

Outlook



Washington University in St. Louis

SCHOOL OF MEDICINE

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AUTUMN 2012

A quest for lifelong bone, joint and muscle health

The living skeleton



Sandell
Medic Sup

Robert M. Bell

LINDA SANDELL



Rites of passage

Graduates celebrated at recognition and hooding events across the School of Medicine at Washington University's 151st Commencement held on May 18.

Ceremonies recognized medical students, graduates of the school's programs in Occupational Therapy, Physical Therapy

and Audiology and Communication Sciences, and doctoral graduates from the Division of Biology and Biomedical Sciences. At left, former students prepare to join their families and friends following Commencement at America's Center in downtown St. Louis.

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Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU AUTUMN 2012



7 Zebrafish lab



10 Pediatric research

Waterworld

7 Washington University's advanced zebrafish facility, with more than 6,500 automated tanks, offers advantages for medical research.

It's For the Kids

10 Clinicians and investigators unite, tackling childhood diseases, conducting innovative research and translating results into care.

Making Connections

16 Understanding the biological underpinnings of musculoskeletal diseases is made easier by the creation of a focused new center.

Serving a Need

21 A doctor's dream becomes reality, and an underserved population of African women reap the medical and societal benefits.

COVER Researchers Linda J. Sandell, PhD, and Roberto Civitelli, MD, lead a new, interdisciplinary effort aimed at better understanding musculoskeletal health. The Washington University Center for Musculoskeletal Research includes researchers from more than 50 laboratories. To learn more, please turn to page 16.

PHOTO BY ROBERT BOSTON

2 Pulse

24 Viewpoint

26 Alumni & Development

26 Mentor Memorial Funds

28 Hardesty Professorship

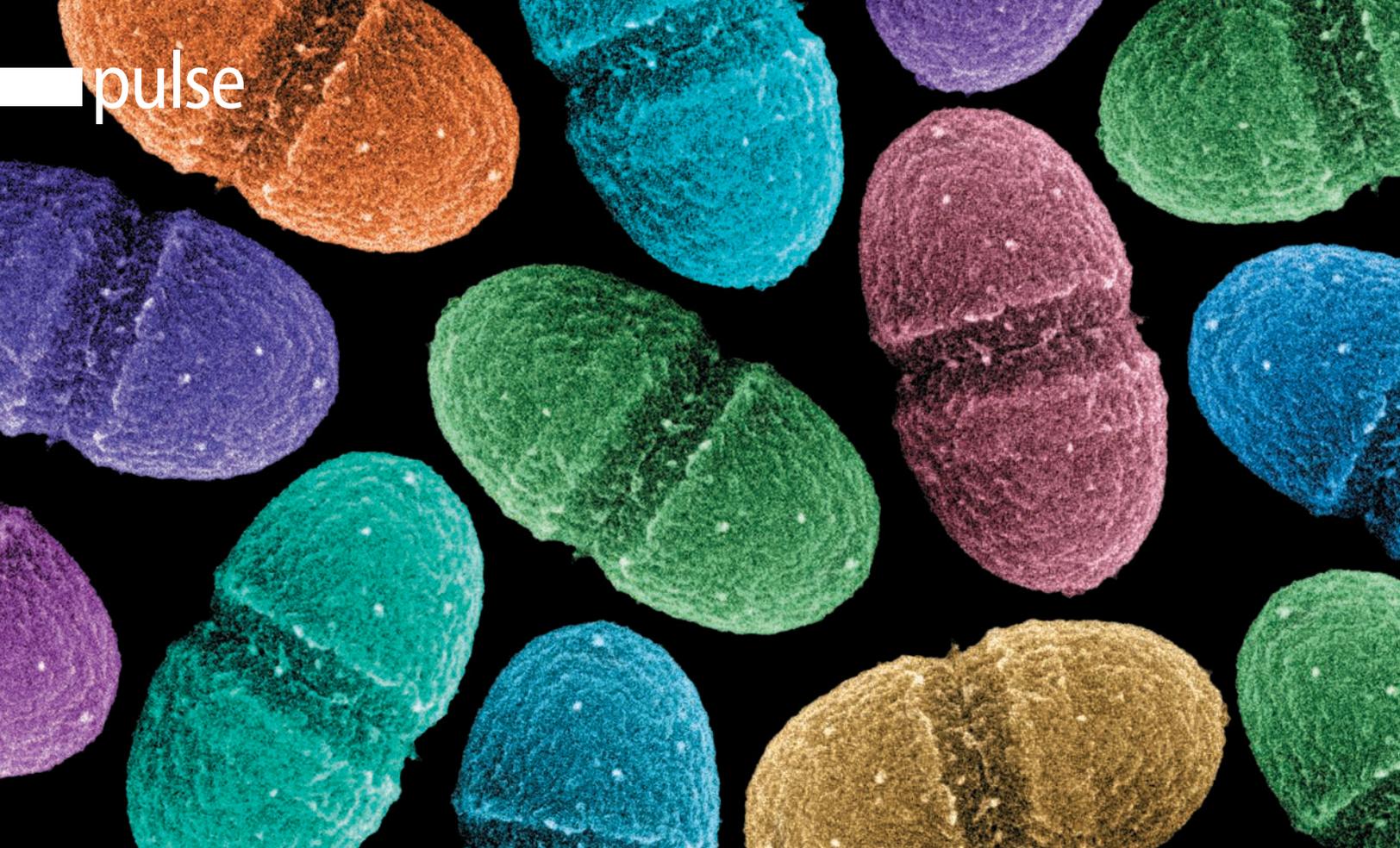
30 MD Reunion 2012

31 Hornsby Professorship

32 Class Notes



30 A tradition begins



Microbial zoo

Viruses, bacteria and fungi abound in healthy people

T trillions of microbes inhabit the human body, occupying virtually every nook and cranny. And most of the time, this relationship is a friendly one, with microbes helping to digest food, strengthen the immune system and ward off dangerous pathogens.

But despite microbes' prominent roles, researchers have understood little about which of them reside in specific sites of the body. Now, a consortium of some 200 U.S. scientists reports findings from the most comprehensive census of the microbial makeup of healthy humans.

The research, published June 14, 2012, in *Nature* and in several *Public Library of Science* (PLOS) journals, offers new details and even some surprises.

For example, the researchers found that even healthy people typically carry low levels of harmful bacteria in and on their bodies. But when a person is healthy, these

pathogens don't cause disease; they simply coexist in an abundance of beneficial microbes. Now, scientists can investigate why some pathogens suddenly turn deadly, which will refine current thinking on how microorganisms cause disease.

"It's not possible to understand human health and disease without exploring the massive community of microorganisms we carry around with us," says George M. Weinstock, PhD, associate director of The Genome Institute at Washington University

Scientists identified more than 10,000 species of microbes that occupy the human ecosystem, documenting the impressive diversity of microbial life in the human body.

The bacterium *Enterococcus faecalis*, which lives in the human gut, is just one type of microbe studied as part of the Human Microbiome Project funded by the National Institutes of Health (NIH).

and one of the project's principal investigators. "Knowing which microbes live in various ecological niches in healthy people allows us to better investigate what goes awry in diseases that are thought to have a microbial link, like Crohn's and obesity, and why dangerous pathogens sometimes, but not always, cause life-threatening illnesses."

Washington University and its Genome Institute played a major role in the research, known as the Human Microbiome Project. The five-year initiative was funded with \$153 million from the National Institutes of Health (NIH), with some \$32 million coming to Washington University.

Genome Institute scientists decoded about half of the 5,000 specimens from nearly 250 healthy volunteers.

"Data generated from this study has the added potential to provide scientists with new insights into how local environments shape the composition of microbes that are found in healthy individuals," says co-investigator Mark A. Watson, MD, PhD, associate professor of pathology and immunology.

Global team of scientists to study childhood malnutrition

Washington University to lead effort

Jeffrey I. Gordon, MD, the Dr. Robert J. Glaser Distinguished University Professor and director of Washington University's Center for Genome Sciences and Systems Biology, will lead an international team of scientists to find new ways to diagnose, treat and prevent a critical global health problem: malnutrition in infants and children. The work is funded by an \$8.3 million grant from the Bill & Melinda Gates Foundation.

Gordon's research first established a link between obesity and the trillions of friendly microbes that live in the intestine, where they extract nutrients and calories from food. His studies have shown that diet helps shape the mix of microbes in the intestine and that these microbes, in turn, influence how efficiently nutrients and calories are harvested from foods. This dynamic interplay has led Gordon to suspect that an imbalance of certain types of gut microbes conspires with an inadequate diet to trigger malnutrition.

"A complex relationship exists between diet, gut microbial communities and the immune system in severely malnourished children," says Gordon. "We now have a way to tease apart these influences. This project seeks to discover novel dietary and microbial therapeutics that can be targeted to infants and children living in countries with rampant malnutrition."

The new research builds on ongoing clinical studies in Africa, South Asia and South America of malnourished and healthy infants and children and their mothers.

The community of intestinal microbes and their vast collection of genes, known as the gut microbiome, are assembled right from birth and influenced by babies' early environments and the first foods they consume, such as breast milk. As part of the Breast Milk, Gut Microbiome and Immunity Project, Gordon will work with other scientists to evaluate the relationship among first foods, the developing community of microbes in the intestine and the developing immune system.

Gordon's research underscores the need to understand the workings of gut microbiomes among people of different ages living in different parts of the world, especially as scientists consider manipulating intestinal microbes to improve health and nutrition.



ROBERT BOSTON

Summer school Lawrence M. Lewis, MD, professor of emergency medicine, studies a sonogram in the emergency room with Amanda Fletcher, a student from Meharry Medical College. Fletcher and 10 other Meharry students visited Washington University School of Medicine over the summer to participate in a program coordinated by the Office of Medical Student Research. Each student is paired with a faculty mentor and given the opportunity to conduct research. Fletcher is studying whether higher health literacy correlates with better self-management of hypertension. As part of her experience, she is shadowing Lewis in the emergency room and interviewing patients.

Pediatric quintet tapped as leaders

Washington University's Department of Pediatrics and St. Louis Children's Hospital once again have been catapulted into the national spotlight — this time by the simultaneous election of five pediatric faculty into the top national leadership roles in large and distinguished medical societies.

Thomas W. Ferkol Jr., MD, was installed as vice president of the American Thoracic Society. Keith A. Hruska, MD, was elected president of the American Society for Bone and Mineral Research. David M. Jaffe, MD, was installed as president of the Academic Pediatric Association. Alan L. Schwartz, PhD, MD, will become president of the American Pediatric Society. Gregory A. Storch, MD, is president-elect of the Pan American Society for Clinical Virology.



"Election to lead a major academic society is a mark of distinction," says Schwartz, the Harriet B. Spoehrer Professor and head of the Department of Pediatrics. "We are very proud of the recognition of Drs. Ferkol, Hruska, Jaffe and Storch by their peers nationally. This is a most unusual concurrence, and one that highlights Washington University School of Medicine."



ROBERT BOSTON

Heavy lifting

Workers prepare to place a new MRI scanner into the East Building at Washington University School of

Medicine. The 18,000-pound scanner, delivered in June, is customized for use in the Human

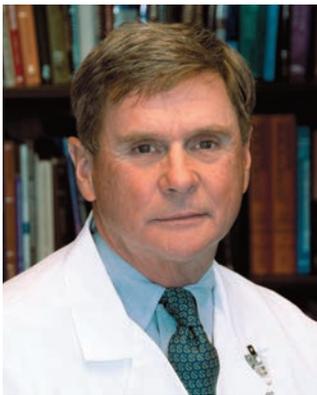
Connectome Project, a research study that will trace the anatomical and functional

connections between different regions of the human brain. David C. Van Essen, PhD, the Edison Professor and head of the Department of Anatomy and Neurobiology, is co-investigator of the project, which began scanning brains of research participants in August. The project aims to compile unparalleled neural data and to create an interface to graphically navigate this information.

Dacey heads neurosurgery society

Ralph G. Dacey Jr., MD, the Henry G. and Edith R. Schwartz Professor and head of the Department of Neurosurgery, is now president of the Society of Neurological Surgeons (SNS).

The SNS is the American society of leaders in neurosurgical residency education and is the oldest neurosurgical society in the world. Dacey, who is neurosurgeon in chief at Barnes-Jewish Hospital, joins an exclusive group of neuro-



Ralph G. Dacey Jr., MD

surgical leaders that includes Harvey W. Cushing, MD, who is regarded as the father of modern neurosurgery and served as the SNS's first president in 1920. Additionally, each of Dacey's predecessors as head of the Department of Neurosurgery served terms as president of the SNS: Ernest Sachs, MD, the first professor of neurological surgery in the world and founding director of the Department of Neurological Surgery at the School of Medicine; Henry G. Schwartz, MD; and Sidney Goldring,

MD. Sachs was a founding member of the society in 1920.

The group's goals include promoting improvements in education and training for neurosurgical students and postgraduates; recognizing outstanding neurosurgical care, instruction and research; and encouraging the highest standards of care for patients with neurological diseases.

Dacey plans to work with the Accreditation Council for Graduate Medical Education to optimize a new set of procedures for accrediting neurosurgical training programs and to establish a web portal to help meet the educational needs of neurosurgeons at every point in their careers, from neurosurgical residents to practicing neurosurgeons.

Examining the link between diabetes and heart disease

Grant to fund collaborative research

Researchers at the School of Medicine have received a \$4.7 million grant from the National Heart, Lung, and Blood Institute to investigate heart disease in patients with diabetes.

