

Outlook

FALL 2004

 Washington
University in St. Louis
SCHOOL OF MEDICINE

.....
AUTOIMMUNITY
.....
VARICOSE VEINS
.....
SAVING HIPS
.....

Gleaning genes

Comparing humans,
algae and plants





Row, row, row... Stephen Warner (front), a first-year MD/PhD student in the university's Division of Biology and Biomedical Sciences, guided his men's lightweight-four boat during competition in the recent summer Olympic Games in Athens, Greece. The former University of Michigan rower deferred his acceptance to the School of Medicine for four years to continue training. He and his teammates finished ninth overall in the rowing event.

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Outlook

Reaching Out!

Construction proceeds on the atrium that will connect the Farrell Learning and Teaching Center with the North Building.

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 for personal network access.
- 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.

Outlook

Washington University School of Medicine
VOLUME XLI • NUMBER 3 • FALL 2004

COVER Susan K. Dutcher, PhD, professor of genetics and of cell biology and physiology, among the flora at St. Louis' Missouri Botanical Garden. Dutcher's research on cilia, hairlike structures on the surfaces of cells, led her on a computerized search through genetic information from algae, plants and humans. For more on this story, please turn to page 16.

PHOTO BY ROBERT BOSTON



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Understanding why the human immune system sometimes attacks its own host may lead to new therapies or even the prevention of autoimmune diseases.

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Young adults with hip dysplasia — who often go undiagnosed — can benefit from a surgical procedure that radically changes the structure of the hip joint.

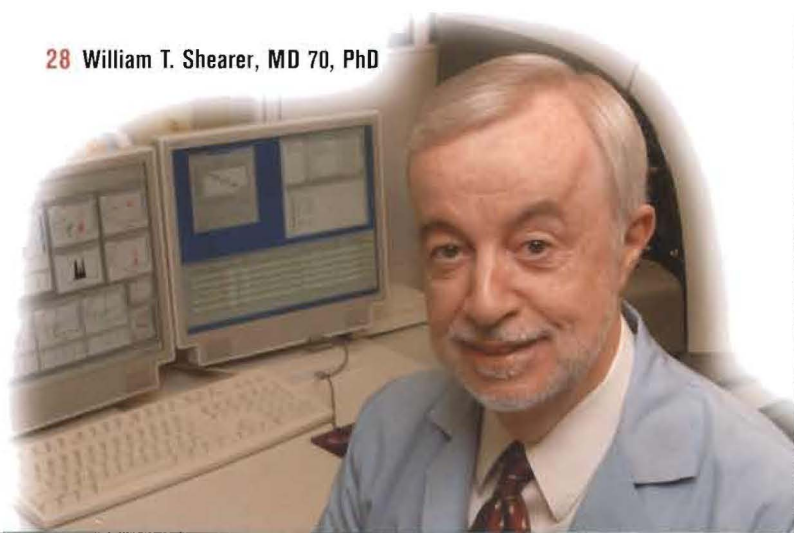
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An innovative method of culling specific genes for study helps researchers to determine which genes carry out important functions or contribute to human diseases.

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Minimally invasive treatment for varicose veins and other leg vein problems is not for looks alone — the procedure can cure these often painful and debilitating conditions.

28 William T. Shearer, MD 70, PhD





All aboard! The Class of 2008's 122 incoming members enjoy a tour of the St. Louis Zoo by train during Dean Larry Shapiro's annual welcoming party held on August 19, 2004. The new first-year medical students and their guests enjoyed a barbecue dinner and dancing at Rivercamp during the event.

WUSTL awarded select distinction

THE ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS (AAHRPP) recently awarded full accreditation to Washington University, one of only a few organizations in the nation to gain this recognition.

The AAHRPP, a non-profit organization, works to protect the rights and welfare of research participants by fostering and advancing the ethical and professional conduct of scientists and organizations that engage in clinical research.

"We are very proud that Washington University is one of only 14 organizations awarded accreditation by the AAHRPP," says Theodore J. Cicero, PhD, vice chancellor for research.

"The safety and protection of human participants has always been at the forefront of patient care at Washington University."

THEODORE J. CICERO, PHD

The AAHRPP was founded by seven prestigious organizations, including the Association of American Medical Colleges, the Association of American Universities and the

Federation of the American Societies of Experimental Biology, "to foster a culture of science and responsibility within institutions seeking its services." The clinical research accreditation process was initiated by AAHRPP in 2002.

Powell to head Radiation Oncology

SIMON POWELL, MBBS, PHD, a cancer physician-scientist from Massachusetts General Hospital and Harvard University, has been appointed head of the Department of Radiation Oncology.

"Simon is a talented research scientist who has done much to uncover the molecular mechanisms that allow normal tissues and cancer cells to repair their DNA after exposure to ionizing radiation," says Larry J. Shapiro, MD, dean of the School of Medicine and executive vice chancellor for medical affairs.



Simon Powell, MBBS, PhD

"He possesses the leadership skills and vision to move our Department of Radiation Oncology forward in a continued effort to achieve excellence in all of its missions."

Powell is a leader in research into BRCA1 and BRCA2, two genes that can sharply increase a woman's risk of developing breast cancer. Among other accomplishments, Powell developed new tests that let doctors interpret formerly ambiguous results from tests for the risk-enhancing forms of BRCA1 and BRCA2.

Originally from England, Powell was head of the Breast Cancer Service and Clinical Director of the Gillette Women's Cancer Center Program at Massachusetts General, which is affiliated with Harvard Medical School. He earned both his MBBS (the British equivalent to the MD) and his PhD in cell and molecular radiation biology at the University of London. Powell trained at the Royal Marsden Hospital and the Institute of Cancer Research in England before coming to the United States in 1991 as a clinical oncology fellow at Harvard.

Powell also will become a professor of radiation oncology. As department head, he succeeds Carlos A. Perez, MD, who served as the department's head since it was founded in September 2001.

