Tiny technology
Nanomedicine holds big potential
Musical tradition  The John Ford Highland Bagpipe Band, a pipe-and-drum ensemble that has been a regular fixture at School of Medicine graduation ceremonies since 1996, ushered in the graduates during the Academic Processional of the 2005 Commencement Recognition Ceremony. The School of Medicine conferred 114 degrees on May 20: Ninety students received the MD degree, 18 received the MD/PhD degree, and six received the MD/MA degree.
Outlook
Open Soon

Workers put the finishing touches on the Farrell Learning and Teaching Center.

medicine.wustl.edu/ltc
Farrell Learning and Teaching Center

Located in the heart of the Washington University Medical Center, at the intersection of Euclid and Scott avenues, the Farrell Learning and Teaching Center will serve as the school's main venue for medical education.

- The first classes are scheduled to be held there in fall 2005.
- The latest technology throughout the building means, for example, that every seat in the lecture halls will be wired with power and data connections.
- New spaces emphasize small group learning.

Giving opportunities

- Prominent naming opportunities are available throughout the building, starting at $25,000.
- Annual Fund support, at any level, will help enable this important addition to medical education.

Contact the Office of Medical Alumni and Development at (314) 286-0086.
The nano-scale technology created by Samuel A. Wickline, MD, and Gregory M. Lanza, MD, PhD, is poised to make a mega-scale impact on medical care. For more on this story, please turn to page 16.

PHOTO BY ROBERT BOSTON

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Goldstein awards honor top educators

Three outstanding educators recently received the Samuel R. Goldstein Leadership Awards in Medical Student Education, which recognize faculty members who have made outstanding contributions to medical education.

The 2004 recipients of the Goldstein awards are Martin I. Boyer, MD, associate professor of orthopaedic surgery and chief of hand and wrist service; Lewis R. Chase, MD, professor of medicine and chief of medical services at St. Louis Veterans Affairs Medical Center; and Robert J. Rothbaum, MD, professor of pediatrics and clinical director of the division of pediatric gastroenterology and nutrition.

The annual leadership awards were established in 2000 in honor of Goldstein, a longtime supporter of the School of Medicine. The recipients were selected by faculty and peers after a formal nomination process.

The Goldstein awards aim to acknowledge the dedication of faculty members and are among the highest honors teachers at the medical school can receive.

"When it comes to educating medical students, Drs. Boyer, Chase and Rothbaum represent the best of the best," says Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine. "They are not only a credit to the School of Medicine, but also the entire medical profession. But it is our students who benefit most from these physicians' dedication and extraordinary teaching abilities."

Medical school places among top three

Third-best medical school in the nation is the rating the School of Medicine received in the 2005 U.S. News & World Report rankings of graduate and professional programs.

The School of Medicine ranked third after Harvard University and Johns Hopkins University, which moved into the second spot in this year's ranking. The No. 4 slot went to the University of Pennsylvania.

The report also revealed that the School of Medicine's students had the highest undergraduate grade point averages and the highest scores on medical school entrance exams. Additionally, the medical school ranked second in National Institutes of Health grant dollars awarded per faculty member.

"This is the eighth consecutive year the School of Medicine's students have had the highest undergraduate grade point averages and highest scores on medical school entrance exams," says Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine. "The medical school has remained in the top 10 since U.S. News began its annual rankings in 1987."

Specialty areas at the medical school also were listed among the nation's best. Internal medicine and pediatrics both ranked sixth in the nation, the drug and alcohol abuse program tied for 12th, women's health tied for 11th, and the AIDS program tied for 19th.
Cicero to step down as vice chancellor for research, search committee to form

After 10 years of leading the university's research enterprise, Theodore J. Cicero, PhD, vice chancellor for research, plans to step down in June 2006. At that time, he will return to his former position as vice chairman for research in the Department of Psychiatry.

Cicero will spend the next year making the transition from heading the office that coordinates the research efforts of the entire university to focusing on his own research.

"Ted Cicero has served Washington University extraordinarily well as vice chancellor for research," says Chancellor Mark S. Wrighton. "He has significantly strengthened our research infrastructure, launched the Office of Technology Management and contributed to the development and implementation of policies governing all aspects of our research program."

Under Cicero's leadership, the university's research enterprise has greatly expanded. In fiscal year 1996, total research funding was just more than $244 million. Today, that funding has more than doubled, with research support reaching almost $535 million in fiscal year 2004.

Hematology

Gene therapy completely corrects hemophilia in laboratory animals

Newborn mice and dogs with hemophilia A were restored to normal health through gene therapy developed by researchers at the School of Medicine. The technique supplied the animals with a functioning gene for clotting factor VIII, a vital blood protein missing in hemophilia A.

"The animals produced about 20 times more factor than in prior attempts using gene therapy for hemophilia A in dogs," says senior author Katherine Parker Ponder, MD, associate professor of medicine and of biochemistry and molecular biophysics.

The immune system often blocks the clotting activity of introduced factor VIII. But the researchers found that the newborn animals did not raise an immune response against their new factor VIII. In addition, the cells receiving the new gene multiplied as the animals grew, providing the adult animals with higher amounts of active factor VIII genes.

The study was reported in the April 26, 2005 issue of the Proceedings of the National Academy of Sciences.

Hemophilia is an inherited bleeding disorder with two forms, A and B, caused by genetic mutations that prevent normal production of key blood-clotting factors. Hemophilia A is the form occurring in 80 percent of cases. An X-chromosome-linked disorder, hemophilia almost always occurs in males, and one in 5,000 human males are born with the disorder.

"Hemophilia greatly restricts patients' lives," says Ponder, who also is a hematologist at Barnes-Jewish Hospital. "People with the disease don't heal well after injuries. Even running can cause bleeding into the joints."

Over the long term, hemophiliacs suffer from joint damage and other complications related to excess bleeding. Gene therapy offers the chance that hemophilic patients could be freed from dependence on injected clotting factor.

In the study, blood tests demonstrated all of the animals treated with the viral vector carrying the new gene produced factor VIII. The mice achieved an average of 139 percent and the dogs an average of 115 percent of normal factor VIII activity. In comparison, untreated animals with hemophilia A have less than one percent of normal factor VIII activity.

"The ultimate goal is for gene therapy to work in humans, but humans have a more mature immune system at birth than mice," Ponder says. "In animals more closely related to humans, there will probably be more risk of an immune response against factor VIII. So, next we will investigate gene therapy trials in newborn primates with hemophilia to see if we can successfully treat hemophilia A."

The gene supplies the clotting factor (blue) otherwise missing due to hemophilia A.
Jost to chair radiological society

R. GILBERT JOST, MD, the Elizabeth Mallinckrodt Professor and head of radiology, has been named chairman of the board of directors of the Radiological Society of North America (RSNA).

Active within the organization for years, Jost will serve a one-year term as RSNA chair before becoming president-elect and then president of the group.

The society comprises more than 37,000 radiologists, radiation oncologists and related scientists committed to promoting excellence in radiology through education and research, with the ultimate goal of improving patient care.

Jost is also the director of the Mallinckrodt Institute of Radiology at the School of Medicine and an affiliate professor of computer science at the university. He is internationally known for his work to expand and improve the use of information technology in the practice of diagnostic radiology.

Fixing diabetic heart complications is focus of new clinical research grant

A FIVE-YEAR, $14 MILLION GRANT will establish a center at the School of Medicine that will develop better ways to prevent and treat heart disease in diabetic patients. The grant was awarded by the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH).

Diabetics who have heart attacks currently confront a poor prognosis, according to Daniel P. Kelly, MD, professor of medicine, pediatrics and of molecular biology and pharmacology.

“Heart disease is the leading killer of diabetics. When we treat diabetic patients following a heart attack with standard cardiac therapies, they do not respond as well as non-diabetic patients,” Kelly says. “We want to improve the way we understand and care for diabetics who are at risk of or who have suffered a heart attack.”

The new grant establishes a Specialized Center for Clinically-Oriented Research (SCCOR) in Cardiac Function and Disease. Kelly will direct the center, one of the first of a new generation of NIH-sponsored research centers designed to encourage heavy emphasis on clinical research.

