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Outlook

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WINTER 2013-14



Washington
University in St. Louis
SCHOOL OF MEDICINE



**fresh
start**

toward a life
without sickle cells

What's COOKING

Guided by international guest chefs, occupational therapy students learn food traditions — planning meals, following recipes, wearing native dress and setting the table according to custom. Then, they enjoy the fruits of their labor. Students cooked food from Ireland, Asia, India, Poland, Argentina, Colombia and Ukraine. Leading the Nigerian cooking lab is Mary Adeniyi (back row, center), whose husband and co-instructor, Sydney, is a Nigerian native.



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Outlook

Washington University School of Medicine

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Encore!

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COVER Gabby Carter is among the earliest sickle cell patients in the country to be treated via an umbilical cord blood transplant from an unrelated donor using a reduced-intensity conditioning procedure refined by Shalini Shenoy, MBBS, MD. To learn more, turn to page 10.

PHOTO BY ROBERT BOSTON

2 Pulse

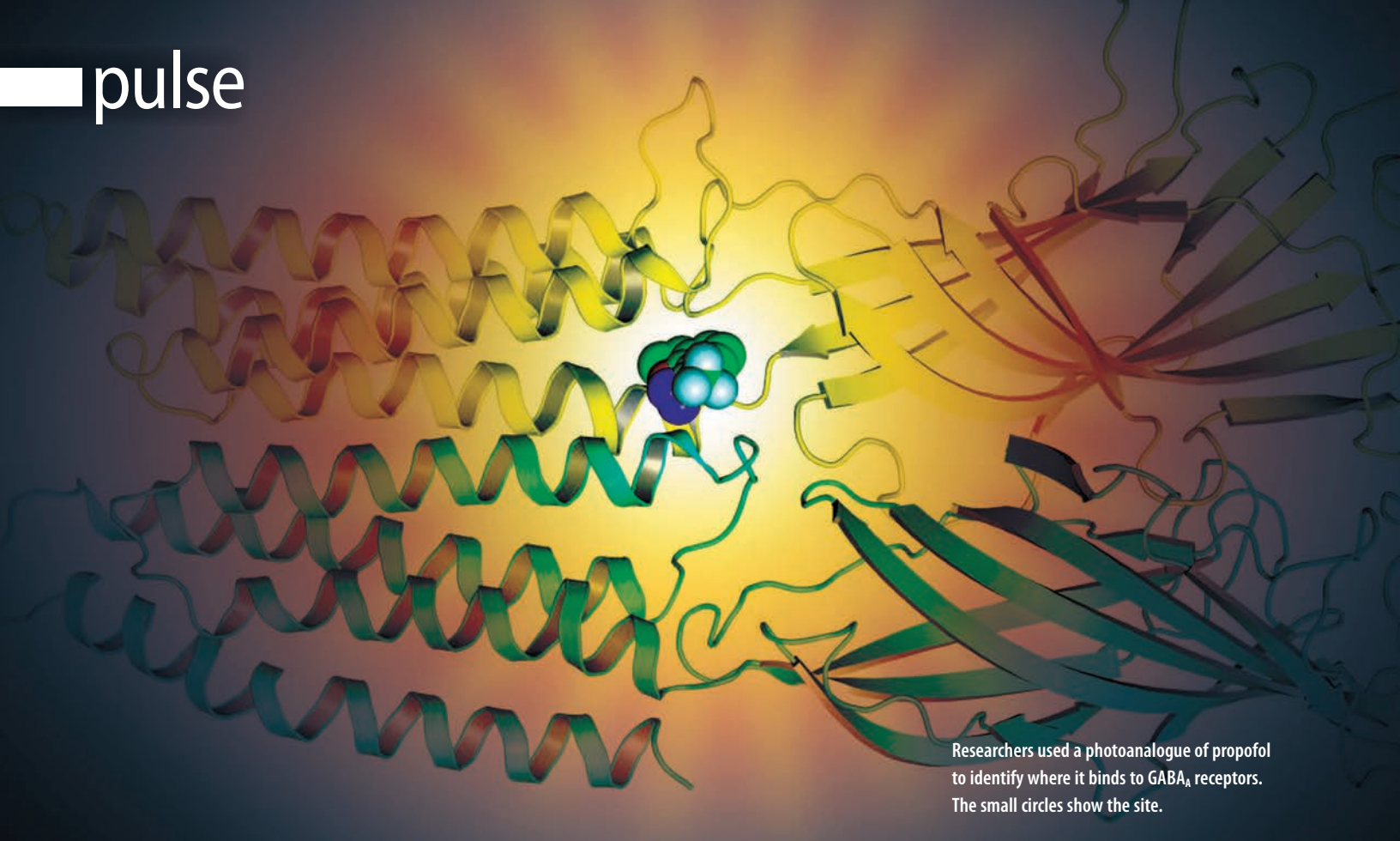
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Researchers used a photoanalogue of propofol to identify where it binds to GABA_A receptors. The small circles show the site.

Reducing risks

Propofol discovery may aid development of new anesthetics

Researchers at Washington University School of Medicine and Imperial College London have identified the site where the widely used anesthetic drug propofol binds to receptors in the brain to sedate patients during surgery.

Until now, it hadn't been clear how propofol connects with brain cells to induce anesthesia. The researchers believe the findings, reported online in the journal *Nature Chemical Biology*, eventually will lead to more effective anesthetics with fewer side effects.

"For many years, the mechanisms by which anesthetics act have remained elusive," explained co-principal investigator Alex S. Evers, MD, the Henry E. Mallinckrodt Professor and head of the Department of Anesthesiology. "We knew that intravenous anesthetics, like propofol, act on an important receptor on brain cells called the GABA_A receptor, but we didn't really know exactly where they bound to that receptor."

Short-acting propofol often is used in surgical patients. It wears off quickly and is less likely to cause nausea than many anesthetics. But the drug isn't risk-free. Potentially dangerous side effects include lowered blood pressure and interference with breathing.

To understand how propofol induces anesthesia during surgery, scientists have tried to identify its binding site within the gamma-aminobutyric acid type A (GABA_A) receptor on brain cells. Activating these receptors — with propofol, for example — depresses a cell's activity.

"For many years, the mechanisms by which anesthetics act have remained elusive."

— ALEX S. EVERS, MD

Evers' laboratory teamed up with a group at Imperial College led by Nicholas P. Franks, PhD, professor of biophysics and anaesthetics. The group had created a photoanalogue of propofol that behaves in precisely the same way as propofol and contains a labeling group that permanently attaches to its binding site on the GABA_A receptor when exposed to a specific wavelength of light.

In creating the analogue, it's as if the researchers put a tiny hook onto the molecule so that when it binds to the GABA_A receptor, it grabs onto the receptor and won't let go.

"The next step was to extract the receptor, cut it into pieces and identify the precise piece of the protein where the propofol analogue had attached to the receptor. This was the tricky step that the Evers group at Washington University had perfected," Franks said.

Evers and Franks believe this technique has implications for other types of drugs beyond anesthetics, such as psychiatric agents and anti-seizure drugs.

"By understanding precisely what the binding sites look like on the proteins that induce those potential problems, we eventually hope to design and select for drugs that have the benefits we want without dangerous side effects," Evers said.

Genetic errors found repeatedly in 12 of the major cancer types

Setting the stage for new diagnostic tools

Examining 12 major types of cancer, scientists at Washington University School of Medicine have identified 127 repeatedly mutated genes that appear to drive the development and progression of a range of tumors in the body. The discovery sets the stage for devising new diagnostic tools and more personalized cancer treatments.

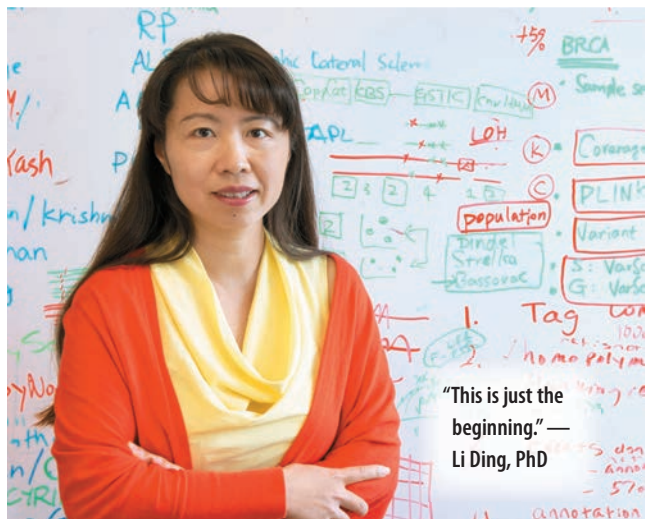
The research, published Oct. 17 in *Nature*, shows that some of the same genes commonly mutated in certain cancers also occur in seemingly unrelated tumors. For example, a gene mutated in 25 percent of leukemia cases in the study also was found in tumors of the breast, rectum, head and neck, kidney, lung, ovary and uterus.

Based on the findings, the researchers envision that a single test — one that surveys errors in a swath of cancer genes — eventually could become part of the standard diagnostic workup for most cancers. Results of such testing could guide treatment decisions for patients based on the unique genetic signatures of their tumors.

While earlier genome studies typically have focused on individual tumor types, the current research is among the early studies to look across many different types of cancer.

“This is just the beginning,” said senior author Li Ding, PhD, of The Genome Institute at Washington University. “Many oncologists and scientists have wondered whether it’s possible to come up with a complete list of cancer genes responsible for all human cancers. I think we’re getting closer to that.”

Researchers analyzed genes from 3,281 tumors — a collection of cancers of the breast, uterus, head and neck, colon and rectum, bladder, kidney, ovary, lung, brain and blood.



“This is just the beginning.” —
Li Ding, PhD

ROBERT BOSTON



ROBERT BOSTON

Model program Local youth celebrate the fifth anniversary of The SPOT (Supporting Positive Opportunities with Teens). Federal and Illinois health officials recently tapped The SPOT as a mentor for a similar center in East St. Louis, Ill. Aimed at 13- to 24-year-olds, The SPOT offers free testing for HIV and sexually transmitted diseases, health care and counseling, social support and more. School of Medicine clinicians and staff provide many of the services.

Breast cancer test earns FDA approval

A lab testing kit that estimates the risk of breast cancer returning after anti-hormone treatment has received U.S. Food and Drug Administration approval. The technology could help standardize breast cancer diagnosis, according to School of Medicine researchers, who led the development.

The research team, including collaborators at the University of North Carolina, the University of Utah and the BC Cancer Agency in Canada, designed a test that categorizes breast tumors into four main types by looking at the expression of 50 genes. Each subtype has a distinct genetic signature and requires a different treatment approach. These subtype data then are combined with a standard pathology variable to deliver a “risk of recurrence” score that predicts the likelihood of that patient’s disease returning within 10 years.

The test, Prosigna, removes some of the subjectivity that goes into breast cancer diagnosis, which still involves looking at cells under a microscope and, based on visual cues, determining how aggressive the tumor is likely to be.

“With this test, we are moving toward a standardized diagnosis based on the genetics of the tumor,” said Matthew J. Ellis, MB, BChir, PhD, test co-inventor and oncologist at Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.



Will the cancer return?



CLAUDIA BURRIS

Mindful approach Kevin Parks, third-year medical student and volunteer with the Young Scientist Program, recently shared the wonders of the brain with the general public at Brain Works. The event at The Ritz-Carlton, St. Louis, featured hands-on demonstrations, including the chance to hold a real human brain, and a presentation by Washington University neurosurgeons Eric Leuthardt, MD, and Albert Kim, MD, PhD. Among other topics, attendees learned about innovative therapies and technologies.

Evaluating red blood cell storage

Washington University School of Medicine has received a \$7.8 million grant to determine whether the length of time red blood cells (RBCs) are stored affects organ failure in critically ill children who receive RBC transfusions.

The five-year grant, from the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH), will

fund a trial involving more than 1,500 critically ill children who require RBC transfusions at St. Louis Children's Hospital and some 30 other medical centers in the U.S. and Canada. The trial will be one of the largest studies performed in pediatric critical care.

