- Sensation of the skin
- Scratching can cause pain
- Two itch types: histamine-dependent and not
- Pain-control drugs cause itching that cannot be controlled with an antihistamine

ITCH



Poison ivy



Perhaps the most famous chronic itch plagued Napoleon Bonaparte. The body's response to an itch is to scratch, but scratching itself can cause tissue damage. In some serious cases, itch sufferers have scratched through to the underlying bone.

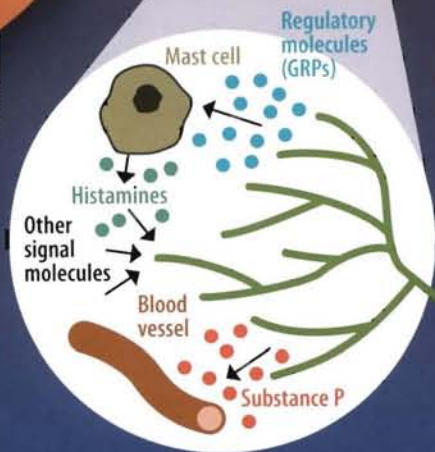
Developing a new view

The complexity of these sensory functions is revealed in the research of Zhou-Feng Chen, PhD, and colleagues. They have identified neurons that express receptors of regulatory molecules called GRPRs. In a mouse model, inhibiting or destroying these neurons appears to limit scratching, without dampening the withdrawal response to pain. Chen calls it "a very striking and unexpected result, because it suggests there is an itch-specific neuronal pathway in the spinal cord." Controlling this mechanism in humans could mean better pain control without the common side-effect of itching.

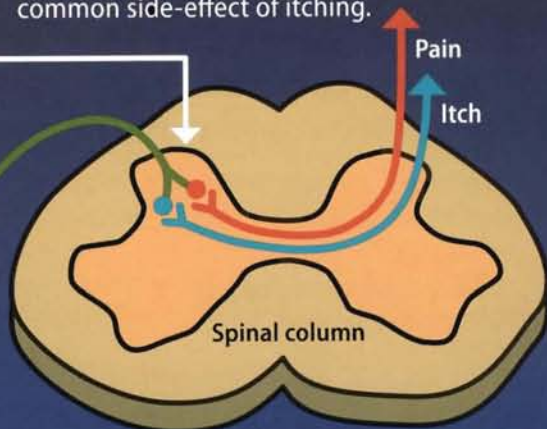
An itch relay: GRP receptor-expressing neurons (dark spots) within the spine

ITCH INTERACTIONS

Cellular communication within the skin



Relay station for sensory information: Dorsal root ganglion neuron





Critical differences count

A highly efficient — and effective — method for finding disease-related genes takes a shortcut via complex math

BY CAROLINE ARBANAS

Photo above, from left: Todd E. Druley, MD, PhD, Robi D. Mitra, PhD, and Francesco Vallania

A major motivation behind the \$3 billion project to decode the human genome was that it would enable scientists to sift through the sequence of letters that make up DNA to find common changes that predispose individuals to common diseases, such as cancer, diabetes or Alzheimer's.

But this first step toward personalized genomic medicine has turned out to be far more complex than expected.

Many genetic studies have compared common variations in the DNA of healthy people and sick patients, finding dozens of changes linked to diseases. But variations identified to date account for only a small percentage — typically 1 percent to 3 percent — of overall genetic risk for any particular disease.

That disappointment has led a growing number of scientists to suspect that rare genetic variants lie at the root of many common diseases. But short of sequencing the complete genomes of many thousands of individuals — a highly expensive and time-consuming task even with the latest DNA sequencing technology — no reliable method exists to identify rare variants or interpret their influence on disease.

"There's intense interest in rare variants right now," says pediatric oncologist Todd E. Druley, MD, PhD. "We couldn't wait until whole-genome sequencing became cost effective before we started our search."

The urgency hits home every time Druley has to tell parents their child has cancer. "Of course, the first thing parents want to know is whether their child will die. Then, invariably, they ask: 'Why did this happen to my child?'"

Not knowing the answer was the driving force behind Druley's efforts to find a way to search for rare variants. Toward that end, he teamed with Robi D. Mitra, PhD, assistant professor of genetics, who specializes in the development of experimental and computational tools that allow biologists to collect large volumes of genetic data.

"We think children with cancer are likely to have a unique collection of rare, inherited DNA variations that predispose them to their disease or to difficulties metabolizing the medications used to treat cancer," Mitra says. "Rare variants likely contribute to disease in adults, too, but until now, we haven't even had a way to investigate the link."

With funding from the Children's Discovery Institute, the team developed a way to find and quantify all the inherited rare genetic variants in a complete set of human genes. Their method is fast and inexpensive — and incredibly accurate, they reported in the April 2009 issue of *Nature Methods*.

The approach, which combines next-generation DNA sequencing technology with a computer program the research team developed, has attracted the attention of other scientists. The team now is working with the Children's Oncology Group, the global clinical trials cooperative, to identify rare variants in pediatric cancer patients with an aggressive form of leukemia.

$$Q_{j,d,s}^n(E) = 2^{-n_{j,d,s}} D(P_{j,d,s} \| Q_{j,d,s})$$

Adapting Sanov's theorem resulted in a more efficient variation-finder.

Doing the math

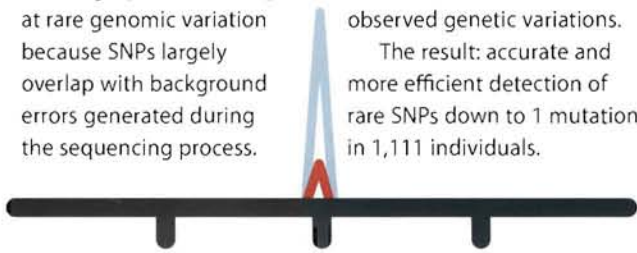
The question was how to tell an unusual gene from a technical glitch.

Researchers sought to determine variations that altered a single letter in the genetic code (A, C, G or T), called single nucleotide polymorphisms (SNPs). This problem becomes really challenging when looking at rare genomic variation because SNPs largely overlap with background errors generated during the sequencing process.

In order to distinguish a real SNP from sequencing noise, the research team developed a novel algorithm based on an application of Sanov's theorem, which was borrowed from the field of information theory.

An added mathematical model of known error rates aided comparisons with the observed genetic variations.

The result: accurate and more efficient detection of rare SNPs down to 1 mutation in 1,111 individuals.



SNPs (red) align with expected errors (blue) in this detail of a larger graph.

The bulk of the 3 billion pairs of chemical bases that make up DNA — represented by the letters A, T, C and G — are identical from one person to the next. But the exact order of the letters varies, often at a single location, in some 10 million common spots in the genome. These variations are what make each individual unique.

Each person also has about 300,000 rare genetic alterations buried within the genome. These variations mean nothing by themselves; it's only in the context of a large group that scientists can identify their links to a particular disease.