Powell is currently principal investigator or co-principal investigator for six federal research grants, and he has served on various committees for the NIH including site visit committees that have reviewed major cancer-related grants at other institutions. He was associate editor for the *International Journal of Cancer* for eight years and currently serves on the editorial boards of the journals *Radiation Research* and *Cancer Biology and Therapy*.

HIV care for uninsured, underserved patients to be funded by three-year grant

MISSOURI FOUNDATION FOR HEALTH (MFH) has awarded a three-year, \$1.1 million grant to the Infectious Disease Clinic at Washington University School of Medicine and Barnes-Jewish Hospital. The new grant will support care of low-income patients with HIV and conditions that complicate HIV treatment.

"The foundation's funds will be committed to serving the growing needs of people with HIV disease who, due to lack of insurance or other issues of access, would otherwise receive little or no care for their complex illnesses," says project director Victoria J. Fraser, MD, professor of medicine and co-director of the division of infectious diseases.

MFH was created in 2000 as part of an agreement between Blue Cross/Blue Shield of Missouri, the Missouri Department of Insurance and the Missouri Attorney General. The largest health care foundation in the state, Missouri Foundation for Health works to support public and private health care services for the uninsured and the underserved.

The grant also will be used to expand and improve psychiatric counseling and to better monitor HIV's effects on the liver. Though 85 percent of the grant's funds will be used directly for patient service, the grant also is structured to help the clinic seek future funding from other agencies and plan for future partnerships.

PSYCHIATRY

Holidays, special events have no proven effect on timing of death

The idea that dying people hang on to life in order to celebrate one more birthday or holiday has no firm scientific basis, according to behavioral medicine researchers.

"I've worked in hospitals since I was about 16 years old, and I've seen that people in medicine have a lot of very strongly held beliefs, like the idea that certain people hang on," says Judith A. Skala, PhD, research associate at the university's Behavioral Medicine Center. "But none of the studies have convincingly established that the time of death can be postponed

through force of will or hastened by loss of the desire to live."

Skala is the lead author of a review article that appeared in the May issue of the journal *Psychosomatic Medicine*. With Kenneth E. Freedland, PhD, professor of psychiatry, Skala reviewed a number of studies that have looked at whether death rates increase or decrease before, during or after symbolically important occasions such as holidays or birthdays.

They examined studies dating back to the early 1970s but found no convincing evidence that people can delay or hasten their own deaths.

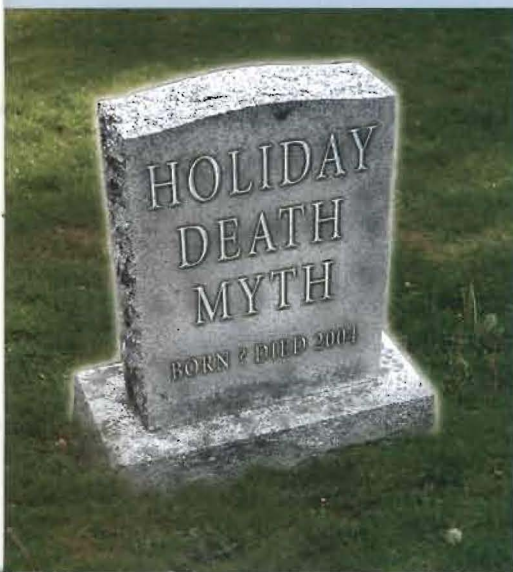
If it were possible to learn how people might tip the balance one way or the other, Freedland says, it could provide some insight into the psychological processes that can enhance or inhibit survival.

The available research analyzed by Skala and Freedland is contradictory, shows only modest effects, and some is of poor quality. In many cases, the studies also fail to explain the mechanisms that might delay or advance death.

For instance, one study claimed there was a 19 percent dip in deaths among prominent Americans in the month before their birthdays and a 14 percent rise in deaths in the month afterward. However, Skala and Freedland say, the original authors included the birth month itself in the "after" category. That meant some post-birthday deaths may have occurred before a person's actual birthday.

Two other studies analyzed deaths among members of certain religious groups before and after major holidays. A study of Catholic priests found no variation in mortality around Christmas, Easter, birthdays or anniversaries of their ordinations.

To truly learn whether people can "hang on" or "give up," it will be necessary to pick a group of people with the same disorder at the same stage – say, terminal cancer. Then, studying those people during the time they have left, Freedland and Skala say it may be possible to identify psychological factors that seem to lengthen the time that a person survives.



ERIC YOUNG

Baum to lead national organization

M. CAROLYN BAUM, PHD, has been elected president of the American Occupational Therapy Association (AOTA), a professional society that represents the interests and concerns of occupational therapy professionals and works to improve the quality of occupational therapy services.

Baum is the Elias Michael Director of the School of Medicine's Program in Occupational Therapy, which is ranked third among occupational therapy schools by *U.S. News & World Report*.



M. Carolyn Baum, PhD

"My goals are to lead the association and its members as they form partnerships with consumers and policymakers," Baum says.

"We hope to foster the participation, health and well-being of people whose health condition or disability threatens or limits their performance."

The AOTA is a national professional society established in 1917 to represent the interests and concerns of occupational therapy professionals and to improve the quality of occupational therapy services. Occupational therapists focus on enhancing the quality of life for individuals who may be recovering from illnesses or injuries, coping with developmental disabilities or experiencing the normal sensory changes that result from aging.

Baum, who also is professor of occupational therapy and of neurology, has developed three measurement tools used worldwide by clinicians working with patients with neurological conditions. The instruments enable therapists to assess what a patient is able to do now versus before an illness or injury, how much support a patient may need to perform daily tasks such as paying bills or taking medications, and the level of care a patient may need in the home or an assisted-living facility.

Much of her research focuses on helping older adults live independently. "Rather than focusing on people's deficits, I try to understand what a person with a chronic disease or disability can do," Baum says.

Her current research includes a project to identify the relationship between a person's vision and the ability to continue living at home. Baum also is principal investigator of an interdisciplinary team studying brain injuries caused by stroke or trauma. She and her colleagues hope this research will lead to more effective rehabilitation strategies.