"We want to know whether fresh red cells can improve outcomes in critically ill children," said Philip Spinella, MD, associate professor of pediatrics at the School of Medicine and a principal investigator in the study.

"No studies have evaluated whether storing RBCs for more than a week affects clinical outcomes for these children."

The researchers will compare the risk of new or progressive multiple organ failure in two groups of critically ill children ages 3 days to 16 years randomly assigned to receive RBC transfusions as a course of treatment. One group will receive RBCs stored for a week or less, and the other will receive RBCs stored an estimated average of 21 days.

Generally, patients who require RBC transfusions receive cells stored anywhere from three to 42 days. The standard approach is to use those stored the longest first.



Trio of Wolff Professors honored in Department of Medicine

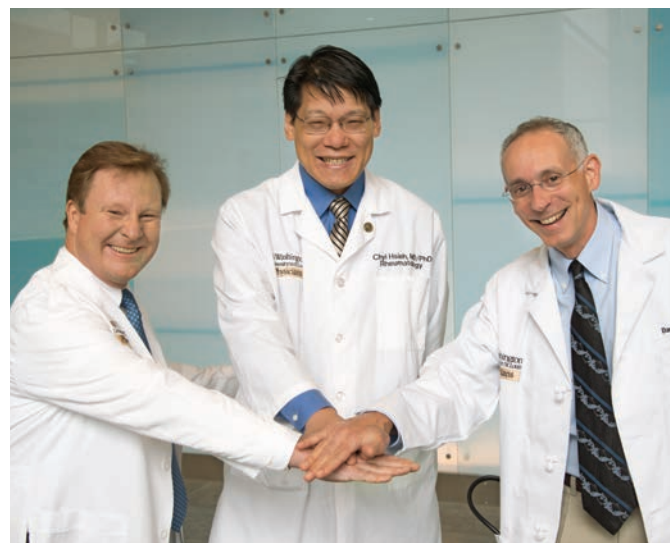
Three highly regarded faculty members in the Department of Medicine have been named Alan A. and Edith L. Wolff Professors in their fields. They are Daniel C. Brennan, MD, Chyi-Song Hsieh, MD, PhD, and Daniel S. Ory, MD.

A bequest by the late Edith L. Wolff to enable these and other professorships continues the legacy of support for medical research that characterized Edith L. Wolff's life and that of her husband, the late Alan A. Wolff.

Daniel C. Brennan, MD, is the Alan A. and Edith L. Wolff Professor of Renal Diseases. He is a professor of medicine and director of transplant nephrology at the School of Medicine. Brennan joined the faculty in 1993 as the first director of transplant nephrology. He is internationally known for his studies on infectious complications of kidney transplants, and his research has resulted in new anti-rejection strategies that have markedly improved kidney transplantation outcomes.

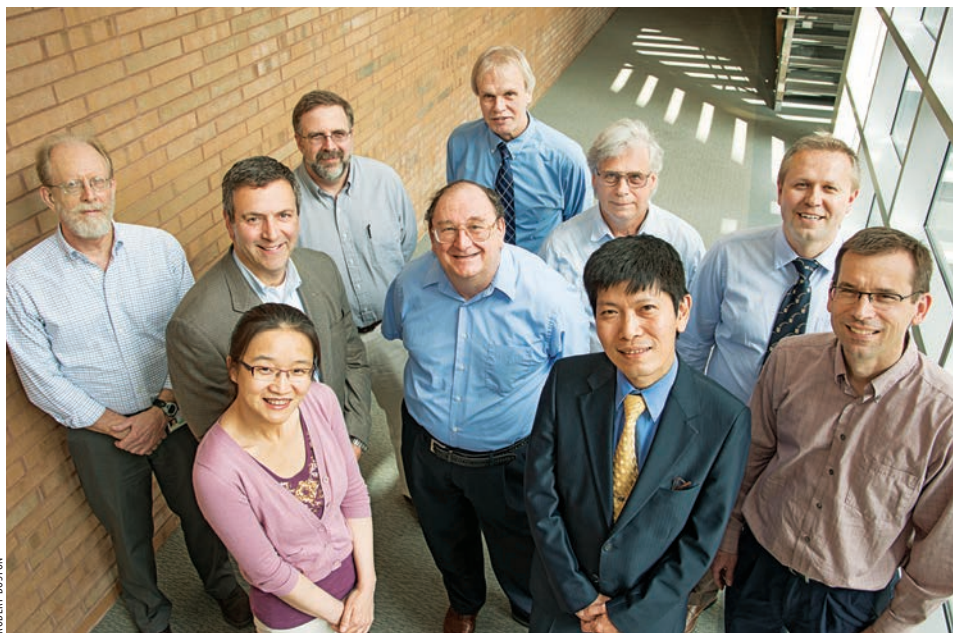
Chyi-Song Hsieh, MD, PhD, the Alan A. and Edith L. Wolff Professor of Rheumatology, is an associate professor of medicine and of pathology and immunology. Hsieh, who studies autoimmune diseases, joined the medical school in 2005 and has conducted groundbreaking research in basic immunology.

Daniel S. Ory, MD, the Alan A. and Edith L. Wolff Professor of Cardiology, is a professor of medicine and of cell biology and physiology. He is co-director of the BioMed 21 Diabetic Cardiovascular Disease Center and director of the Washington University metabolomics facility. He also is director of admissions for the Division of Biology and Biomedical Sciences. He joined the faculty in 1995.



ROBERT BOSTON

Daniel C. Brennan, MD, Chyi-Song Hsieh, MD, PhD, and Daniel S. Ory, MD



ROBERT BOSTON

Shown are Taylor Family Institute investigators: (back row, left to right) David Wozniak, PhD; David Reichert, PhD; Charles Zorumski, MD; Joe Henry Steinbach, PhD; (middle row) Alex Evers, MD; Douglas Covey, PhD; Gustav Akk, PhD; (front row) Ziwei Chen, PhD; Yuki Izumi, MD, PhD; and Steven Mennerick, PhD.

Taylor Institute launch

An Oct. 1 celebration marked the official launch of the Taylor Family Institute for Innovative Psychiatric Research. Dedicated to developing new and more effective therapies for psychiatric disorders, the institute was created with a \$20 million gift from Andy and Barbara Taylor and the Crawford Taylor Foundation, the charity of the entire Jack C. Taylor family. The institute, housed in the Department of Psychiatry, includes members from four School of Medicine departments. Research initially will focus on neurosteroids, naturally occurring chemicals in the brain involved in regulating cognition, emotion and motivation. For more information, visit taylorfamilyinstitute.wustl.edu.

USER-FRIENDLY DATABASE

Matching genes with potential therapies

A massive online database now matches thousands of genes linked to cancer and other diseases with drugs that target those genes. Some of the drugs are approved by the U.S. Food and Drug Administration, while others are in clinical trials or just entering the drug development pipeline.

The database was developed by identical twin brothers, Obi Griffith, PhD, research assistant professor of medicine, and Malachi Griffith, PhD, research instructor in genetics, whose interest in pairing drugs with genes is as much personal as it is scientific. Their mother died of breast cancer 17 years ago, weeks before their high school graduation.

"We wanted to create a comprehensive database that is user-friendly, something along the lines of a Google search engine for disease genes," explained Malachi Griffith. "As we move toward personalized medicine, there's a lot of interest in knowing whether drugs can target mutated genes in particular patients or in certain diseases, like breast or lung cancer. But there hasn't been an easy

way to find that information."

Details of the Drug Gene Interaction Database were reported online Oct. 13 in *Nature Methods*. The database also includes genes involved in Alzheimer's disease, heart disease, diabetes and many other illnesses. The Griffiths created the database with a team of scientists at The Genome Institute at Washington University.

The database is easy to search and geared toward researchers and physician-scientists who want to know whether errors in disease genes — identified through genome sequencing or other methods — potentially could be targeted with existing drug therapies. Additional genes included in the database could be the focus of future drug development efforts because they belong to classes of genes that are thought to make promising drug targets.

"Developing the database was a labor of love for the Griffiths," said senior author Richard K. Wilson, PhD, director of The Genome Institute. "There's an amazing depth to this resource, which will be invaluable to



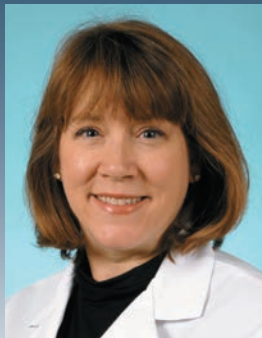
researchers working to design better treatment options for patients."

Wilson and his colleagues caution that the database is intended for research purposes and that it does not recommend treatments. The primary purpose of the database is to further clinical research aimed at treating diseases more effectively.

The free, publicly available database brings together information from 15 publicly available databases in the U.S., Canada, Europe and Asia. To access it, visit dgidb.genome.wustl.edu.



Michael M. Awad, MD, PhD



Valerie S. Ratts, MD

Educational leadership Michael M. Awad, MD, PhD, assistant professor of surgery, now is associate dean for medical student education and Valerie S. Ratts, MD, professor in obstetrics and gynecology, has been named associate dean for admissions. Awad will oversee the medical student curriculum (managing schedules, evaluations, assessment, course planning and the Career Counseling Office). Ratts will direct all aspects of medical school admissions, working to attract, recruit and enroll the best students.

Two elected to Institute of Medicine

Evan D. Kharasch, MD, PhD, and J. Evan Sadler, MD, PhD, have been elected to the Institute of Medicine of the National Academy of Sciences, one of the highest honors medical scientists in the U.S. can receive.

Kharasch and Sadler, both widely regarded physician-scientists at Washington University School of Medicine, are among 70 new members and 10 foreign associates whose elections to the Institute of Medicine recently were announced by the National Academy of Sciences.

Members are selected based on their professional achievements and commitment to service. As members, Kharasch and Sadler will devote a significant amount of volunteer time on committees engaged in a broad range of health-policy issues.

Kharasch, the Russell D. and Mary B. Shelden Professor of Anesthesiology and professor of biochemistry and molecular biophysics, is also the vice chancellor for research at Washington University.

Sadler is professor of medicine and of biochemistry and molecular biophysics and chief of the Division of Hematology at the School of Medicine.

NIH grants total \$26 million for leukemia research

Support for basic science, clinical trials

The National Cancer Institute, part of the National Institutes of Health (NIH), has awarded two major grants totaling \$26 million to leukemia researchers and physicians at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and the Washington University School of Medicine.

The funding helps establish the medical school as a premier center for innovative leukemia research, with a bench-to-bedside approach that has the potential to lead to novel therapies that improve survival and reduce treatment-related side effects.

The first award is a five-year, \$14.3 million Program Project Grant (PPG) in leukemia. The grant initially was funded at the medical school in 2003 and has been renewed

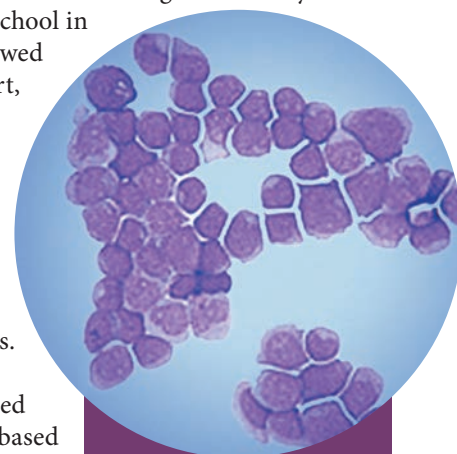
twice. With new support, the scientists aim to identify all the genetic changes underlying the development and progression of acute myeloid leukemia, the most common type of acute leukemia in adults. This information may lead to more personalized treatments for patients based on the unique genetic and molecular signatures of their leukemia cells.

The second award is a prestigious Specialized Program of Research Excellence (SPORE) grant in leukemia. The \$11.3 million, five-year award capitalizes on research advances at the medical school to bring new investigational treatments into clinical trials.