"Diabetes is an incredibly common problem," says Jean E. Schaffer, MD, the Virginia Minnich Distinguished Professor of Medicine. "It affects a huge swath of the population. Importantly, people with diabetes don't just have a metabolic disorder. They develop complications in many organs. And one of the most deadly complications is heart disease. We're particularly interested in why people with diabetes suffer from unusually severe forms of heart disease."

For reasons not fully understood, people with diabetes are more likely to develop blockages in arteries. After a heart attack, the course of the subsequent heart disease is more aggressive than in people without diabetes. Even independent of blocked arteries, there is evidence that their hearts do not function like those of individuals without diabetes.

"Diabetes is an incredibly common problem that affects a huge swath of the population. We're particularly interested in why people with diabetes suffer from unusually severe forms of heart disease."

JEAN E. SCHAFFER, MD

According to the Centers for Disease Control and Prevention, almost 26 million Americans are living with type 2 diabetes and another 79 million with undiagnosed diabetes or

pre-diabetes, a condition that increases their risk of developing the full-blown variety. With such statistics, it is becoming increasingly important to explore the reasons behind the aggressive progress of cardiovascular disease in patients whose bodies do not properly regulate blood sugar.

Schaffer and her colleagues suspect a likely culprit is abnormal lipid metabolism. Lipids are a class of molecules that includes fats, such as fatty acids and triglycerides. Past studies have shown that patients with diabetes store higher levels of these lipids in their heart muscle, likely impairing cardiac function. These lipids appear to lead to inflammation and can also damage important parts of heart cells, such as proteins and DNA, leading to heart muscle dysfunction. The goal of the new research program is to identify better measures of heart disease in patients with diabetes.

Washington University will serve as the coordinating center among five institutions chosen to receive this funding from the National Institutes of Health (NIH). The other participating centers are the Cleveland Clinic, Emory University, National Jewish Health and Weill Cornell Medical College.



Global health Henish A. Bhansali, MD, instructor in medicine, Victor G. Davila-Roman, MD, professor of medicine, and Yeshey Penjore, MD, a cardiologist from the National Referral Hospital in Thimpu, Bhutan, review a heart echocardiogram. Penjore trained at the School of Medicine for two months as part of the Global Health Scholars in Medicine Program, a Department of Medicine initiative designed to expand global health education. Penjore also attended continuing medical education courses and worked alongside Washington University cardiologists, experiences he will use to better diagnose and treat his patients in Bhutan, where there is a high prevalence of congenital heart disease.

GASTROENTEROLOGY

Poor colonoscopy prep hides polyps

What happens the day before a colonoscopy may be just as important as the test itself.

Gastroenterologists at the School of Medicine have found that when patients don't adequately prep for the test by cleansing their colons, doctors often can't see potentially dangerous pre-cancerous lesions.

Reporting in the journal *Gastrointestinal Endoscopy*, the researchers say that doctors often missed at least one pre-cancerous growth in about one-third of patients who did not properly prepare for their colonoscopy. Polyps and other markers of cancer risk were then discovered in subsequent colonoscopies.

Although several studies have found that up to a quarter of colonoscopy patients don't prepare adequately for the test, the new study is the first to point out the potential consequences of poor bowel preparation in outpatients at average risk.

"Because so many of the patients had a follow-up screening less than a year after the initial test, we strongly suspect that most of the pre-cancerous growths found during the

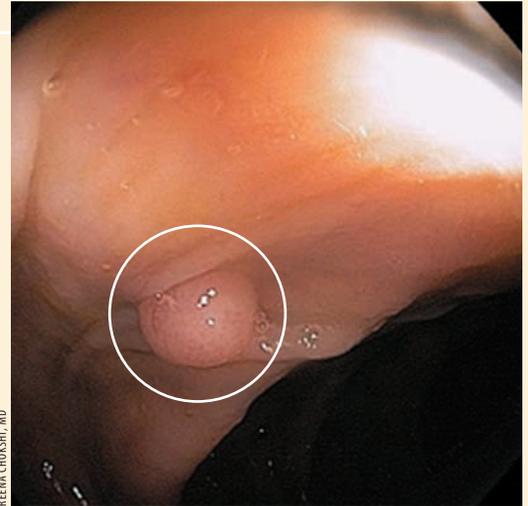
second colonoscopy already were present at the time of the initial test," says first author Reena Chokshi, MD, a gastroenterology fellow at Washington University.

Researchers say their findings suggest that if a physician is having difficulty seeing the colon due to inadequate bowel prep, the colonoscopy should be stopped and rescheduled.

"Rather than subjecting a patient to the potential risks of a full colonoscopy when we may not be able to detect polyps, or other pre-cancerous growths called adenomas, it may be better to bring that patient back as soon as possible for a repeat procedure with better bowel preparation," says Chokshi.

On the day before a colonoscopy exam, people are asked to stop eating solid food and to consume only clear liquids. Later in the day and the next morning, patients drink bowel-cleansing mixtures to empty the colon prior to the examination.

The test itself usually takes less than an hour, and patients are sedated during that time. Using a tiny camera, doctors are able to look at the walls of the colon in an attempt



REENA CHOKSHI, MD

Doctors discover a polyp during a repeat colonoscopy conducted on a study patient who had not prepared adequately for the initial exam.

to detect polyps and other pre-cancerous growths. Once detected, those growths can be removed during the procedure.

"It generally takes several years for an adenoma to become cancerous," Chokshi says. "So it certainly is possible that any lesion we miss during a colonoscopy could develop into a malignancy before a person's next colonoscopy, especially if it doesn't happen until 10 years later."



ROBERT BOSTON

Research rewarded Morton E. Smith, MD, councilor for the Washington University chapter of Alpha Omega Alpha (AOA), congratulates first-year medical student Gregory C. Ebersole, the 2012 recipient of the AOA's Carolyn L. Kuckein Student Research Fellowship. Ebersole is studying the responsiveness and validity of a postsurgical functional assessment survey for cubital tunnel syndrome, a condition brought on by increased pressure on the ulnar nerve at the elbow.

Siteman welcomes Komen funding

With more than \$5 million in new grants from Susan G. Komen for the Cure, Washington University scientists at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine are developing innovative treatments in the fight against breast cancer.

The largest portion — \$4 million — will be used to better identify which women with estrogen receptor-positive (ER-positive) breast cancer, the most common form of the disease, are at highest risk for recurrence and to determine more effective treatments for those individuals.

“There are so many new drugs out there for breast cancer patients that we need a way to establish which ones are most likely to be the home run,” says

Matthew J. Ellis, MD, PhD, professor of medicine and chief of the breast oncology section. “Our goal is to screen drugs to find the one that will produce the best outcome for the patient with the least toxicity.”

Ellis is a co-recipient of the grant along with Elaine R. Mardis,

PhD, co-director of The Genome Institute at the School of Medicine, and Pascal Meier, PhD, of The Institute of Cancer Research in London.

Using DNA sequencing to compare a patient's normal and cancerous cells, the researchers are learning why traditional anti-hormone drugs often are only partially effective in reducing tumor growth. The study involves developing a test to predict which patients are most likely to experience recurrence after five years and determining which combination of drugs now in development will kill all ER-positive cancer cells and prevent recurrence.

A new test under development will predict breast cancer recurrence and also protect women from unnecessary treatment and follow-up visits.

Largest-ever share of cancer genome data released

Free access will accelerate research

To speed progress against cancer and other diseases, the St. Jude Children's Research Hospital-Washington University Pediatric Cancer Genome Project has announced the largest release to date of comprehensive human cancer genome data for free access by the global scientific community.

The amount of information released more than doubles the volume of high-coverage, whole-genome data currently available from all human genome sources combined. This information is valuable not just to cancer researchers, but also to scientists studying almost any disease.

The release of this data was announced as a part of a perspective published online May 29 in *Nature Genetics*.

The 520 genome sequences released are matched sets of normal and tumor tissue samples from 260 pediatric cancer patients. The St. Jude and Washington University researchers are analyzing the genomic sequences to determine the differences between each child's normal and cancerous cells to pinpoint the causes of more than a half-dozen of the most deadly childhood cancers, an effort which has already produced a number of key discoveries reported in top scientific journals.

Launched in early 2010, the Pediatric Cancer Genome Project is the world's largest effort and investment to date to understand the genetic origins of childhood cancers. The three-year project will cost an estimated \$65 million. St. Jude is covering \$55 million of the cost, including a \$20 million commitment from Kay Jewelers, a long-standing partner of St. Jude. This is the first major privately funded human genome sequencing project to share its data as soon as it becomes available.

“This approach has been more valuable than anyone could have predicted,” says Richard K. Wilson, PhD, director of The Genome Institute. “We have identified unusual, ‘cryptic’ changes in many patients’ cancer cells that we would not have found using other methods. We are pleased to be able to share this data with the research community in hopes that others can build upon our initial discoveries.”



more information
pediatriccancergenomeproject.org

A large number of zebrafish (Danio rerio) are swimming in a blue tank. The fish are arranged in various directions, some facing left and some facing right. The background is a solid blue color, and the lighting is bright, highlighting the silver and blue stripes on the fish's bodies.

WATERWORLD

Take a look inside a
splashy research facility



A common type of minnow, the zebrafish is increasingly popular in scientific research.

Because its tiny embryos are transparent and develop outside the body, zebrafish are useful for observing growth and development. In addition, while less expensive than mice, research results from studying zebrafish have been shown to be just as valuable as those from mice.

Washington University is home to one of the largest zebrafish facilities in the world. And with robotic feeding and cleaning systems, it is the world's most modern, says Lilianna Solnica-Krezel, PhD, professor and head of the Department of Developmental Biology at the School of Medicine.

"This facility allows us to do large-scale, collaborative projects that would not be possible for individual investigators."

The work of more than 30 researchers is currently supported by the facility. Beyond sheer numbers of fish, other resources abound, such as capabilities for obtaining, viewing and manipulating fish embryos and calling on the expertise of colleagues who can help in evaluating experiments.

zebrafish.wustl.edu



Fish larvae beginning their life cycles



Infertile eggs are extracted using a stereomicroscope.



Zebrafish develop rapidly; at 36 hours, an embryo has a complete body with most organs and a beating heart.



Fertilized eggs filter through a false-bottomed mating cage, which prevents the fish from eating the eggs and facilitates embryo collection.



Large numbers of fish grow quickly as robotic feeding machines travel to each tank, providing frequent small meals.

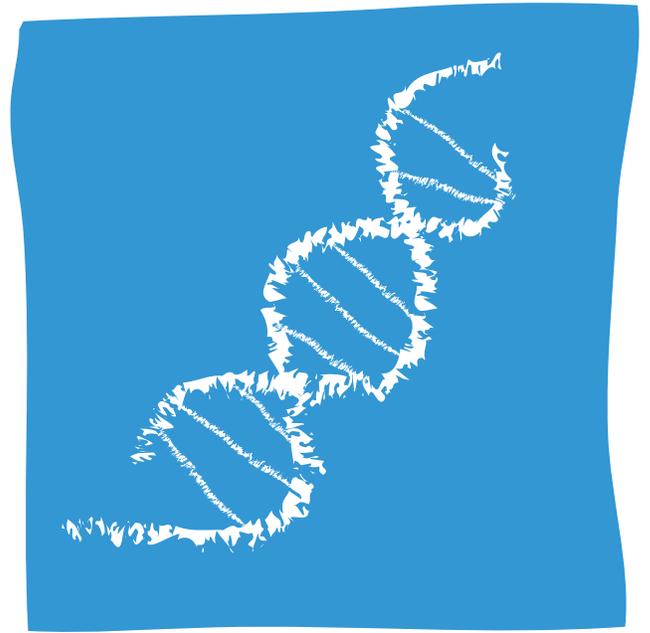
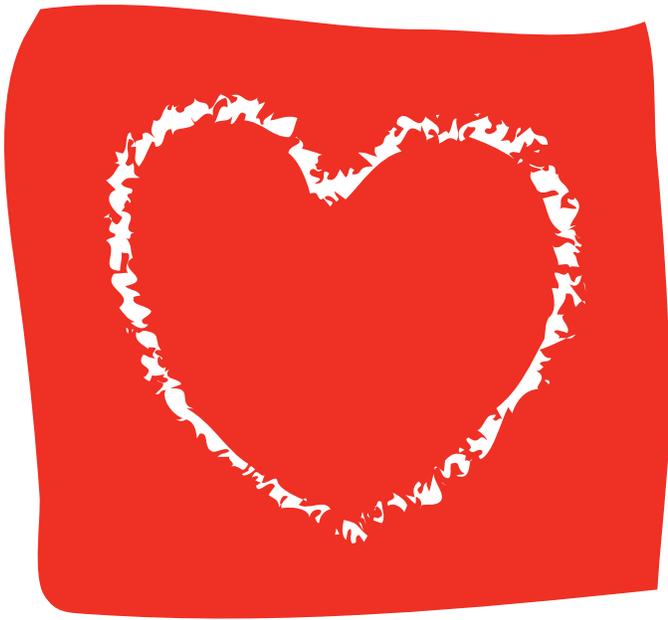


Systems automate water, temperature and more. Each room has its own centralized life support, including an innovative filtration system that passes used water through a biological filter (below) before reuse. Alarms can alert responders to a systems failure.



ROBERT BOSTON

Fish capacity	200,000	Current occupancy	80,000
Fish tanks	6,780	Total water capacity, in liters	17,898



It's for the kids



Advances in pediatric care are no longer enough. Today researchers are focused on an even higher goal — discovering cures for the most serious disorders of childhood. The **Children’s Discovery Institute**, a joint initiative of Washington University School of Medicine and St. Louis Children’s Hospital, is designed to change the way pediatric research is conducted. [▶ childrensdiscovery.org](http://childrensdiscovery.org)

By funding innovative research and translating discovery into treatment, Institute investigators hope to make significant advances in caring for sick children.