To find individual DNA samples to search for rare variants, Druley and Mitra turned to F. Sessions Cole, MD, the Park J. White MD Professor of Pediatrics and director of the Division of Newborn Medicine, who provided his collection of thousands of blood samples collected from the heels of newborns.

The researchers pooled the DNA of 1,111 newborns and targeted four genes. To ensure accurate results, they created thousands of copies of the four genes and sequenced them many times to identify the full spectrum of genetic variation.

The genes of interest included surfactant protein B, which Cole discovered in 1993 and linked to respiratory distress syndrome in infants. Cole had painstakingly sequenced the gene in all 1,111 individuals with traditional sequencing methods; Mitra and Druley used the gene as a control.

"We wondered whether we would find the same variants at the same frequencies in our pooled sample that Dr. Cole had already identified," Mitra says.

They also looked for rare variants in two genes important in cancer — p53 and APC — as well as in beta actin. None of these three genes had been sequenced in the 1,111 individuals.

In all, the team sifted through a haystack of 4.5 billion DNA bases. They found 64 variants in the four genes, nearly two-thirds of which were identified in less than 1 percent of the individuals, making them rare. These included four variants that had not been previously identified. Three of them occurred in the two cancer genes.

The computer algorithm, developed in collaboration with graduate student Francesco Vallania, accurately distinguished between rare variants and sequencing errors most of the time. "This is crucial because rare variants can easily look like sequencing errors," Mitra says. "How do you tell the difference? The algorithm we developed could do that."

The researchers accurately recapitulated all of Cole's data, finding variants at the predicted frequencies in the surfactant protein B gene. They also went back to verify the frequencies of variants in the other three genes. In all, they accurately identified all the rare variants in the pooled sample. They also identified sequencing errors as mistakes 99.8 percent of the time. Overall, the algorithm was 96 percent accurate.

With the new method, the sequencing that took Cole 2.5 years at a cost of \$200,000 was completed in just four months for \$6,000.

"This provides proof of principle," Druley says. "We're now testing the approach in children with aggressive leukemia and in healthy children to see whether we can find rare variants linked to the disease."

Ideally, the team hopes to identify rare variants linked to prognosis that could be evaluated in newly diagnosed patients. These variants may tell doctors which patients need aggressive therapy or which treatment works best in

a particular patient.

Rare genes, found faster

FULL-GENOME SEQUENCE	COMPARISON METHOD
2.5 years	4 months
\$200,000	\$6,000

Since the original publication, they have expanded their approach by adding a DNA barcode onto each individual's contribution to the pooled

DNA sample. This enables them to trace rare variants back to individual patients, which was not previously possible.

The investigators also are collaborating with other Washington University researchers by using the method to find rare variants in other complex diseases: newborns with lung disease, children with clubfoot, brain tumors or sickle cell disease, adults with heart failure and lung disease.

"Ultimately, we think we'll be able to use this simple method to find important genetic variations," Mitra says. "Lots of people have done genetic studies and have come up empty-handed. They're anxious to get at rare variants, and we think this method will get us there, not just for cancer but for many important diseases." □

SAFER passage

Surgeons collaborate on a device that offers less pain and faster recovery for pituitary surgery patients.

BY GWEN ERICSON

Richard A. Chole, MD, PhD, was in his home workshop, and the sparks were flying. Chole is an ear, nose and throat specialist and surgeon. But on this day he was grinding away at a short length of stainless steel, trying to shape the hard metal

into a gentle curve.

His intention was to create a surgical instrument for removing tumors near the brain.

Chole often teams up with neurosurgeons Ralph G. Dacey Jr., MD, and Michael R. Chicoine, MD, on pituitary tumor surgeries. Dacey sometimes mentioned that he would like a better

surgical retractor, one that would give him a wider, clearer view of the pituitary and surrounding areas.

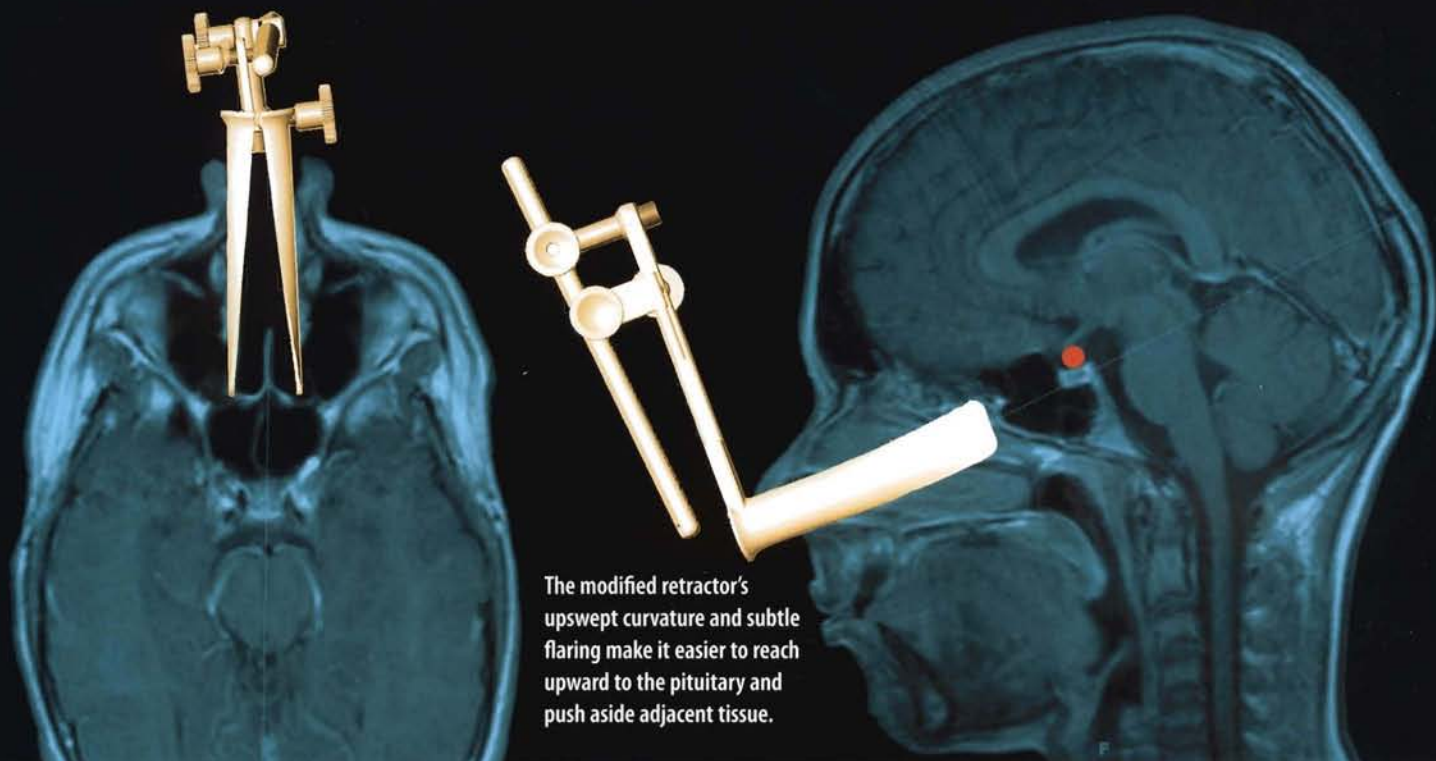
The two discussed what kind of instrument would fill the bill; they envisioned a retractor that would fit through a patient's nostril and hold aside tissues to help expose the pituitary gland lying deep inside the head. Chole's long experience with rebuilding old cars and other metalwork meant he could go to his shop and put together prototypes. Together, the two surgeons tweaked the design until they had what they considered an optimal pituitary retractor.