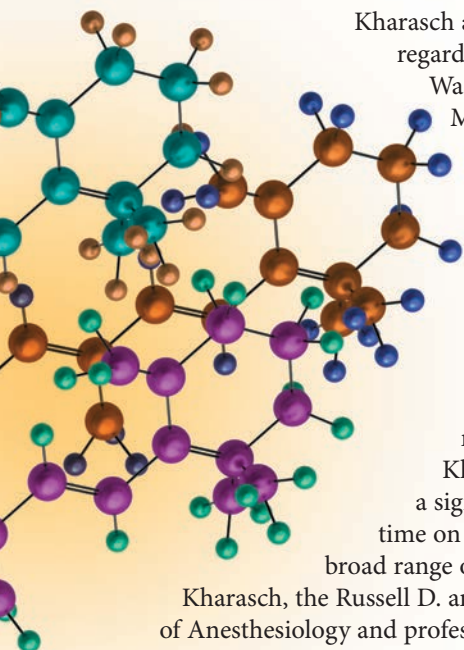
Timothy Ley, MD, the Lewis T. and Rosalind B. Apple Chair in Oncology, is principal investigator of the Program Project Grant; Daniel Link, MD, the Alan A. and Edith L. Wolff Distinguished Professor of Medicine, is principal investigator of the SPORE grant.

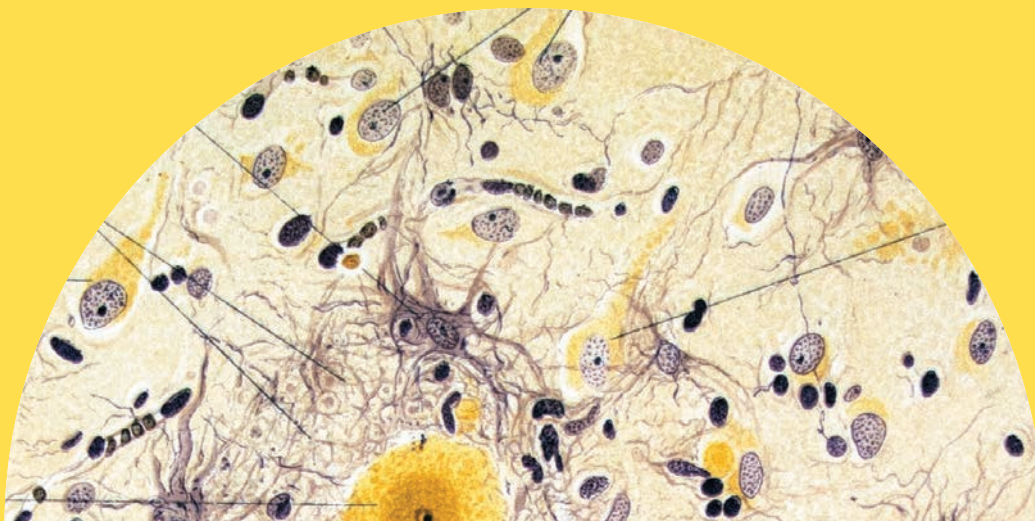
"There's important synergy between the two grants," said Ley. "The PPG focuses on basic research to generate ideas, concepts and technologies that can be evaluated in clinical trials via the SPORE grant."

As part of the research, Division of Oncology scientists will work closely with researchers at The Genome Institute to further explore the genetic basis of leukemia.



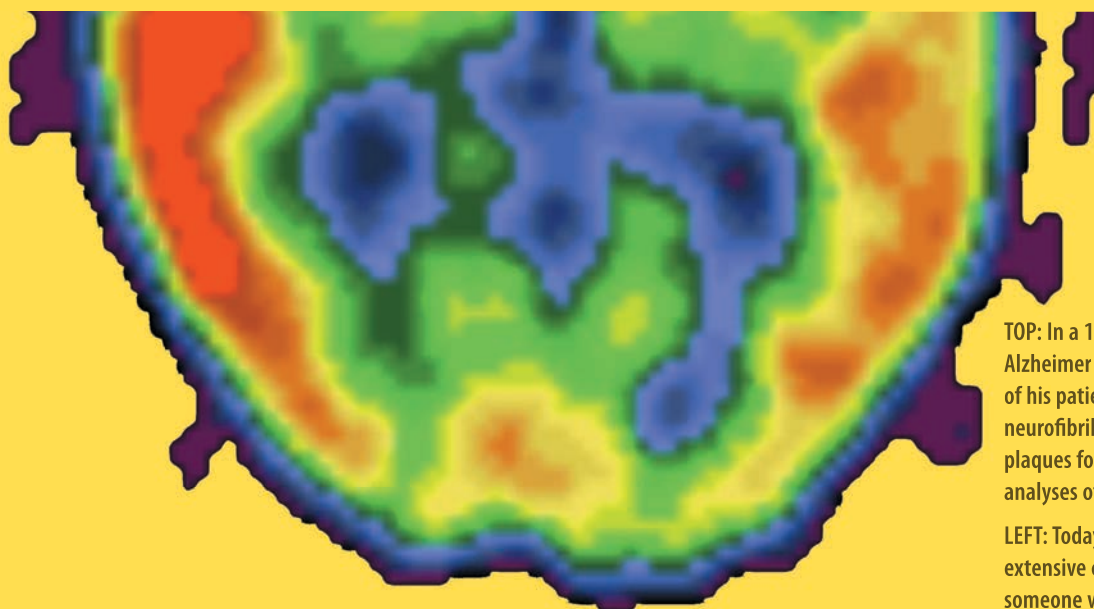
Investigating the genetic origins of acute myeloid leukemia





PREVENTING ALZHEIMER'S

Can it be done? A groundbreaking study aims to find out.



BY MICHAEL
C. PURDY

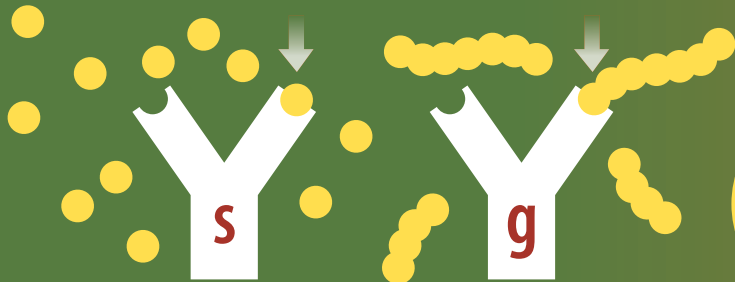
TOP: In a 1911 article, Alois Alzheimer described the symptoms of his patients and illustrated the neurofibrillary tangles and amyloid plaques found during post-mortem analyses of their brains.

LEFT: Today, scanning confirms extensive changes in the brain of someone with Alzheimer's disease.

ALZHEIMER'S DISEASE TRIAL

Before damage is done

Two drugs targeting the protein amyloid beta ($A\beta$) could stop it from damaging the brain before any symptoms occur. As visualized below, an antibody called solanezumab (s) removes soluble molecules of $A\beta$ (yellow). Another antibody, gantenerumab (g), binds to and removes larger aggregates of $A\beta$.



Is it possible to curtail Alzheimer's early stages?



~20–30 YRS PRIOR

Cerebrospinal fluid analysis reveals abnormal levels of precursor proteins, an early warning sign

~15 YRS PRIOR

Neurofibrillary tangles (gray) have already gnarled some tissue; amyloid beta protein (yellow) deposits in clumps

MORE THAN A CENTURY AGO,

Alois Alzheimer, a German psychiatrist, first identified the neurodegenerative brain condition that came to be known as Alzheimer's disease.

Finding ways to diagnose and treat this devastating disease has frustrated scientists and clinicians ever since.

Now the long and hard-fought campaign against Alzheimer's has reached a potentially significant milestone: the launch of the first clinical trials to test whether new drug treatments given before dementia can prevent the disease.

The trial is being conducted by the Dominantly Inherited Alzheimer's Network Trial Unit (DIAN-TU), led by principal investigator Randall J. Bateman, MD, the Charles F. and Joanne Knight Distinguished Professor of Neurology at Washington University School of Medicine.

Learn more about the registry:

www.DIANXR.org

Steps on the journey School of Medicine researchers have made many key contributions along the journey to the new DIAN-TU trial.

The late Leonard Berg, MD, the founding director of the university's Knight Alzheimer's Disease Research Center, and current director John C. Morris, MD, were among the first to assert and prove that Alzheimer's harms patients' brains for many years prior to dementia onset and memory loss.

Washington University scientists have led the quest for new treatments and for biological markers that can identify people who seem normal but whose brains are actively being damaged by presymptomatic Alzheimer's disease.

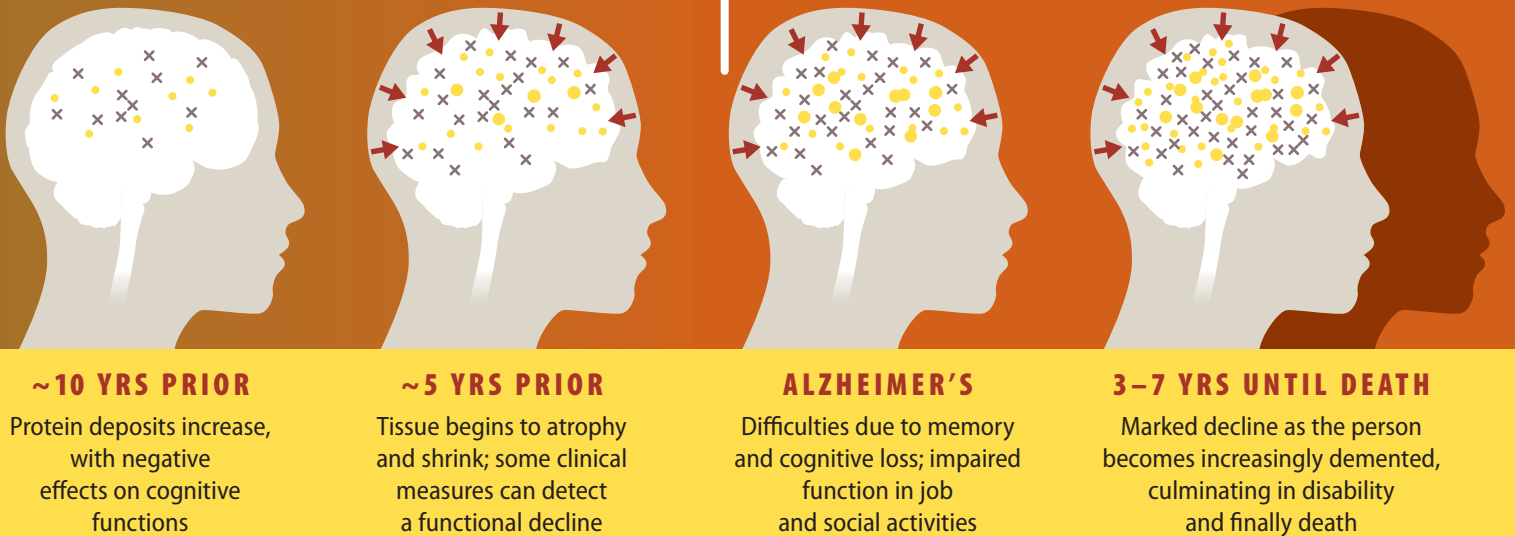
Researchers have characterized disease markers in cerebrospinal fluid and have tested neuroimaging techniques for detecting Alzheimer's, making it possible to diagnose the disease much earlier.

A long, slow descent Rare, inherited forms of Alzheimer's are particularly devastating — striking much earlier in life than sporadic forms of the disease — with symptoms becoming apparent in some mutation carriers in their 30s or 40s. Children who inherit one of the mutations typically show signs of Alzheimer's at about the same age as their parents.

To expand researchers' opportunities to work with these families, Morris founded the Dominantly Inherited Alzheimer's Network (DIAN) in 2008. This global network generated a pool of qualified volunteers and forged a research partnership determined to understand forms of Alzheimer's caused by genetic mutations.

With the help of DIAN family members, researchers created a detailed timeline of the brain's long, slow descent into Alzheimer's dementia, showing, for example, that brain plaques can be detected 15 years prior to symptoms. These plaques are made mostly of amyloid beta. This protein, which abnormally accumulates in the brain of people with Alzheimer's, is thought to play a role in brain cell damage and death.