Since its launch in 2006, the Children’s Discovery Institute has awarded nearly \$29.5 million to researchers tackling deadly pediatric diseases ranging from cancer to malaria. The targeted effort has united clinicians and investigators from all corners of Washington University, reaching across 16 departments in three schools.

“In seeking new answers to questions about pediatric disease, we need to collaborate and think in bold new ways,” says Mary C. Dinauer, MD, PhD, scientific director of the Children’s Discovery Institute and professor of pediatrics and of pathology and immunology at the School of Medicine.

Institute-funded projects in four areas — childhood cancer, musculoskeletal and metabolic diseases, pulmonary disease and congenital heart disease — are “discovery research,” preliminary studies that may eventually yield new treatments.

“The Children’s Discovery Institute is an interesting concept developed to fund early-stage research that will lead to a better understanding of childhood disease and treatment, and in some cases, even prevention,” says Dinauer, who also

serves as the Fred M. Saigh Distinguished Chair in Pediatric Research at St. Louis Children’s Hospital.

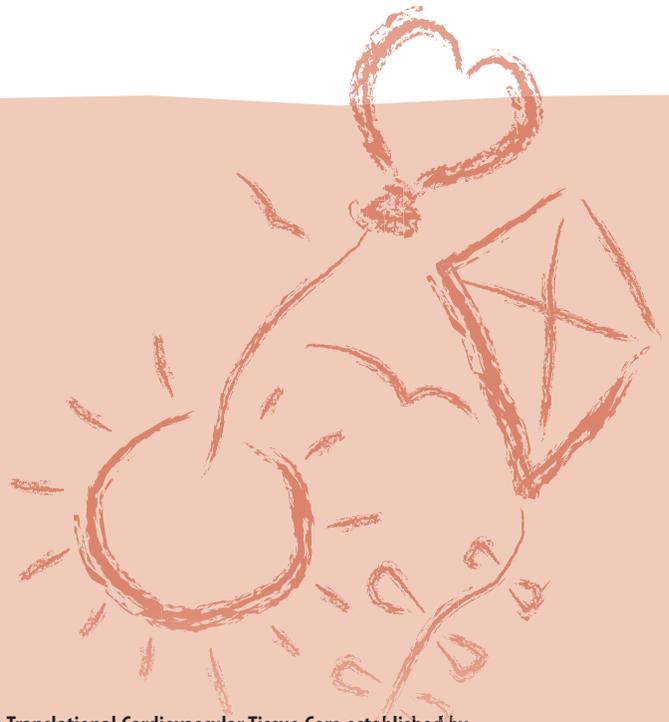
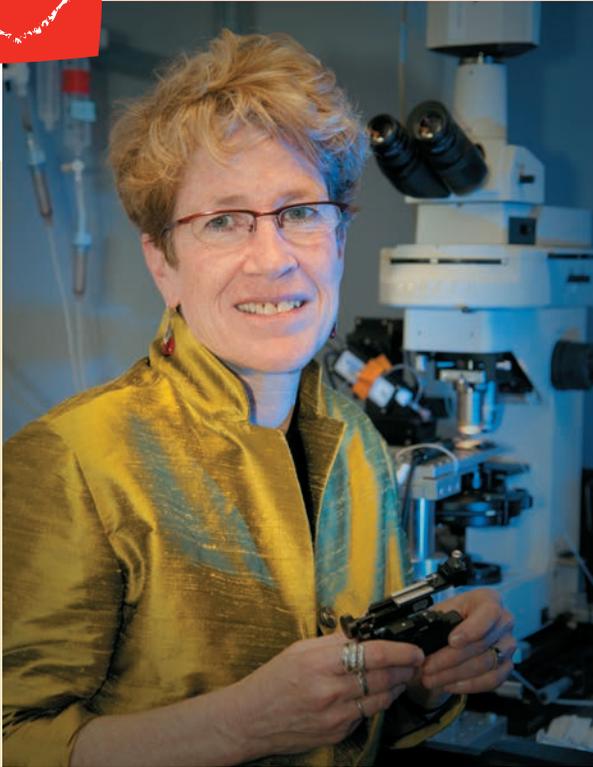
Of the 92 grants awarded to researchers since the Institute’s inception, 55 percent were to researchers outside the Department of Pediatrics. According to Dinauer, that’s unique among children’s disease research.

“We want these grants to bring people from multiple disciplines together to study in this research area,” she says. “Other institutions have in-house funding for research, but it stays within the department.”

The Children’s Discovery Institute also funds a Faculty Scholars Award that provides three years of support to junior faculty, allowing them to set up their laboratories, as well as a summer research opportunities program for undergraduate students.

“In the end, we want to establish new areas of pediatric research,” Dinauer says. “Creative collaborations will allow us to conduct outstanding investigations that otherwise wouldn’t have been possible.”

BY BETH MILLER



The Translational Cardiovascular Tissue Core established by Jeanne M. Nerbonne, PhD, and colleagues allows scientists to study hypertrophic cardiomyopathy from all angles.

PHOTOS BY ROBERT BOSTON - ILLUSTRATIONS BY ERIC YOUNG

Understanding a silent danger

A healthy teenager suddenly collapses during soccer practice and dies. After his death, physicians find he was harboring a silent killer known as hypertrophic cardiomyopathy, a condition in which the heart muscle becomes thickened, making it harder to pump blood out of the heart.

The condition generally has no symptoms, but it is the most common killer of adolescents who are otherwise healthy and is the leading reason for heart transplants in children.

There is no way to predict when a seemingly healthy adolescent might experience sudden and fatal heart failure.

Despite its prevalence, very little is known about the genetic and molecular makeup or the electrical phenotypes of the hearts of children with hypertrophic cardiomyopathy. New research funded by the Children's Discovery Institute may change that.

Jeanne M. Nerbonne, PhD, the Alumni Endowed Professor of Molecular Biology and Pharmacology in Developmental Biology, and her colleagues received a large initiative grant from the Institute to develop the Translational Cardiovascular Tissue Core, a centralized system for acquiring, banking, annotating with clinical data, and distributing tissue from diseased hearts.

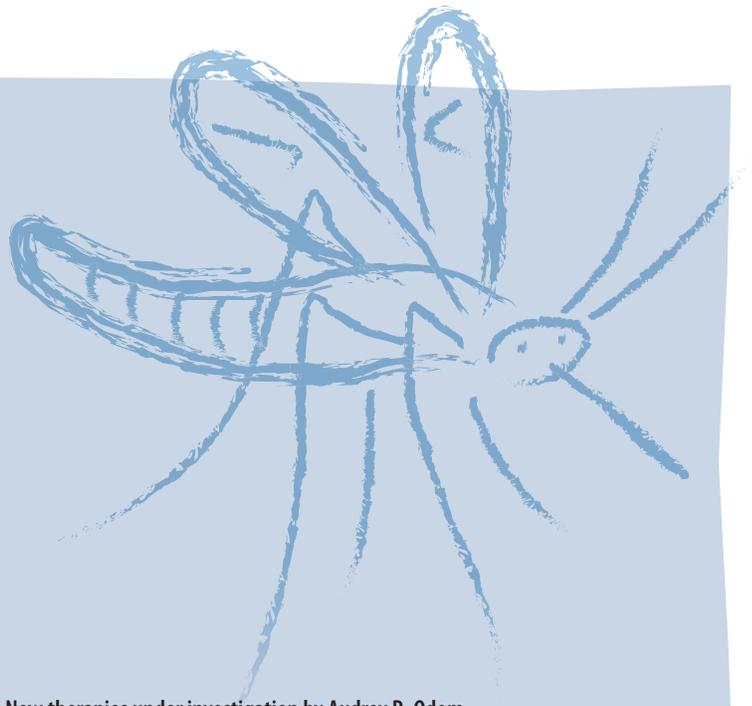
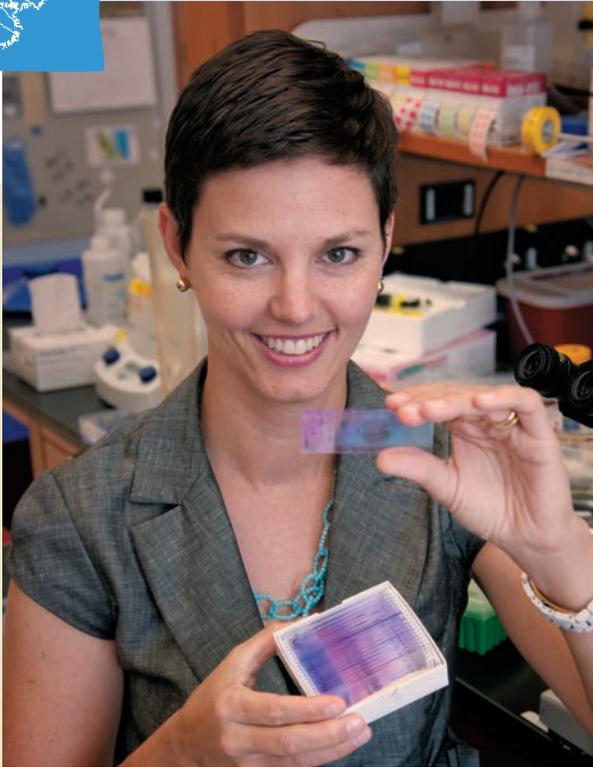
It is directed by Kathryn A. Yamada, PhD, professor of medicine in the Cardiovascular Division.

"As individuals develop heart failure," says Nerbonne, "we do not know how to predict who is going to have the fatal sudden death incident. It has become increasingly clear that detailed electrophysiological and molecular analyses of diseased and non-diseased human hearts are urgently needed to advance the field."

Nerbonne, professor of medicine, and her team take tissue samples from the diseased hearts of children at the time they get a ventricular-assist device, which helps the heart pump blood and is often used as a bridge to a heart transplant. Investigators then perform various studies on these tissues, looking at the proteins, RNA, cellular and whole tissue physiology, as well as bank tissue for genetic and epigenetic analyses. They also collect diseased hearts at the time of transplant and perform similar studies, comparing what they find with non-diseased heart tissue.

Notably, the banked tissue and associated data will be available to all Washington University investigators for further types of analysis.

"As the science moves forward," Nerbonne says, "other researchers will be able to take a different look at the data for new discoveries."



New therapies under investigation by Audrey R. Odom, MD, PhD, could stem the threat of malaria, spread by mosquitoes to millions of children worldwide every year.

Swatting malaria more effectively

Internationally, there are 250 million to 350 million cases of malaria each year, resulting in about 1 million deaths. Most of those deaths are children under age 5.

Audrey R. Odom, MD, PhD, wants to cure malaria. The pediatric infectious disease specialist has been working toward that goal since she came to the School of Medicine in 2008 with a Children's Discovery Institute Faculty Scholars Award.

Odom's background in cell signaling in eukaryotic organisms, or microbes that have a nucleus and organelles like human cells, led her to apply that knowledge to a eukaryotic pathogen in child health. An assistant professor of pediatrics and of molecular microbiology, Odom says malaria is hard to control because the parasite has become resistant to nearly all currently available anti-malarial drugs.

"Chloroquine, a mainstay drug for nearly 100 years, is resistant to malaria worldwide," Odom says. "Every time we develop a new drug, we're going to encounter resistance, so we need to establish a continual pipeline of new drugs."

With funding from a separate grant from the Children's Discovery Institute, Odom has made progress with that pipeline. She has identified a metabolic pathway that is present in the malaria parasite and is required for it to grow, but that is not present in humans.

"In theory, we can create a safe antimalarial drug," she says. "What makes this pathway even more exciting is that it's also present in the mycobacteria that cause tuberculosis, and there's also a real need for new drugs for TB."

Odom and her colleagues are testing new compounds to see if they inhibit the enzyme and kill the malaria parasite. Her research team also is screening a large number of existing compounds to determine if they have any effect.

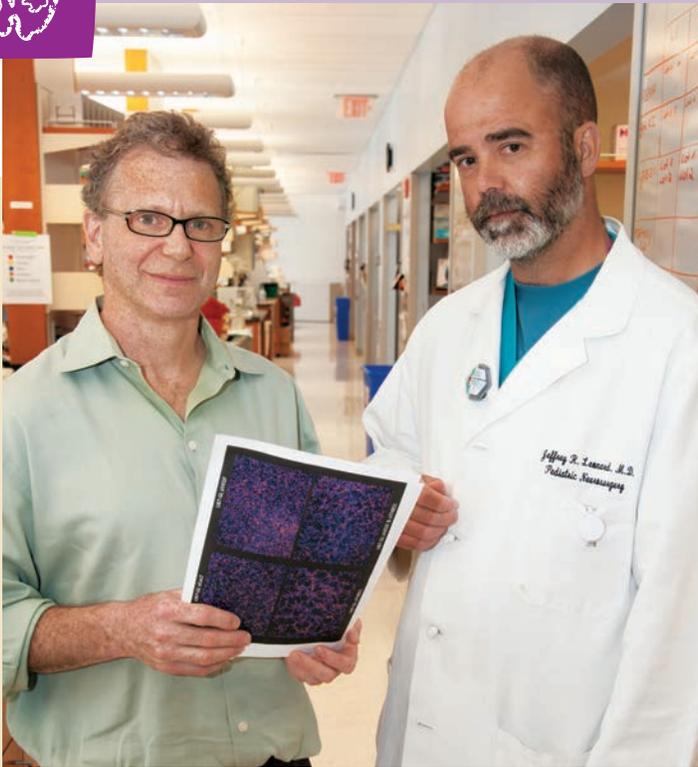
But that's not her ultimate goal.