“One of the main goals of the new SCCOR grants is to aggressively link research discoveries to improving patient treatments,” Kelly explains. “More than 50 percent of our center’s research will be patient-oriented.”

A major research initiative of the new center, led by Kelly, will be to study heart attacks in animal models and apply the findings toward development of new diagnostics and treatments for human diabetics.

John Spertus, MD, professor of medicine and health outcomes research at Mid-America Heart Institute and the University of Missouri-Kansas City, will apply animal model results to patient populations, as well as study differences in outcomes based on patient race and ethnicity.

Howard L. McLeod, PharmD, associate professor of genetics at the School of Medicine, will examine how genetic differences in diabetic patients affect their response to drug therapies.

“The final goal is to develop something called a diabetic cardiovascular panel,” Kelly says. “It will help us stratify diabetic patients based on the severity of the metabolic disease, a key step toward choosing treatment strategies.”
If a woman goes into labor before her baby is full term, her obstetrician must make a crucial recommendation: delay labor or allow it to continue. Delivering prematurely may increase the baby's risk of suffering from neonatal respiratory distress syndrome (RDS), a potentially fatal condition.

School of Medicine researchers have generated new RDS risk estimates, published in the January 2005 issue of the American Journal of Obstetrics and Gynecology, that allow physicians to make those delivery decisions with far greater confidence.

The syndrome occurs when newborn lungs have not fully matured and lack the normal coating in the tiny sacs where air is exchanged. RDS causes difficulty breathing and not only threatens survival, but also poses a risk of long-term health effects caused by oxygen deprivation.

Physicians considering a preterm delivery estimate lung maturity by testing the amount of lung coating, or surfactant, present in amniotic fluid. Previous recommendations for RDS prediction listed one surfactant level indicating mature lungs and another lower number indicating immature lungs—but that left a gray zone in the middle that required educated guesswork by physicians.

"Not only was there a gray zone, but when the surfactant tests were designed, they didn't consider the gestational age of the fetus," says senior author Ann M. Gronowski, PhD, associate professor of pathology and immunology and of obstetrics and gynecology. "Everyone suspected that the cutoff numbers changed over the weeks of gestation, which meant the old guidelines weren't adequate."

Using a statistical model designed by Curtis A. Parvin, PhD, associate professor of pathology and immunology and biostatistics, the researchers set out to create recommendations taking gestational age into account. The research group combined data from three studies of women and babies whose doctors had administered a test for amniotic surfactant shortly before delivery. The data showed whether the newborns had RDS, their gestational age and surfactant level.

The results of the statistical analysis were arranged into convenient tables and graphs to determine the potential RDS risk based on both surfactant level and gestational age. For example, the absolute risk chart the team built shows that at 34 weeks, a baby with a surfactant level of 20 has a 73 percent risk of RDS, while a baby showing a level of 60 has only a 3 percent risk.

Having detailed information about the RDS risk in each situation gives physicians more choice in patient treatment.
Heuser elected AAAS fellow

JOHN E. HEUSER, MD, professor of cell biology and physiology, has been elected a fellow of the American Academy of Arts and Sciences.

He is among 213 men and women elected this year by the academy, an organization formed in 1870 to cultivate the arts and sciences and to recognize leadership in scholarship, business, the arts and public affairs.

The academy's membership of more than 4,500 includes more than 150 Nobel laureates and 54 Pulitzer Prize winners. Fellows are selected through a highly competitive process that recognizes individuals who have made preeminent contributions to their disciplines and to society at large.

Heuser created "quick-freeze, deep-etch" electron microscopy, a pioneering technique that lets biologists take detailed pictures of fleeting events inside living cells. For decades, Heuser has used this technique to capture the molecular mechanisms that underlie many basic biological activities, including nerve cell signal-transmission, muscle contraction and, most recently, the fusion of viruses with cells during the spread of infection.

New genetics, genomic medicine division aims to transform pediatric patient care

The separate worlds of patient care and genomic science will be brought together in the new Division of Genetics and Genomic Medicine in the School of Medicine's Department of Pediatrics. Plans for the division map out a model of individualized medical care in which physicians look to their patients' genetic makeups to determine the most effective treatment.

"We've unraveled the human genome, and in that genetic blueprint are answers to medical problems," says Jonathan D. Gitlin, MD, director of the new division and the Helene B. Roberson Professor of Pediatrics and professor of genetics. "Right now it isn't possible to get all the answers we need and apply them to patients, but this division will establish a structure with which to begin that effort."

The division will receive research grants and support from Washington University School of Medicine and St. Louis Children's Hospital. Its goals mesh with those of Washington University's strategic research initiative BioMed 21, which focuses on translating basic genetic data into new therapies and includes faculty from the schools of Medicine, Engineering & Applied Science and Arts & Sciences.

Morris garners Potamkin Prize

The American Academy of Neurology has awarded the 2005 Potamkin Prize for Research in Pick's, Alzheimer's and Related Diseases to John C. Morris, MD, the Friedman Distinguished Professor of Neurology and director of the Alzheimer's Disease Research Center (ADRC) at the School of Medicine.

The annual prize, regarded as the most prestigious in Alzheimer's research, honors scientists for outstanding contributions to the understanding and treatment of Alzheimer's disease and related disorders. Ronald Petersen, MD, PhD, of the Alzheimer's Disease Research Center at the Mayo Clinic College of Medicine, also was awarded the prize this year. Both were recognized for their pioneering efforts in early diagnosis of Alzheimer's disease.

"I accept individual prizes on behalf of the entire Alzheimer's Disease Research Center," says Morris, "because our studies truly represent the group effort of many wonderful colleagues."
Closing in on a vaccine for breast cancer

Progress toward development of a breast cancer vaccine has been reported by researchers at Washington University School of Medicine and the Siteman Cancer Center in St. Louis.

Cancer-fighting vaccines stimulate immune cells to recognize tumor cells as foreign and destroy them. Physicians believe a vaccine-induced immune response could be used to supplement other cancer therapies or to immunize high-risk people against cancer.

"We've been studying a protein called mammaglobin-A found in 80 percent of breast tumors," says Thalachallour Mohanakumar, PhD, the Jacqueline G. and William E. Maritz Professor of Immunology and Oncology in the Department of Surgery and at the Siteman Cancer Center. "The protein is especially interesting for cancer immunotherapy because of its frequent occurrence and because breast tumors express it at high levels."

In articles in the Journal of the National Cancer Institute and Breast Cancer Research and Treatment, the researchers report that they constructed a vaccine consisting of copies of the DNA sequence that makes mammaglobin-A in humans.

Researchers theorized the DNA vaccine would rev up special immune cells (T cells) to recognize mammaglobin-A as a foreign molecule when displayed on cell surfaces as an antigen (a small protein that the immune system may recognize). The primed T cells then would proliferate and attack when they met with mammaglobin-A antigens.

"Mammaglobin-A is involved in breast development and secreted in breast milk," Mohanakumar says. "So we had to prove first that we could elicit an immune response to a protein that is in the body normally."

They injected the DNA vaccine under the skin of test mice that had been engineered so that their immune systems would react to the human mammaglobin-A like a human immune system. The researchers loaded specific cells in the mice with mammaglobin-A antigens and found that the vaccine-primed T cells attacked those loaded cells.

The research team also transferred vaccine-primed T cells into mice with growing tumors that had or didn't have mammaglobin-A antigens. Tumors with mammaglobin-A antigens stopped growing and shrunk in volume, while those without the antigens continued to grow at the usual pace.

According to Mohanakumar, "the results demonstrated that the vaccine-primed immune response is specific to mammaglobin-A antigens."

Breast tumors with mammaglobin-A antigens on their surface also may display antigens that come from multiple parts of the mammaglobin-A molecule. Further experiments confirmed the importance of generating T cells that can react to a variety of different mammaglobin-A antigens.

When the research team tested a DNA vaccine containing the DNA code for just one part of the mammaglobin-A molecule, they found T cells reacting to only that antigen, indicating that the method can generate immune cells that target specific parts of the mammaglobin-A protein.

"Now that we've found how effectively an immune response can be generated to mammaglobin-A, we plan to conduct clinical trials in patients who are at very high risk for breast cancer and in patients who have had a relapse after initial treatment," Mohanakumar says.