Treatments at later stages have been unsuccessful



Starting the new trial With the support of these findings and other groundwork from the DIAN study, Bateman established the DIAN Trials Unit. Now, DIAN participants and others who have an inherited Alzheimer's mutation are undergoing the first trials of preclinical treatments that target amyloid beta. Many of these participants do not have any symptoms, but researchers know these patients will get Alzheimer's disease and approximately when they will get it.

"Trying to prevent Alzheimer's symptoms from occurring is a new strategy, but much of what we've learned in recent years about Alzheimer's and the brain has suggested that prevention has a significantly better chance of succeeding than treatment after cognitive impairment," said Morris, the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology.

The trial is testing two drug treatments designed to eliminate amyloid beta from the brain at different points in the plaque production process. Researchers plan to test additional treatments with different mechanisms of action in this and future trials. The treatments were nominated by the DIAN Pharma Consortium, composed of 11 pharmaceutical companies that have been advising researchers on the planning of the trial. From those nominations, the Alzheimer's researchers chose the trial drugs.

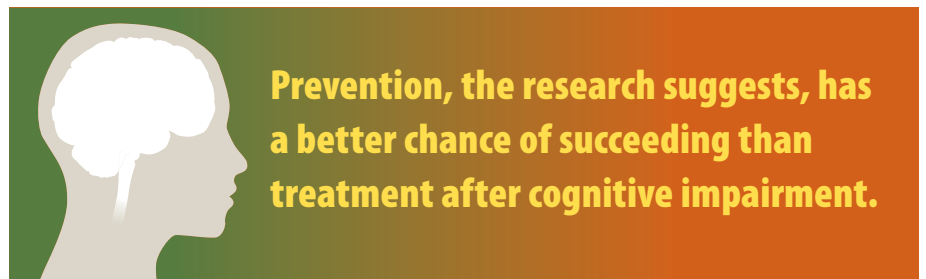
"We believe that the diverse portfolio of drugs and approaches of the DIAN-TU trial will accelerate the discovery of an effective treatment for Alzheimer's," Bateman said. "This trial is possible because of the outstanding support of multiple stakeholders, including patients and family members, pharmaceutical partners, the Alzheimer's Association, the National Institutes of Health, academic researchers and highly dedicated trial operations groups."

The trial is funded by a unique mix of private and public resources, including: major grants from the National Institutes of Health (NIH) and the Alzheimer's

Association; treatment donations and funding from the drugs' manufacturers Roche and Eli Lilly & Co.; donation of a new agent for imaging brain plaques, Amyvid, by Avid Radiopharmaceuticals Inc., a wholly owned subsidiary of Lilly; and donation by CogState of computerized cognitive skills tests to help assess function in participants.

Renewed hope This initial study involves 210 participants. Three of every four will receive active forms of trial drugs; the fourth will receive a placebo. Researchers will track biological markers of Alzheimer's in participants' cerebrospinal fluid and on brain scans, looking for any indicators that the disease process is slowing or stopping.

If successful, scientists plan to move directly into Phase III clinical trials to prove that Alzheimer's can be slowed



or stopped. The hope is that knowledge gained in the trials can be applied to the more common late-onset Alzheimer's.

Brent Whitney, 34, of Grove, Okla., is asymptomatic, but has an inherited form of Alzheimer's and is a DIAN participant. The lives of his grandmother and 10 of her 13 siblings were cut short by the Alzheimer's gene mutation, and the mutation continues to affect succeeding generations of the family.

"The start of this trial is a very exciting moment in Alzheimer's disease research, and it gives me renewed hope for a future without Alzheimer's," Whitney said. "I hope my grandchildren someday learn of this condition in history books, like I learned about polio." □



improving options

sickle solut

ROBERT BOSTON

for transplants cell ions

BY STEVE KOHLER

A reduced-intensity conditioning process — gentler than the harsh chemotherapies used in the past — will safely prepare Judah Wilks' body to accept a stem cell transplant for his sickle cell disease.

refining a safer, gentler process that promises a long-term fix for sickle cell disease



GABBY June 2012

IN JUNE OF 2012, 6-year-old Gabby Carter reached a watershed moment in her young life. Having lived with sickle cell disease and its debilitating effects since the time of her first medical crisis at 10 months of age, she arrived at transplant day.

Gabby needed more than 30 blood transfusions and made 50 trips to St. Louis Children's Hospital from her Cape Girardeau, Mo., home to manage her condition. Sickle cell disease (SCD) is marked by a host of symptoms, including sudden pain throughout the body. Although Gabby never suffered a stroke, many SCD patients do, and the threat is always present.

The transplant itself must have seemed eerily anticlimactic. Right there in her all-too-familiar hospital room, a bag of what appeared to be oddly colored blood hung next to her, and, under the direction of Shalini Shenoy, MBBS, MD, its contents flowed into Gabby's veins. No operating room, nary a scalpel, and the next day, Gabby was up and moving around.

If all went as planned, these donated cord blood stem cells would find their way to Gabby's bone marrow and begin producing normal, oxygen-carrying red blood cells, replacing her defective sickle cells.

Although the procedure was less than dramatic, Gabby's pre-conditioning to receive it was finely tuned. And the 18 months post-transplant have been a closely monitored "tightrope walk," according to Shenoy.

Today, Gabby's sickle cell disease (SCD) is gone — cured. Now, her mom, Debbie, says Gabby's a vibrant 7-year-old who has played in the snow, gone swimming and attends second grade with her classmates.



CAITLYN May 2013

fresh starts

first recipients of
unrelated cord blood
transplants using
reduced-intensity
conditioning



JUDAH October 2013

Gabby is among the earliest sickle cell patients in the country to be cured via an umbilical cord blood transplant from an unrelated donor using a reduced-intensity conditioning procedure refined at Washington University School of Medicine.

The novel procedure is remarkable for two primary reasons: It is much gentler on patients than earlier procedures; and it dramatically will expand an extremely limited donor pool.

Upping the odds

A renowned leader in pediatric stem cell transplantation, Shenoy is the Teresa J. Vietti, MD Scholar in Pediatrics and directs the Pediatric Bone Marrow Transplant Program at St. Louis Children's Hospital and the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.

Shenoy is leading a 20-center pilot study focused on reduced-intensity cord blood transplants from unrelated donors. The study has a safety restriction: three patients must have successful transplants before three more can be performed. Following the completion of nine patients, Shenoy is hopeful that the pilot study will extend to a fully funded national trial by the end of 2014.

Since Gabby's transplant, two other children — Caitlyn Hill and Judah Wilks — have undergone the procedure at St. Louis Children's Hospital.

Up until now, treatment options for children were limited. One option was to find an exact bone marrow match, but that's difficult. African Americans, who make up the majority of the



sickle cell population, are vastly underrepresented in national marrow registries. The other option was to use umbilical cord blood from a tissue-matched sibling free from the disease.

Nimble newborn cord blood offers significant benefits over bone marrow, requiring a less stringent match and fewer cells to effect a cure. Even so, tissue-matched sibling donors often are not available. Unrelated cord blood is easier to find because many public banks have made minority cord blood donation a priority. However, unrelated cord blood transplants simply weren't very successful.

"You have better chances of finding a cord match than a marrow," Shenoy said. "It was important for us to find a successful way."



Checking in post-transplant, Caitlyn Hill and her mom, Lena, review progress with nurse practitioner Monica Hente. Inset: Some of the meds Caitlyn was taking to help her body readjust as the transplant takes hold.

5 things to know about sickle cell disease

About 100,000 Americans live with SCD. It is the most common inherited blood disorder in the U.S.

Sickle cell affects those with African, Spanish, Mediterranean and Indian ancestry. In the U.S., about one in 500 African Americans and one in 1,200 Hispanic Americans are born with SCD.

SCD occurs when a child inherits two sickle hemoglobin genes, one from each parent. People are born with sickle cell; it doesn't develop later in life and it's not contagious.

The dysfunctional genes produce red blood cells with a distinctive sickle shape, jagged edges and a brittle structure. These cells clump together, and

intense pain results as blocked and damaged arteries starve organs and systems of oxygen. Anemia is the No. 1 symptom.

SCD is a chronic illness, but with new therapies, many people are living more productive lives. Life expectancy has increased from 14 years to 50 and older.



Shalini Shenoy, MBBS, MD, gives Gabby the OK to stop taking protective post-transplant medications — and jump into a life without sickle cells.

Researcher sets national standards

That the reduced-intensity unrelated cord blood transplants succeed is a tribute to Shenoy's tenacity. The wider medical community largely abandoned reduced-intensity cord blood transplants following early failures, reverting to myeloablative conditioning with siblings only.

Just eight years earlier, myeloablative conditioning in bone marrow transplants from unrelated donors also was considered too toxic for patients. But Shenoy devised a reduced-intensity transplant approach. Based on her experience, the first unrelated donor bone marrow transplant trial for sickle cell disease was opened through the National Heart, Lung and Blood Institute's Bone Marrow Transplant Clinical Trials Network. Shenoy is principal investigator for this trial.

Reduced-intensity unrelated transplants for sickle cell began succeeding with bone marrow, but initially failed with umbilical cord blood. Shenoy persevered, further fine-tuning the pharmaceutical cocktail and tweaking the protocol until unrelated cord blood trans-

plants also began working.

Despite the disease's severity and the procedure's complexity, Shenoy now achieves successful donor cell engraftment using both unrelated donor bone marrow and cord blood products.

John F. DiPersio MD, PhD, chief of the Division of Oncology and deputy director of the Siteman Cancer Center, hails Shenoy's work. "Her clinical studies will have a transformative impact on the future success of both related and unrelated stem cell transplant for children with sickle cell anemia, resulting in restoration of normal blood production while minimizing the usual toxicities of unrelated stem cell transplants."

Shenoy's reduced-intensity approach since has been applied in bone marrow transplants for another condition, thalassemia, in a national trial, which used the modified approach successfully and included unrelated cord blood transplants. Shenoy and others now are testing similar methods to treat several non-cancerous immune and marrow failure disorders.

CONTINUED FROM PG.13

improving the process

Cord blood transplants — regardless of source — carried an important drawback: they required that all of a recipient's blood-producing cells first be eliminated via high-dose chemotherapy, a toxic pre-transplant process known as myeloablative conditioning. Despite this, many patients rejected cord blood cells from unrelated donors. Even if the cells engrafted successfully, curing the disease, patients often had unwanted collateral organ damage, a high incidence of sterility and liver dysfunction. A less toxic option using cord blood was needed.

Shenoy's reduced-intensity conditioning avoids major organ damage. It forces the patient's immune system to accept the new cells — a balancing act that requires judgment and experience. Too little conditioning will cause the donor cells to be rejected, but too much can cause prolonged immune suppression.

In particular, to prevent rejection, the T-cells of the recipient's immune system must be depleted, making it possible to slip in the new cells. This is done via low-dose chemotherapy and monoclonal antibodies.

In this method, the donated cord blood still must be tissue-matched for compatibility, but importantly, can come either from a sibling or from the widely available unrelated donor pool.

this therapy avoids the long-term damages of prior methods

watching the risks

For the critical month following the cord blood transplant, the patient is sustained by transfused red blood cells and platelets. Over time, the new cells begin to work. SCD patients need as much as a year of recovery as the new cells become prolific and establish an operative immune system.

Shenoy monitors what she calls the "big three" risks. First is infection. With a downsized old immune system and a new one not yet fully functional, infection is a constant threat and must be treated promptly.