A new beginning First-year medical student Funmi Okuyemi accepts a little help from Will Ross, MD, associate dean for diversity programs and assistant professor of medicine, at the School of Medicine's White Coat Ceremony held August 13, 2004, at the Eric P. Newman Education Center. Each member of the incoming class was presented with a white coat, long a symbol of the medical profession, as they began the journey to becoming physicians.

Barrack named Knight Professor

ROBERT L. BARRACK, MD, has been named the Charles F. and Joanne Knight Distinguished Professor of Orthopaedic Surgery. He also will serve as chief of staff for orthopaedic surgery at Barnes-Jewish Hospital and chief of the Adult Reconstructive Surgery Service for the Department of Orthopaedic Surgery at the School of Medicine.



Robert L. Barrack, MD

"We are very excited to welcome Dr. Barrack as the Knight Distinguished Professor," says Larry J. Shapiro, dean of the School of Medicine and executive vice chancellor for medical affairs. "The School of Medicine and Barnes-Jewish Hospital owe a great debt to Chuck and Joanne Knight, and this distinguished professorship is emblematic of their commitment to our institution."

Richard H. Gelberman, MD, the Fred C. Reynolds Professor and head of the Department of Orthopaedic Surgery, says Barrack's appointment is another key step in building the department's reputation as one of the finest orthopaedic surgery departments in the United States.

Peck named to national committee on health insurance benefits and payments

THE NATIONAL ACADEMY OF SCIENCES' Institute of Medicine has named William A. Peck, MD, a member of a national committee that will address ways to redesign health insurance benefits, payment and performance improvement programs. Peck is the Alan A. and Edith L. Wolff Distinguished Professor of Medicine and director of the Center for Health Policy at Washington University's Olin School of Business.

The committee's purpose is to identify options for redesigning insurance benefits, provider payment policies and performance improvement programs in ways that will encourage and reward improvements in health and health care delivery. The primary focus is on the



William A. Peck, MD

Medicare program, but the findings and recommendations may have broad applicability to all public and private insurance programs.

The committee, chaired by Steve A. Schroeder, MD, Distinguished Professor of Health and Health Care at the University of California, San Francisco,

includes 22 national health care executives, educators and policy makers.

Peck, the former dean of the School of Medicine, is a nationally recognized health care leader.

RADIATION ONCOLOGY

PET scans after therapy improve cervical cancer survival predictions

Post-treatment positron emission tomography (PET) scans can be used to predict cervical cancer patients' chances of survival, according to radiologists at the School of Medicine.

PET scans are used to diagnose cervical cancer, but post-therapeutic PET scans are not covered by most insurance plans and are rarely used to look for signs of cancer recurrence. Current follow-up practices include regular pelvic exams and occasional X-rays or CAT scans.

The new study's results suggest that making post-treatment PET scans standard therapy practice could give doctors a potentially lifesaving headstart at prescribing follow-up therapy.

Their results appeared in the June 1, 2004 issue of *Journal of Clinical Oncology*.

"Right now, we're forced to wait until a patient comes back with a lump or with symptoms before we can begin follow-up treatments, and by then it's often too late," says Perry W. Grigsby, MD, professor of radiology and of radiation oncology.



Post-treatment PET scans: Potential lifesaving head start on follow-up treatments.

While X-rays and CAT scans reveal structural details of the body, PET scans can detect functional differences in tissues, allowing physicians to highlight tumors.

Grigsby and colleagues retrospectively examined post-treatment PET scans from 152 cervical cancer patients taken after their treatment at the Siteman Cancer Center at Washington University and Barnes-Jewish Hospital. They used scan data to separate patients into groups based on indications of recurrent or continued tumor growth: those with no signs, those with moderate indications, and those with strong signs.

After five years, 90 percent of the patients in the moderate indications group were still alive, compared to less than half in the group with strong signs of surviving tumor cells.

"The hope is that we might be able to catch patients in that second or third group before their cancers get too far ahead of us and try to do something to make their survival rates better," says Grigsby.



Showcasing Sickle Cell Disease Clayvon Wesley, program development specialist, State of Missouri, left, and Elam King III, executive director, Prince Hall Family Support Center, discuss the center's new sickle cell display wall, installed in September during National Sickle Cell Awareness Month. The educational display is designed to inform the community about sickle cell disease and the need for blood and cord blood donations. The wall, sponsored by Lone Star Lodge #2, was developed by the Sickle Cell Medical Treatment and Education Center at St. Louis Children's Hospital and the School of Medicine.

Gordon to lead Genome Sciences Center

THE NEW CENTER FOR GENOME SCIENCES, an interdepartmental, university-wide program, will be directed by Jeffrey I. Gordon, MD, the Dr. Robert J. Glaser Distinguished University Professor.

The center is an interdisciplinary and university-wide program strategically located adjacent to the School of Medicine's Genome Sequencing Center (GSC),

which played a major role in the success of the Human Genome Project.

The new Center for Genome Sciences is the first of three major components to be implemented as part of BioMed 21, the univer-

sity's visionary initiative dedicated to using the latest knowledge of the human genetic blueprint to develop new ways to diagnose, treat and ultimately prevent a variety of common human diseases.

The Center for Genome Sciences will provide space for faculty and students and bind together research and educational programs. Center members also will provide new tools to their GSC neighbors to help interpret the information generated from ongoing sequencing projects.

The community of scientists will address fundamental questions in comparative genomics and systems biology.

Siteman Cancer Center receives donations

PLEDGES OF \$1 MILLION EACH toward the Siteman Cancer Center's Emerson-Busch challenge grant have been made by the May Department Stores Foundation and Edward Jones.

The challenge grant, a \$10 million gift from Emerson's Charitable Trust and the Anheuser-Busch Foundation, will be used to expand research space at Siteman and to support and help ensure that patients have access to the most advanced cancer treatments.

"These gifts from May and Edward Jones will benefit efforts to lessen the burden of cancer on communities in the St. Louis area, the Midwest and beyond for years to come," says Washington University Chancellor Mark S. Wrighton.