"We want to see if giving patients the DNA vaccine can prevent or eliminate breast cancer or at least slow its growth."
DOMINO EFFECTS

Intensivists strive to understand the science of critical care and improve survival rates of critically ill patients

BY MICHAEL PURDY

Many paths lead to the intensive care unit. Nearly 5 million people are admitted to U.S. ICUs each year, and while trauma, violence and accidental injury are leading causes of those admissions, other maladies ranging from pneumonia to cancer to obstetrical disorders also can necessitate an ICU stay.

The variety of conditions that pass through the ICU and the transitory nature of most patients' stays have orphaned these units and the physicians who work in them. No patient advocacy groups exist for ICU patients, and no federal agency is mandated to fund critical care research. Although other countries, notably Canada and Germany, have national research networks dedicated to systematically improving the care of critically ill patients, funding in the United States is fragmented among organ- or disease-specific institutes.

But change is coming. J. Perren Cobb, MD, associate professor of surgery and of genetics, is leading a growing movement to increase public awareness of the value of critical care medicine. He and his colleagues, who practice in the ICU at Barnes-Jewish Hospital, are laying the groundwork for an integrated U.S. research network that will bring the latest methods in high-speed genetic analysis, systems biology and molecular biology to bear on the question of how to better help critically ill patients fight for their lives.

Washington University intensivists at Barnes-Jewish Hospital battle many challenges in critical care, among them multiple organ dysfunction syndrome, in which one organ's failure can bring other organs tumbling down like dominoes.
The condition of being critically ill is a relatively new component of the human experience.

"Since the mid 20th-century or so, we've been able to put people on ventilators and keep them alive in states that never existed before," Cobb says. "Nature has never had the opportunity to engineer a solution for these states, because, prior to that time, people simply died."

According to Cobb, medicine's ability to treat these patients still mostly amounts to a holding measure — an ability to keep patients alive temporarily while factors within "normal" levels of factors like blood pressure, water or potassium in their patients, Cobb notes, they target levels based on studies of healthy persons at rest.

"It's often unclear how truly helpful our efforts are to maintain these normal levels in the critically ill," he says. "We could be trying to alter an adaptive response that might actually help the patient recover."

"It's very common for the lung expert to tell us we need to give a patient medicine to dry them out," he notes. "But then a kidney expert may come in and look at the same patient and tell us to give them lots of fluids. And we have to decide what to do."

An intensivist has to span the gamut of expertises, knowing a great deal about every organ and system while not necessarily specializing in any one of them, according to Cobb.

"In a way, we're experts in the process of how people die," he says. "That's what we study — the process of death and how we can prevent it."

FROM A SYSTEMIC PERSPECTIVE, one of the key challenges intensivists have to deal with is the inflammatory response.

"Inflammatory mediators are released into the bloodstream, so when this process of inflammation gets out of control, it's not just confined to the area of the injury, it involves the entire body, affecting every organ," Cobb says.

This can lead to multiple organ dysfunction syndrome, a condition in which one or more organs fail, and the supportive links between organs bring them all tumbling down like dominos.

Researchers have identified and detailed the properties of several different inflammatory mediators over the last 20 years. However, in all but one case, their strategies for controlling these factors have been uniformly unsuccessful when tested in human patients.

It's this frustration — having so much new information but still being able to clinically apply so little of it — that motivated Cobb to give up his role as a trauma surgeon in favor of pursuing opportunities
to advocate for and advance change in the field of critical care.

"When a previously healthy person arrives at the hospital after an accidental injury, and we treat them using very advanced technology only to basically have them ebb away and die over a period of 24 to 48 hours, it’s very frustrating” says Cobb.

Scientists showed that the protocols they established produced consistent results. This benchmark was essential for future plans to establish large, long-term studies of genetic factors in critical care patients. A second major concern was whether the analyses were sensitive enough to detect changes in gene expression triggered by trauma. In blood samples from 34 trauma patients and 23 healthy persons, scientists found significant changes in the activity levels of several key genes related to inflammation.

COBB SUSPECTS the complex connections between various inflammatory factors, genes, organs and major systems in the body may be one of the biggest reasons why efforts to improve critical care treatment have so far met with relatively little success.

“For example, as we try to get a fix on the optimal levels of minerals in the bloodstream of critical care patients, we have to keep in mind that changing the level of one mineral will affect the levels of other minerals,” he explains.

He hopes that the new technology for rapidly assessing gene activity levels and other advanced scientific techniques will finally provide scientists with the ability to identify and fully understand these connections.

“We’ve been like a driver trying to fix a car without knowing the names of all the engine parts or how they’re interconnected,” Cobb says. “Now, we finally have the tools we need to begin to identify all the parts and their connections.”

Assembling that list of parts and connections will be a massively complex undertaking. To that end, Cobb, who chairs an annual NIH meeting on critical care and genomics, has been recruiting scientists nationwide with a range of expertise to collaborate with critical care experts. This includes intensivist researchers locally who formed the Washington University ICU (WICU) group.

He and other leaders of this movement have resolved to apply the guiding principles of the NIH’s Roadmap Initiative and Washington University’s own Biomed 21 initiative: to take new insights from the lab to the patient’s bedside as quickly as possible, bringing together experts from many different fields with the latest genomic assessment technology.

“We’re very hopeful that in this decade and the next, the frustrations we experienced in the 1990s are going to give way to real advances in understanding the complexity of these systems,” he concludes. “And that will allow us to begin to metabolically engineer new solutions that can actively help patients fight their way back to recovery.”

"Finding new ways to improve these patients’ chances for survival is my professional passion. It’s what I think about day in and day out.”

J. Perren Cobb, MD
Mentors of tomorrow
One-of-a-kind program
steers budding physicians
toward a lifetime of discovery

BY STEVE KOHLER

TIM W. SCHLOSS, MD, IS A CONVERT. He was a first-year intern in the Department of Medicine, focused intently on a career as a clinical cardiologist, when he encountered the Mentors in Medicine program. Now he's a senior resident with a successfully completed research project and a follow-up study in design. More broadly, he's become a believer in academic medicine and the value of clinical research. Schloss is now certain that his cardiology career will include a research component.

Schloss' prior lack of participation in research is not unusual. The Association of American Medical Colleges reports that only about 11 percent of graduating medical students say they will be significantly involved in research during their medical careers. “My exposure to research in medical school was limited,” Schloss says, “and finding the time in a resident's schedule to undertake a research project has been a challenge.” But participating in Mentors in Medicine and producing meaningful results, along with a first place poster award from the Society of Geriatric Cardiology and impending publication of his paper in a national cardiology journal, is “exciting,” he says.

Working with his research mentor, noted geriatric cardiologist Michael W. Rich, MD, Schloss designed a project which showed, counter-intuitively, that using aggressive approaches to treating heart attacks — cardiac catheterization, stent procedures or even bypass surgery — in the very elderly is twice as effective in the long term as more conservative medical therapy. It's information that will imbue his practice of cardiology and a mindset that will guide his pursuit of medical knowledge.

Michael W. Rich, MD, introduced senior resident Tim W. Schloss, MD, to the academic side of clinical cardiology.
THE FOCUS OF MENTORS IN MEDICINE is not so much on specific results as on broad philosophy. The idea is to provide eye-opening research opportunities to bright, young physicians who are "hungry to answer clinically relevant questions but may not know exactly how to proceed," says Daniel M. Goodenberger, MD, professor of medicine and chief of the division of medical education in the Department of Medicine. Begun by Goodenberger and his colleagues three years ago, Mentors in Medicine aims to use mentorship to demystify the processes and challenges of research, both clinical and basic. The program has evolved to provide everything residents need to pursue a research question, from help with experimental design through laboratory and statistical techniques to securing funding.

Today, Brian Dieckgraefe, MD, PhD, whom Goodenberger calls the "energy" of Mentors in Medicine, directs the program. Dieckgraefe, assistant professor of medicine, says, "The reality of medicine today is that those interested in academic careers often get little formal help. Many people may abandon their goals of doing research because of a lack of information and no familiarity with what's required. This program formalizes a mentorship. And successful academic investigators all share one quality: They all sought career mentors to guide them."