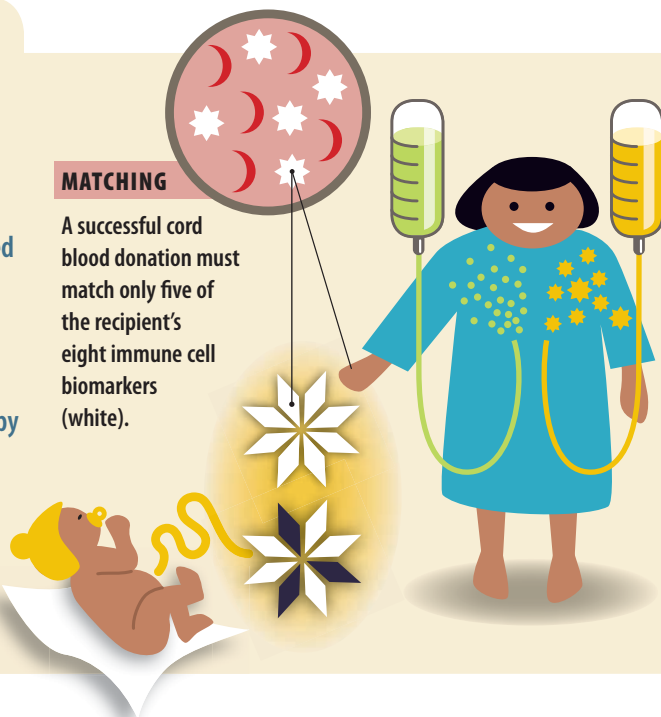
The second is rejection. Rejection can occur when the patient's remaining immune system identifies the transplant as foreign and attacks the

transplants, made better

The standard sickle cell treatment — engrafting a new hematopoietic (blood-forming) system created from donor cells — has been harsh medicine. Donor bone marrow cells must exactly match eight cellular biomarkers in the recipient. Further, recipients endure strong chemotherapy to destroy the old system before building a new one. By contrast, an improved treatment draws from a larger pool of cord blood donors and uses safer, gentler conditioning.

MATCHING

A successful cord blood donation must match only five of the recipient's eight immune cell biomarkers (white).



CONDITIONING Reduced-intensity conditioning agents “downsize” the recipient’s immune system to avoid rejection without causing problems during or after the transplant.

TRANSPLANT The donor cells are implanted. Caregivers must balance risk factors and manage the recipient’s health for a few months until the transplanted cells establish a stable new blood and immune system.

new cells. Shenoy uses DNA tests to determine the source — new or old — of the gradual increase in red blood cells. She says some mixed chimerism — carrying two DNA sets (patient and donor) — is acceptable, even long term, but she stays alert to any drop in productivity of the new cells.

The third is rejection’s sneaky counterpart: graft versus host disease (GVHD), which can quickly ruin everything. In GVHD, the transplanted cells’ immune components identify the patient’s body as foreign and attack it. The results are difficult to treat, and treatment causes further immune suppression resulting in a cycle of infection and GVHD.

expecting the best

For many, Gabby included, the year post-transplant is tough. She needed 50 medications, including 15 IVs for blood pressure control, diabetes regulation and steroids to manage GVHD. It wasn’t easy avoiding crowds and eating a healthful diet. But she followed the regimen and came through, with the benefits afforded by reduced-intensity conditioning: no cognitive impairment, no liver or kidney dysfunction and no discernible fertility damage. Not surprisingly, mom Debbie now struggles to maintain the tight control she adopted to protect her daughter.

Because strokes often recur with SCD and damage accumulates over time, Shenoy said it’s advantageous to intervene early. But only when the risk-to-benefit ratio with transplant has been shown to be positive.

That’s why 2-year-old Judah Wilks underwent a transplant last fall. Whereas the average age of

first stroke for a SCD patient is 9 years, Judah suffered his first stroke 10 months ago.

Judah’s parents, Bryce and Maryl Wilks of Marshfield, Mo., adopted him and his brother, David, from the Democratic Republic of the Congo. The family learned of Judah’s SCD only when the standard tests that all U.S. infants receive were run upon his arrival in this country.

People of deep faith, the Wilks firmly believe it is no accident that they found Judah and that he is now part of their Missouri family and close to Shenoy’s groundbreaking program. Bryce said of the post-transplant future, “We expect the best.” That fervent belief — along with Shenoy’s attention to balance in applying her novel approach to transplant — suggests they will get nothing less. ☐

Judah Wilks with Megan Holtmann, stem cell transplant nurse coordinator at St. Louis Children’s Hospital. The conditioning already underway, Judah played with Megan, read books with his brother, hugged his mom and mugged for the camera — testimony to the general mildness of the transplant preparations.





Exploring A N

A traditional course of study evolves with its field and embraces contemporary technologies. From left: anatomy instructors Jane Phillips-Conroy, PhD, Glenn Conroy, PhD, and Krikor Dikranian, MD, PhD.



PHOTO ESSAY BY ROBERT BOSTON

Human anatomy is the flagship course of first-year study. Students unravel miles of vessels, dissect masses of tissue, find and name interlinking parts and consider functional systems. Dry textbook abstractions become viscerally real. During a life-changing semester, students ponder the human organism, developing the respect and detachment physicians must cultivate in their duties.

Students huddle, four to a cadaver, around each stainless steel table. "The first day is daunting," said course master Glenn C. Conroy, PhD. "For many, it's their first exposure to death. And it's a challenging and humbling experience to make that first incision into the human body."

Many donors beforehand write letters about their lives and medical histories, which are placed alongside their bodies. "Their last wish was to provide useful information to tomorrow's physicians," Conroy said. "We tell the students, 'You are the instrument through which their final wishes are manifested.'" The donors, in a sense, become the students' first patients.

Recently renovated, the century-old lab showcases the school's expansive anatomical specimen collection. Anatomists of old would marvel at the glowing high-definition wall monitors and iPads.

Throughout weeks of exploration, feelings of insecurity eventually yield to fascination. "You can see the students evolving in front of your eyes," Conroy said.

Practicing specialists visit the class to offer clinical contexts for the examples upon the tables. During exams,

students must think on their feet when asked questions designed to synthesize their analyses of the cadavers.

The course concludes with an evening of reflection; students offer memorial poems, essays and musical tributes to the donors.

Through exploring these human bodies, future physicians come to better know themselves: a vital passage toward mastering the art and science of improving human health.



Students employ electronic tablets and study radiologic anatomy on large wall monitors in the renovated lab.

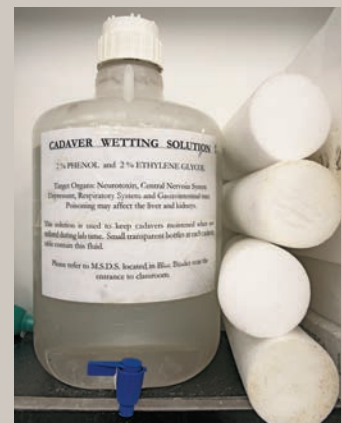
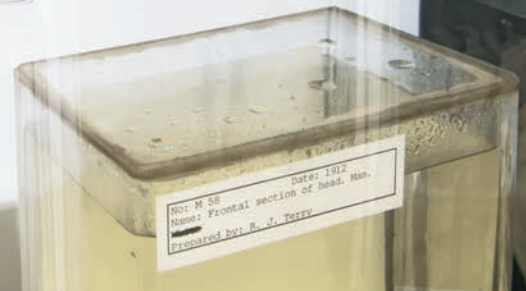
human

A T O M Y





see the variability of
THE BODY



nosce te ipsum

KNOW THYSELF





A quartet of arts specialists, photographed at Powell Symphony Hall in St. Louis:
Devyani Hunt, MD, Lynnette Khoo-Summers, PT, DPT, Heidi Prather, DO, Aaron Chamberlain, MD



The Medical Program for Performing Artists rehabilitated Alicia Graf Mack, dancer with the Alvin Ailey American Dance Theater, now on a 24-city tour.

THIS YEAR, DEVYANI HUNT, MD, HAD AN EPIPHANY. During Dancing in the Streets, a St. Louis outdoor festival featuring more than 60 dance companies and 1,000 dancers, Hunt saw many dancers who might not have been on stage without her help. In one instance, Hunt realized she had treated 10 of a company's 18 dancers.

Encore!

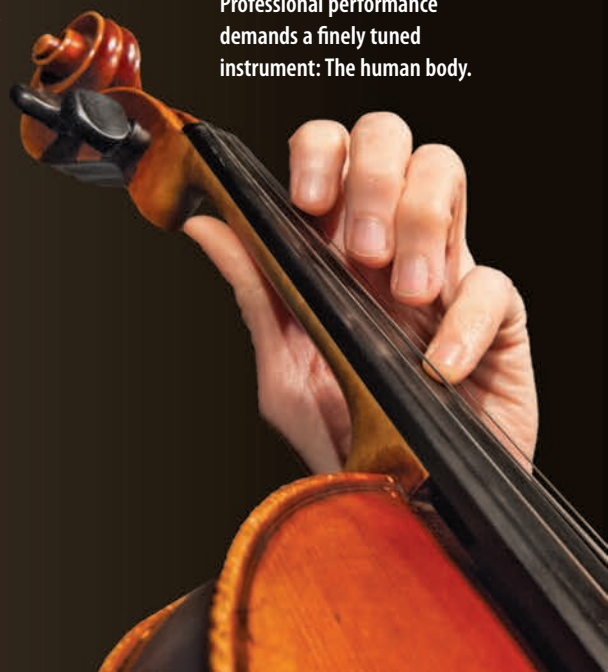
When the healing arts enhance the arts

BY DEB ARONSON

"It was great to see that," said Hunt, a physiatrist and associate professor in the Department of Orthopedic Surgery. "It was an 'aha' moment for me that I really am making a difference."

Along with physical therapist Lynnette Khoo-Summers, PT, DPT, Hunt co-directs Washington University's Medical Program for Performing Artists (MPPA). This program helps a variety of arts professionals — musicians, dancers, circus acrobats, ice skaters, painters and singers — return to their beloved stage, abiding passion and, in many cases, their livelihood. Frequently, without the help of the MPPA team, these unique patients might have to give up the very things that animate their lives.

Professional performance demands a finely tuned instrument: The human body.



Encore!

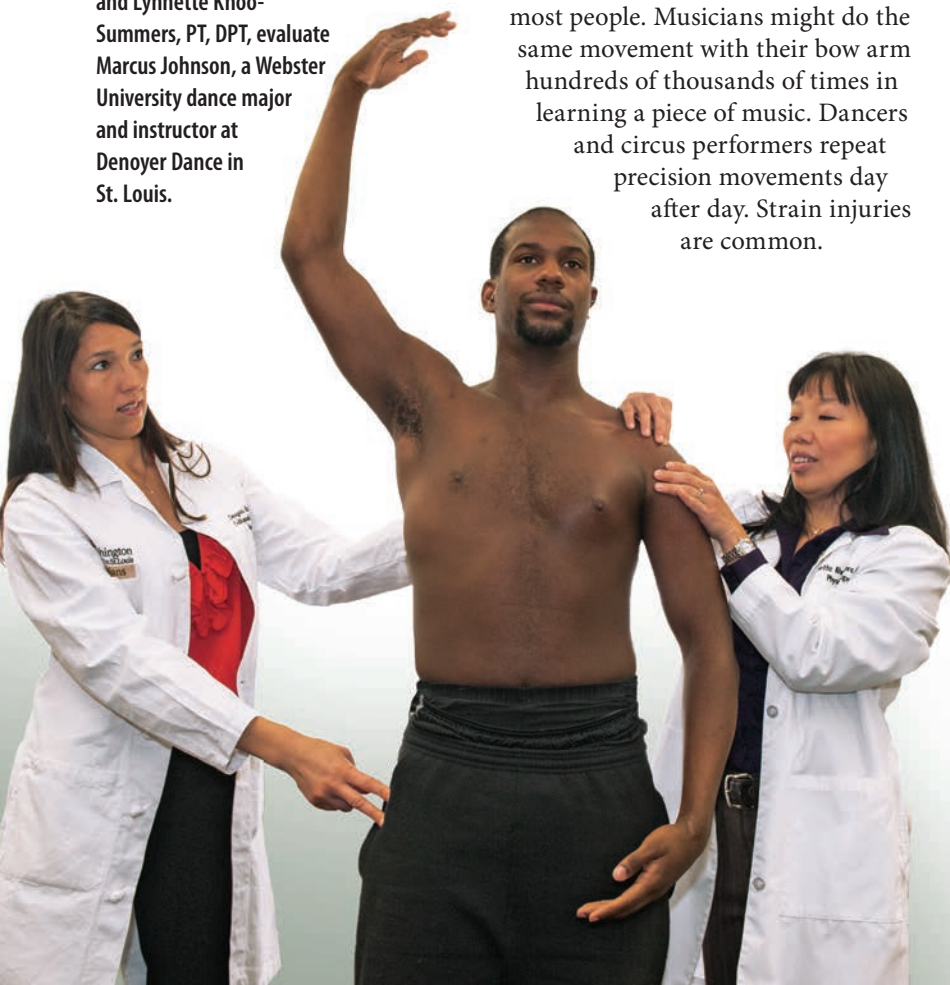
MPPA CLINICIANS primarily treat local artists but also see performers from many different tours — “So You Think You Can Dance,” Disney on Ice and Cirque du Soleil, for example — performing locally at The Fabulous Fox Theatre, the Blanche M. Touhill Performing Arts Center or other venues.