The challenge grant will further St. Louis' role as home to a nationally recognized cancer research and treatment program.

First priority for funding through the Emerson-Busch challenge grant is expansion of cancer research space and programs in a new cancer research facility. The basic and applied research supported by this gift are crucial in finding new treatments and diagnostic techniques for cancer patients.

Second opinion service debuts

NO MATTER HOW EXPERIENCED your physician, the need for a major medical procedure can be daunting.

To address this issue, School of Medicine cardiologists and cardiothoracic surgeons at Barnes-Jewish Hospital have introduced a second opinion service for patients with a heart disease diagnosis who have been recommended for any heart procedure, including surgery. The service also is available for any lung or esophageal condition for which surgery is recommended.

For a fee of \$50, physicians in the School of Medicine's divisions of cardiothoracic surgery and cardiovascular diseases will review a patient's medical records within 48 hours of receipt. If a patient prefers to be seen in person, the staff will arrange an office visit, for which the patient's insurance will be billed.

The service is open to Missouri and Illinois residents. To learn more, call toll-free (866) TOP-DOCS.



Strep bacteria spreads infection via wasplike “stinger”

The bacterium responsible for strep throat, scarlet fever and other disorders appears to use a single wasplike “stinger” to spread infection, according to surprised microbiologists at the School of Medicine.

Researchers studying the surface of *Streptococcus pyogenes*, also known as Strep A, had expected to find a disordered jumble of several pumps for spraying compounds onto cells targeted for infection. Instead, they found a single dedicated stinger — a feature Strep A may share with other bacteria that could provide an easier target for new drugs designed to treat infections.

“It’s certainly a long time down the road, but this gives us new ways to think about how strep and other bacteria might one day be stopped,” says Michael G. Caparon, PhD, professor of molecular microbiology and the study’s lead investigator. “With better understanding of how bacteria interact with the cells they infect, we can start to develop better approaches for intervening.”

Strep A is one of the most common human pathogens. Epidemiologists estimate that at any given time, 5 to 15 percent of humans carry asymptomatic Strep A in their respiratory tracts. Strep bacteria has become increasingly resistant to antibiotic drugs during the last decade, and serious infection by the bacteria can produce a “flesh-eating” condition called necrotizing fasciitis.

On the basis of the Strep A’s outer membrane, microbiologists classify it as

a Gram-positive bacteria. Gram-positive bacteria only have one outer membrane; Gram-negative bacteria have two outer membranes separated by a small space.

That space between the inner and outer membranes serves as a prep room for proteins and other agents that Gram-negative bacteria secrete to infect host cells. Many proteins won’t function properly unless they have folded into a

its infectious processes,” he says. “Some are toxins, some interact with host cell receptors and make the cells die or behave differently. We wanted to know how Strep A emits these agents: Is it organized in any fashion, or does it just happen randomly?”

Most microbiological evidence had suggested the latter hypothesis might be a better bet. Bacteria seemed to have little

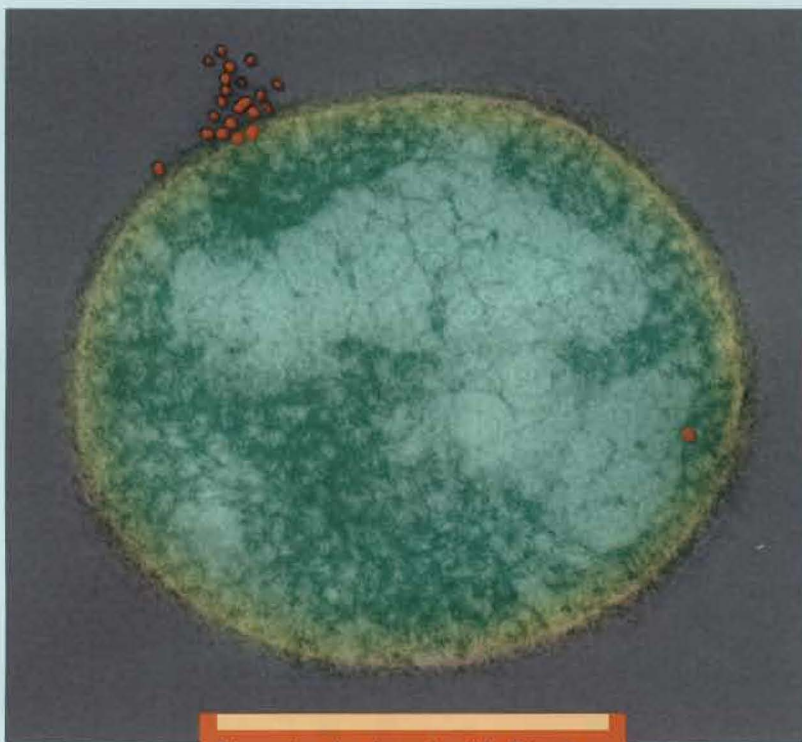
structural organization beyond the shape of the cells they came in, which can vary from round to cigar to corkscrew shapes. But a few studies, including some from Caparon’s lab, recently hinted that Strep A bacteria might be more organized than scientists suspected.

For the study, Caparon and graduate student Jason Rosch used modified antibodies to tag an infectious agent secreted by Strep A. They then took micrographs of the bacteria. The antibodies consistently

showed up at a single focal point where the cell was secreting the infectious agent.

After follow-up tests confirmed their findings, Caparon decided to name the new structure that secretes infectious agents. He calls it the “exportal,” a combination of export and portal.

“We’d like to now look at how the cell actually puts this together,” Caparon says. “If we can identify the factors that are involved in structurally putting the exportal together, those may be the most interesting points of intervention for devising new drug treatments.”