"I want to identify a small molecule inhibitor that we can pitch to pharmaceutical companies to treat bacterial infections in the United States and that they can then give away to treat malaria and TB in the developing world," Odom says.

But the malaria parasite also likely will become resistant to that drug, she says, so her strategy is to pair it with another compound.

"Combination therapy," Odom says, "will be the way forward."

Malaria is hard to control because the parasite has become resistant to current anti-malarial drugs.



Researchers Joshua B. Rubin, MD, PhD, and Jeffrey R. Leonard, MD, use the data bank they created to study treatment of pediatric brain tumors.

PHOTO: BY ROBERT BOSTON - ILLUSTRATIONS BY ERIC YOUNG

Banking on a store of knowledge

Cancer is the leading cause of death by disease among U.S. children between infancy and age 15. Among major childhood cancers, leukemia and brain and other central nervous system tumors make up more than half of new cases.

A child with leukemia — a cancer of the blood cells — has a 90 percent chance of long-term survival. But only two of three children with a malignant brain or central nervous system tumor will live beyond five years.

Brain tumor treatments — while effective — can cause brain damage and other toxic side effects.

According to researchers Jeffrey R. Leonard, MD, and Joshua B. Rubin, MD, PhD, that needs to change.

Part of the reason pediatric brain tumors are so deadly is the lack of samples on which to do research. With funding from the Children's Discovery Institute, Leonard, associate professor of neurosurgery and of pediatrics, and Rubin, associate professor of pediatrics, of neurology and of neurobiology, have developed a pediatric brain tumor data bank. It contains tissue samples from brain tumors in children they have treated, along with individual patient data such as age, sex, type of tumor and type of treatment. New data is automatically entered into the databank.

Leonard and Rubin implant the brain tumor samples into mouse brains. By studying how the tumors grow in the mice, they can screen thousands of existing compounds to determine if any work to slow the tumor's growth or eliminate the tumor.

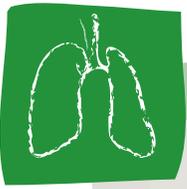
Rubin says that current treatments can be effective, but they also can cause long-term damage to children's brains. "So," he says, "even when tumors are cured, we are still looking for new treatments with less toxicity."

Data from the tumor bank also is available to other researchers to study brain tumors, perform genetic screens or test for new drugs.

"We have a large number of resources here," Leonard says. "We want people around the country to view Washington University as the place to come for pediatric and adult brain tumor research."

The Children's Discovery Institute provides a unique mechanism to support innovative ideas and collaborative efforts among departments and across campuses, Rubin says.

"What's smart about setting it up that way is it requires people to come up with a novel, collaborative approach to pediatric disease," he says. "That prompts research that might not have happened without support from the Institute."



Thomas W. Ferkol, MD, and a team of diverse researchers from across the university are studying persistent respiratory, sinus and ear infections in children.



Linking rare and common diseases

Painful middle ear infections are among the most common infections seen in toddlers and young children. Many children find relief in a course of antibiotics, but others experience recurrent ear infections.

To find answers to what causes these and other pediatric respiratory infections, the Children's Discovery Institute awarded a large initiative grant to Thomas W. Ferkol, MD, the Alexis Hartmann, MD, Professor in Pediatrics. Ferkol, also professor

of cell biology and physiology, is a world-renowned expert on primary ciliary dyskinesia (PCD), a rare, inherited lung disease that results in chronic infections of the respiratory tract.

He and his team are studying the functional, structural and genetic characteristics of cilia diseases in children using a single-celled algae model that is structurally identical to a human cilium. Ultimately, they will learn more about common childhood diseases that could lead to better care, prevention and identification of new treatments.

The cilia are tiny, hair-like structures in the lungs, nose, sinuses and ears that help clear out mucus, foreign particles, fluids and bacteria.

When the cilia don't function correctly, children develop respiratory, sinus and ear infections.

In PCD, which occurs in about one in every 12,000 to 20,000 births, cilia are unable to clear out bacteria-filled mucus from the lungs, sinuses and ears, resulting in persistent infections. Ferkol and the research team suspect a link between common ear infections and the relatively rare PCD.

"Children who get chronic ear infections, requiring repeated treatment with antibiotics and sometimes surgeries, also may have genetic and functional defects of the cilia, similar to children with PCD, but much less severe," he says.

The team has found genetic mutations that may impact cilia and flagella, another hair-like structure that functions much like cilia. The mutations disrupt the biochemical pathways of motor proteins that surround each cilium and make it move.

"Our goal is to connect specific abnormalities of cilia motion with a child's genetic profile, then connect that with a child's disease," Ferkol says. "One day, we could potentially personalize treatment to the genetics and cilia motion abnormalities present in each child."

Ferkol says the collaboration and support from the Children's Discovery Institute have been instrumental in bringing about these insights. □

Though treatable, ear infections and other respiratory infections have a high rate of recurrence.



ROBERT BOSTON



Advocating a systems view of musculo-skeletal health: Roberto Civitelli, MD, and Linda J. Sandell, PhD

Making connections

50+ labs integrate bone, muscle and connective tissue research
BY JIM DRYDEN





The focus of bone health has long been repair. Broken bones, torn ligaments and damaged cartilage either can be put in a cast to heal or surgically repaired to restore normal function. Or, a worn joint can be totally replaced. But that only fixes the mechanical breakdown. It doesn't address the underlying problems that led to the breakdown of bones, muscles, tendons, ligaments and cartilage.

"If you're going to have biological solutions," says Linda J. Sandell, PhD, the Mildred B. Simon Research Professor of Orthopaedic Surgery and professor of cell biology and physiology, "you need to reach back from the structure to the things that are performing the function."

"Exactly," echoes Roberto Civitelli, MD, the Sydney M. and Stella H. Schoenberg Professor of Medicine and chief of the Division of Bone and Mineral Diseases. "We must cover the spectrum, from the basic biology to cell biology to the signals between cells that regulate breakdown and healing. It is much cheaper to prevent problems such as fractures than to treat them after they occur."

At the new Washington University Center for Musculoskeletal Research, researchers are attempting to do just that. By employing a collaborative approach, they hope to better understand the biological underpinnings of problems with bones and connective tissue. CONTINUED ON PAGE 20 »



Core *concepts*

UNLIKE A PIECE OF CHALK, bone is no dry, static thing wearing away with use. A structure at rest, a machine in motion, the living skeleton renews itself in cycles, regulating and interacting with tissues and systems throughout the body. Musculoskeletal performance peaks in adulthood and then declines, a precursor to pain, disease and fractures.

At the Musculoskeletal Research Center, collaborative teams strive to understand the complex foundations of bone, joint and muscle health. These findings will be applied to osteoporosis, osteoarthritis and other musculoskeletal conditions.

Earlier detection and treatment — or finding the means to avoid disease altogether — will help to ensure a skeleton's long and active life.

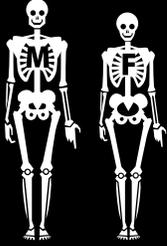
Musculoskeletal hotspots

Daily stress makes these areas trouble-prone. Healthy eating and staying active will maintain the skeleton. But in some cases, targeted drug therapies may forestall disease, prevent fractures and limit the need for costly joint replacements.



Balancing act

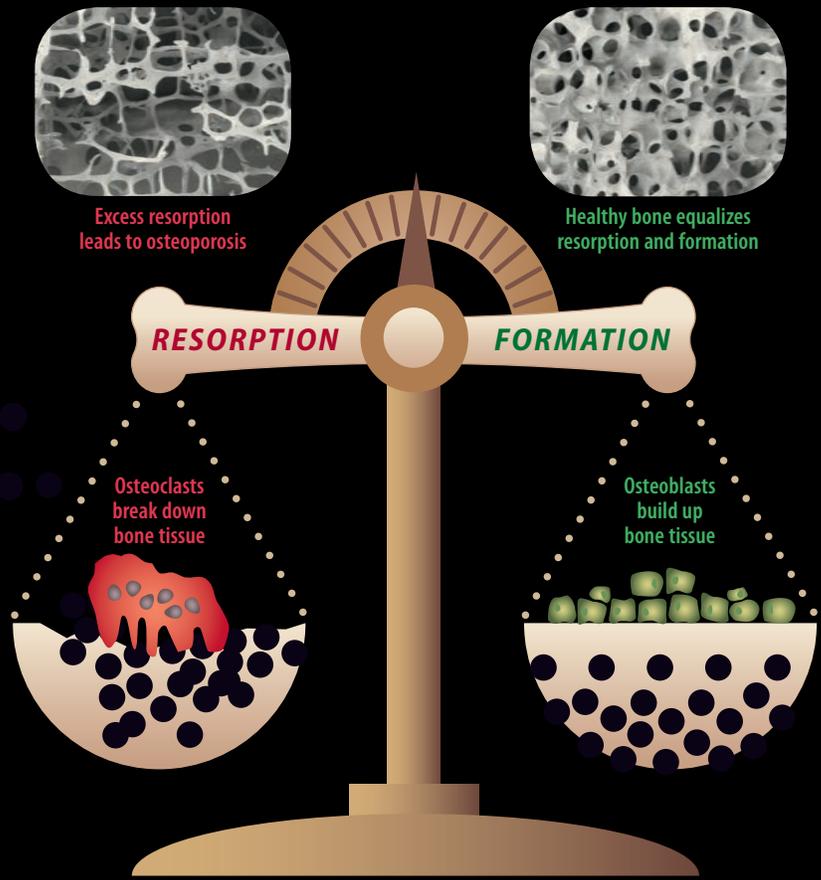
osteoporosis



25% **40%**

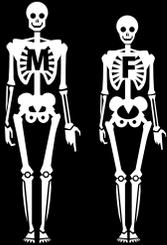
RISK
Age 50+

A body tears down and rebuilds its skeleton every 10 years or so. This natural cycle is key to skeletal health — that is, as long as the resorption and formation processes remain balanced. Once bone formation slows later in adulthood, however, excess resorption can weaken bones, increasing the risk of fractures. Drug therapies that rebalance the cycle can mitigate the disease known as osteoporosis.



Painful legacy

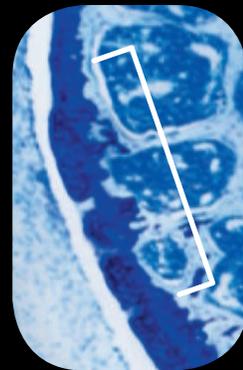
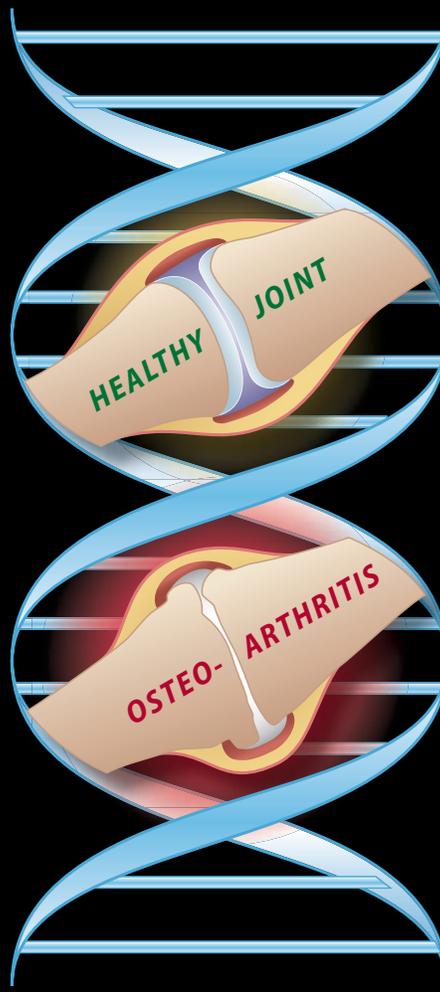
osteoarthritis



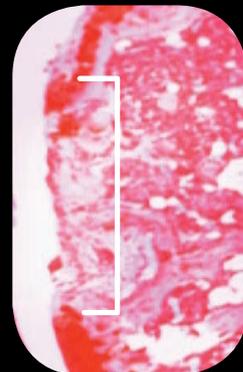
50% **50%**

RISK
Age 50+

Why doesn't everyone get osteoarthritis (OA)? The disease affects skeletal joints and cartilage, the "cushion" between the bones. Research shows that some animals inherit the ability to repair damaged cartilage. Understanding and possibly enhancing this repair process in humans is one goal of OA research.



"Repair genes" heal injured cartilage (dark blue)



Without repair genes, injured area does not heal



“The skeleton and its components are part of the organism,” says Civitelli, professor of orthopaedic surgery and of cell biology and physiology and the leader of an NIH-funded training program in skeletal disorders. “Without the skeleton, you don’t have any way for muscles to function. You would have no protection of soft tissues, and you would have no way of regulating many key cellular processes. We’re even learning that bone is necessary for normal glucose metabolism.”

“Roberto’s point is that the bone is doing more than just taking care of itself,” Sandell adds. “We’ve got cells that make bone and cells that resorb bone, the so-called osteoblasts and osteoclasts. Those regulate the bone, but the bone appears to be regulating other things. There are clear connections between diabetes and obesity and inflammation and the skeleton. That’s why we need all of these investigators working together. One specialty just doesn’t bring enough to the table to understand this anymore.”