Last year, during the St. Louis production of “The Lion King,” one of the lead actors, outfitted with a heavy headpiece, suffered acute neck pain. The role was physically demanding, Hunt explains, and the actor no longer could perform in costume. In the clinic, Hunt diagnosed him with a pinched nerve and treated him to decrease inflammation and muscle spasms. Khoo-Summers also addressed the muscle spasms, and taped his shoulder girdle to provide more support. Within a few days, he rejoined the “Lion King” cast.

Hunt once treated a physical comedian from Branson, Mo., who injured himself after doing the splits nightly for 15 years. “He wasn’t one to be told not to do the splits anymore!” Hunt said.

Performing artists use their bodies more intensively and repetitively than most people. Musicians might do the same movement with their bow arm hundreds of thousands of times in learning a piece of music. Dancers and circus performers repeat precision movements day after day. Strain injuries are common.

Poetry in motion:
Devyani Hunt, MD (left),
and Lynnette Khoo-
Summers, PT, DPT, evaluate
Marcus Johnson, a Webster
University dance major
and instructor at
Denoyer Dance in
St. Louis.



Functioning within “normal” limits simply is not good enough. St. Louis Symphony cellist Alvin McCall found he could not exert enough force on the end of his bow. Because of damage to his ulnar nerve, his fingers were sluggish. Initially, McCall’s doctor told him that the strength in his left hand was “within the normal range.”

“Diagnosticians and therapists have to understand the demands you make on your body,” said McCall’s wife, Anna Lackschewitz, who is also a professional musician. “Lots of doctors just shrugged off his concerns about needing a higher level of performance.” Another doctor told him ‘wait and see.’ They have no appreciation that this is our livelihood.”

Not so with the MPPA, where McCall found support and help to strengthen weak muscles and adapt his playing style. Lackschewitz and McCall were so happy with how McCall was treated that they referred all four of their children, two who now dance professionally. Recently, Lackschewitz, principal violist of the Fox Theatre Orchestra, underwent therapy for a pinched nerve in her neck.

The MPPA was established in 1988 by the late Jerome Gilden, an orthopedic specialist in the School of Medicine and Barnes-Jewish Hospital. He retired in 1998, but, in 2004, the program was revived by Hunt, Khoo-Summers and Heidi Prather, DO, orthopedic surgery professor and chief of the section of physical medicine and rehabilitation. Prather and Hunt are physiatrists — specialists in physical medicine and rehabilitation who focus on non-surgical musculoskeletal care. They excel at linking symptoms to root causes and, unlike orthopedic surgeons, are not body-part specific.

Two years ago, Aaron Chamberlain, MD, a shoulder and elbow surgeon and assistant professor of orthopedic surgery, joined the group.

Because of their experience as performing artists, they bring zeal and understanding to their clinical work: Hunt and Khoo-Summers as dancers, Prather on trumpet and Chamberlain on violin.

“We understand where they (the artists) are coming from,” said Khoo-Summers, who danced professionally in Chicago before injuring her knees. Now an assistant professor in the Program in Physical Therapy and the Department of Orthopedic Surgery, she found her niche in rehabilitating performing artists. “We understand that need to perform, to make your body do things it is not built for. Most often, if you go to clinicians who don’t understand that need to perform, they’ll say, ‘If it hurts to dance, don’t dance.’”

Together, Hunt and Khoo-Summers diagnose problems by observing patients in motion. In addition to traditional exercise equipment, such as treadmills, an elliptical, bikes and a universal gym, the physical therapy clinic boasts a ballet barre and special flooring for dancers.

“If you test performing artists in the office in standard fashion to see if they have good muscle strength, their strength will be fine,” she said. “But if they can’t maintain the posture they need because of fatigue, then you have to develop a training program to work more toward endurance and posture retraining.”

While the MPPA physicians’ efforts help decrease symptoms, Khoo-Summers corrects the movement impairments that are causing the symptoms. This is done by attaining better alignment, correcting muscle imbalances, building stamina and developing adaptive strategies.

“The MPPA is cutting edge — designed to maintain high levels of performance in those who push the limit of what is physically possible on a sustained basis,” said Richard Gelberman, MD, the Fred C. Reynolds Professor and chair of the Department of Orthopedic Surgery. “The clinicians are to be congratulated for bringing exceptional care for this ultra-committed population to St. Louis and to our region.”

Not surprisingly, the field of performing arts medicine is a small and tight-knit community. There are fewer than 50 such programs nationwide and many have sprung up in cities with major performing arts centers. Harkness Center for Dance Injuries, for example, was founded in 1989 in response to the New York dance community’s critical need for specialized and affordable health care. Washington University’s program, while not one of the nation’s largest, is well known and respected.

“Washington University’s program in performing arts is a wonderfully integrated and multi-disciplinary program,” said Monica Rho, MD, assistant professor of physical medicine and rehabilitation at Northwestern University’s Feinberg School of Medicine. “Dr. Hunt worked hard to develop a clinic where both she and Lynnette co-evaluate and co-treat the patient. The coordination of these services places the performing artist’s needs first and makes Washington University’s program a model to emulate.”

“We understand that need to perform, to make your body do things it is not built for.”

LYNNETTE KHOO-SUMMERS, PT, DPT



Such coordination may sound simple, but most programs cannot coordinate co-evaluations, said Rho, who also sees performing artists in her practice. Because it’s critical for these artists to maintain their performance schedules, the MPPA team offers same-day appointments whenever possible.

Besides working in the clinic, Hunt or Khoo-Summers often are on-call or backstage at performances. Recently, Khoo-Summers accompanied Dance St. Louis pro bono on a three-city tour.

Because most patients have chronic overuse injuries, it’s important that artists adopt preventive strategies early in their careers. The MPPA holds outreach programs with young dancers, musicians and circus performers, recently leading a symposium for Western University’s Department of Music and Community Music School.

But no matter how much prevention they preach, injuries will occur. With proper intervention, however, injuries don’t have to result in a sidelined career; performing artists can get back on the road and back to following their passion. □

Warming up for a Metropolitan Orchestra of St. Louis concert: Alvin McCall, St. Louis Symphony cellist, and his wife, Anna Lackschewitz, principal violist of Fox Theatre Orchestra, who both were treated through the Medical Program for Performing Artists.







INFECTIOUS DISEASES AND GLOBAL HEALTH

Improving health is among the world's most pressing challenges,

and infectious diseases research has become one of the largest areas of concentration within the School of Medicine. As new diseases appear, there is an ever-greater risk of rapid transmission and spread of infection. By traveling to foreign countries to provide basic health care or by offering programs in St. Louis aimed at preventing sexually transmitted diseases, our faculty, students and staff are dedicated to making a difference — locally, nationally and globally.

Research in the gut microbiome, hospital-acquired infections, and parasitic diseases are but a few examples of the breadth and depth of our leadership. The potential to solve some of the most vexing questions of population health is growing as our research teams forge a rapid pace toward discoveries.

Private philanthropy is essential to advance the initiatives described in the following pages.

Partner with us in support of these initiatives.

The global reach of Washington University extends to sub-Saharan Africa. Mark Manary, MD, the Helene B. Roberson Professor of Pediatrics, developed a revolutionary peanut butter-based therapeutic food to combat severe childhood malnutrition. A proven lifesaver with a 95 percent recovery rate, the blend has become standard treatment worldwide.



Victoria J. Fraser, MD, and her team lead infection control training programs in health care and community settings.

NO PLACE FOR INFECTION

Hospital-acquired infections (HAIs) remain a significant cause of illness and death. Too frequently, bacteria or other microorganisms lurking on medical devices, bed rails, a bandage or a caregiver's hands find their way into a patient's body via a wound, catheter, ventilator or invasive procedure.

School of Medicine researchers have developed infection surveillance and control guidelines that have been adopted worldwide.

Despite these measures, new virulent, antibiotic-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* have emerged. People are living longer, but also are more susceptible to HAIs — through advances in cancer therapy, the use of immunosuppressants and long-term management of multiple chronic diseases. “The key to preventing the spread of infections is

vigilance and attention to strict patient care guidelines,” said Victoria J. Fraser, MD, the Adolphus Busch Professor and chair of the Department of Internal Medicine and a world-renowned infectious diseases expert.

Among critical advances made by the medical school's infectious disease research team and BJC HealthCare Infection Prevention Consortium:

- Safer IV insertion techniques and use of the antibacterial antiseptic chlorhexidine to lower the risk of bloodstream infections. In 10 years, central line-associated bloodstream infections in the U.S. decreased 60 percent.
- Standardized procedures to reduce surgical site infections, including improved hand hygiene, skin antiseptic use, clippers instead of shaving, perioperative glucose control, better temperature control in the operating room and precise timing of antibiotic use.
- Improved patient management policies — including elevating the head of hospital beds, use of disinfectant mouthwashes and standardized order sets to wean patients off ventilators and sedatives — which reduced ventilator-associated pneumonia in ICUs. This campaign, named “Whap VAP,” subsequently was replicated across the country.

Our ability to advance research, recruit the best individuals and train health care workers to protect patients is greatly helped by private philanthropy.

Washington University researchers have developed infection surveillance and control guidelines that have been adopted worldwide.



With support from FIHTM, students designed and implemented a diabetes prevention program in Majuro, Republic of the Marshall Islands.

LIFE-CHANGING JOURNEY

Interest in global health among U.S. medical students has grown dramatically. But, only a small fraction of students who work overseas during medical school will pursue careers in international health.

Faculty say it is clear, however, that early international experiences can have long-term impact on medical students and their future patients. Global

training broadens students' perspectives on disease prevention, care delivery and health care systems.

The Forum for International Health and Tropical Medicine (FIHTM) is a student-led group devoted to promoting interest and understanding of global health at the School of Medicine. With support from the dean's office and the Washington University Medical Center Alumni Association, FIHTM annually sponsors one- to two-month overseas electives for 25 students and spring break experiences

in the Navajo Nation and Central America.

FIHTM fellows participate in a wide range of research and clinical activities, such as studying tuberculosis in India, working on malaria prevention in rural Uganda and examining respiratory

disease in stonemasons in Colombia.

"Many of our students say their international experience was life-changing," said Gary Weil, MD, professor of medicine and faculty adviser to FIHTM. "They quickly learn to adjust to reduced resources and they see that culture, behavior and environment dramatically affect health, outcomes and the delivery of care."

Working with diverse populations in low-resource settings requires students to rely heavily on physical exams and the patient's history to make a diagnosis. These electives often strengthen "soft" skills, such as compassion and cultural sensitivity, which are valuable regardless of where students practice.

"It taught me how to establish a rapport with patients in spite of a language barrier and to see things from another cultural perspective," said Christelle Samen, a second-year medical student who completed a rotation in Guatemala.

Student demand for these experiences outpaces the resources of FIHTM. Private philanthropy can support summer internships around the globe.

"There's a growing interest in global health issues, and many of these issues are relevant to U.S. medical practice and policy," Weil said. "Through FIHTM, the medical school is preparing young doctors who will work to change the world."