An accomplished researcher himself, Dieckgraefe also is pleased that the program may be forestalling endangered species status for academic physicians, a career path he says is under attack from uncertainties in funding, salary differentials and the debt that stalks so many medical school graduates.

"Mentors in Medicine provides resources, a framework and illustrations of how it is possible to be successful," Dieckgraefe says. The program's assistant director, Thomas M. De Fer, MD, assistant professor of medicine, adds that Washington University is the perfect place for such a program: "Residents in more common hospital settings have no exposure to research. Here, this is the way we think; we see the ongoing need for academicians."

The one-of-a-kind program — nothing like it exists anywhere else in the country — has several parts. Every intern who begins training in the Department of Medicine is assigned a general mentor in a nod to the fire-tested practice of senior guiding junior. Beyond that, trainees can choose to seek out a research mentor, most often from among department faculty, involved in the pursuit of questions of interest to the trainee.

With that mentor's help and the support of Dieckgraefe, De Fer and others (notably Sharon Morgan, the department's assistant director of development and corporate education), the trainee, who by this time is usually in the first year of residency, develops a design for a research project and completes an application, learning grant-writing skills along the way.

Rich, associate professor of medicine, who currently mentors four residents and fellows, says he volunteers both because he enjoys working with young investigators and finds their research projects interesting. "These are not huge, randomized trials, obviously, but the studies do make contributions to the field, and it's great for them to have an opportunity to work with a career investigator." He points to Schloss' project as one that has been well-received and generated interest.
It helps that the trainees come to their chosen labs with funding to cover the costs of their projects, Rich says. Otherwise, he and other mentors would be limited by what their own labs could bear financially. But Mentors in Medicine is also a grant-making organization.

Modeled after government granting agencies to the largest extent possible, the program seats a review board that considers research proposals and takes one of three actions: 1) funds them as is, 2) sends them back to their authors for revision, or 3) disapproves them with comments and a small stipend to encourage their further refinement and later resubmission. Most grants range from $3,000 to $7,000, enough to cover the cost of a laptop computer for data acquisition, statistical analysis and lab materials, De Fer says. Some grants are for more, and Schloss was pleased to learn recently that the follow-up to his initial study had been funded this year for significantly more than the average.

The necessary funds come as grants from pharmaceutical companies interested in advancing the next generation of research physicians, contributions that Dieckgraefe and De Fer characterize as “unselfish and generous.” They also point out that the funding is controlled by the companies’ research offices and not their marketing departments, with no strings attached and no corporate input whatsoever into what research ultimately is funded and pursued. All funding is pooled and then distributed so that no company is tied in any way to a particular research project.

A smaller part of the program, but one that endows huge benefit, is the inclusion of noon lectures and casual dinners with eminent researchers invited to campus. Dieckgraefe says that the chance to interact casually with renowned investigators, asking questions such as “What mistakes did you make early in your career?” demystifies the research life and humanizes highly successful people. “Examples of how a career can be structured are particularly helpful,” he says. Goodenberger points out that such networking opportunities can be invaluable for junior researchers, as when they are introduced by their mentors as scientists of promise.

In another bow to the reality of researchers’ lives, every participant is expected to present the results of his or her study at an annual symposium; if the project is not complete, then progress must be detailed. Presentation skills are fostered, and pharmaceutical house representatives are invited to learn how the funds they contributed have been spent.

Mentors in Medicine is growing. The Department of Medicine has approximately 160 graduate physicians in training at any one time, with about 50 senior residents graduating each year. This program now touches nearly half of those graduates. In the first year, 11 grant proposals were made, and all were funded. Last year, the number rose to 18. Most recently, 28 proposals were entertained, and 20 were accepted for funding, so competition is now a factor. Dieckgraefe believes that the program is approaching its optimum size, and he hopes to achieve a steady state.

Goodenberger underscores the purpose: “Washington University is a leader at turning out people who excel in academic medicine. We want to continue that tradition in all available venues.”

Tim Schloss and his commitment to make research a permanent part of his career illustrate how it is being done. □

Visit outlook.wustl.edu for more on the Mentors in Medicine program.
Microscopic particles aid diagnosis and treatment of disease

BY GWEN ERICSON

Imagine replacing numerous medical tests, scans or surgeries with a simple injection. That’s the hope offered by nanoparticles — extremely small, bead-shaped carriers of medicinal agents. Using these tiny spheres, doctors will be able to locate disease sites deep within the body and at the same time determine their size, shape and diagnostic features. They can then adapt the nanoparticles to deliver a load of therapeutic drugs exactly where needed. Readily manufactured to contain a variety of components, the particles can be tailored to each patient’s unique condition.

Co-inventors Samuel A. Wickline, MD, and Gregory M. Lanza, MD, PhD, have already seen their technology work against such major health challenges as cancer and cardiovascular disease in laboratory animals. Now they are set to test its effectiveness in human patients.

Samuel A. Wickline, MD, and Gregory M. Lanza, MD, PhD

Nanoparticles, illustrated at right, have an inert core coated with a layer of active components — homing agents, imaging substances or drugs. Here, the particles (blue) are engineered to target strings of fibrin in a blood clot.

ILLUSTRATIONS BY ERIC YOUNG
Going with the flow

Increased angiogenesis, formation of new blood vessels, accompanies atherosclerosis and cancer. Nanoparticles offer a means for precise imaging and treatment.

Atherosclerosis

Detection
With the buildup of artery-clogging deposits comes an enhanced network of vasa vasorum — small vessels that feed blood to the walls of arteries and veins greater than 1 mm in diameter. Treating atherosclerosis after major vessels are dangerously constricted is reactive medicine. Nanoparticles could provide clues early on.

A forest of vasa vasorum feeds an atherosclerotic vein (above). Nanoparticles bind to extra vessels, revealing atherosclerotic deposits (above right, and right).

Treatment
Drugs delivered by the nanoparticles a week earlier reduced plaque angiogenesis.

Cancer

Detection
Tumors often are spotted only when they are dangerously large and it is too late for nonsurgical treatment. Earlier detection of smaller tumors would greatly boost a cancer patient's prospects. Nanoparticles target the growing mass of blood vessels that feeds the tumor and fosters its spread.

Here, angiogenesis surrounding a melanoma measuring 2 mm is identified 120 minutes after injection of nanoparticles.

Treatment
Delivered via nanoparticle carriers, drug components and lipids enter the membrane of a targeted melanoma cell.

Like a truck delivering cargo to an assigned dock in a warehouse, a nanoparticle transfers its drug cargo to a targeted cell, contrasted with the typical model in which drugs diffuse throughout the body.
homining in and lighting up
Although the nanoparticles are a few thousand times smaller than the dot above an “i,” each can carry hundreds of thousands of molecules on its surface.

To induce the particles to homing in on a target, the researchers attach molecules on the surface that recognize and bind to complementary molecules on the surface of target cells, whether the target is a cancerous tumor or a plaque in an artery.

A suspension of the nanoparticles can then be injected into the bloodstream where the particles travel until they reach their objective.

The ability to target internal disease sites with an externally administered therapy is a leap forward, but the ability to visually confirm that they are reached adds an important dimension.

When loaded with an imaging agent in addition to a homing agent, the particles can both find disease sites and “light them up”; that is, make them easy to visualize using widely available scanning methods such as MRI, CT or ultrasound.

“In the past, experiments with targeted molecular imaging using other types of carriers failed because the signal at the target site was too faint,” says Lanza, associate professor of medicine and a cardiologist at Barnes-Jewish Hospital. “But our nanoparticles vastly increase the density of imaging agent at the site so that the signal becomes quite strong.”

That’s because the amount of surface area available for attaching imaging agents to the nanoparticles is enormous. Say you have a cube just one inch on each side. To cover that cube would require just six square inches of paint, a spot about two and one-half inches wide. But if you cut the cube into a bunch of tiny cubes about the size of the nanoparticles, you would need 600,000 square inches of paint to cover them. That’s enough paint for a wall 10 feet high and 400 feet long.

In a set of laboratory experiments, the researchers loaded their particles with about 100,000 molecules of a metal that provides contrast in MRI scans and a few thousand molecules of an agent that homed in on growing tumors. The high payload of metal molecules allowed the researchers to see tiny, two-millimeter-wide melanoma tumors in mice using MRI scans identical to those in standard use for human heart or brain scans. The same tumors were invisible when scanned in the absence of the nanoparticles.