Chole and Dacey are good friends and joke about their respective importance in the process: "He likes to call it the Chole-Dacey pituitary retractor, but I call it the Dacey-Chole retractor," Dacey says, smiling. There's no argument about the quality of their invention, though. Both men say that the instrument has significant advantages over previous retractors. "We use it for most of the pituitary operations we do now," Chole says.



RICHARD A. GIBBLE, MD, PhD

Ralph G. Dacey Jr., MD, assisted by scrub technician Tinika Noldin, uses an endoscope to examine a pituitary tumor. On the monitor: a pituitary gland.



The modified retractor's upswept curvature and subtle flaring make it easier to reach upward to the pituitary and push aside adjacent tissue.

Even though brain surgeons perform pituitary surgery, the pituitary gland isn't really part of the brain. The pea-sized gland nestles in a protective bone cavity in the center of the head, directly beneath the brain. That puts it right next to critical arteries, nerves and brain regions, making pituitary surgery a very delicate operation indeed.

By far, the most common reason for pituitary surgery is to remove benign tumors called pituitary adenomas, which account for about 15 percent of brain tumors. If these grow large enough, they can cause headaches and dizziness or press on the optic nerves and lead to vision problems.

The pituitary is a hormonal jack-of-all-trades, secreting hormones that help regulate growth, blood pressure, reproductive functions, energy metabolism, fluid balance and body temperature. Pituitary adenomas can increase or decrease pituitary hormone production, leading to disorders like Cushing's syndrome, which is characterized by weight gain, high blood pressure and other health issues, gigantism, enlarged thyroid, inappropriate milk production and many others.

During pituitary tumor surgery, doctors have to take care to avoid injury to the carotid arteries running on either side of the pituitary and to the membrane covering the brain, which is directly behind the pituitary. Damaging the healthy portions of the pituitary during surgery could harm hormone production.

The bone cradling the pituitary sits right at the back of one of the nasal sinuses. So most of

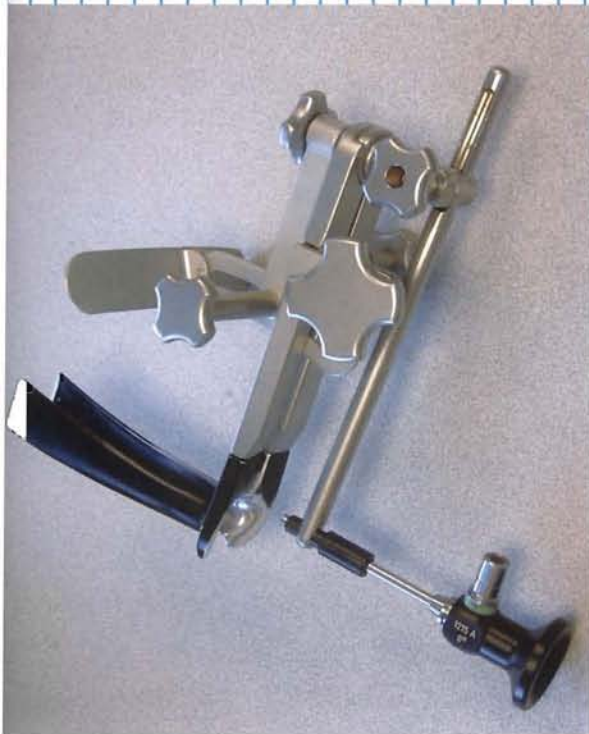
the time, surgeons can reach pituitary tumors by going through these sinuses instead of opening the skull and moving aside brain tissue.

For this kind of pituitary tumor operation, Chole and Dacey divide tasks. Chole starts the procedure by cutting through or removing bone and cartilage structures within the nasal sinuses to expose the bone covering the pituitary. Then Dacey goes in to excise the tumor.

Until recently, it was routine to get to pituitary tumors through an under-the-lip, or sublabial, approach. That involves pulling up the upper lip and making incisions under it to get to the sinus cavities.

Unfortunately, after such operations, patients might have lip swelling, as well as lingering numbness of the upper front teeth and lip. Sometimes patients' dentures don't fit well after the surgery and have to be remade. Packing the area with absorbent materials to prevent bleeding and fluid leakage often causes face and head pain during the recovery period.

To alleviate those problems, Chole and Dacey started performing the operation by entering the nasal cavity through a nostril and then going into the sinus cavities at the back of the nasal cavity. At times, neurosurgeons perform this surgery without a retractor, but many situations call for use of the instrument. Unfortunately, he found that available retractors weren't all that practical for doing this procedure through a nostril.



The main component of pituitary retractors is something that looks like a metal tube, about three to four inches long, split lengthwise; the halves of this tube are called blades. Attached to one end of the blades at a right angle are handles that allow surgeons to manipulate the instrument and to spread the two blades apart. The blades hold tissues out of the way and give surgeons a clear pathway to insert implements for cutting out the tumors.

“We started doing through-the-nose surgery with existing instruments,” Chole says. “But we found they didn’t angle correctly and the size was wrong. We could get by most of the time, but the view of the pituitary wasn’t as good as we wanted.”

So, in his home workshop, Chole made new blades for one of the standard retractors. These new blades had an upswept curvature at the end and a subtle flaring that made it easier for the surgeons to reach upward to the pituitary and push aside adjacent tissue. Chole also made the blades small enough to fit through a nostril.

That patched-together instrument was better, but the surgeons found a few more ways to improve the design. Working with instrument manufacturing company Anspach, Chole and Dacey have developed a final product, a stainless steel pituitary retractor with aluminum blades in three sizes suitable for children and small and large adults. The company will market the device.

Their completed retractor design is unique in allowing the blades to move in two ways: opening in parallel or opening at an acute angle. It also has a bar that rests on the patient’s forehead to stabilize the instrument.