"Through FIHTM, the medical school is preparing young doctors who will work to change the world."

— GARY WEIL, MD



Global Health Scholars learn sensitivity to other cultures and develop solutions in resource-limited environments, such as this ICU in Guatemala City.

WORLDVIEW OF HEALTH

A catalyst for innovation, the Global Health Scholars in Medicine program takes residents out of the academic medical setting with its latest technologies and collaborative, multidisciplinary teams and places them in underresourced parts of the world.

On these month-long rotations, medical residents hone their skills — overcoming language barriers, broken equipment and cultural sensitivities. Often, they work without the benefit of a translator, attending physician or nearby lab.

These new physicians gain a global mindset, understanding not only disease, but also the impact of culture and poverty on public health.

Ten residents are selected yearly to participate in the highly competitive program administered by the Department of Internal Medicine.

The program began in 2007 with support from Jack Ladenson, PhD, the Oree M. Carroll and Lillian B.

Ladenson Professor of Clinical Chemistry.

Ladenson and David Windus, MD, professor of medicine, led residents to Eritrea and Bhutan to create diabetes education and disease management programs.

Now it includes more faculty and sites in Honduras, India, Japan and Guatemala. Also, the program offers a locally based “international” rotation: students work with refugees and the homeless in St. Louis — people they might not typically see during an inpatient rotation — at Family Care Health Centers and Casa de Salud.

Scholars conduct research, develop outreach initiatives and share best practices.

“It strengthens several aspects of our curriculum, including training in cultural sensitivity and preventive care,” said Melvin Blanchard, MD, FACP, chief of the Division of Medical Education. “As a university with a global view, we hope that our trainees develop an appreciation for the wider world in which we live and become engaged in a manner that advances longevity and a high quality of life in our immediate community and abroad.”

Rachel Kilpatrick, MD, an endocrinology fellow at the School of Medicine, finished a rotation in Eritrea and now hopes to work with Hispanic immigrants. “I’m motivated to work with the underserved here in the United States, particularly with immigrant populations that may have difficult access to care,” she said. “My time as a Global Health Scholar was one of the most valuable experiences of my entire medical training so far.”

These new physicians gain a global mindset, understanding not only disease, but also the impact of culture and poverty on public health.



MARK KATZMAN

A study of young twins living in Malawi showed that intestinal bacteria play a key role in malnutrition. Center: Jeffrey Gordon, MD, is senior author.

ENDING MALNUTRITION

International leaders in addressing childhood malnutrition, Washington University researchers are working to devise innovative solutions.

Jeffrey Gordon, MD, the Dr. Robert J. Glaser Distinguished University Professor and director of the Center for Genome Sciences and Systems Biology, leads an international team of scientists trying to understand how gut microbes (the “microbiota”) help determine nutritional status.

Recent study findings point to a role for the microbiota in childhood malnutrition. The research, published in the journal *Science*, involves 317 sets of twins in Malawi followed from birth to age 3.

Childhood malnutrition is all too common, and scientists wonder why some children are afflicted but not others, even those in the same household who eat the same foods. Gordon and his team focused on twin pairs in which one child

remained healthy and the other became malnourished. This ‘discordance’ occurred equally in fraternal and identical twins, suggesting an underlying factor besides human genetics. So the team turned to the microbiota.

Therapeutic food interventions reduced mortality in children with severe undernutrition, but healthy growth was not completely restored and proper neurodevelopment lagged.

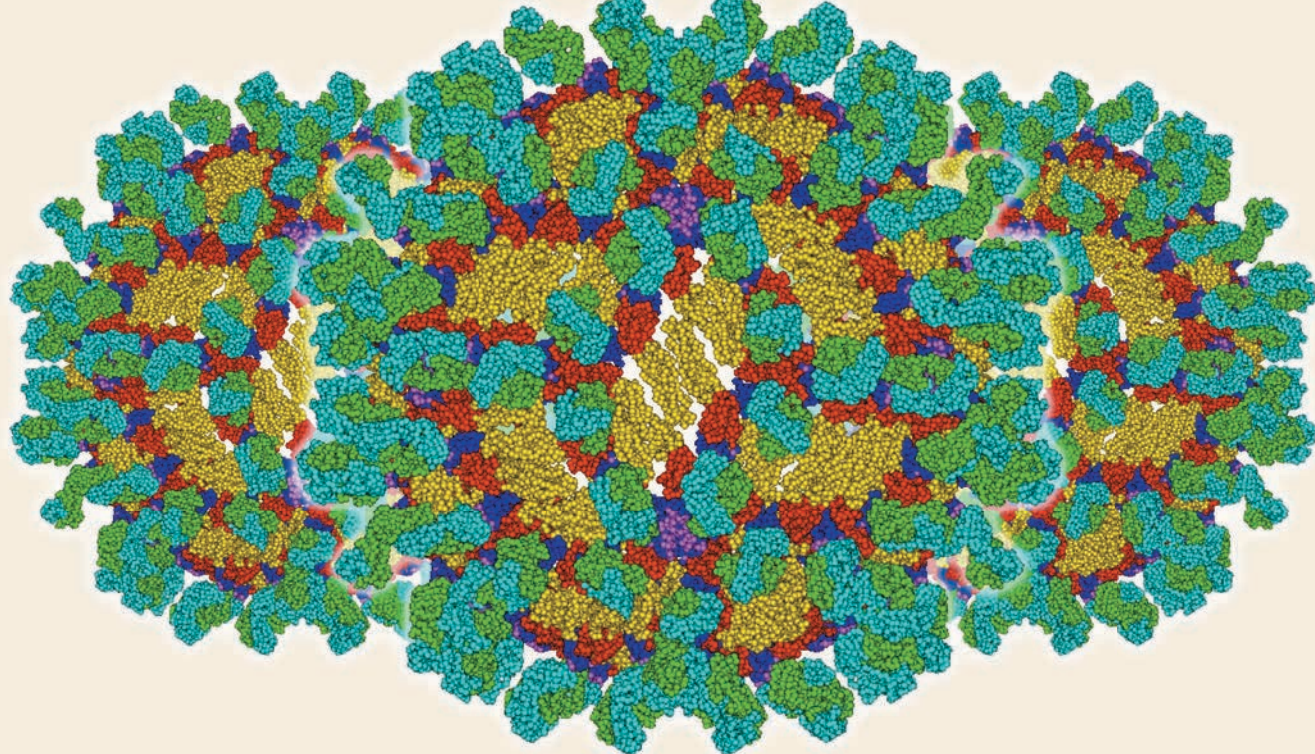
The team found that the microbiota of malnourished children appeared immature. Therapeutic foods helped, but once they were stopped, the immature state reappeared.

By transplanting microbiota from twins into formerly sterile mice, the researchers showed that the combination of immature microbiota from a malnourished child and a Malawian diet produced disease in recipient animals; this was not the case when mice received a healthy child’s microbiota.

Their work provides a microbial view of human postnatal development and suggests that healthy growth requires a properly maturing microbiota. An important implication is that prolonged food-based interventions and/or addition of gut microbes may be needed for durable repair of microbiota immaturity in childhood malnutrition and improved clinical outcomes.

“With support of the Bill & Melinda Gates Foundation, we are studying the gut microbiota in malnourished children living in other low-income countries, and working to develop new types of safe, effective interventions to treat and ultimately prevent this devastating disease,” Gordon said.

Researchers believe there is a link between gut microbes and the diets of malnourished children.



COURTESY OF DAVID FREMONT, PhD

Researchers are investigating how humans respond to potentially lethal viruses such as West Nile, modeled above.

TARGETING VIRAL DANGERS

Washington University has broad research focused on the viral causes of infectious disease.

Stephen Beverley, PhD, is researching viruses that make parasitic diseases more dangerous. In doing so, Beverley, the Marvin A. Brennecke Professor and chairman of the molecular microbiology department, is forging a pathway in his field, which he calls “parasite virology.”

In 2011, Beverley’s team, working with scientists at the University of Lausanne in Switzerland, found that a particular virus increased the severity of a parasitic disease called Leishmaniasis.

About 12 million people are infected worldwide with this potentially lethal disease, and 2 million new cases develop each year.

“The fact that there was a viral target within the Leishmania parasite immediately led us to thinking that an antiviral therapy could control the spread and impact of

the disease,” Beverley said. “We’re now exploring several leads in this area.”

Michael Diamond, MD, PhD, professor of medicine and an expert on West Nile virus, is part of a new multi-institution collaboration

looking for similarities in how humans respond to three potentially lethal viruses.

The National Institutes of Health (NIH) study will focus on West Nile, Ebola and influenza, using advanced computational models to find common traits. Diamond expects that finding similarities could lead to new, more effective treatments.

David Wang, PhD, associate professor of molecular microbiology and pathology and immunology, was part of an important team in 2003 that successfully hunted down the severe acute respiratory syndrome (SARS) virus.

Emerging viruses pose constant threats to public health. Today, Wang continues efforts to identify and characterize novel viruses.

His current research attempts to understand why 70 percent of viral encephalitis cases and 30 percent of respiratory tract infections defy the most sophisticated diagnostic tests now used — suggesting that unknown agents likely are involved in the pathogenesis of these diseases.

Philanthropy plays a vital role in funding fellowships and research opportunities. Support from donors is critical to our continued leadership in infectious diseases.

Emerging viruses pose constant threats to public health.



Improving global health is among the world's most pressing challenges. Please consider funding this or other opportunities to advance human health.

Infectious Diseases and Global Health

- Endowed professorships for specific departments or diseases
- Endowed research funds for specific departments or diseases
- Endowed gifts to be recognized by naming an institute, center or research laboratory
- Annual or endowed fellowship support for physician-scientists
- Expendable support for three- to five-year pilot projects
- Annual unrestricted support

The Brain

Cancer and Personalized Medicine

Diabetes, Heart Disease and Obesity

Annual or endowed fellowship support for graduate and physician-scientists

The Annual Fund

For information about these and other opportunities, please contact:

Pamela Buell

Associate Vice Chancellor for Medical Alumni and Development

Phone:
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Email:
meddev@wustl.edu

Website:
medicalalumni.wustl.edu/
campaign

Reply card:
See inside back cover

Together,
we can change lives.

1940s

Carl Woolsey, MD 43, is retired and living in Salt Lake City. He enjoys "being with his family, drinking whiskey and telling lies with friends, relatives and neighbors." He is proud to have three generations of OB/GYNs in the same family practice and hospital.

1950s

Bernice Oshita, NU 50, was honored by The American Red Cross as a "Volunteer of the Week" for contributing 10,716 service hours to the Tripler Army Medical Center in Honolulu. She describes herself as the "gofer," lending a hand as needed in the office and helping nurses.

Rudenz "Rudy" Douthat, MD 54, was honored at the American College of Emergency Physicians (ACEP) Scientific Assembly as one of two surviving founders of emergency medicine and ACEP.

1960s

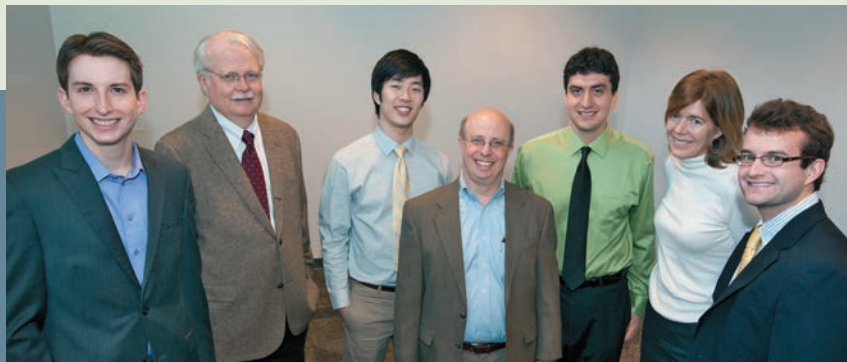
Ronald Evens, MD 64, has been appointed chairman of the Board of Regents for the National Library of Medicine (NLM), the world's largest medical library. The NLM board guides the library as it manages the worldwide flow of medical information.