Because they can pinpoint and then illuminate tiny regions, the nanoparticles have great potential for spotting disease sites at the early stage when treatment is most effective. They also can take uncertainty out of patient follow-up by definitively highlighting areas where disease symptoms have just begun to recur.

targeted treatment
With the capacity to carry therapeutic agents also in the nanoparticles’ array, doctors will have a full-function medical missile available to them. “We’ve reached the era of targeted drug delivery where you now can see drugs being delivered to the right place,” asserts Wickline, professor of medicine and also a cardiologist at Barnes-Jewish Hospital.

“With nanotechnology, we’ve been able to bring Paul Ehrlich’s concept of a magic bullet to realization,” Lanza adds.

Ehrlich, winner of the 1908 Nobel Prize in Physiology or Medicine, sought compounds that would be specifically attracted to and kill disease-causing organisms, with no harmful effect on the body.

“Like Ehrlich’s magic bullet, our nanoparticles are attracted to a particular disease site. Because they accumulate at a well-defined location, they have little effect on the rest of the body,” Lanza says.

In contrast, standard drug administration dilutes medication throughout a person’s system. While a portion of the medication eventually reaches the area where it is needed, it also goes where it isn’t needed in equally toxic concentrations.

Already-tested versions of the nanoparticles locate tumors and atherosclerotic plaques using small homing molecules attracted to proteins abundant on the cells of newly forming blood vessels.

As tumors grow, they recruit new blood vessels to obtain nutrition. Arterial plaques also stimulate the growth of capillaries around them. So, both abnormal growths can be detected using the same homing strategy.

Drugs specifically designed to kill cancer cells or to dissolve plaques can be included on these nanoparticles.
along with homing and imaging agents. Then the brightness of the image at the site reveals both the size of the lesion and the amount of drug that reached the site. The treating physician would have complete information about dose achieved the same day the treatment was given and could quickly adjust treatment as needed.

**personalization**

“The nanoparticle technology is really the next step in personalized medicine,” Wickline says. “There’s a lot of interest in individualizing medicine by analyzing each patient’s genome. The genome interacts with its environment in very complex ways so that the results often can’t be predicted exactly.”

“On the other hand,” Lanza says, “the nanoparticles locate what’s already present in the body.”

“Right,” Wickline says. “We’re not reading the script — the genes — we’re looking at the actors — the proteins. We’re the critics watching the play as it happens, not reading it as it was written.”

That means that each patient’s health status can be analyzed and treated as a unique case, instead of a generalization. The nanotechnology can be designed to peer directly at the biochemical and molecular markers in the body and report what it sees. This ability is unavailable through even the most sophisticated of scanning devices, blood tests and genetic analyses.

“Our nanotechnology is very flexible,” Wickline says. “During the course of treatment, a doctor could decide to target a different biomarker or numerous markers simultaneously.”

Flexibility allows the nanoparticles to be loaded with combinations of compounds and used as a one-step diagnostic test. One injection could reveal the proportions of different biomarkers and indicate the nature of a disease — how aggressive a cancer is or how likely a plaque is to rupture, for example.

The medical school’s BioMed 21 initiative calls for efficient development of laboratory discoveries into practical medical applications, and Wickline and Lanza have support from both the medical school and corporate partners to ensure their technology will be rapidly put to use for the benefit of patients.

They have built collaborations with Phillips Medical Systems, Dow Chemical, Bristol-Meyers Squibb Medical Imaging, and a local company they founded called Kereos Inc., which will set up clinical trials. They also have received $15 million in support from the National Institutes of Health.

“We’ve maintained control of the technology instead of licensing it out so that we can make sure it develops to its fullest potential,” Lanza says.

“This technology can strongly affect the practice of medicine, and we intend to have it do so,” Wickline emphasizes. \(\square\)
shades of gray

examining uncertainty: ethics and human values

by candace o’connor
T H E  P A T I E N T  I S  H O S P I T A L I Z E D,
seriously ill, with no hope of a cure. Although he
had never wished to linger, he is tethered to life-
sustaining equipment through a tangle of tubes and
lines. Day after day, he is pricked and prodded by
well-meaning medical personnel, simply doing their jobs.
How can such a patient achieve a dignified death?

"The answer is palliative care, in
which an interdisciplinary team of
physicians, nurses, chaplains and
social workers come in and say:
"What did your dad really want?"
and "What can we do?" says Ira J.
Kodner, MD, director of the Center
for the Study of Ethics and Human
Values, which has helped launch this
new program.

Gathering people from around
the university to tackle thorny ethical
issues is the mission of the center,
founded in 2003. Faculty, students,
community leaders, even national experts gather for thoughtful debates
of such questions as embryonic stem
research, medical malpractice and tort reform or nationalized
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cence this April called "Democracy
and Global Justice" or a lecture in
February by former Senator Robert
Kerrey on "Uncovering Truth in a
Democratic Society."

The result is a program that is
already assuming a leadership role
nationally for its unusual, interdisci­
plinary focus in which social workers
talk to medical practitioners, lawyers
to philosophers, surgeons to econo­
mists. Some of its projects are also
unique. Currently, Barnes-Jewish
Hospital is the largest teaching hos­
pital in the United States to have a

palliative care program. This sum­
mer, the Internal Revenue Service
Office of Professional Responsibility
will circulate to IRS field offices
across the country a Tax Ethics DVD
for lawyers, certified public accountants, and other tax professionals
developed by the center.

"This university-wide program
is of vital importance, because ethics
and human values affect all students
and faculty and all programs of
education and scholarship," says
Chancellor Mark S. Wrighton.
"I am grateful to Dr. Kodner for
taking an impressive leadership
role in building a program of high
quality having great value to our
university community."

The center also collaborates with many
groups and institutions in sponsor­
ing programs, such as the Interfaith
Partnership of St. Louis and the
University of Missouri-Columbia
for a program on religious views of
stem cell research, and the Jewish
Community Relations Council for
a discussion of the Darfur crisis.
Recently, the center teamed up with
Edison Theatre on a panel discussion
in conjunction with performances
of "Hiroshima Maiden," based
on the story of Japanese women,
disfigured by the atomic blast,
who were brought to the U.S. for
reconstructive surgery.

Sometimes center-sponsored
discussions focus more narrowly on
the needs of a single department.
In surgery, for example, Mary E.
Klingensmith, MD, coordinates
monthly sessions in which residents
can eat pizza and discuss ethical
issues that they have faced, includ­
ing religious prohibitions on blood
transfusions.

"The personnel, expertise and
programs of the Center for the Study
of Ethics and Human Values are a
very valuable resource to the entire
Washington University community,"
says Larry J. Shapiro, executive vice
chancellor for medical affairs and
dean of the medical school. "The
School of Medicine has long been
noted for its excellence in fundamen­
tal investigation, clinical care and
educational programs. Through
the work of the center, we will
become acknowledged as leaders
in the development of important
ethical principles that will guide
decision making in the future."

But the center does not limit
itself to fostering discussion: It
also sponsors ethical research and
education through faculty and stu­
dent grants of up to $5,000 each.
Students, in fact, play a key role
in planning the center's programs
and setting its agenda. On a recent
Saturday, Kodner hosted a picnic at
his home to discuss with interested
students which areas should be a
priority this year. Soon, sheets of
newsprint were filled with project
suggestions, including health care
for the underinsured, "isms" such
as sexism or racism, and most of all,
basic ethics communication.

"That was surprising to us:
There is a significant interest in
simply the idea of what ethics is
all about," says Stuart D. Yoak, the
center's executive officer. “One thing the center focuses on is that different professions have different terms and concepts about values, so the students wanted to understand the lawyer's concept, the business person's concept and the medical view in order to move toward a common approach.”

Ideas for new ventures may also come from the center's executive committee, headed by University College dean Robert E. Wiltenburg and composed of senior faculty and administrators, or its program committee, made up of other interested university faculty. Last year, they set “truth” as the theme for their activities and this year are shifting to a related topic — “responsibility” — which ties in to a range of issues, from environmental policy to academic integrity.