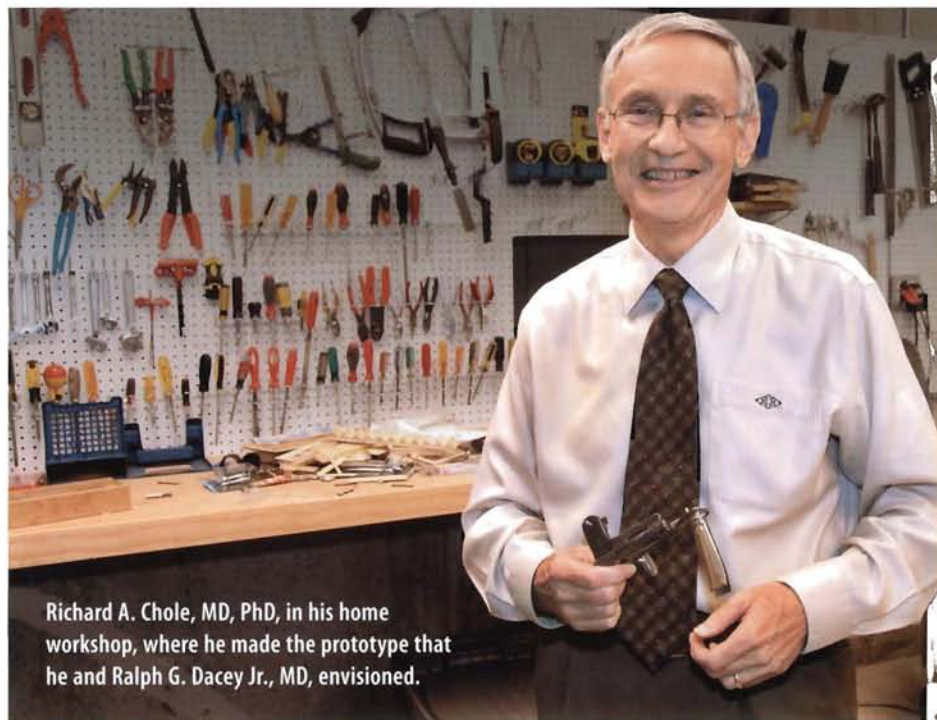
The retractor can grip on to an endoscope, a lighted tube with a wide-angle lens. The endoscope can be fed through the retractor and back to the area of the tumor. But it also can be moved aside so it doesn’t get in the way of the surgical instruments needed to take out the tumor.

“Because the retractor can hold an endoscope, that frees a surgeon from having to hold it,” Dacey says. “The retractor also makes it easier to go back and forth between using an endoscope and using an operative microscope to see the tumor. It’s also very good that the retractor is adjustable to allow us to deal with an individual patient’s anatomy.”

Patients are likely to be pleased at the chance for pituitary surgery with fewer complications and no external stitches or scarring. Chole says one patient was surprised when he awoke from anesthesia after a recent operation.

“He felt so good,” Chole says, “that he accused us of not doing the surgery at all.” □

The completed device — in three sizes suitable for children and small and large adults — will be marketed.



Richard A. Chole, MD, PhD, in his home workshop, where he made the prototype that he and Ralph G. Dacey Jr., MD, envisioned.

viewpoint

The Ochieng brothers wanted nothing more than to be physicians. Little did they realize that their dedication to giving back would bring them to the attention of the world with the making of an extraordinary documentary.

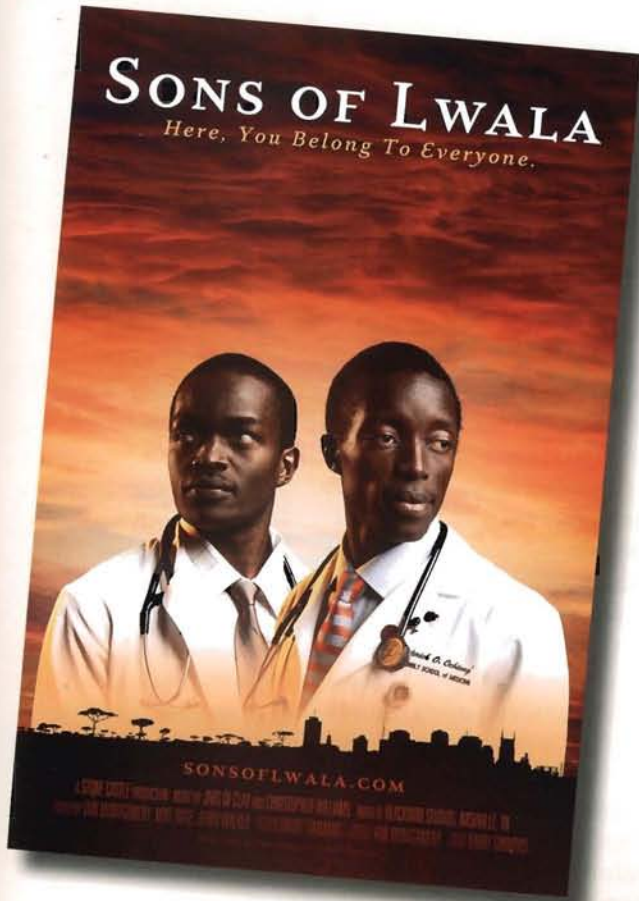
PLEDGE — *and* — PASSION



TWO BROTHERS FROM KENYA say they owe much to their home village of Lwala, a community that has supported them throughout their educational careers. In turn, the brothers wanted to give back to Lwala and, at the same time, honor their parents, Erastus and Margaret, who had both died from complications of HIV/AIDS. While studying in the United States, both Milton, an internal medicine resident at Barnes-Jewish Hospital and Washington University School of Medicine, and Fred, a medical student at Vanderbilt University, worked tirelessly to raise funds to build a health clinic in Lwala. The Ochieng Memorial Lwala Community Health Center opened in 2005; to date, more than 32,000 patients have been treated there. “For us,” says Milton, “it’s been realizing that every ounce of our energy — every extra second we spend answering an e-mail, making a phone call, or giving a talk somewhere — can translate to a life saved.”



Patients await treatment at the Ochieng Memorial Lwala Community Health Center.



St. Louis premiere event

The red carpet was unfurled on November 3 at the Missouri Botanical Garden to showcase "Sons of Lwala," a moving documentary that examines the challenges and triumphs of Milton Ochieng, his brother, Fred, their friends, family and fellow villagers in building a health clinic in their hometown of Lwala, Kenya. Washington University School of Medicine, Barnes-Jewish Hospital and others partnered to host the viewing.

learn more and view the trailer at: lwalacommunityalliance.org

The film, directed by Barry Simmons, chronicles the journey of the brothers, who left Lwala to attend college and then medical school in the United States, but never forgot their impoverished village. The Ochieng Memorial Lwala Community Health Center they founded is the first medical facility in Lwala, a village that has no electricity or running water.

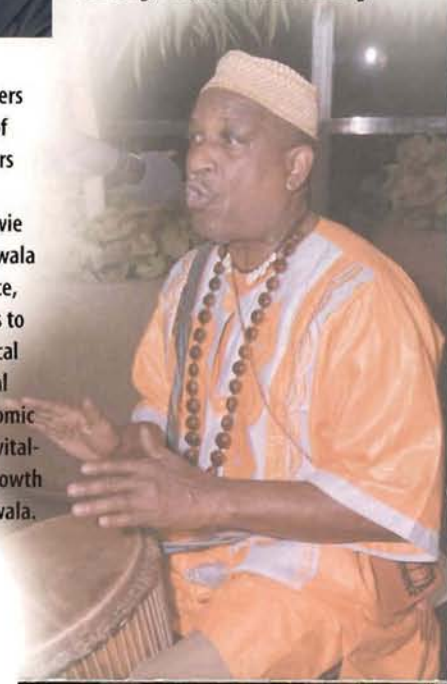
Proceeds from the sale of the documentary support the Lwala Community Alliance in sustaining existing programs and developing new initiatives, such as a maternity program and medical training. Overall, the Alliance works to empower the people of Lwala by providing jobs, training, education and improved health.