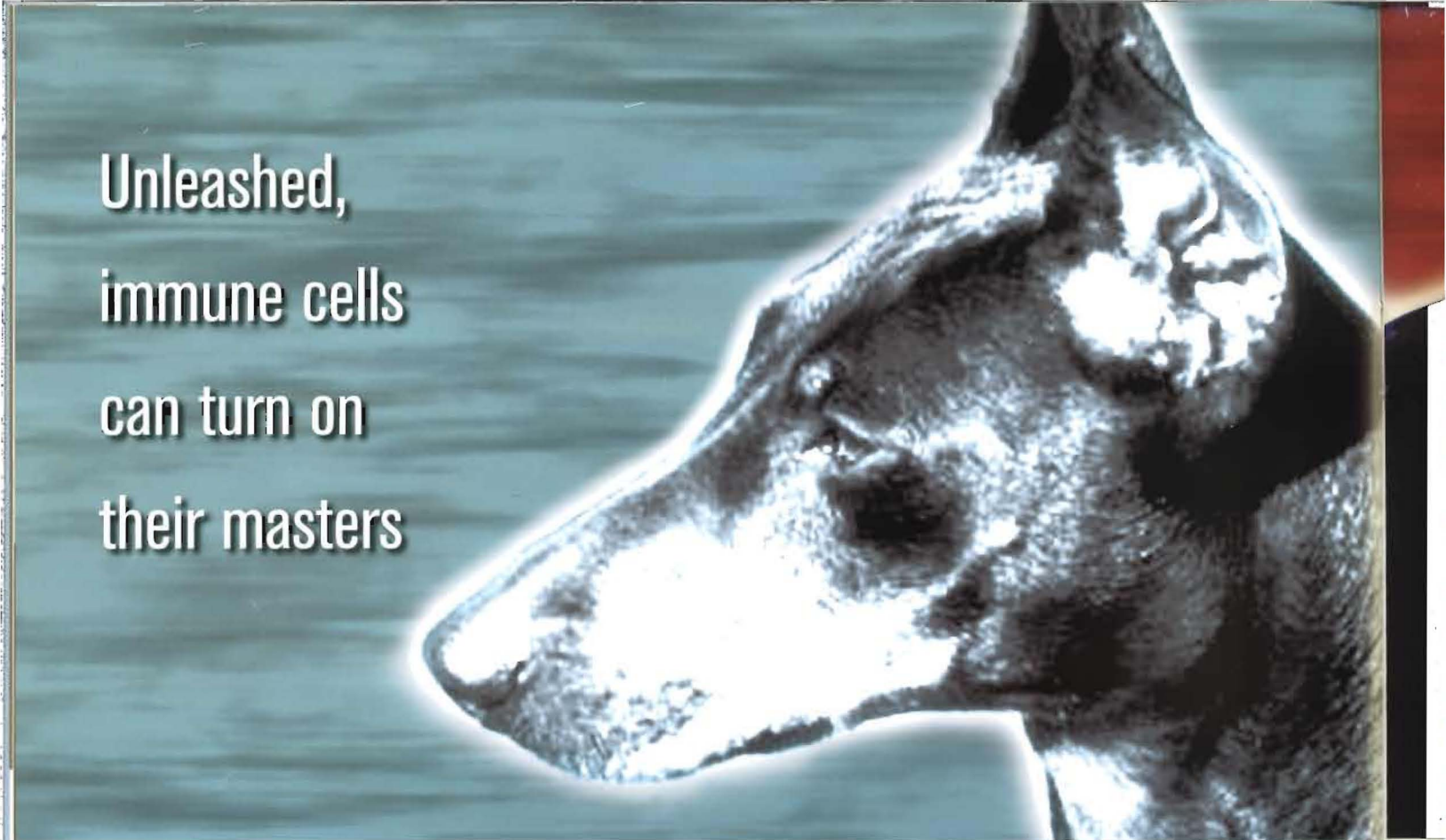


The grainy structure atop this Strep A bacterium, a newly discovered feature known as an exportal, emits substances that help the bacterium infect host cells.

particular configuration, and scientists believe the space between the two membranes provides Gram-negative bacteria with a place to ensure the right folding and other preparatory steps take place.


Caparon was curious about how Gram-positive bacteria like Strep A prepare their infectious agents without this airlock-like space between membranes.

“Strep A is known to secrete more than 30 different substances as a part of



Unleashed,
immune cells
can turn on
their masters

IMMUNITY



Stanford Peng, MD, PhD, reviews lab results with, from left, graduate students Stephanie Lathrop and Barbara Schraml and laboratory technician Ling Lin.

SCIENTISTS ARE UNCOVERING new complexities in the innermost workings of the human immune system that could make big differences for patients with autoimmune diseases. Thousands of Americans are diagnosed with these disorders each year as cells in their bodies that normally attack invaders like bacteria and viruses instead turn their fury on the body's own tissues. This about-face causes conditions such as lupus, myasthenia gravis, allergies, psoriasis, diabetes, Graves' disease, rheumatoid arthritis and multiple sclerosis.



ERIC YOUNG

BITES

BY MICHAEL PURDY

For decades, scientists assumed that these disorders were caused mostly by bad instructions to the cells that serve as the immune system's attack dogs. These cells, which are collectively referred to as lymphocytes and include B cells and T cells, rely on a complex signaling and detection system that tells them when, where and what to attack. If immune attack cells were assaulting the wrong targets, researchers reasoned, something had to be going awry in that signaling system.

Thanks to the work of researchers like Stanford Peng, MD, PhD, assistant professor of medicine in rheumatology and of pathology and immunology, a much more complicated picture of the causes of autoimmune diseases is beginning to emerge. Expanded insights into these causes may soon be offering scientists new frontiers for developing drugs that can ease or prevent such disorders.

One of the biggest new developments in autoimmune theory focuses on what immune attack cells are like when they're not on the job battling invaders. Scientists previously assumed that mature, unused versions of T and B cells were "sleeping" or dormant. But a new theory starting to gain widespread acceptance suggests that the cells are constantly spoiling for a fight, and healthy immune systems have to constantly work to restrain them, in effect putting a "leash" on the attack dogs.

In both T and B cells, Peng has identified the first-ever examples of these leashes — proteins that actively work within the cells to keep them quiet when they're not needed.