The Center for Musculoskeletal Research, a joint effort primarily involving investigators from the Department of Orthopaedic Surgery and the Department of Medicine’s Division of Bone and Mineral Diseases, is located in the BJC Institute of Health at Washington University School of Medicine. In all, the center includes investigators from 54 laboratories. Not all of those laboratories are housed in the new space, and not all of those investigators work mainly with the muscles of the skeleton, but all are contributing in some way to an interdisciplinary effort to better understand the biologic causes that underlie skeletal problems.

“We have a historic interaction because most of us used to be housed in the Yalem Research Building,” says Sandell, who directs the NIH-funded program that supports the center’s core activities. “We had collaborations between investigators that allowed us to put together a center grant, and that greatly facilitated the creation of a center on this floor. Now we hope to launch a number of major projects that will help us diagnose and treat bone and connective tissue problems earlier so that we can prevent more serious problems later on.”

Like other floors in the Institute, workspace in the new musculoskeletal center is organized with cores in the center and laboratories surrounding those cores. Investigators’ offices line a hallway along the north side of the building.

It’s designed, says Civitelli, so that investigators in the center will see each other... a lot. “All of this didn’t just come out of the blue,” he explains. “This is the end of a long process of nurturing trainees, attracting investigators to this field, and building infrastructure.”



Intricate computer scans offer inside views of bone and joint health in animal models.

And the way the space is designed — with open labs and open administrative suites — it’s natural to bump into one another on a daily basis, which we believe will spur new collaborations across disciplines and foster creativity within the research base.”

Other key members of the center include associate directors Matthew J. Silva, PhD, and Steven L. Teitelbaum, MD. Deborah V. Novack, MD, PhD, directs a core devoted to microscopic and molecular analysis of bone, muscle, cartilage, tendons and ligaments, while David M. Ornitz, MD, PhD, and Fanxin Long, PhD, lead a mouse genetic core. One of the center’s investigators produces mice with genetic traits that mimic various bone and connective tissue diseases, while other researchers are developing animal models to find

better ways to regenerate bone, cartilage and muscle.

Ultimately, all of the studies will provide not only a better understanding of the biology of skeletal problems, but more insight into multiple disorders and how they interact. But it all starts with individual investigations.

Civitelli’s primary research focus is osteoporosis. As with other problems, he says it once was true that many cases of osteoporosis were discovered only after a fracture. Now it’s possible to screen for weakening of bones long before they break. Doctors can use a machine called a DXA scanner (Dual-energy X-ray Absorptiometry) to measure bone mineral density and determine who is at risk for fractures. The center also has a small DXA scanner and other more sensitive techniques to study bone structure and strength in mice. By studying how bone cells work, investigators are developing new approaches by which weak bones can be made stronger.

Sandell focuses on osteoarthritis. For the most part, early diagnosis of osteoarthritis isn’t yet possible. Patients don’t go to the doctor until they’re already having pain and stiffness. But there are some known risk groups.

“Half a million people have arthroscopic knee surgery each year to treat torn meniscus cartilage,” she says. “When those injuries occur in young people, they’re likely to develop arthritis later in life. So we have to find some way to repair these injuries, other than just treating the structural problem in the knee with surgery. We need to understand what’s going to happen to that person 10 or 20 years later.”

That expanded understanding is the center’s reason for existence. Although not all associated investigators are pulling in a single direction, working together will allow the researchers to better understand what goes wrong not only in osteoporosis and osteoarthritis, but in other musculoskeletal problems. □



A tree-lined dirt road leads to a new hospital for African women.

Serving a Need

An unspeakable problem. An underserved population.
An undeterred physician who championed their cause.

BY DIANE DUKE WILLIAMS



PHOTOS COURTESY OF L. LEWIS WALL, MD

For L. Lewis Wall, MD, a dream has come true. For almost 20 years, he worked doggedly to build a hospital in one of the world's poorest countries to treat women with a devastating childbirth injury. His dream became reality this past February, when the 42-bed Danja Fistula Center opened in Niger, a landlocked, arid country in West Africa. The facility is dedicated to repairing obstetric fistulas, childbirth injuries that result from untreated prolonged labor, which leave women — and often girls — with a complex mixture of medical and social problems.

"It was wonderful to be there that day," says Wall, professor of obstetrics and gynecology and of anthropology. "This hospital may seem small by American standards, but it will make a huge difference in the lives of so many women who have suffered needlessly for too long."

Obstetric fistulas are holes between body cavities that open up following severe tissue damage. They occur in women of all ages but are more common among those

In Niger, the largest nation in West Africa, a serious health problem went largely untreated until recently. L. Lewis Wall, MD, and his wife, Helen (far left, above), donned traditional African garb for the opening of the Danja Fistula Center earlier this year. The new facility offers hope to thousands of women who have suffered severe injury during childbirth. Accommodations for patients' families (far right, above) give them a place to stay during treatment and recovery.

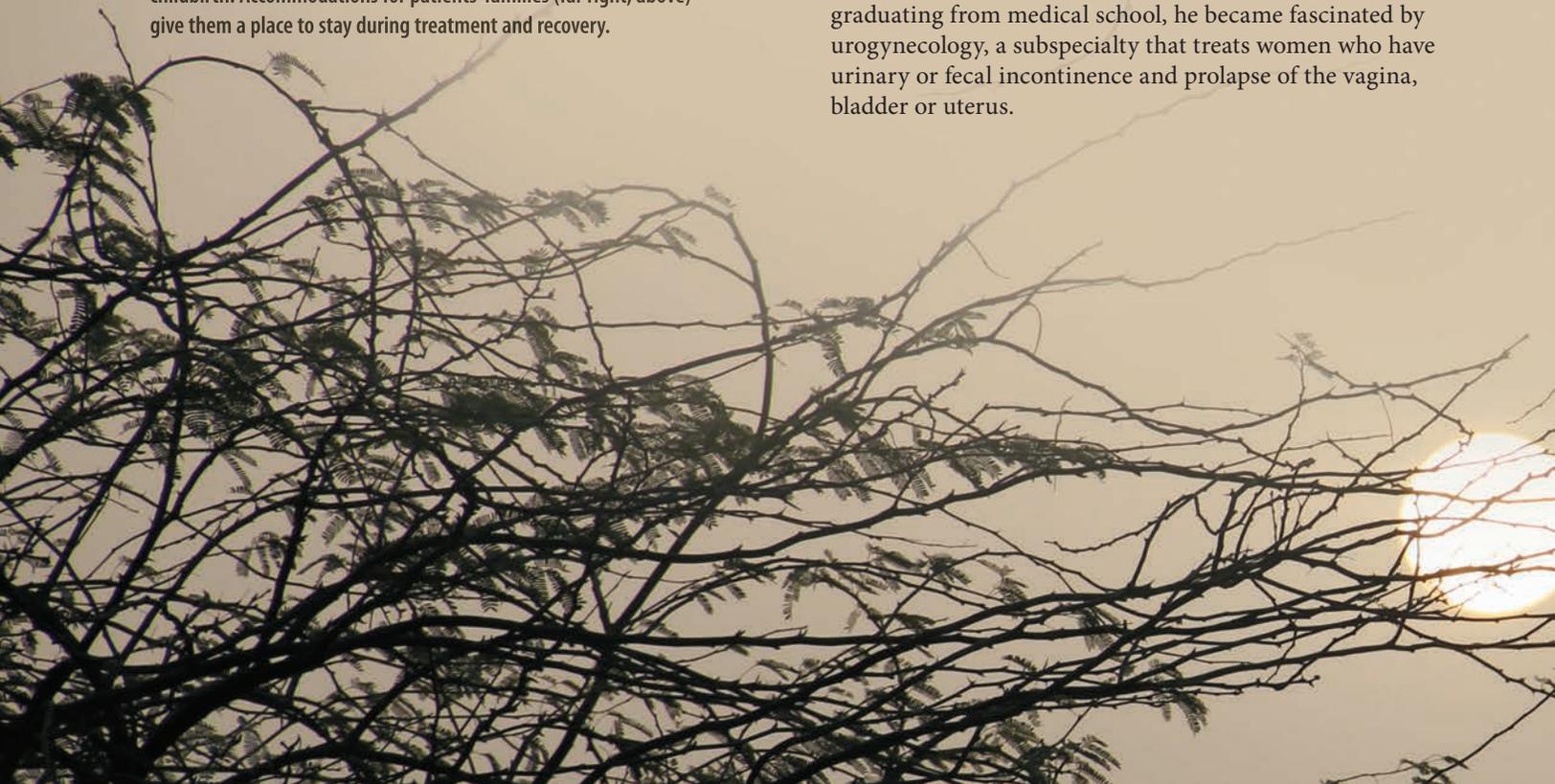
who marry young and whose narrow pelvises make them susceptible to childbirth trauma. In developing countries, where women tend to give birth at home rather than in a hospital, days of pushing during difficult labor can result in terrible injuries.

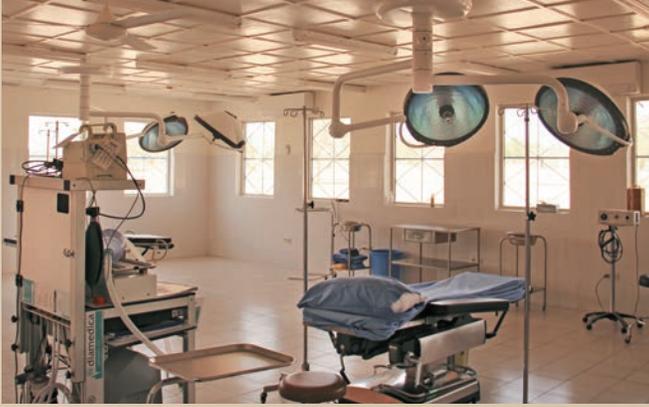
Fistulas can form between the vagina and the urinary tract or rectum. The result is extremely unpleasant; women are left steadily leaking urine and sometimes feces. While the condition can usually be fixed with surgery, a lack of health care options leaves many who suffer in this way with no hope of recovery.

To make matters worse, many African women who develop fistulas are divorced by their husbands, cast out by their families and must eke out a meager living with no marketable skills. Often, they are forced to live humiliating, desolate lives on the edge of their villages.

"When these women get a fistula, life is basically over for them," Wall says. "They become social pariahs. With an inexpensive surgical repair, we are able to give them back their life and dignity. It's astonishing."

Lewis first encountered the problem of fistulas while working as an anthropologist in northern Nigeria on a Fulbright-Hays fellowship. Eventually, he decided the world needed doctors more than it needed anthropologists. After graduating from medical school, he became fascinated by urogynecology, a subspecialty that treats women who have urinary or fecal incontinence and prolapse of the vagina, bladder or uterus.





In 1995, after visiting a large fistula hospital in Ethiopia, Wall envisioned opening a similar facility in West Africa, where fistulas are prevalent.

He founded the nonprofit Worldwide Fistula Fund to raise money to construct hospitals to repair fistulas. The fund has helped support and build a number of fistula centers in Africa. It also has provided money to train local doctors to perform the surgical procedure and to help raise awareness of the problem.

In Niger, among the scattered grasslands on the edge of the Saharan desert, people grow millet and raise sheep, cattle and goats. The majority of people live on less than \$1 a day. There are very few personal or private resources for medical clinics or hospitals, so getting the Danja Fistula Center built was much more difficult than Wall originally anticipated.

“I thought I was fairly realistic because I had lived in West Africa for two years,” he says. “But we had to contend with unexpected obstacles — bureaucratic hassles, insects, a lack of communication and supplies, and people who thought their own interests would be threatened by such a facility.”

He also had to raise about \$1 million.

Large contributions from the Trio Foundation of St. Louis, South African musician Dave Matthews and an executive at Merrill Lynch helped the Worldwide Fistula Fund reach its goal. The fund also received many small personal donations, including \$35 from a potluck hosted by a group of elderly women in New York.

“This was not my individual achievement,” says Wall. “It was a result of the efforts of thousands of people.”

Mark J. Manary, MD, the Helene B. Roberson Professor of Pediatrics, understands some of the obstacles Wall faced in getting the hospital built. Over the past 15 years, Manary has spent a great deal of time in Africa, where he developed Project Peanut Butter, a non-profit organization that produces a peanut-butter mixture to treat children with malnutrition.

“Lewis’ work removes a huge burden, a permanent scar, from the lives of thousands of African women,” Manary says. “I admire his commitment and persistence.”

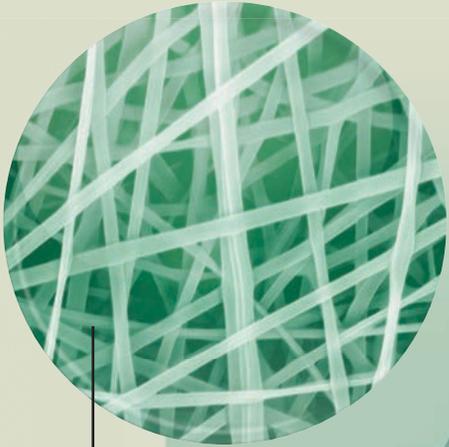
Each year, about 1,000 women will have fistula surgery in the new facility, which is affiliated with an existing leprosy hospital run by a Christian missionary organization. Some will travel hundreds of miles by truck or bus to get there.

Aside from repairing fistulas, the hospital will oversee outreach efforts to promote maternal health and reduce childbirth deaths. It also will educate women about micro-finance to teach them about business and empowerment.

The new hospital is part of a grand vision to eradicate fistulas worldwide by building fistula centers that will serve as focal points for maternity care and public health outreach in the world’s poorest countries.