Of course, mounting programs on such topics takes money. Initial funding for the center has come from 10 community backers who have pledged $50,000 each, and a $100,000 leadership grant from the Arthur and Helen Baer Charitable Foundation. Operational support has come from Arts & Sciences, the School of Medicine, the Barnes-Jewish Hospital Foundation and the Medical Staff Association.

These many facets of the center mean full days for Kodner, also the Solon and Bettie Gershman Professor of Colon and Rectal Surgery, who first became interested in ethical issues years ago while teaching an elective in the medical humanities program, “Dealing with Sick Folks and their Families.”

“We got into issues of truth-telling and delivering bad news and answering religious questions,” says Kodner. “For example, when patients say to us — ‘Why is God doing this to us?’ — how do you respond?”

His own patients, half of whom suffer from colon or rectal cancer, also have taught him about the need for compassion. “We have come to think that the end of life means a defeat for us as physicians and nurses, but I know it isn’t,” he adds. “Sometimes the most gratifying thing we can do is guide a patient to an honorable death.”

That’s where palliative care comes in, one of the most successful center efforts to date. Already, the hospital has hired a palliative care physician and is reviewing applications for a dedicated nurse practitioner. Business planning for the program has been helped by a consulting team of MBA students and faculty at the John M. Olin School of Business, while the cross-campus educational component will be handled by students from social work, medicine and law.

Along with donors Jack and Ellen Deutsch, the other major sponsor of this project is university friend Dorothy Moog.

“All we are doing is bringing together components of a great university,” says Kodner. “And it gives all of us a huge sense of pride that the center is helping to accomplish something as important as this.”

The Center for the Study of Ethics and Human Values

Ripped from the headlines? Through its topical seminars, the center continues to probe some of the most sensitive and ethically challenging issues of our time.

Ira J. Kodner, MD, director (left), and Stuart D. Yoak, executive officer.

MEDICAL TOPICS
Medical Malpractice and Tort Reform
Medical Ethics
Organ Transplantation

Beyond Tuskegee: Human Testing in the Current Age
Religious Perspectives on Stem Cell Research
Nationalized Health Care

OTHER TOPICS
Painted Narratives: The American West, from Both Sides
Corporate Governance and Ethics

Ethics Forum for Tax Practitioners
Democracy and Global Justice
Selling the Presidency
Uncovering Truth in a Democratic Society
Letter-perfect!

MATCH DAY WAS HELD MARCH 17, 2005, and 106 of the 114 graduating medical students took part in the National Resident Matching Program. During the annual ceremony, senior medical students in the United States learn which residency programs they will enter. School of Medicine graduates are highly successful in obtaining competitive training programs. In 2005, 45 percent of the graduating class selected a primary care field and 19 percent matched into highly competitive surgical subspecialty training positions.
Here's to the Class of 2005!

John Campbell, MD 05, and his wife, Colleen, are in good spirits, and good company, as they lift their glasses in Match Day celebration.

Caring resource
Sansone family strives to ease the struggle of depression

Most people with conditions such as diabetes or heart problems don’t hesitate to see a physician for treatment. But when a person has depression, he or she often suffers alone, leaving family and friends feeling helpless as they watch a loved one struggle. One St. Louis family’s tragedy inspired them to help others suffering with depression, a debilitating and sometimes fatal disease. In 2002, Anthony F. Sansone Jr. and his seven children established the Peggy Sansone Special Angel Foundation to offer people with depression and their families a place to turn for support and answers. Improving treatment options to include an examination of how spirituality can become a component of care is one of its many goals.
The family's motivation is personal. Peggy Sansone, Tony Sansone's wife and the mother of their children, took her own life in 2001.

"Peggy was undiagnosed for the most part and didn't receive proper treatment," says Sansone, a principal with the Sansone Group in Clayton MO. "We feel that the system is flawed, and we want to figure out how to help people talk about this disease openly, in addition to developing more effective and compassionate ways of evaluating and treating people with depression."

The Sansones also wish to honor C. Robert Cloninger, MD, the Wallace Renard Professor of Psychiatry, for the support he gave the family in their darkest hours following Peggy's death. In gratitude, they have established the Peggy Sansone Memorial Lecture series and the Sansone Family Center for Well-Being at Washington University School of Medicine.

"I think Tony and his family realized that turning inward wouldn't be helpful for them or for the community," Cloninger says. "They have courageously and generously decided to come forward and raise awareness of depression, in addition to providing a resource for people struggling with this disease."

Peggy Sansone visited numerous therapists but was not diagnosed with depression and referred to a psychiatrist until she was severely depressed. And even when she was hospitalized, her family didn't feel as if her physicians were well prepared to treat her. They saw Peggy become even more hopeless in the hospital environment where she received treatment.

"The facility had bars and wasn't conducive to feeling good or productive," says Anthony F. Sansone III, the couple's eldest son. "It made her feel worse."

Before turning to Washington University, Sansone and his family spent nearly two years desperately trying to obtain effective treatment for Peggy's illness. He was referred to Cloninger by a national expert on depression, who told him: "You don't need to see me; the leading depression specialist is right there in St. Louis." Cloninger responded immediately to Sansone's call for help, telling him he could see Peggy within the hour. Unfortunately, she got only as far as Cloninger's door, then turned back.

"He's a man of compassion and a wonderful human being," Sansone says of Cloninger, who is now director of the Sansone Center for Well-Being. "I've talked to many of his colleagues, and they have unanimously praised his talent, his heart, his faith and his practices. We're as lucky to have him as Washington University is."

The Peggy Sansone Memorial Lecture series addresses topics associated with the treatment, cure and prevention of depression and also examines the role of spirituality in personality development. According to Sansone, the purpose of the lecture series is to inform clinicians of different approaches and of the importance of the physician's role as therapist.

May the spirit of a dear wife, mother and friend help illuminate a path that will save others in the future from ever feeling they are hopeless and alone.

The Center for Well-Being, now housed in the Department of Psychiatry, currently studies the development of positive emotions and life satisfaction using a combination of approaches, including molecular genetics, brain imaging and longitudinal studies.

The Sansones hope that the Center for Well-Being someday will be a separate facility, with a warm and compassionate environment. They envision it as a place of respite and comfort where patients will get better and be able to resume their lives.

The Sansones have received plenty of support from their own extended family — more than 60 members faithful and strong. And they hope their efforts will encourage people with depression to seek help early — to give interventions time to work — and remember that they're not alone. They also want to spare another family the loss and pain they've experienced.

"There are so many people who are suffering and going untreated just as Peggy did," Sansone says. "We want to make getting help easier. It's our challenge to make a difference."
REUNION 2005 brought together a community of medical alumni to celebrate and learn. This gathering of physicians, scholars and longtime friends featured educational programs, medical center tours, dressed-up dinners and down-home fun.

From the Class of 1995 starting the reunion tradition with their 10th to the Class of 1940 proudly feting their 65th, at the School of Medicine, everyone was home again.

PHOTOS BY MARK BEAVEN, ROBERT BOSTON AND DAN DONOVAN
Saundra Hudson and James M. Hudson, MD 75, enjoy the reunion nightlife. Celebrating at the 15th reunion class dinner are Kathleen Cizek and Gregory R. Cizek, MD 90.

Allan H. Pribble, MD 65, looks for familiar faces among the pictures from his student days.

Eric D. Green, MD 87, PhD 87, HS 91, told fellow alumni about his frontline participation in the Human Genome Project.

Learning from each other

David L. Rosenbaum, MD 60, finds out about community outreach from first-year student Kari Wanat.

Five members of the Class of 1940 gathered for what may become a new School of Medicine tradition: the 65th reunion. They looked over student photos, left, compared stories and discussed their careers. Standing at right are Willard D. Rowland, MD, John S. Skinner, MD, and Llewellyn Sale Jr., MD. Seated are Seymour Brown, MD, and Richard L. Landsau, MD.

Looking back, looking forward
Betty Geren Uzman, MD 45, greets lifelong friends.

James S. Louie, MD 65, entertains classmates.

Joseph W. Eades, MD 60, and classmate H. Denny Donnell Jr., MD 60.