Peng, who sees patients at Barnes-Jewish Hospital, specializes in the study of lupus, an autoimmune condition that afflicts approximately 1.5 million Americans with symptoms including arthritis, prolonged fatigue, skin rashes, kidney damage, anemia and breathing pain.

CELLS

Through selective breeding, scientists have developed several mouse models that exhibit one or more lupus-like symptoms. To identify the gene leashes, Peng's research group compared levels of messenger RNA for various genes in normal mice and a lupus mouse model.

Measuring messenger RNA, which acts like an order slip for building a copy of a gene's protein, gives scientists a feel for a gene's activity level in a cell. This in turn allowed Peng's group to highlight genes with distinct differences in activity levels in the mice with lupus-like symptoms.

The first leash they found, a protein called Foxj1, had never previously been linked to immune system functions. Based on messenger RNA levels, though, the gene appeared to be much less active in lupus mice than in normal mice. When Peng and colleagues disabled the gene for the protein in normal mice, the mice developed lupus-like symptoms.

"These symptoms included inflammation in multiple organs like their lungs, their salivary glands, their kidneys, and other organs, which is very characteristic of lupus," Peng explains.

Scientists had previously identified Foxj1 as a transcription factor, a protein that can bind to DNA to increase or decrease the activity of other genes. Further investigation by Peng's group showed that decreased Foxj1 activity led another transcription factor, NF- κ B, to increase its activity.

"This protein belongs to a family of transcription factors heavily implicated in various types of inflammation, including the inflammation caused by infections and by allergies," Peng says. "So our thinking is that without Foxj1, more NF- κ B is activated, possibly triggering the inappropriate activation of T cells and leading to organ inflammation and other lupus symptoms."

Inappropriately activated T cells also are involved in multiple sclerosis and in diabetes, suggesting that Foxj1 also might be a contributing factor in these conditions, Peng notes.

T AND B CELLS FIGHT INVADERS, but when not needed must be kept in check to prevent them from attacking the body's own tissues and causing autoimmune disorders.

The second leash recently identified by Peng's group is known as microphthalmia-associated transcription factor (MITF). Microphthalmia is a genetic condition that causes abnormally small eyes and impaired vision.

Like the Foxj1 protein, Peng's group became interested in MITF when messenger RNA studies suggested the gene was unusually inactive in a mouse lupus model. Peng and colleagues lowered activity levels of the protein in normal mice, and close examination of those mice showed that B cells were spontaneously turning themselves on and making antibodies, clumps of proteins that are normally designed to attack invaders. The new antibodies in the mice were autoantibodies — antibodies targeted to the body's own tissues that are a characteristic symptom of lupus.

"This is the first transcription factor we've found that has to be active in the resting B cell to keep it that way," Peng says.

MITF's sphere of influence is proving a little harder to define than that of Foxj1. It appears to restrain interferon regulatory factor 4 (IRF4), a transcription factor previously linked to the activation of B cells. But it appears to have that effect by proxy through its influence on several other genes that in turn act to keep IRF4 in check.

"We've been focusing our efforts to develop new treatments for autoimmune disease on pathological targets — genes that are overused or are used inappropriately, leading to immune system attacks on self," Peng says. "Another concept we should keep in mind is

CELLS

Two “leash” proteins and a communication protein appear to help keep these trigger-happy cells from erupting into friendly fire.

that the loss of one of these regulatory genes that keep the immune system in check also may be a primary contributing factor.”

In addition to their work with immune cell leashes, Peng and his colleagues recently connected lupus in mice to a protein that is involved in immune system communications.

The protein, SLAM-associated protein (SAP) appears to be involved in exchanges between B cells and T cells. Scientists have long known that T cells “talk” to B cells to help them produce antibodies meticulously customized to destroy the last scattered remnants of a persistent invader. But they’ve had a hard time determining the details of how those interactions take place.

“SAP may give us an important first insight into how this occurs,” Peng says. “But even more importantly, it may provide us with a target for new lupus treatments that don’t widely suppress the immune system.”

Earlier research had shown that higher levels of SAP were present in animals with autoimmune conditions than in normal animals.

Peng affirmed the SAP-autoimmunity connection through work with a lupus model created by exposing mice to a hydrocarbon oil. Such exposures cause normal mice to develop kidney disease, arthritis and other conditions similar to lupus. However, mice with genetically disabled SAP stayed healthy even after exposure.



To their surprise, researchers found that most immune system functions appeared to be working normally in mice lacking SAP.

“We have identified other immune system proteins that are potential targets for new autoimmune disease treatments, but they all affect large portions of the immune system, making weakened immune function a potential side effect of any new drug,” Peng explains. “Our early experiments suggest targeting SAP for treatment may avoid that risk.”

Peng cautions that errors in any one gene are unlikely to be the sole cause of an acute autoimmune disorder like lupus. “It’s very clear now that no single gene or even couple of genes are sufficient to explain lupus,” he notes. “You probably need multiple malfunctions in different genes to cause such a severe autoimmune syndrome.”

The multiple causes of lupus are likely reflected in the multiple mouse models of the disorder, says Peng.

“Each of the animal models has slightly different clinical aspects to it, probably because they represent a slightly different facet of the human disease,” he explains. “It’s therefore going to be very interesting to test if these are findings that can apply to lupus generally or if they’re limited to subsets of lupus.”