“For starters, we hope this hospital will help countless women and alleviate human suffering,” Wall says. “We also hope it will advance women’s rights and gender equality. There still is a lot of work to do. But for now, I’m just going to enjoy this accomplishment.” □

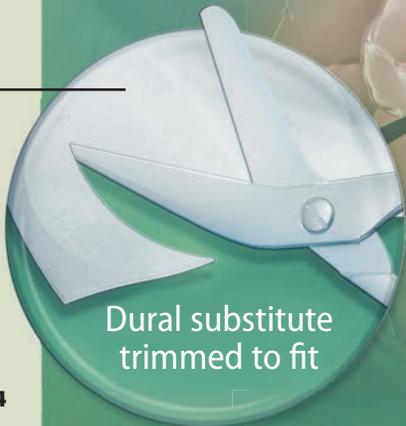
Think SMALL



Magnified view of the dural substitute mesh

Skin
Skull
Dura mater
Arachnoid
Cerebral cortex

Cerebral cortex
Dura mater
Skull
Dural substitute
Skin



Dural substitute trimmed to fit

DURASTAR

A student's "big" vision will help surgeons and patients alike

Matthew R. MacEwan is no ordinary medical student. The neurosurgeon-to-be, a student at the School of Medicine, also is pursuing a doctorate in biomedical engineering at Washington University. And, at 29, he recently started his own local company, Retectix LLC, aimed at revolutionizing the surgical mesh used in operating rooms worldwide.

The company's lead product, invented by MacEwan and Jingwei Xie, PhD, a former postdoctoral researcher in engineering, is a synthetic polymer mesh made of synthetic nanofibers. The mesh was developed to repair defects in the membrane surrounding the brain and spinal cord, but also could be used to mend tissues as well. The nanofiber material has the potential to make operations easier for surgeons and reduce the rate of complications experienced by patients.



Co-inventor of promising nanofiber:
Matthew R. MacEwan

Existing surgical mesh used to repair the protective membrane that covers the brain and spinal cord is thick and stiff, making it difficult to work with. But the novel material MacEwan and Xie developed is thin and flexible and more easily integrated into the body's own tissues.

"It's almost like a cloth," MacEwan says. "But it's designed on a nanoscopic scale. To put that into perspective, every thread of the mesh is hundreds to thousands of times smaller than the diameter of a single human cell."

The technology's promise has caught the attention of the business world. In 2011, MacEwan won the Olin Cup, sponsored by Washington University's Skandalaris Center for Entrepreneurial Studies. In June he won the Licensing Executives Society Foundation's International Graduate Student competition in London, and last November, the Idea to Product Global Competition in Stockholm. The winnings of more than \$100,000, along with other investments and in-kind services, have helped MacEwan get the company off the ground.

The nanofiber material developed by MacEwan and Xie, now a senior scientist at Marshall University in West Virginia, along with collaborators Younan Xia, PhD, the James M. McKelvey Professor of Biomedical Engineering, and Zack Ray, MD, now an attending neurosurgeon at the School of Medicine. MacEwan has worked closely with Washington University's Office of Technology Management, which has filed patents on the technology.

"We've taken the whole idea of surgical mesh and pushed it into a new direction," MacEwan says. "It's not just a foreign material you're putting into the body. The nanofabricated nature of the mesh creates a scaffold that cells can easily penetrate and populate to recapitulate the body's tissues."

The surgical mesh looks like gauze but feels sticky, like a spider web. It is typically composed of multiple layers of nanofibers and can be cut to size for different uses. Once the mesh is placed in the body, cells grow along the individual nanofibers, which gradually degrade in nine to 12 months, leaving only the body's own tissue in their place.

One advantage of the new technology is that different patterns of nanofibers can be created in the mesh to promote the healing of different kinds of wounds. For example, in a starburst pattern used to repair ulcers and other circular wounds, the nanofibers originate from a central point and radiate outward. This encourages cells to migrate and grow toward the center of the wound. For linear defects like tears and incisions, nanofibers can be aligned perpendicular to the wound, encouraging cell growth across the injury, which provides reinforcement to the new tissues.

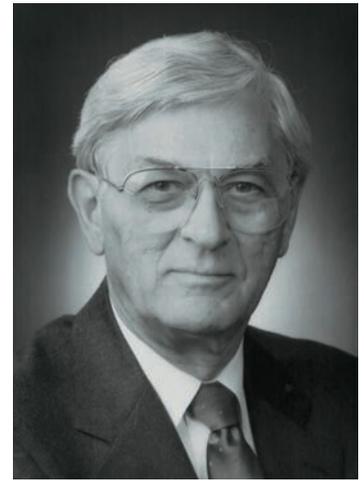
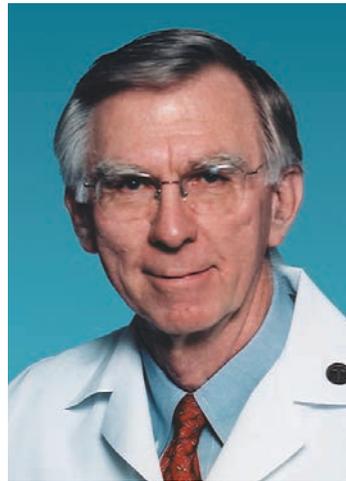
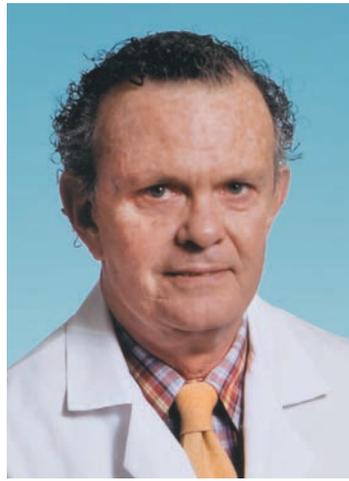
MacEwan is currently evaluating the product in animal models, a first step toward gaining U.S. Food and Drug Administration approval. Preliminary studies indicate the nanofiber material is safe and effective; MacEwan is hopeful that clinical trials in patients will begin later this year.

For now, MacEwan is finishing his doctorate and has two years left before he receives his medical degree. He's planning a career in academic medicine, where he can spend time in the laboratory and the operating room. There, he hopes to use the nanofiber surgical meshes he developed to improve the care and surgical outcomes of his own patients.

"At Washington University, I have continually focused on moving discoveries beyond the laboratory," MacEwan says. "I hope to see this technology have a positive impact on many patients. Nothing would be more thrilling." □

Leaving their marks

Diverse physicians honored with lasting legacies for education



Four distinguished former faculty honorees, left to right: Walter F. Ballinger, MD, John P. Boineau, MD, Paul R. Manske, MD, and J. Neal Middelkamp, MD

Walter F. Ballinger, MD, embodied the spirit of rigorous and broad-based learning at Washington University School of Medicine. Former head of the Department of Surgery, Ballinger relished his role as an educator.

“He thrived on teaching and cared deeply about training the next generation of surgeons,” says his wife, Mary Randolph Ballinger. “He always wanted to bring out the excellence in their talents.”

Timothy J. Eberlein, MD, the Bixby Professor and head of the Department of Surgery says, “Dr. Ballinger often said that training the next generation of surgeons would be the most important, and among our most challenging, tasks.”

So it was a fitting tribute that shortly before Ballinger passed away last year at the age of 85, one of his first surgical interns, Gordon W. Philpott, MD, suggested a fund that would support the establishment of the Dr. and Mrs. Walter F. Ballinger Surgical Academic Education Program. The initial endowment was funded by the Ballingers, and former residents and friends made generous contributions.

The program enables the Department of Surgery to expand the knowledge of surgical training beyond the clinical practice of surgery to include topics such as ethics, public health and health care delivery.

“This is a way to honor the school and the person and to benefit society through advancement of education,” says Philpott, emeritus professor of surgery and a former member of the university’s Board of Trustees. “It fits with Walter’s own passion of continuous learning.”

Washington University School of Medicine has received many gifts to honor faculty who have been outstanding mentors and colleagues. The outpouring of generosity for recent memorial gifts reflects the school’s collegial spirit.

In the Cardiovascular Division, the first John P. Boineau Lecture was held in April 2012 to honor Boineau’s contributions in the fields of cardiothoracic surgery and cardiology. The lecture fund was created through the generosity of current and former faculty and former residents.

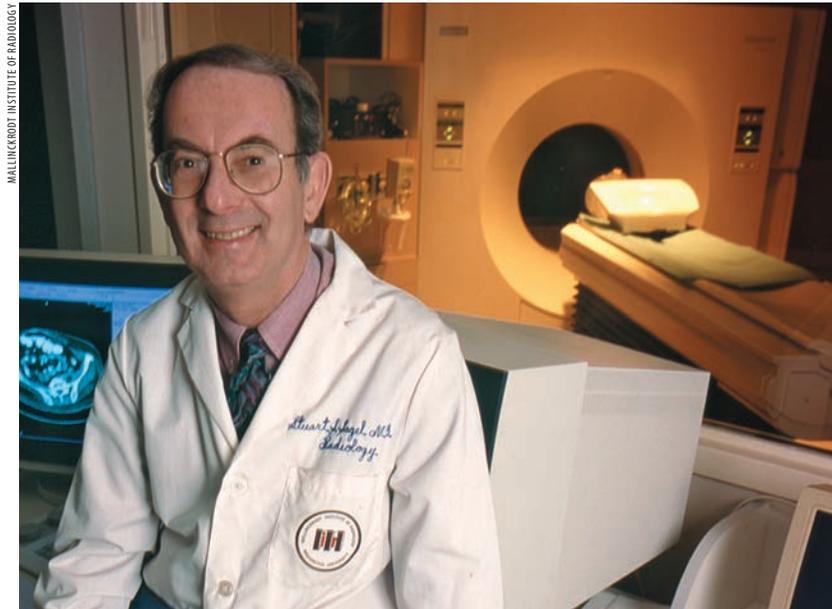
“Dr. Boineau made substantial contributions to the Cox-Maze procedure for the treatment of atrial fibrillation, the most common arrhythmia that we treat,” says Douglas L. Mann, MD, Lewin Professor and chief of the Cardiovascular Division. “This procedure formed the basis for ablation therapy and is practiced by electrophysiologists on a daily basis. Dr. Boineau’s contributions will continue to be felt for the next decade, and likely well beyond that.”

In the Department of Orthopaedic Surgery, the Paul Manske, MD Resident Learning and Teaching Center debuts next year to honor his memory. Manske, the former chairman of the department, died in April 2011.

“We are dedicating this space in honor of Dr. Manske because he was a world-renowned hand surgeon and a true gentleman who also was a highly effective teacher. This center will enable us to honor his legacy and his life here at the medical center where he spent nearly his entire career,” says Richard H. Gelberman, MD, the Fred C. Reynolds Professor and head of the Department of Orthopaedic Surgery. “It will be a state-of-the-art learning center for residents and house staff encompassing individual computer carousels, an anatomical dissection facility, and an arthroscopy and surgical skills simulation center.”

Former orthopaedic surgery resident Bruce A. Bollinger, MD, was among those who made a memorial gift to recognize Manske. “Dr. Manske was an excellent surgeon, research scientist and educator and was always very approachable with questions or issues,” says Bollinger. “I feel I owe much to him and the rest of the faculty during my time at Barnes, and I hope the new center will facilitate education and training through easier access to information and hands-on simulator equipment.”

In November, the Department of Pediatrics will host the



Stuart S. Sagel, MD

11th annual J. Neal and Lois Middelkamp Lecture. The lectureship rotates topics between Middelkamp’s passions — infectious diseases and medical education. “The establishment of this lectureship enables us to bring in national and world leaders to inform and inspire the Washington University community,” says Alan L. Schwartz, PhD, MD, the Harriet B. Spoehrer Professor and head of the Department of Pediatrics. The Middelkamps established the endowed fund in 2001 and, upon his death in November 2011, gifts in tribute to his accomplishments and mentorship were directed to the fund. The comments from former students and residents reflect a tremendous depth of gratitude for the role he played in their lives.

Washington University School of Medicine has received many gifts to honor faculty who have been outstanding mentors and colleagues. The outpouring of generosity for recent memorial gifts reflects the school’s collegial spirit.

Another beloved mentor and colleague, Stuart S. Sagel, MD, will be recognized in the Mallinckrodt Institute of Radiology with a conference room named in his honor. “Residents, fellows and faculty members alike benefited from his excellence as a clinician and teacher for decades,” says R. Gilbert Jost, MD, the Elizabeth E. Mallinckrodt Professor and head of the Department of Radiology and director of Mallinckrodt Institute of Radiology. Teaching conferences will be held in the renovated space and will serve as an ongoing reminder of Sagel’s many contributions. Sagel passed away in November 2011, and the Mallinckrodt Institute of Radiology will keep his legacy alive through this constant reminder. □

An eye for patient care

John F. Hardesty, MD, spent his career caring for the needs of visually impaired children and their families. He dedicated his life to improving the quality of life for all with whom he came in contact. It is in his memory that his daughter, Jane Hardesty Poole, established the John F. Hardesty, M.D. Distinguished Professorship in Ophthalmology and Visual Sciences. Hardesty's life and work were honored on May 31, 2012, at the installation ceremony and lecture of R. Lawrence Tychsen, MD, the inaugural professorship holder.

Hardesty (1887–1953) was an eminent St. Louis ophthalmologist, teacher, writer and war hero whose heritage dates to Colonial and early Missouri settlers. He received bachelor of science and doctor of medicine degrees simultaneously from Saint Louis University in 1914. Following his graduation from medical school, he spent two years as an intern and later a resident at St. Louis City Hospital.