Far left: Kenneth S. Polonsky, MD, Busch Professor and head of the Department of Internal Medicine, left, and Melvin S. Blanchard, MD, associate professor and director of the department's residency program. Left: Kenyan ambassador Peter Ogego, center, with Fred Ochieng, left, and Milton Ochieng.



The Ochieng brothers pose with School of Medicine volunteers who raised nearly \$20,000 at the movie premiere for the Lwala Community Alliance, a group that works to advance the physical health, educational opportunity, economic freedom, cultural vitality and spiritual growth of the people of Lwala.



TIM PARKER

Financial tipping point

Scholarships help future medical professionals train to serve others

For many students, receiving a scholarship to Washington University School of Medicine represents a tipping point — that critical moment when a person arrives at a decision. A scholarship provides an extraordinary opportunity to train at an acclaimed institution alongside world-class scientists, physicians and health care professionals. It also represents faith in individuals and their futures.

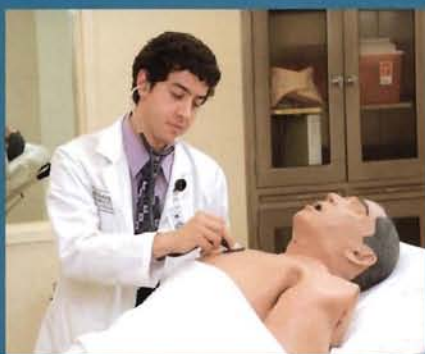
Students who enroll at Washington University School of Medicine come from diverse ethnic, geographic, economic and social backgrounds. They arrive on campus with distinct professional goals and career aspirations, while being bound together by a common desire to heal the patients that they will serve later in their careers. It is this unique balance between the dissimilar and similar that enriches the robust academic environment in which all students train as physicians, research scientists, physical therapists, occupational therapists and audiologists.

“I want to practice medicine in underserved and underdeveloped areas,” explains Joseph B. Song, a first-year medical student. “However, the cost of a medical education

presented a significant hindrance.” Song received a scholarship to attend Washington University and plans to pursue his goal to practice in underserved areas. He is getting a head start through his involvement in community outreach efforts offered at the School of Medicine.

Many students at Washington University have similar stories. More than 70 percent of students currently receive scholarship support during their academic career. Scholarships, in combination with student loans, enable many students to attend Washington University School of Medicine and fulfill their tremendous potential.

“Washington University has enjoyed wonderful success in its ability to recruit many outstanding students to the School of Medicine and our top-ranked Programs in Audiology and Communication Sciences, Physical Therapy and Occupational Therapy,” says Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of Washington University School of Medicine. “Despite our past success, we must continue to find ways to lessen the overwhelming financial burden challenging our students.”



THE COSTS

Direct interaction among teachers and students, rapidly advancing technologies, and specialized equipment and training all contribute to educational costs at the School of Medicine.



THE BENEFITS

Scholarship support provides a critical tipping point that helps make the School of Medicine both desirable and affordable for scholarship recipients like Jonathan Byrd, Catherine N. Le and Alton C. Williams.



Opening Doors to the Future

The Scholarship Initiative for Washington University School of Medicine

Q: How much student financial aid was provided in 2009–10?

A: More than \$15 million. Of this, scholarship support exceeded \$6 million.

Q: What is the average student debt?

A: Medical students graduate with an average debt exceeding \$100,000. Students in the Programs graduate with average debts ranging from \$85,000 to \$96,000.

Q: Who will receive my scholarship?

A: You may direct your scholarship to support students in medicine, audiology and communication sciences, occupational therapy or physical therapy.

Q: What are the giving options?

A: Giving options include an annual scholarship with a single gift or an endowed scholarship with a gift that is invested and provides income in

perpetuity. Giving methods include outright gifts of cash or securities, multi-year pledges, and planned gifts including estate and life-income gifts. Donors may name their annual or endowed scholarships to honor themselves, their family, a friend, a current or former faculty member, or in memory of a loved one.

For more information, please contact Pamela Buell at 314-935-9691.

Opening doors to the future

The need for scholarships is significant and expected to increase in the years ahead, which is why Washington University has launched Opening Doors to the Future: The Scholarship Initiative for Washington University. This five-year effort was formally launched on November 7, 2009, in conjunction with Founders Day and is designed to augment support for student scholarships.

The School of Medicine effort, led by co-chairs Gordon W. Philpott, MD 61, and Jay Kaiser, MD 72, has a goal of \$25 million and will be part of the university-wide goal of \$150 million. Through this effort, the School of Medicine has enlisted the help of alumni who have seen the tangible benefit of scholarships. As volunteers, they will assist the School in its efforts to boost scholarship support for students.

“The students who come to Washington University are of exceptional ability. Scholarship support is often the decisive factor that enables so many of these talented individuals to achieve their true potential,” observes Philpott.

“Scholarships allow students to pursue careers based on passion and not financial circumstances,” adds Kaiser. “The Scholarship Initiative will ensure that current and future students have the same opportunities that we had as students.”

Broadening the margin for excellence

The scholarships that are offered by Washington University School of Medicine comprise both endowment income and annual contributions from alumni, friends and organizations and have enabled the school to recruit the nation’s best students for more than a decade. Many of the other leading medical schools are quickly closing the gap. These institutions possess endowments that surpass that of Washington University School of Medicine, and they are able to offer larger scholarships to the most outstanding students.

The Scholarship Initiative will help to maintain and expand Washington University’s competitive edge as well

as keep professional education affordable for a greater percentage of students.

Annual scholarships will offer opportunities to students currently enrolled at the School of Medicine, while endowed scholarships provide support for students who will study here now and in future years. Regardless of the type of scholarship a donor chooses, the students will benefit.

The cost of excellence

During the 2009–10 academic year, the School of Medicine awarded more than \$15 million in financial aid to its students, including those enrolled in the Programs in Audiology and Communication Sciences, Physical Therapy and Occupational Therapy. Of this total, scholarship support exceeded \$6 million.

And yet, the burden of debt remains daunting for many of our students.

Approximately three quarters of medical students graduate with debt, and more than half of these students leave with debt exceeding \$100,000. Similarly, the average debt of students graduating from the Programs in Audiology and Communication Sciences, Physical Therapy and Occupational Therapy exceeds \$85,000 — a burden made more severe by an average professional salary of \$50,000.

Second-year medical student Lucy Zhang was at a tipping point. Faced with a choice of schools that were affordable but not a great fit and schools that were desirable but unaffordable, scholarships made the difference. “Having to take on less debt during my medical education eliminates many stresses and affords me the opportunity to explore various fields of medicine,” Zhang says.