T.S. Park, MD, and Mee-Aeng Park were among the celebrants who attended the reunion awards banquet to honor faculty colleagues and friends.

Newest alumni: Days before graduation, the Class of 2005 was welcomed to the Alumni Association during the reunion awards banquet. Pictured are Karen Reisiger and Kara Barnett with Ashley Steed, a student in the Medical Scientist Training Program.

Ann E. Starr, MD, catches up with Class of 1995 colleagues Christopher M. Palmer, MD, and David J. Caccamo, MD, at the Welcoming Reception.

Inspecting new digs

Hardhat tour: Alumni receive a sneak peak at the Farrell Learning and Teaching Center as it nears completion. With its wi-fi cafe and clinical skills instruction suite, the building will open a new door in medical education, reported the student leaders who led the tour. For one tour participant, wearing the hard hat is as cool as it gets.
The School of Medicine honored five outstanding members of the Washington University Medical Center community at the Reunion 2005 Awards Banquet. Alumni, faculty, family and friends gathered to celebrate these physicians for their laudable contributions to clinical research, basic science and patient care.

Distinguished Service Award

Robert L. Grubb Jr., MD, HS 73, is the Herbert Lourie Professor of Neurological Surgery and professor of radiology at Washington University School of Medicine.

Alumni/Faculty Awards

M. Gilbert Grand, MD, HS 76, is professor of clinical ophthalmology and visual sciences at Washington University School of Medicine.

Alan Permutt, MD 65, is professor of cell biology and physiology and of medicine at Washington University School of Medicine. He is also director of the Diabetes Research and Training Center at the School of Medicine and of the Institutional National Service Research Training Program in Endocrinology and Metabolism.

Alumni Achievement Awards

James E. Darnell, MD 55, is the Vincent Astor Professor and Head of the Laboratory of Molecular Cell Biology at Rockefeller University.

Eric D. Green, MD 87, PhD 87, HS 91, is the scientific director of the National Human Genome Research Institute of the National Institutes of Health.

Walter L. Meyer, MD 50, and Meredith J. Payne, MD 50, live it up at their 55th reunion.

From the Class of 1955: Miles C. Whitener, MD, Robert C. Drews, MD, Waller W. Cooper, MD, and Glendall L. King, MD.

Generosity

Next stop, Super ATM: Executive Vice Chancellor and Dean Larry J. Shapiro, MD 71, thanks reunion alumni for their more than $1.85 million in gifts this year.

Yearbook review:

Brian E. Lawner and David P. Miller, both MD 95, make a list of those who didn't come to the 10th reunion.
50th Reunion pride: Harold L. Stratton, MD 55.

James W. Fleshman Jr., MD 80, chaired reunion sessions as president of the Washington University Medical Center Alumni Association while celebrating his 25th reunion.

Willard O. Rowland, MD 40, and Llewellyn Sale Jr., MD 40, take a look down Memory Lane (a.k.a. Euclid Avenue).

Way back whens

Bruce R. Brodie, MD 70, and Dora Brodie compare the St. Louis sunset to those seen back home in Greensboro NC.

Robert B. Stewart, MD 50, proudly shows his copy of the Evarts Graham biography to his wife, Sandy Stewart.


Let’s meet next year!

Peg Dunner, OT 64, and David L. Dunner, MD 65, share a laugh with Margaret C. Telfer, MD 65.

2006 MD REUNION
May 11, 12 & 13, 2006
physicians, safety net clinics and local hospitals that provides care for more than 15,000 low-income, working uninsured, and other vulnerable adults and children.

Warren B. Howe, MD 65, is the recipient of the 2005 Citation Award of the American College of Sports Medicine, granted to an individual who has made significant and important contributions to sports medicine, the exercise sciences, or both. He is student health physician and university team physician at Western Washington University in Bellingham WA.

Lynn M. Taussig, MD 68, has announced that he will retire as president and CEO of National Jewish Medical and Research Center in Denver in January 2006, having served in that role since October 1993. He writes, "I was fortunate to receive the Distinguished Achievement Award from the American Thoracic Society in 2002. My wife, Lisa, and I are delighted to be able to spend a fair amount of time with our two granddaughters in Denver. Except for a mitral-valve repair in 2002, and some of the health issues that come with the aging process, we have been quite healthy and able to travel extensively. I would be delighted to see classmates who are passing through Denver."

Peter J. Stern, MD 70, the Norman S. and Elizabeth C.A. Hill Professor and chairman of the Department of Orthopaedic Surgery at the University of Cincinnati College of Medicine, has been elected president of the American Board of Orthopaedic Surgery. He is a recent past-president of the American Society for Surgery of the Hand.

Richard A. Linneberger, HA 79, received his Doctor of Ministry degree from Wesley Theological Seminary in Washington DC in May 2004. Linneberger lives in Chesapeake VA.

Cathy J. Lazarus, MD 81, HS 86, who formerly held a position at Tulane University, became Associate Dean for Student Affairs and Medical Education at Chicago Medical School at Rosalind Franklin University of Medicine and Science on Feb. 1, 2005. She commutes to New Orleans to be with her husband and 16-year-old daughter, who are remaining there until their daughter graduates from high school. They also have a son in college.

John C. Morris, MD, HS 83, is the recipient of two prestigious awards: the Lifetime Achievement Award from the Alzheimer's Association and the 2005 Potamkin Prize for Research in Pick's Alzheimer's and Related Diseases from the American Academy of Neurology (see Pulse, page 6). He has been a pioneer in searching for ways to achieve early diagnosis of Alzheimer's. Morris is the Harvey A. and Doris Mac Hacker Friedman Distinguished Professor of Neurology and principal investigator at Washington University's Alzheimer's Disease Research Center.

Jeana D. O'Brien, MD, HS 92, recently transitioned from director of the internal medicine residency program to assistant medical director for the Scott & White Clinic in Temple TX.

Stasi A. Gormley, OT 93, gave birth to her third son on Sept. 8, 2004. His name is Luke, and he joins brothers Andrew, 5 1/2, and Michael, 3.

Gormley continues to expand low vision rehabilitation outpatient and home health practice with the Association for the Blind and M.U.S.C. Feldberg Center in Charleston SC.

Robert A. Bane, MD 96, and his family, Amy E. Bane, MD 98, Thomas, 7, and Laura, 4, have moved to Mahomet IL, near Champaign, where he works for Carle Clinic Association and is a team orthopaedic surgeon for University of Illinois varsity athletics.
Matthew M. Bruckel, MD 97, is now practicing emergency medicine at St. Vincent's Hospital in Jacksonville FL, after his discharge from the U.S. Navy. He and his wife, Katy, had a daughter, Ava Morgan Bruckel, last year.

Patricia D. Short, MD 98, and her husband, Jon, celebrated the birth of their first child on July 14, 2004. Anna Joy is named in honor of her great-grandmothers.

Julie C. Holschen, MD 99, has moved to Ann Arbor MI, where she has a joint appointment in emergency medicine and orthopaedic sports medicine at the University of Michigan.

Jennifer M. Dunn, MD 00, recently joined Northwest Pediatrics, a group practice in St. Louis County MO. She and her husband, Eric, welcomed Alison Ruth Dunn on July 11, 2004.

Tisa McLaughlin Barry, PT 01, writes that she married Matt Barry, a professional engineer, on May 15, 2004. She is currently working at Athletic and Children's Pediatric Specialists. They live in Palatine IL.

Ethan and Elena Korngold, MDs 01, are the proud parents of Gabriel Jonah Korngold, born July 29, 2004. They live in Allston MA.

Kari B. Wisinski, MD 01, and her husband, Mark, welcomed their first child, a son named Caden Paul, "a sweet, healthy boy with a charming smile," on Jan. 9, 2005. The Wisinskis are moving to Chicago where she will begin a fellowship in hematology/oncology at Northwestern University.

IN MEMORY

Torrence A. Makley Jr., MD 43, died Jan. 3, 2005, in Columbus OH at age 86. He was professor emeritus and former chair of the Department of Ophthalmology at Ohio State University School of Medicine. The Torrence A. Makley Lecture and the Torrence A. Makley Research Professorship in Ophthalmology have been established at OSU in his honor. His first wife, Anne, preceded him in death. Survivors include his wife, Claudette, three sons and three daughters.