Peng’s group recently identified another leash protein from the same family of genes as Foxj1. They are currently working in the lab to further understand the activity of all the proteins and also have begun studying human lupus patients to see if they can detect signs of abnormal activity in these proteins. □

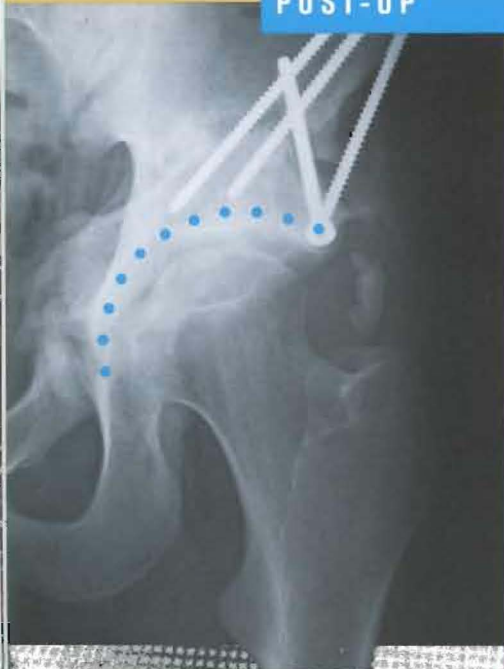
NORMAL



HIP DYSPLASIA



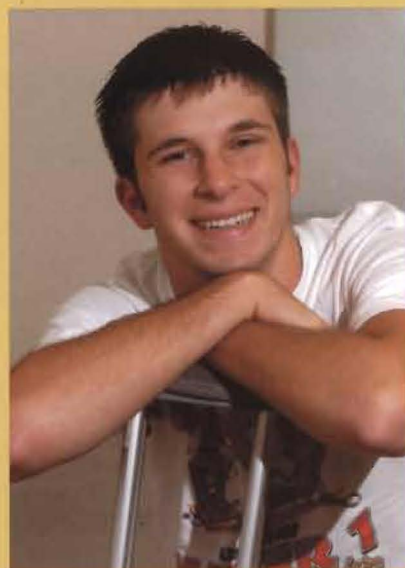
POST-OP



YOUNG HIP JOINTS

Retirement is no
prerequisite
for hip surgery

BY JIM DRYDEN



Christopher Mackey didn't realize he needed hip surgery.

For several months, he didn't really know what was wrong. All he knew was that when he pitched a baseball, a popping sound came from his left hip. At first, there wasn't really any pain involved, but then his groin muscle started to hurt. It turned out the groin was being aggravated by a deformity in his hip, the same deformity that was causing it to pop.

Later, when his right hip also popped out of its socket, Mackey experienced significant pain. In fact, he was unable to move, and his baseball coach had to lay him flat on the ground in order to help move the joint back into place.

"That time it hurt!" he says.

Mackey was suffering from a congenital deformity of the hip joint called hip dysplasia. The hip joint is commonly thought of as a "ball and socket" joint. The "ball" is the top of the thighbone, called the femoral head. It rests within the hip's "socket," known as the acetabulum. When those two structures are out of sync, problems can develop.

People with hip dysplasia lack a normal hip's solid ball and socket structure (left, top and middle). Rather than replace the hip joint, orthopaedic surgeon John C. Clohisey, MD, (below, right) radically cuts and repositions the bones in young patients such as Christopher Mackey, returning them to normal, pain-free motion.



John C. Clohisy, MD, examines Christopher Mackey's range of motion. The outcome? Ask anyone who's faced Mackey's 92-mph fastball.



“Most of these patients have an underlying deformity, and many of them have some degree of osteoarthritis in the hip,” says John C. Clohisy, MD, assistant professor of orthopaedic surgery. “As people like Christopher get older, they can begin to experience symptoms. Among people in their 60s and 70s, those symptoms would make us think about total hip replacement, but our goal with younger patients is to delay joint replacement surgery and to prolong the life of their true hip joint.”

To do that, Clohisy and his colleague Perry L. Schoenecker, MD, professor of orthopaedic surgery, radically change the hip joint's structure. In an operation that takes two to four hours, they cut the bones around the hip socket and reposition them. The patients don't need a cast, but they do need to stay in the hospital for several days and must walk with the help of crutches for several weeks afterward.

The surgical technique, called the Bernese Peri-Acetabular Osteotomy, isn't for everybody. Clohisy says it's designed for relatively young, healthy patients. Those with multiple

medical problems or those who are obese are not good candidates.

And while hip replacement surgery can provide pain relief and improved function for patients with advanced hip disease, it's not a great solution for people under age 50.

“For patients in the 15 to 50 age group, a hip replacement is sub-optimal due to activity restrictions

“Our goal with younger patients is to delay joint replacement surgery and to prolong the life of their true hip joint.”

JOHN C. CLOHISY, MD

and the fact that the synthetic hip joint is going to wear out with time,” says Clohisy. “A patient who gets a hip replacement at a very young age may require multiple hip surgeries over the course of his or her lifetime.”

Traditionally, treatment for hip disorders in young adults involved little more than restriction of activities,

anti-inflammatory medicines and painkillers. But the pain usually gets worse. At first, it occurs during or just after physical activity, but over time, as the pain becomes more frequent, many people may have hip pain even when at rest.

“One way to explain why patients like Christopher don't get symptoms until they are young adults is that although the cartilage in the hip can function in an adverse environment for a long time, eventually just as the tread on a tire will go bad, the cartilage begins to wear out over time,” Clohisy says.

A person with Mackey's condition could look forward to pain, difficulty with daily and recreational activities, and doctor's orders to stop doing things that put stress on the hip joint. There also are problems involving failure to diagnose early hip disease.

That could easily have happened to Mackey.

“I live in Springfield, and a lot of the doctors I saw around here didn't really know what was wrong with me,” he says.

According to Clohisy, that's not uncommon. “Very frequently, patients of this age have a deformity or hip joint problem that is not easily recognized,” he says. “Patients don't get a definite diagnosis, so some go for many years without treatment.”

That's why Clohisy developed the Young Adult Hip Program at Washington University and Barnes-Jewish Hospital. He treats not only patients who need major rebuilding of the hip joint, but also young people who are candidates for hip arthroscopy or for a process called

hip joint debridement, a procedure that involves a trimming of the bones around the joint to correct subtle abnormalities and relieve impingement problems of the hip joint.

Many of these surgical techniques have only been used regularly in the past few years at selected medical centers. As recently as 15 years ago, most of these patients would have been untreated. That would have contributed to the development of osteoarthritis at a young age, and most would have needed a hip replacement by the time they reached their 30s or 40s.