Similarly, Washington University School of Medicine stands at a tipping point. The Scholarship Initiative can provide necessary resources that will enable the School of Medicine to sustain its momentum well into the future. “We have incredible students at Washington University School of Medicine who graduate with a significant debt load,” says Shapiro, “and we are compelled to alleviate this burden.”

Linda and Harvey Saligman

Taking research to the next level

Harvey Saligman, a St. Louis-area private investor, was in New York for a business trip when suddenly his hip began hurting. The pain was severe and persistent. "I was having great difficulty walking," Saligman says. "I had always prided myself that I could walk to almost anything, but I had to hire a car to get around because my leg hurt so badly."

Back home in St. Louis, Saligman was diagnosed with multiple myeloma, a type of blood cancer that originates in the bone marrow. He came to the School of Medicine for care under myeloma specialist Ravi Vij, MD, associate professor of medicine in the Division of Oncology.

Today, Saligman is in remission, but the experience inspired a new venture. He and his wife, Linda, talked about how they could make a difference to others facing myeloma.

"Having been associated with the university for more than 20 years, I know it has great physicians and researchers," Saligman says. He has served as a member of the Washington University Board of Trustees since 1986 and has been on the Washington University School of Medicine National Council since the mid-1990s.

"Linda and I saw that other places were better known for myeloma research, but we thought, why not here?" he says. "So with the goal of moving the university to the forefront in myeloma research, we set up a fund, and we hope it will attract additional support."

The Harvey and Linda Saligman Multiple Myeloma Research Fund will support basic and clinical research in the Division of Oncology to understand the causes of myeloma and to develop improved treatments and ultimately a cure for the disease.

"We are at a critical point and ready to go from a local and regional center to a national myeloma center," says division director John F. DiPersio, MD, PhD, the Lewis T. and Rosalind B. Apple Chair in Oncology. "We have a nationally and internationally recognized clinical program now further strengthened by strong basic science focused on the biology and genomics of myeloma. But to go to the next level, we need community philanthropic support; that will make the difference."

The division conducts a number of clinical studies to evaluate new myeloma treatments, many of which Vij heads. Washington University is a member of the Multiple Myeloma Research Consortium, an organization of 13 leading U.S. academic centers designed to speed development of new myeloma therapies. As a member, the medical school can provide patients access to new medications that wouldn't otherwise be available.

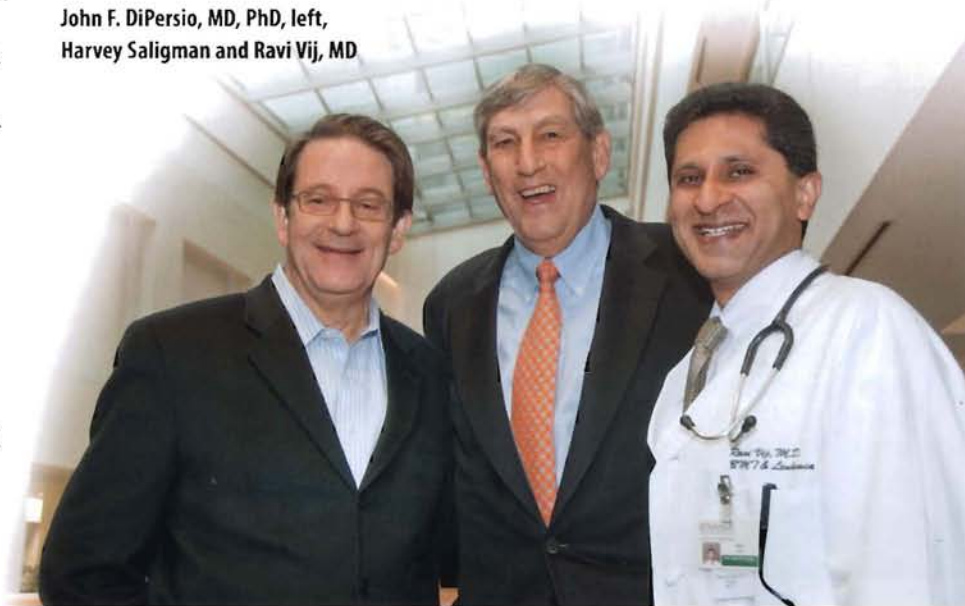
"Multiple myeloma is rapidly undergoing a therapeutic revolution,"

Vij says. "We have already made great strides in improving the life expectancy of myeloma patients and hope that we can someday come up with curative therapies."

At the basic-science level, three key research areas contribute to the investigation of myeloma at the School of Medicine. Researchers tap into the rise of genome science and the presence of the Genome Center to identify the genetic abnormalities that initiate the disease and contribute to its progression. They also study the effect of novel compounds in laboratory models of myeloma and conduct research in basic bone biology to find out how to prevent bone damage from myeloma. Other projects look into myeloma incidence and distribution to isolate the disease's risk factors.

Ultimately, generosity such as the Saligmans' will move this critical research forward, helping Washington University School of Medicine to quickly develop a leading program for multiple myeloma research.

**John F. DiPersio, MD, PhD, left,
Harvey Saligman and Ravi Vij, MD**





Where you belong!

REunion 2010

APRIL 29–MAY 1

- ◆ **REnew** friendships
- ◆ **REthink** medicine with CME opportunities
- ◆ **REconnect** at the fun Family Picnic
- ◆ **REdiscover** St. Louis
- ◆ **REvisit** the ever-changing medical campus



Reunion 2010 is right around the corner, with an exciting new schedule of events! You will have an opportunity to take CME courses offered by fellow alumni and current faculty members. There will be trips to the St. Louis Zoo, the Science Center and the Missouri Botanical Garden. You can enjoy a jog through Forest Park and take in a Cards game! And of course, you will have the opportunity to reconnect with classmates at the Friday night class parties and the Saturday night Alumni Banquet.

**Look for registration materials in January 2010,
or talk to a member of your Reunion Class Committee.**

The School of Medicine is aided in its Reunion planning by many loyal alumni. We are grateful to the following individuals who have volunteered to make the 2010 event a special weekend.