Pediatric ophthalmologist R. Lawrence Tychsen, MD, examines the eyes of young patient Clark Griffin.





**Washington University
Chancellor Mark S. Wrighton,
R. Lawrence Tychsen, MD,
Jane Hardesty Poole and School of
Medicine Dean Larry J. Shapiro, MD.**

Hardesty enlisted in the U.S. Army Medical Corps and was later transferred, at his own request, to the Seaforth Highlanders in the British Military Service. In this capacity, he served on the front lines of World War I until March 1918, when he was captured by the German army and held at Baden-Baden for eight months as a prisoner of war until the armistice. He received an honorable discharge as a captain in March 1919.

Hardesty joined the Saint Louis University School of Medicine faculty in 1920, advancing to senior instructor in 1928, assistant professor in 1931, and associate professor in 1934. He served with distinction in that role until 1953. During his tenure, he served as acting chair of the school's Department of Ophthalmology.

Hardesty's pioneering 1934 thesis for membership in the prestigious American Ophthalmological Society was titled "Treatment of Glaucoma by Systemic Measures." Although the first recorded treatments for glaucoma date to the mid-19th century, Hardesty performed research and published papers on treating the disease using "systemic" medication, drugs introduced to the body intravenously or subcutaneously. This represented the first attempt to treat glaucoma in systemic form. Hardesty's idea of using epinephrine to treat glaucoma is still in use today in eyedrop form, and his work was foundational to the development of the oral drug Diamox in the 1950s by Bernard Becker, MD, at Washington University.

Often described as "a gentleman and a scholar," Hardesty left among his papers a list entitled "Things I Wish I had Known Before I was Twenty-One." The last item noted: "the greatness of the opportunity and joy of serving a fellow man." Nothing guided the life and work of Hardesty more than this.

"My father gave so much of himself to help individuals from all walks of life to retain their sight," says Poole, a 1961 graduate of Washington University. "He was very modest and humble, yet a towering figure. I am so pleased that I can honor him in this way."

The inaugural recipient of the Hardesty Professorship, R. Lawrence Tychsen, MD, graduated from Georgetown University with majors in biology and philosophy, receiving his medical degree from Georgetown in 1979. He finished residency training at the University of Iowa Hospitals in

1983, followed by fellowships at the University of California San Francisco (pediatric and neuro-ophthalmology) and the Smith-Kettlewell Institute, San Francisco. He also was a neuroscience research postdoc both at the National Eye Institute/National Institutes of Health (NIH) and at UCSF.

From 1985 to 1989, Tychsen served in the U.S. Air Force as a flight surgeon/pediatric ophthalmologist at the School of Aerospace Medicine and the Wilford Hall Medical Center, San Antonio.

In 1989, Tychsen joined the Washington University School of Medicine faculty, where he is professor of ophthalmology and visual sciences in pediatrics and professor of anatomy and neurobiology. He is ophthalmologist-in-chief at St. Louis Children's Hospital.

Tychsen's clinical work focuses on three topics: surgical repair of vision in children with ocular and brain damage (including prematurity, cerebral palsy, Down syndrome and autism), refractive surgery (excimer laser and intraocular implants) for children who have major difficulties wearing eyeglasses or contact lenses, and eye muscle surgery for children and adults who have crossed eyes (strabismus) and eye movement abnormalities (nystagmus). He is principal investigator on NIH R01-funded studies of visual brain maldevelopment and repair in infant primates, as well as clinical studies of visuomotor abnormalities in cerebral palsy and pediatric refractive surgery.

Tychsen has published more than 200 clinical and basic science journal articles or book chapters. He serves on the editorial boards of several journals, as well as panels for national and international ophthalmology associations, the National Eye Institute of the NIH, the Pediatric Eye Disease investigator group, and the Food and Drug Administration. Tychsen has mentored more than 30 undergraduate and medical students over the course of his teaching career and has received numerous awards, lectureships and honors.

"It is humbling and inspiring to be named as the first Hardesty professor," Tychsen says. "Dr. Hardesty was not only an accomplished ophthalmologist, but beyond this a great husband and father, and a brave patriot. He knew that he had been called to a vocation, not just a profession, and that he was the instrument of a purpose. I'll embrace his spirit in the work of the professorship that his daughter, Mrs. Poole, has so generously provided." □

MD Class of 1962 begins new Reunion tradition

Members of the Class of 1962 welcomed this year's graduates into the medical profession and a unique camaraderie of colleagues with a new Washington University School of Medicine alumni pin. The pins were presented at the Alumni Awards Banquet on April 28, 2012, marking the culmination of a busy Reunion weekend of activities for alumni and guests.

The idea behind the pin and the beginning of a new tradition was sparked by conversations with alumni and Washington University physicians who have alumni pins from other medical schools. The pins can be worn on white coats and allow alumni to subtly display school pride.

The pins also presented an opportunity to introduce new graduates to the Washington University Medical Center Alumni Association, while bridging the 50-year gap that separates the Golden Anniversary and current graduating classes. Advancements in medical training, treatments and technology make the experiences of both groups of physicians very different, but the common bond of Washington University represented in the alumni pin unites them.

The 50th Class Speaker, William H. Gondring III, MD, introduced the tradition and announced that he and his fellow classmates would present

each of the graduates with a pin as a token of congratulations. The 2012 graduates surrounded the Class of 1962 and a hush fell over the ballroom. Heartfelt comments and genuine gratitude were expressed by the young physicians to the senior alumni. It was an intimate moment between individuals, but its impact was palpable throughout the entire ballroom.

A general sense of awe and respect for one another was evident. The new graduates took the pinning ceremony seriously, with a reverence for the older alumni that might at first come as a surprise. But then again, the respect they demonstrated is a natural byproduct of the long years of training, the unique skill sets required of physicians, and the important regard held for the mentors who guide students through the process of medical education.

"I remember admiring the Class of 1962 and especially noting their sense of humor and ease of interaction with all of us," reflects 2012 graduate Tara C. Jackson, MD. "They were encouraging about our future prospects and careers. I enjoyed the support and connection we all felt to the alumni. It was inspirational! They were once in our shoes and it means the world to see where they are now.

"Seeing how they kept in touch with their class at Washington University and maintained the informal, friendly relationship they had as students 50 years ago was also priceless," says Jackson, "and very encouraging during this emotional time in our lives."

According to Gondring, the ceremony represented more than a transfer of 50 years of health care commitment from one medical class to another. "It also represents recognition of new skill sets obtained by the new graduates as a continuation of a similar learning experience obtained by the presenting alumni," he says.

The pinning ceremony, a huge success, will now be a featured event at Reunion, and takes its place alongside long-held School of Medicine traditions such as the White Coat Ceremony and Match Day.

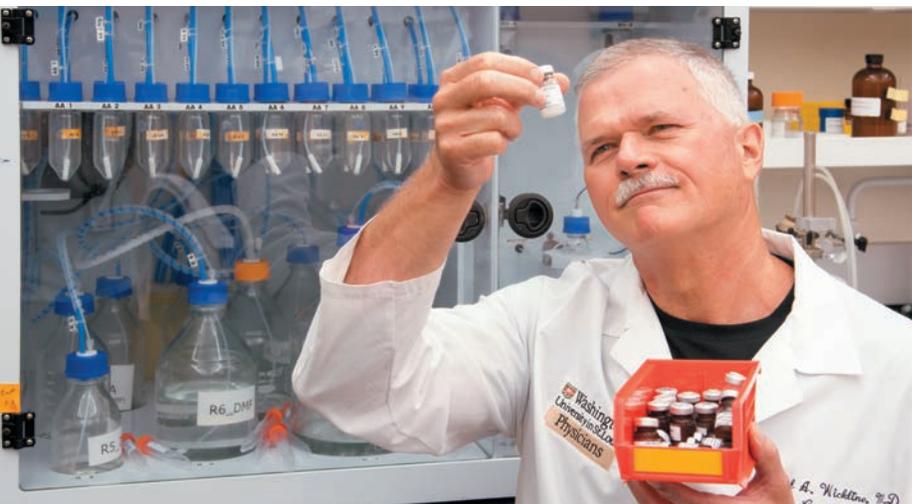


2012 graduate Mark D. Mangano, MD, visits with members of the Class of 1962 after receiving his alumni pin.

MARK BEWEN

Interested in seeing more of the people, events and activities of MD Reunion 2012?
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A blending of entrepreneurial spirit



Samuel A. Wickline, MD, the inaugural recipient of the J. Russell Hornsby Professorship in Biomedical Sciences

James Russell Hornsby’s company, Cepia Inc., was founded on the premise that sufficiently advanced technology is indistinguishable from magic. With that in mind, he has created a world of electronic toys that entertain and delight children and adults alike.

Chief among the company’s successes are the popular robotic Zhu Zhu Pets, included on *Time* magazine’s “All-TIME 100 Greatest Toys” list. But Hornsby’s interest in technology doesn’t end with his devotion to toys; he’s also fascinated with how technology can spur advancements in medical research, with a particular focus on curing cancer and other major diseases.

A former undergraduate parent, his affiliation and appreciation of Washington University were already solidified. As an avid supporter of various community philanthropic organizations, the St. Louis-based Hornsby expressed interest in building a relationship with the School of Medicine that would support medical science and the groundbreaking achievements of the school’s physician-scientists.

That determination to give back resulted in the establishment of the J. Russell Hornsby Professorship in Biomedical Sciences. This significant gift will be used to support the work of the professorship’s inaugural recipient, Samuel A. Wickline, MD, professor of medicine, of physics, of cell biology and physiology, and of biomedical engineering.

A successful entrepreneur in his own right, Wickline established the Washington University Consortium for Translational Research in Advanced Imaging and Nanomedicine, known as C-TRAIN. Located at the St. Louis CORTEX Center, C-TRAIN is devoted to diagnostic and therapeutic development of nanotechnology for broad-based clinical applications, in conjunction with corporate and academic partners.

Mirroring Hornsby’s premise, Wickline’s pioneering nanoparticle research has shown that truly advanced, groundbreaking technology can be used to create another type of magic — changing the way medical diagnoses are made and improving the safety and efficacy of drug treatment, thereby benefitting patients.

Imagine being able to replace multiple medical tests, scans and treatments with a single injection. That’s the promise offered by nanoparticles, extremely small, bead-shaped units that can become carriers of medicine. Using these tiny particles, doctors will be able to locate disease sites deep within the body and at the same time determine their size, shape and molecular features. They can then adapt the nanoparticles to deliver therapeutic drugs exactly where needed and personalized to each patient.

In addition to his research, Wickline created the Siteman Center of Cancer Nanotechnology Excellence at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. The center is devoted to nanomedical therapeutics for cancer. He also established the St. Louis Institute of Nanomedicine, a consortium of academic and commercial partners devoted to enhancing regional infrastructure for the translational advancement of nanotechnology in medicine.

Hornsby’s entrepreneurial spirit is a perfect match for Wickline’s research efforts. The J. Russell Hornsby Professorship in Biomedical Sciences and Wickline’s development of nanoparticle technology will continue to give hope that one day we will see the magic and no longer have to only imagine.

1930s

Benjamin Milder, MD 39

Milder published a sixth book of poetry, *From Adolescence to Senescence—A Life in Light Verse*, in 2010.

1940s

Robert Royce, MD 42

Royce is retired and enjoying life to the fullest. His interests include golf, bridge, ecology, and being on the ranch.

George Prothro, MD 45

Prothro enjoys traveling and volunteer work. He has participated in a program which makes unused, sealed prescriptions from nursing homes available to the indigent.

Stanley Wald, MD 46

Wald, though retired, participates in life-long learning courses and volunteers at a local grade school.

Theodore Bryan, MD 47

Bryan retired from practice in 1998. His hobbies include reading and the occasional round of golf. He continues to enjoy his time with his wife of 62 years, Bertha "Benny" Benadine.

1950s

Edgar Draper, MD 53

Draper was the 50 Year & Life Medal and Distinguished Fellow Award recipient from the American Psychiatric Association in May 2011.

J. Roger Nelson, MD 53

Nelson wrote and published a novel, *The God Whom Moses Knew*, in August 2010.

Rillah Owen, NU 54

Owen retired in 1997 and has moved to Lewes DE. She took up watercolor (plein air painting), volunteers for the risk manager at Beebe Hospital in Lewes, and is active in swimming, traveling, baking and playing bridge. Owen belongs to three art leagues and has gone on a jazz cruise every year for the past seven years.

Donald Harkness, MD 58

Harkness is still playing tennis several times a week. Last June he took his 12-year-old granddaughters to Japan. He is still helping in a hematology course.

1960s

John Crane, MD 64

Crane is still working part-time. He is enjoying life, doing some (non-medical) writing, traveling and sailing his old Pearson P-30.

Michael Reif, MD 68

Reif retired from private practice in 2004. He spent more than six months in North Carolina's Blue Ridge Mountains. He has been married 47 years and has eight grandchildren.

Penelope Shackelford, MD 68

Shackelford is still restoring land in Wisconsin and enjoying her grandchildren.

Michael Pacin, MD 69

Pacin has been awarded the Intercultural Human Rights Award at St. Thomas University School of Law in recognition of his commitment to diversity, the fight against human trafficking, and assistance to those in need in the community. Pacin, who is the founder and was the CEO for 35 years of the Florida Center for Allergy & Asthma Care, expanded his practice from two to 17 offices and implemented a policy of "giving back" by providing affordable or free medical care to indigent patients. He continues to work full time, caring for patients, administering a large practice, and serving his community.