Josh Grossman, MD 65, colonel (retired), U.S. Army Medical Corps, MD, FACP, spoke to the Washington County Bar Association on "Landmark Medical Ethical Matters."

Michael Treister, MD 67, attended the National Flute Association annual convention. As a previous chair and current member of the Performance Health Care Committee and Editorial Board, Treister enjoyed getting away from the office to "jam" with other flautists.

1970s

Francisco Garriga, MD 70, published *Tell Me How You Die Easy*, a book aimed at educating medical and nursing students on the importance of compassionate care.



Distinguished Alumni Scholars honored Four first-year medical students recently were honored as Distinguished Alumni Scholars. Each scholarship is named to honor an alumnus or alumna who has served on the School of Medicine faculty. Distinguished alumni honorees and scholars, from left: Jeffrey Marinshaw; William F. Stenson, MD 71; Kevin Li; Leonard Bacharier, MD 92; Jordan Jacquay; Linda Peterson, MD 90; and Michael Madigan.

Scott Frankel, MD 79, an allergy specialist with Kansas City Allergy & Asthma in Overland Park, Kan., was named a "Top Doctor" by *U.S. News & World Report* and Castle Connolly Medical Ltd.

Cecil Holliman, MD 79, presented the opening plenary lectures on "Trauma System Development" and "Prehospital Trauma Triage" at the 2013 International Conference and Training on Emergency Trauma Care held in Vietnam last March. Holliman is president-elect of the International Federation for Emergency Medicine.

1980s

David Baltzer, HA 81, has been elected to the Board of Directors of the Missouri Health Executives Group, the state chapter of the American College of Healthcare Executives, and will chair the communications committee.

Ayse Kilfoy, DE 87, was named to St. Louis Magazine's "Top Dentists" list for the fifth consecutive year.

1990s

Kirk Gasper, MD 93, was promoted to U.S. Navy captain and served as a senior medical officer at the Naval Branch Health Clinic in Bahrain. In August, he returned

to Oak Harbor, Wash., to his family, which includes **Michele (Francoeur) Gasper, MD 93**, who also serves in the Navy.

Tadd Pullin, HA 94, GR 94, was named senior vice president of marketing and strategy development at the Nebraska Medical Center in Omaha, where he provides senior oversight for marketing, strategic planning and human resources.

Brett Kissela, MD 95, has been appointed the Albert Barnes Voorheis Chair of Neurology and Rehabilitation Medicine at the University of Cincinnati (UC) College of Medicine and UC Health, effective Jan. 1, 2014. He joined the neurology department as an assistant professor in 2000.

2000s

Marc Herant, MD 00, will spend the next two years in Rwanda as an adviser to the Ministry of Health.

Elizabeth Foglia, MD 05, is completing a neonatology fellowship at Children's Hospital of Philadelphia this fall and will transition to a faculty clinical research position and study neonatal resuscitation. Her husband, **Ted Satterthwaite, MD 06**, works in imaging research in the Department of Psychiatry at the University of Pennsylvania. They recently welcomed their third child.

Leana Wen, MD 07, co-authored the book *When Doctors Don't Listen: How to Avoid Misdiagnoses and Unnecessary Tests*. She is an attending physician and director of patient-centered care research in the Department of Emergency Medicine at George Washington University.

IN MEMORY

Ernesta Grace Mira, NU 41

Mira died Thursday, Aug. 1, 2013, at age 95. Mira grew up in Roodhouse, Ill., and dreamed of becoming a nurse. Upon graduating from Washington University, she was called to active duty in the Army Nurse Corps and sent to O'Reilly General Hospital in Springfield, Mo. Later, she opened a medical practice in Alton, Ill., with her husband **Joseph Mira, MD 41**, who preceded her in death.

Charles Nicolai, LA 43, MD 46, HS

Nicolai died Friday, May 31, 2013, at the age of 91. He completed undergraduate and medical degrees at Washington University before serving in the U.S. Navy Medical Corps from 1947-49. After the war, he returned to the university and co-founded the Division of Urology in 1953. For a time, Nicolai practiced urology at Missouri Baptist and Deaconess hospitals, serving as chief of staff and chief of urology. Nicolai returned to the School of Medicine in 1990 in the office practice of Urology and Prostatic Cancer research until retiring in 2005. He was a founding and life member of the Society for Pediatric Urology, a fellow of the American Academy for Pediatrics and a consultant to the Shriners Hospitals for Children. He was a 32 degree Master Mason K:C:C:H. Moolah Shriner.

Margaret Burge McChesney, MD 49

McChesney died Friday, April 26, 2013, in Newport News, Va. She is remembered as a devoted wife, mother and pediatrician.

David Reed Holmes, MD 51

Holmes died Sunday, March 17, 2013, at age 90. A graduate of Missouri State Teachers College in Springfield, Mo., Holmes joined the U.S. Navy during World War II and became a pilot. He attended

the School of Medicine and opened a general practice in Warrensburg, Mo. He later returned to Washington University to become an OB-GYN, completing an infertility fellowship. For 30 years, Holmes practiced as an OB-GYN in Springfield, delivering 9,000 babies. At one point, he was the only infertility specialist in Southwest Missouri.

Henry Baker Lorentz, DE 53

Lorentz died Tuesday, Feb. 12, 2013, at Peace Hospice in Great Falls, Mont. He was 86. Lorentz earned a bachelor's degree from Montana State College and attended Washington University Dental School. During World War II, he served as a naval air gunner and later joined the Army Dental Corps. A practicing dentist for 40

years, Lorentz was elected president of the Montana State Dental Association and was honored for distinguished service by the Montana State Dental Society.

Mitchell E. Goldenberg, LA 52, MD 55

Goldenberg, a plastic and reconstructive surgeon in Northwest Indiana for more than 40 years, died Sunday, Jan. 20, 2013, at age 81. After attending Washington University for undergraduate and medical studies, he completed a general surgery residency at Albert Einstein Medical Center in Philadelphia, a plastic surgery residency at Meadowbrook Hospital in Hempstead, N.Y., and a hand surgery fellowship at Memorial Sloan Kettering. He served as a U.S. Army captain and as a physician in a MASH unit in Korea.

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Gregory Clawson Rosenberger, PT 59

Rosenberger, a physical therapist for 34 years in Indiana, Iowa and Wisconsin, died Monday, June 17, 2013, at age 82. He served in the U.S. Army for three years during the Korean Conflict. Rosenberger earned a bachelor's degree in physical therapy from Washington University and a master's degree in public health from the University of Michigan. He particularly enjoyed working with elderly patients.

O. Michael Colvin, MD 61

Colvin, a prominent cancer researcher, died Saturday, March 16, 2013. He was 77. Born in Princeton, Ind., he graduated from Indiana University in 1957 and Washington University School of Medicine in 1961. He completed an internal medicine internship and residency at Johns Hopkins University. Following a fellowship at the National Cancer Institute, Colvin worked at Johns Hopkins for 30 years — as a professor of medicine and pharmacology, director of the pharmacology division, research director for the oncology center and associate dean for research. Colvin later moved to Duke University, becoming director of its cancer center and the William W. Shingleton Professor of Cancer Research and professor of pharmacology and cancer biology.

Perry Dyson Inhofe II, MD 88, HS 89

Inhofe died unexpectedly Sunday, Nov. 10, 2013, of injuries sustained from a plane crash. He was 52. Inhofe completed an undergraduate degree, first in his class, in biomedical and electrical engineering from Duke University in 1984. He earned a medical degree at Washington University and completed an internship at Barnes Hospital and residency at the University of Oklahoma College of Medicine, Orthopedic Surgery and Rehabilitation. Inhofe met his wife, Nancy Rader Inhofe, MD, at Washington University when he rotated through the Pediatric Emergency Department. They were married in 1989. Inhofe was an active orthopedic surgeon at Central States Orthopedics in Tulsa, Okla. He was the son of U.S. Sen. James

Inhofe with whom he shared a love of flying. He is remembered as a devoted and loving husband, father, son and physician.

Andrew Zupan, LA 84, MD 92, GM 92

Zupan, a pediatrician in St. Peters, Mo., died Friday, Feb. 15, 2013. He was 50. Originally from Columbus, Ohio, Zupan completed undergraduate studies at Washington University and earned an MD/PhD from the School of Medicine. Zupan completed a pediatrics residency at Cincinnati Children's Hospital. He practiced pediatrics in Batesville, Ind., and later in Washington and St. Peters, Mo.

FACULTY

Bernard Becker, GR 90

Becker died Wednesday, Aug. 28, 2013, at his Central West End home. He was 93. Becker grew up in Brooklyn, N.Y., and graduated from Princeton University and Harvard Medical School. He trained as a U.S. Army psychiatrist during World War II and later in ophthalmology at Johns Hopkins University. Becker is largely known for his work to find glaucoma treatments. During the 1950s, he helped Washington University medical school build its Department of Ophthalmology and Visual Sciences, and headed it for 35 years. Additionally, he helped establish the National Eye Institute. Becker donated a 600-volume collection of medical books to the medical school and, in 1995, the medical library was renamed in his honor.

Thomas B. Ferguson, HS 57

Ferguson, professor emeritus of cardiothoracic surgery, died Sunday, May 26, 2013, at age 90. A pioneer in heart surgery, Ferguson helped bring the first heart-lung machine to St. Louis in the late 1950s. In 1958, he and his colleagues performed Washington University's first open-heart surgery with the aid of the new heart-lung pump. A graduate of the Duke University medical school, Ferguson trained in surgery at Duke, Barnes Hospital and Washington University. Except for four years in private practice, Ferguson spent his career at Washington University, training residents and fellows in cardiothoracic surgery and serving on the admissions

committee. He was president of the American Association for Thoracic Surgery and the Society of Thoracic Surgeons, of which he was a founding member.

Elmer Brown Jr., MD 50

Brown, a distinguished hematologist and emeritus professor of medicine, died Saturday, Sept. 8, 2012, at his home in Dana, N.C. He was 86. A native of New York City, he attended Oberlin College, then earned a medical degree from Washington University. After a residency at Columbia-Presbyterian Center in New York, Brown served two years in the U.S. Naval Medical Corps. Afterward, he trained in the Division of Hematology at Barnes Hospital, serving for nine years as division chief before becoming associate dean for postgraduate education.

Charles Ward Parker, MD 53

Parker died Tuesday, April 23, 2013, at his home in Webster Groves, Mo. He was 83. His pioneering research helped improve treatment of allergies and asthma. Parker, who founded the university's Division of Allergy and Immunology in the early 1960s, served on the faculty for more than four decades. Parker attended Washington University for undergraduate and medical studies. Afterward, he spent two years in the U.S. Navy before completing an internal medicine residency at Barnes Hospital and serving as chief resident. Parker took emeritus status in 1998, but continued to work in his lab.

Thomas H. Steinberg, MD

Steinberg, associate professor of medicine, died Sunday, June 16, 2013, in St. Louis of complications from amyotrophic lateral sclerosis. He was 61. A cell biology researcher and infectious diseases physician, Steinberg joined the School of Medicine's Division of Infectious Diseases in 1989.

If you wish to make a tribute gift in honor of any of the above alumni or faculty, please contact: Pamela Buell, Washington University Medical Alumni and Development, Campus Box 1247, 7425 Forsyth Blvd., Suite 2100, St. Louis MO 63105-2161, (314) 935-9691.



EXHIBIT Not many art careers begin in a pathology lab. As a teenager, Marilynne Bradley illustrated a lab's blood chemistry book, helping her earn a chemistry scholarship to Washington University. She studied pre-med, but eventually committed fully to art. The Webster Groves (Mo.) Arts Commission recently presented Bradley, FA '60 — a watercolorist, illustrator, historian and educator — with its Lifetime Achievement in the Arts Award and St. Louis Mayor Francis Slay declared Oct. 11, 2013, "Marilynne Bradley Day." Her works are showcased around the world in museum exhibits and corporate collections. Following cataract surgery at the Center for Advanced Medicine, Bradley saw the Medical Center through fresh eyes. The resulting paintings are on exhibit in the Farrell Learning and Teaching Center through February 2014.

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