Robert Drews, MD 55
John Martin, MD 55
E. Robert Schultz, MD 55
Nathan Simon, MD 55
W. Yates Trotter, MD 55
Miles Whitener, MD 55
Floyd Bloom, MD 60
Paula Clayton, MD 60
Robert Edmonds, MD 60
David Rosenbaum, MD 60
Gustav Schonfeld, MD 60
Eli Shuter, MD 60
Gabriel Zatlín, MD 60
James Louie, MD 65
James Marks, MD 65

F. Thomas Ott, MD 65
Margaret Telfer, MD 65
Donald Anderson, MD 70
William Blair, MD 70
William Blattner, MD 70
Joann Data, MD 70
Marilyn Escobedo, MD 70
Francisco Garriga, MD 70
Scot Hickman, MD 70
Paul Mennes, MD 70
David Orbals, MD 70
William Shearer, MD 70
David Clifford, MD 75
Jo-Ellyn Ryall, MD 75
Robert Cooper, MD 80

James Fleshman, MD 80
Thomas Loeb, MD 80
Bert Mandelbaum, MD 80
William Morgan, MD 80
David Mutch, MD 80
Herluf Lund Jr., MD 85
Paul Miller, MD 90
Linda Peterson, MD 90
Martha Terry, MD 95
Po Wei Wang, MD 95
Michael Kappelman, MD 00
Michael Peelle, MD 00
Clare Pipkin, MD 00
Geoffrey Uj, MD 00
Erik Wallace, MD 00

~ For more details on MD Reunion 2010, visit: medicalalumni.wustl.edu ~

1940s

Morris Alex, MD 43

Alex is retired and resides in St. Louis MO. He enjoys writing and consulting for ALU Social Security. He is most proud of his children, grandchildren and great-grandchildren.

Sarah Arpe Malin, MD 48

Malin, who is retired from pediatrics, is an active member of hospice. Her late husband was **Jacob Malin, MD 48**. She is a member of the North Lake Tahoe Historical Society, as well as the American Association of University Women. She enjoys studying French and exercising daily. Malin resides in Kings Beach CA.

1950s

Lowell A. Gess, MD 51

Gess retired as a missionary with United Methodist Committee of Relief (UMCOR) as a member of the General Board of Global Ministries in 1975. He first traveled to Africa as an eye surgeon in 1953 with his wife, Ruth, a registered nurse, and their four children. He has remained involved with three eye hospitals in Sierra Leone, Nigeria and Zimbabwe for many years and

is thrilled that all of them are doing well with excellent staff. He had the opportunity to visit the Kissy United Methodist Eye Hospital in Sierra Leone in April and May of 2009, where it was rewarding to see the highly trained ophthalmologist at Kissy providing the best eye care in the least developed country of the world. Gess currently resides in Alexandria MN.

William Shieber, MD 53

Shieber has retired from surgery and lives in St. Louis MO with his wife, Horty. He plays golf in his spare time and enjoys being a docent at the Saint Louis Zoo.

1960s

Robert Hunt, MD 63

Hunt is retired. As he reflects on his surgical career, he is most proud of his development of a breast care diagnostic and treatment center. In his spare time, he likes to travel, play golf and read. He resides in Cape Girardeau MO with his wife, Sue.

Edgar C. Boedeker, MD 68

Boedeker left the University of Maryland and moved to Placitas NM where he is a professor of medicine at the University of New Mexico. He enjoys sailing when he visits Maryland. He is a member of the American Society for Microbiology.

1970s

Bela S. Denes, MD 73

After practicing urology for 23 years, Denes joined the pharmaceutical industry. Currently head of urology drug development for Spectrum Pharmaceuticals in Irvine CA, he also has provided urology services at clinics for the indigent in Orange County. He resides in Laguna Beach CA.

Robert Schmitz, MD 78

In 1985, Schmitz left medicine to pursue a career in real estate. He is married to Amy Csorba, MD, who practices family medicine. They have three children and reside in Durham NC.

1980s

Mark Boothby, MD 83

Boothby is a professor in the Department of Microbiology and Immunology at Vanderbilt University School of Medicine. In recent years, he has published many research articles. He also has stayed funded, taught students, and had lots of great times with his family. He resides in Nashville TN with his wife, Jin Chen, and their son.



2nd Century Award recipients: Gerald Medoff, MD 62, left, Doris Schnuck and Carl Frieden, PhD.

2nd Century Awards

The 2009 2nd Century Awards were presented at a dinner held at the Ritz-Carlton Hotel in Clayton MO on October 3. The awards, bestowed annually since 1991, mark Washington University School of Medicine's entry into its second century of leadership in patient care, teaching and research. The 2nd Century Award recognizes individuals whose long-term commitment and participation truly have made a difference, enabling the School of Medicine to look to the future with strength and confidence.

Janie Cox, MD 83

Cox recently retired so that she can spend more time with her children and volunteer in their schools. She loves her time with her family; they often go hiking and camping. Cox resides in Portland OR.

Eric Stevens, MD 86

Stevens is a member of a 12-person pulmonary, critical care and sleep medicine group in Loveland and Fort Collins CO. He is married and has two girls, ages 14 and 10. He enjoys cycling, rowing and playing bass guitar.

1990s

Peter M. Bridge, MD 93

Bridge is a private practice plastic surgeon. He spends his free time reading, traveling and swimming. He resides in Temple Terrace FL with his wife, Donna, and his two sons, Holden and Blake.

Lynne Champagne, MD 93

Champagne has a private practice in internal medicine. She works a reduced schedule in order to spend time with her young children. She lives in San Diego CA with her husband, Wilfred Kearsse.

Pablo Adler, MD 98

Adler is the director of education for the Department of Anesthesia at Christian Care Health System. He resides in Wilmington DE with his wife, Christina. He enjoys lifting weights, martial arts, traveling and seeing his kids grow.

2000s

Cynthia Chiu, OT 04

Chiu recently returned to St. Louis from Kansas City KS to be closer to family. She has two small children: Lucas, 2, and Peter, 1. She resides in Kirkwood MO.

Beth Schukman Daze, PT 06

Daze, who works at an outpatient physical therapy clinic in Raytown MO, recently was promoted to clinic manager. She enjoys her new position and looks forward to many years within the same company. She was married on May 9, 2009, and bought a house in Kansas City KS this past summer.

IN MEMORY

Marjorie S. Dunlap, NU 42

Dunlap died in Santa Rosa CA on July 20, 2009, at age 91. She was a professor and dean of nursing at the University of Hawaii and at the University of California—San Francisco, from which she retired in 1982.

Elmer LeVerl Barrett, MD 43

Barrett died at home on Aug. 27, 2009, at the age of 93. He liked to note that he practiced internal medicine in an era when doctors took phone calls and made house calls; his medical training also coincided with the introduction of antibiotics when, as he said, "people who used to die lived."

Phillip Comens, MD 51

Comens died on January 9, 2009, at his home in Sunset Hills MO. He was 85. An assistant professor of medicine at Washington University School of Medicine, he carried out extensive research in hypertension and cardiology before going into private practice. He also was a flight surgeon with the Missouri National Guard.

Clifton Brooks Sr., HS 52

Brooks died on May 8, 2009, in Norman OK at the Oklahoma Veterans Center. After graduating from Washington University School of Medicine, he attended UCLA, completing a masters degree in public health. His military service spanned 34 years and three branches of the military. He enjoyed his life and family, was an Eagle Scout and a Past Master of Lexington Lodge #72, and spent many hours researching family genealogy.

Rhys A. Williams, MD 53

Williams died on April 19, 2009, in San Antonio TX. He practiced general surgery for 32 years at the North Arkansas Medical Center, from which he retired in 1991. He and his wife, Bina, then moved to Aspen CO. He was a medical expert for the Social Security Administration until shortly before his death.