Dorothy T. (Pulliam) Magallon, MD 46, of New Albany IN, died July 18, 2004, at age 81.

James T. Brown, MD 48, of Springfield MO, died of cancer on Jan. 24, 2005, in Durham NC, where his son, James Trig Brown, MD 77, practices. A general surgeon, Brown was the founder of the Singing Doctors of Springfield. The group entertained widely with humorous musical shows for nearly 40 years, raising more than $400,000 for scholarships for over 200 medical students. In addition to his son, Brown is survived by a daughter, Mary Louise Brown, SW 76.

Joseph A. Norton, MD, HS 49, died Dec. 22, 2004, in Little Rock AR, at age 85. Following service in the U.S. Army Medical Corps and radiology residency at Washington University, he practiced for 35 years at Radiology Associates in Little Rock. After retiring, he taught at the University of Arkansas for Medical Sciences and at Pennsylvania State University Medical Center in Hershey PA. He served as president of the Arkansas State Medical Society and was active in community groups. Norton is survived by a daughter.

David M. Weible, MD 50, an ophthalmologist, died Dec. 28, 2004, in Belleair FL.

William T. Hill, MD, HS 52, died Jan. 7, 2005, at age 80, in Houston TX. He had been chief of pathology at the U.S. Army area medical lab and chief of staff of Rosewood Medical Center Hospital and Sam Houston Memorial Hospital. Hill was a founding member of the Gulf Coast Regional Blood Center and a past-president of the Texas Society of Pathology. After he retired, he and his wife spent time in medical mission work, establishing a clinic in Mexico and working with Mexican medical students, as well as serving in Nairobi, Kenya, through Pathologists Overseas. His wife, Anna Mary Cornell Hill, a daughter and a son survive.

William F. Turner Jr., MD 56, died Oct. 28, 2004. He was an internist and oncologist in Fort Smith AR.

Casimer Jasinski, MD 57, died in Honolulu on March 16, 2005, at the age of 80. He was a retired Federal Aviation Administration flight surgeon, a World War II Navy pilot, a Hawaii National Guard physician, and had practiced at The Queen's, St. Francis, Kuakini and Kaiser medical centers. Survivors include his wife, Doris Reimann Jasinski, MD 56, a son, John, and a daughter, Mary Ann McAndrew.

John S. Spratt, MD, HS 59, died February 13, 2005. He lived in Charleston SC and had practiced general surgery. Among his survivors is a son, John A. Spratt, MD 80, a cardiothoracic surgeon.

Edgar G. Givhan, MD 60, died on Nov. 15, 2004, in Montgomery AL at age 70, following an 11-year battle with prostate cancer. After graduation from medical school, he trained in internal and family medicine at Vanderbilt University and served as a captain in the U.S. Air Force before beginning practice in Montgomery. Givhan was nationally known for his gardening expertise and authored six books on the subject. Survivors include his wife of 23 years, Montgomery County District Judge Peggy Givhan, children and stepchildren.

Maureen M. Fitzpatrick, MD, HS 95, died Oct. 6, 2004. She had lived in Foley MN.
Elizabeth Gray Danforth, University's former first lady

In recognition of her volunteer efforts, Danforth was made an honorary alumnus, and she received numerous other awards, including the Search Award from the University’s William Greenleaf Eliot Society in 1987.

Other honors accorded to Danforth include the 1983 St. Louis Wellesley Award, the 1989 Outstanding Alumna Award from John Burroughs School, and the 1990 St. Louis Woman of Achievement Award for Youth Enrichment.

Danforth served as a member of John Burroughs School’s board of trustees and alumni board, as president of the Wellesley Club of St. Louis, and as a member of the board of the Community School.

In addition to her husband of 54 years, survivors include three daughters: Cynthia Prather, of Anniston, Alabama; Maebelle Reed, of Tucson, Arizona; and Elizabeth Sankey, of Ladue, Missouri; a son, David Danforth, of Clayton, Missouri; a sister, Mary Jane Gray, MD 49, of Philomath, Oregon; and 13 grandchildren.
How to increase your income and benefit the University.

Consider making a life income gift with appreciated securities or cash to:
- Receive a valuable charitable income tax deduction.
- Receive significant capital gains tax savings.
- Turn low-yielding assets into attractive income.
- Receive fixed payments for your lifetime.
- Fulfill your charitable intent for the University.

**GIFT ANNUITY**

Sample Rates of Return

<table>
<thead>
<tr>
<th>one-life</th>
<th>two-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>rate</td>
</tr>
<tr>
<td>60</td>
<td>5.7%</td>
</tr>
<tr>
<td>65</td>
<td>6.0%</td>
</tr>
<tr>
<td>70</td>
<td>6.5%</td>
</tr>
<tr>
<td>75</td>
<td>7.1%</td>
</tr>
<tr>
<td>80</td>
<td>8.0%</td>
</tr>
<tr>
<td>90</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

If you are age 75 and create a $50,000 gift annuity with appreciated securities, which have doubled in value, you will receive the following benefits:

- **Rate of return**: 7.1%
- **Fixed annual income for life**: $3,550
- **Taxed as ordinary income**: $1,331
- **Tax-free portion**: $1,110
- **Taxed at capital gain rates**: $1,109

(Your charitable deduction will vary.)

**Do you own appreciated real estate?**

Consider gifting the real estate to a Washington University unitrust and receive a lifetime income, a charitable income tax deduction, and avoid capital gains tax on the sale.

Seek advice from your tax or legal advisor when considering a charitable gift annuity and/or charitable trust.

For further information or to request a personalized example, please call 1-314-935-5848 or 1-800-835-3503, complete the attached reply card, or e-mail us at plannedgiving@wustl.edu.

Visit us at our Web site at http://plannedgiving.wustl.edu

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A life income gift benefits both the donor and the University. Alice Eliot Schofield, the great-granddaughter of William Greenleaf Eliot, has seen firsthand the benefits of such a gift.

"I am proud to support the William Greenleaf Eliot Scholarship Fund through annual gift annuities."

Alice Eliot Schofield, Robert S. Brookings Partner

How to increase your income and benefit Washington University

☐ Send me a personal illustration of how a charitable gift annuity or a charitable remainder unitrust funded with appreciated assets or cash would benefit me.

Value $_________ In the form of:

☐ Cash

☐ Securities $(_________) (COST BASIS) (ACQUISITION DATE) 

☐ Real Estate $(_________) (COST BASIS) (ACQUISITION DATE) 

First Beneficiary

Second Beneficiary

Birthdate

Birthdate

Relationship

Relationship

☐ I wish to become a Robert S. Brookings Partner.

☐ I have included Washington University in my estate plan through my:

☐ will or trust ☐ retirement plan assets ☐ other

☐ I have a question. Please contact me.

Name

Address

City/State/Zip

Daytime Phone

E-mail

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Office of Medical Alumni & Development

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City/State/Zip ____________________________

Specialty ____________________________ Class/HS Year ____________________________

E-mail ____________________________ May we list your e-mail address in our web page directory? ☐ Yes ☐ No

Signature ____________________________ Daytime phone ____________________________

The University reserves the right to contact contributors to verify entries.
Striking a nerve

Sculptor Jessie Vonk unveils “In Shadow of the Rock” at the Hope Center for Neurological Disorders. Vonk, the widow of former St. Louis Symphony conductor Hans Vonk (who was treated for Lou Gehrig’s disease at Washington University Medical Center), donated the 500-lb. work in granite and bronze. Inset: Vonk with Mark P. Goldberg, MD, professor of neurology and scientific director of the Hope Center, left, and David M. Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor of Neurology and head of the Department of Neurology.
**Sickness in motion**  As a pox virus fuses with a cell it has just infected, it discards the shroud-like covering it uses to "hide" as it spreads from cell to cell within the body (green). The complicated tracks of protein-crystals seen on a "naked" pox virus (inset, without shroud) mix after fusion with the cell membrane, making the collection of "mulberries" (blue). The event is captured using "quick-freeze, deep-etch" electron microscopy, a process created by John E. Heuser, MD, professor of cell biology and physiology, which lets biologists take detailed pictures of fleeting events inside living cells. For more about Heuser's work, please turn to page 6.