1970s

Bruce Broudy, MD 74

Broudy was elected the 2012 president of the Lexington Medical Society. He resides in Lexington KY, where he works in the area of pulmonary medicine.

Charles Newton, MD 75

Newton is currently a private practice cardiothoracic surgeon in Huntsville AL. He celebrated his 30th anniversary as a surgical subspecialist by retiring the

scalpel on April 15, 2012. In June, Newton and his wife, Ann, a former scrub nurse from Brigham and Women's Hospital in Boston, moved to Tampa FL, where he began a palliative medicine fellowship at University of South Florida. He is excited with this invitation to redirect his medical career, enabling him now to devote his energy and expertise to ameliorating the suffering of the terminally ill.

Thomas Cooper, MD 76

Cooper and his wife, **Linda Loney, MD 76**, are both retired. They recently moved to a condominium in the south end of Boston from the suburbs, which they are very happy about.

1980s

Linda Douglas, MD 82

Douglas returned to private practice after 20 years in medical education and residency education at Rush Medical College and Medical College of Wisconsin. She is happy to now have time to concentrate on patients, her kids and life. Her children, Karen and Daniel, are 25 and 21, respectively.

Gary Chun, MD 84

Chun is trying to be a jazz drummer in his free time.

John Donovan, MD 87

Donovan has climbed Mt. Kilimanjaro and participated in five surgical missions in South America in the past five years. His hobbies include biking, swimming and watching his daughters play softball.

Rosalie Hagge, MD 88

Hagge is an associate clinical professor of radiology and nuclear medicine at the University of California, Davis Medical Center.

Robert McMahan, MD 89, HS 92

Robert McMahan, JD, MD, a gastroenterologist, has been elected 2012 president of the St. Louis Metropolitan Medical Society, the association representing physicians in the St. Louis area. He is in private practice with St. Louis Gastroenterology Consultants in south St. Louis County.

1990s

Grant Hoekzema, MD 92

Hoekzema is in his 12th year as director of the Mercy Family Medicine Residency program and a clinical professor of family medicine at Saint Louis University. His hobbies include traveling and watching his children grow and develop career plans of their own. He was elected president of the Association of Family Medicine Residency Directors for this coming year.

Kristin Kjensrud, PT 92

Kjensrud and her partner have a son, Nathaniel, 2. She teaches in the physical therapy assistant program at Mt. Hood Community College.

Corina Norrbom, MD 94

Norrbom spent July 2009 through September 2010 working as a general practitioner in New Zealand. She found it to be a wonderful experience, learning a little and teaching a little every day. This opportunity to experience another health system firsthand was invaluable to her.

Louis Kuchnir, MD 97

Kuchnir and his wife, Karen, are settled in the suburbs west of Boston with their children, who are now in 4th, 7th, 9th and 10th grades. He is now in his 11th year of owning his private practice.

Dina Levin, HS 97

Levin moved to central Vermont, where she is an ob/gyn at Gifford Medical Center. She has two sons.

Richard Tsai, MD 98

Tsai is the medical director and a practicing clinician at Providence Medical Group.

2000s

Linda Cummings, MD 01

Cummings and her husband enjoy spending time with their son Matthew, who is about to turn 2.

Betsy Peterson, MD 02

Peterson is founder and president of Community Pediatrics, SC in Beaver Dam WI and Waupun WI. She started a pediatric clinic in a town east of Madison WI that had no previous pediatrician. In the past

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seven years, it has grown to now have two pediatricians, two pediatric nurse practitioners, and two locations with nine additional employees and more than 3,000 patients. Peterson is involved with the Wisconsin Chapter of the American Academy of Pediatrics and the Section on Administration and Practice Management. She also cheers for Wisconsin sports — Go Badgers and Go Packers!

Kristen Bruno, MD 03

Bruno completed four years of pediatrics in the Air Force and is now working as a pediatric hospitalist with GlennCare.

Stacey Rubin, MD 06

Rubin is a generalist ob/gyn at Crozer Keystone Health System outside Philadelphia PA. She focuses on pediatric and adolescent gynecology and recently accepted a position as associate residency director of Crozer's ob/gyn residency program.

IN MEMORY

Thomas Geppert, MD 43

Geppert, 92, died on Dec. 31, 2011. He is survived by five children and numerous grandchildren and great-grandchildren.

Robert Stowell, PhD 44, HS 44

Stowell, a world-renowned pathologist who was an early leader of the UC Davis School of Medicine, died Nov. 20, 2011. He was 96. Stowell joined UC Davis in 1967 as founding chairman of the pathology department and was vice chairman of the medical school's first admissions committee. In 1969, he was appointed director of the UC Davis Primate Center. He returned to the pathology department after two years and retired in 1982, but continued teaching as a volunteer until 2001. He was an influential leader of national and international pathology groups.

Rosemary Etherton, NU 46

Rosemary Etherton, 85, died on Sept. 5, 2011. She continually gave of herself and was an example of unconditional love and grace. Her children and grandchildren counted on her faithful prayers in every situation. She is survived by her sister, four daughters and 11 grandchildren.

Jack Davis, MD 47

Davis died on Nov. 28, 2011. He was 89. An internal medicine specialist, he was a member of the AMA for 50 years and a founder of the Raytown Clinic. He practiced medicine at both Research Medical Center and Baptist Memorial Hospital. He was a lifelong sports fan — particularly of the Kansas City A's, the Royals and the Chiefs. He was a voracious reader of journals and books. He was a member of the Raytown Christian Church.

Mary Devous, NU 48

Devous, 84, died on Oct. 10, 2011. She retired from more than 25 years of service in the Veterans Administration as a nurse and nurse administrator. She also served in many capacities in the DAV auxiliary, the Ladies Auxiliary of Fleet Reserve Association, Women in Military Service for America, and in her church. She loved nursing and caring for others, but loved her role as mother and grandmother most.

Patricia O'Neal, LA 44, MD 48, HS

O'Neal, a retired clinical professor of psychiatry, died on Dec. 20, 2011. She was 88. She is survived by her husband.

Rosemary Richardson, PT 48

Richardson died on Dec. 28, 2011. She is survived by her husband and many nieces and nephews.

Eva May Dobbins Bundenthal, NU 49

Bundenthal, 83, died on Nov. 30, 2011. She was a registered nurse for more than 50 years and received the Humanitarian Award for Nurse of the Year from the Selma Medical Center.

Sidney Jick, MD 49

Jick died on Nov. 14, 2011. He is survived by his wife, a daughter, and four grandchildren.

Joseph Iwano, MD 50

Iwano died on Oct. 28, 2011. He was 91. After medical school and military service, he established a private urology practice with offices in Alliance and Salem. He was an organic gardener decades before it was fashionable, a skilled furniture-maker and photographer, as well as a teller of corny jokes. His extensive knowledge of history made travels extra meaningful. In 1988, he retired and moved to Mercer Island WA.

Elynor Flitz, NU 51

Flitz, 83, died on Sept. 3, 2011. She was a registered nurse and a nurse educator. She and her husband, Henry, lived in Princeton for many years, later moving to Texas and subsequently made Coralville their summer home. She is survived by her husband, three children and six grandchildren.

James Michael, MD 53

Michael, 83, died on Nov. 10, 2011. After an internship at Barnes Hospital in St. Louis, he was a flight surgeon in the U.S. Air Force. In 1960, he joined the Department of Internal Medicine at the Sheboygan Clinic. He served as president of the medical staff of Sheboygan Memorial Hospital and of the Sheboygan County Medical Society. For many years he was the designated preceptor in the Sheboygan area for senior medical students at the University Medical School in Madison. Michael retired early from medical practice to follow his passion for watercolor painting, which he taught for more than 30 years at the John Michael Kohler Arts Center. He exhibited locally and nationally and more than a thousand of his paintings hang in private and corporate collections. Many were donated to local charity benefit auctions.

Charles Dunaif, MD 54

Dunaif died on Dec. 26, 2011. He is survived by his wife, daughter, and a niece and nephew.

Byron Demorest, HS 54

Demorest died on Oct. 14, 2011. After receiving his medical degree, he completed a residency in ophthalmology at Washington University. He was an assistant clinical instructor in ophthalmology at Stanford University and the founding chairman of the Department of Ophthalmology at the University of California, Davis. He was a member of many organizations, including the American Academy of Ophthalmology for which he served as president. He also had active duty with the U.S. Navy, ending up as a lieutenant commander and chairman of the Eye Department at the Great Lakes Naval Hospital.

Clark Grimm, MD 57

Grimm died on Sept. 13, 2011.

R. Wayne Neal, MD 58

Neal died on Dec. 5, 2011.

Mary Coons, OT 60

Coons, 86, died on Oct. 17, 2011. She was in the civil service in Nagoya, Japan, where her passion for antiques and collecting began. She returned to the United States to finish school and retired as an occupational therapist with the VA hospital in St. Louis MO. She was well-known on Cherokee Antique Row in St. Louis, where she had a store.

George Dueker, MD 61

Dueker died on Dec. 4, 2011. During the Vietnam War he served as a flight surgeon with the U.S. Air Force. After two years on the Stanford faculty, he moved to Carmel CA, where he practiced urology for 30 years. In 2001, he affiliated with the Provident Group in Portland OR and became an avid Trailblazers fan. He never stopped his quest for knowledge or lessened his interest in the world.

Doris Rigg, OT 62

Rigg, of Denver CO, died on Sept. 25, 2011. She was 78.

Margaret Hayes, HS 66

Hayes, of Dayton OH, died on Sept. 8, 2011. She was 84.

Thomas Banton, HS 68

Banton, 76, died on Dec. 25, 2011. He was an orthopaedic surgeon, associated with the Northland Orthopaedic Group in St. Louis, and served on the staff of De Paul Hospital and Christian Hospitals Northeast and Northwest. He practiced 30 years before retiring in 1995. He also served his country as a captain in the U.S. Army. He is survived by his wife, daughter, son and five grandchildren.

John Black, MD 73

Black, 64, died on Dec. 1, 2011. He was an anesthesiologist and worked for Bowling Green Anesthesia at Greenview Hospital. He loved to cook and to attend cooking schools. He also enjoyed travel and was an avid photographer and reader. He was proud of his children's accomplishments and of his two young grandchildren. He also took great pride in his King Charles spaniels, Kona and Hilo. Black is survived by his wife **Toby Black, OT 71**, two children and two grandchildren.

Mark Ginsburg, LA 73, HS 81

Ginsburg, 60, died on Nov. 11, 2011, in St. Louis MO. He attended Washington University for his undergraduate work in biology and returned to intern at Barnes-Jewish Hospital after receiving his medical degree. Following residency, he moved to Florida to start a rheumatology practice and eventually became involved in other interests including Nationwide Laboratory Services of Fort Lauderdale FL, a revolutionary diagnostic laboratory specializing in the needs of dialysis patients. Always seeking the most from life, he was an avid birder, a California wine expert, an aviation enthusiast and an astronomer. Ginsburg traveled extensively to South America to help preserve and rebuild the rain forests. He had an incredibly green thumb when it came to his beautiful orchid garden and also was a huge sports fan, rooting for the Miami Hurricanes teams. Always a research advocate, Ginsburg was honored in 1999 as a Founders Day Distinguished Alumni of Washington University. He was a member of the Board of Trustees and provided scholarships to students. He is survived by his wife, son and twin daughters.

Robert Etienne, HS

Etienne died on Dec. 23, 2011. He is survived by his wife, daughters, brother and sisters. His memory will be cherished by his grandchildren, great-grandchildren, nephews and a host of other family and friends.

Bernard Sarnat, HS

Sarnat, an eminent plastic surgeon and research scientist who advanced the understanding of craniofacial development and the causes of facial deformities, died on Oct. 21, 2011 in Los Angeles CA. He was 99. In 1955, he began a private practice in plastic surgery in Beverly Hills CA. In 1969, he was appointed professor of oral biology at the UCLA School of Dentistry and, in 1974, he was appointed professor at the UCLA School of Medicine in the Division of Plastic Surgery. For more than two decades, he was chief of plastic surgery at Cedars-Sinai Medical Center. He retired from surgical practice in 1991, but continued writing and publishing.

FACULTY

M. Alan Permutt, MD

Permutt, professor of medicine and of cell biology and physiology at Washington University School of Medicine, died on June 10, 2012, in St. Louis. He was 72. A faculty member since 1970 and one of the world's leading diabetes researchers, Permutt demonstrated in 1992 that variations in the glucokinase gene could cause type 2 diabetes. The discovery was the culmination of years of connecting complex genetic linkage studies and molecular biology to a common, chronic disease. Later, his studies of genes and diabetes led him to focus on a particularly devastating form of the illness called Wolfram syndrome. Permutt's laboratory identified a gene for the illness, which causes type 1 diabetes, hearing loss, severe vision loss and hearing and neurological problems. In 2010, with St. Louis Children's Hospital, Permutt led the effort to create the world's first multidisciplinary clinic for patients with Wolfram syndrome, bringing them to St. Louis from all over the world for intensive testing. Because the syndrome is so rare, that first clinic in 2010 also represented the first time Permutt was able to work directly with patients with Wolfram syndrome and their families. Permutt attended Johns Hopkins University in Baltimore MD before earning a medical degree from Washington University School of Medicine in 1965. He later was an intern at Yale-New Haven Hospital and a medical resident as well as a postdoctoral fellow at the University of Washington in Seattle before returning to Washington University for the rest of his academic career. He is survived by two daughters, Joelle Permutt and Robin Winer; dear friend Rhea Oelbaum; four grandchildren; two sisters and a brother.

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.



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