John G. Durham, DE 56

Durham died on Aug. 20, 2009, after a nine-year struggle with cancer. He was 78. An assistant professor of clinical dentistry at Washington University, he ran a private general dentistry practice for 50 years.

Marshal Glyn Maggard, HA 60

Maggard died on March 17, 2009. He worked as an assistant administrator at Hillcrest Medical Center in Tulsa OK, then later as CEO of Galesburg Cottage Hospital in Galesburg IL, until he retired in 1983.

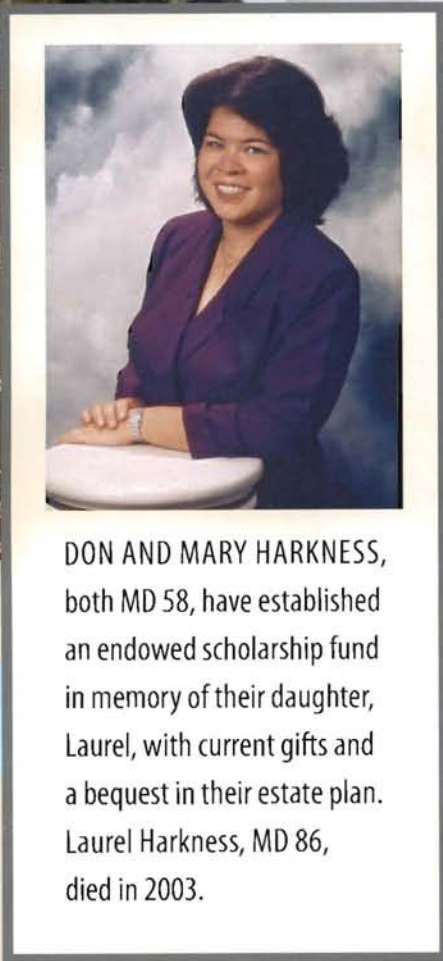
FACULTY

M. Kenton King, MD

King, dean of Washington University School of Medicine for nearly 25 years, died on Oct. 15, 2009, at his home in University City MO. He was 84. He was one of the longest-serving medical deans in the United States, as well as one of the most successful. Under his guidance, the School of Medicine became one of the foremost institutions of medical education in the world. Through his leadership and vision, in particular his instrumental role in recruiting new heads of all medical school departments, he shaped the course of the institution. He also championed a dramatic change in the composition of the student body, recruiting more minority and women students. During his tenure, the school's campus grew tremendously, and he worked to strengthen the amount and quality of research and to bolster alumni relations. He is survived by his wife, June Greenfield King, a 1951 graduate of the Washington University School of Nursing, four sons and eight grandchildren. He was preceded in death by a fifth son, Washington University alumnus and University City Police Sergeant Michael King, who was killed while on duty in 2008.

Lee N. Robins, PhD

Robins, professor emeritus of social science in psychiatry at Washington University School of Medicine, died peacefully at home on Sept. 25, 2009, following a long battle against cancer. She was 87. A world leader in psychiatric epidemiology research, she had worked in the Department of Psychiatry for more than 50 years. She is survived by husband Hugh Chaplin Jr., MD, an emeritus professor in the Departments of Medicine and Pathology and the former head of the Irene Walter Johnson Institute of Rehabilitation, four sons, eight grandchildren and two great-grandchildren.



DON AND MARY HARKNESS, both MD 58, have established an endowed scholarship fund in memory of their daughter, Laurel, with current gifts and a bequest in their estate plan. Laurel Harkness, MD 86, died in 2003.

Your School of Medicine

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- BioMed 21**
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- Specific Department/Division**

- Specific Program**

- Specific Physician/Researcher/Professor**

- Other**

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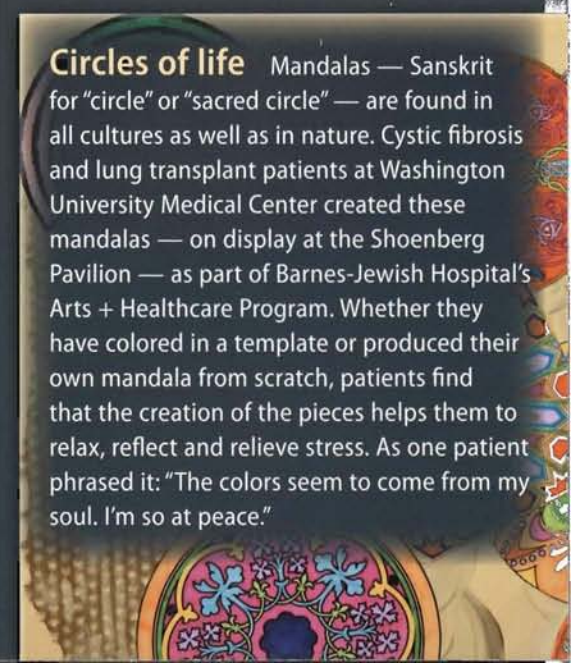
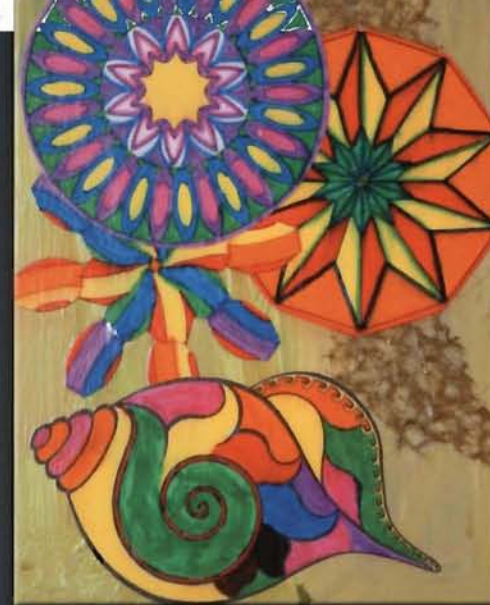
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Circles of life Mandalas — Sanskrit for “circle” or “sacred circle” — are found in all cultures as well as in nature. Cystic fibrosis and lung transplant patients at Washington University Medical Center created these mandalas — on display at the Shoenberg Pavilion — as part of Barnes-Jewish Hospital’s Arts + Healthcare Program. Whether they have colored in a template or produced their own mandala from scratch, patients find that the creation of the pieces helps them to relax, reflect and relieve stress. As one patient phrased it: “The colors seem to come from my soul. I’m so at peace.”

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Music to their ears Rehan A. Hasan, a third-year doctoral student in Washington University's Program in Physical Therapy, sings humorous songs he wrote about relationships at the student coffeehouse held in October 2009 at the Farrell Learning and Teaching Center. Students sang, played instruments and read poetry at the event, which was sponsored by the Student Arts Commission. The commission holds several coffeehouses each year.

Also performing at the event, from left, were second-year medical students Elizabeth A. Davlantes on vocals, Shaun R. Yockelson on bass guitar, Brandon B. Holmes on percussion, and Andrew Y. Lee on guitar.



Washington University in St. Louis
SCHOOL OF MEDICINE