Instead, many of those patients are walking around without pain. Even those who still experience some pain in the hip joint due to underlying arthritis are markedly improved and usually can manage their pain with over-the-counter anti-inflammatory drugs. Most return to full activities after surgery.

Clohisy says some of these young patients may eventually need hip replacement surgery, but even that wouldn't mean the earlier surgery wasn't worth it.

"If we have a patient who gets an osteotomy at age 30 and then ends up having a hip replacement at age 50, to me that's a great success," he says. "The first surgery will have provided that

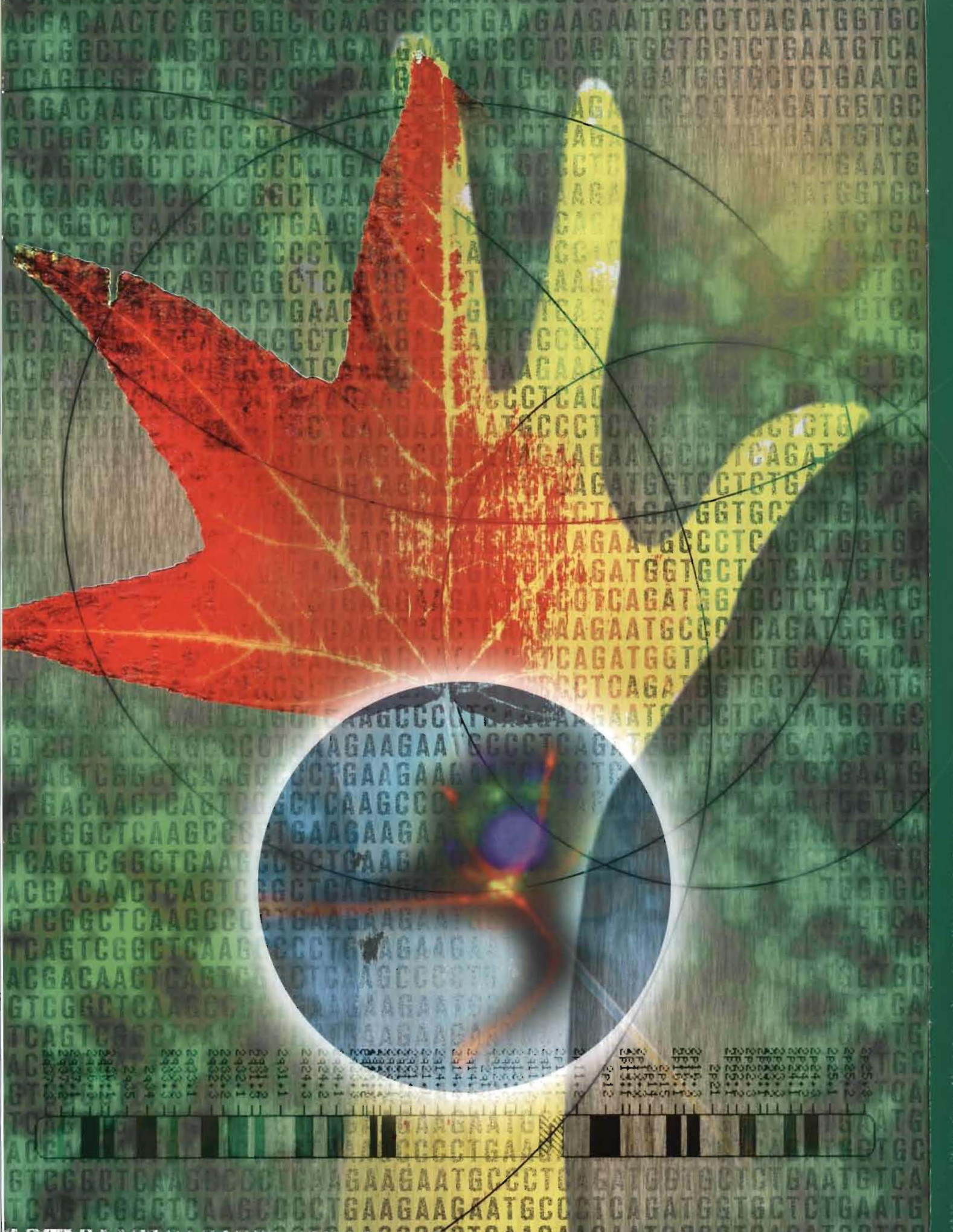
person with 20 years when the hip wasn't causing them problems, giving them the opportunity to do many things they couldn't do if they hadn't had the operation."

Luckily, Mackey can look forward to doing many things he would not have been able to do without surgery. Clohisy and Schoenecker surgically repaired his left hip on Valentine's Day of 2003. When baseball season started in March of that year, Mackey had to watch the Fighting Irish of Springfield Catholic from the dug-out. But in spite of pain in his right hip, he came back for his senior season last spring and featured a fastball in the 92-mile-per-hour range. He waited to have that hip operated on in June of this year because he wanted to make it through baseball season first.

Young athletes like Mackey make up a large part of Clohisy's surgical practice. After osteotomy surgery, they can return to competition, although he discourages them from taking up distance running or other repetitive-impact activities that can damage a diseased hip. Nonetheless, his patients have returned to a variety of sports, including basketball, gymnastics, cycling, swimming, hiking and tennis.

Following the rehabilitation of his right hip, Mackey plans to pitch in college next season for Southwest Missouri State University. He says his hip problems probably cost him a shot at being drafted by a major league baseball team, but even with the injury, he was able to earn a college scholarship. And who knows, if his pitching improves as much as his hips have, he might go a long way. □





Susan K. Dutcher, PhD, and
Gary D. Stormo, PhD, with
research assistant Lin Ya Li
(left, seated) and graduate
student Jin Billy Li.



Strands of *Life*

Unraveling the
roots of cilia

BY MICHAEL PURDY

WITH SEVERAL GENOME SEQUENCING PROJECTS COMPLETE, scientists now know where to find all the genes for organisms ranging from humans to fruit flies to yeast. But knowing where a gene is found and what information it typically contains still leaves two critical questions: What jobs does the protein made by the gene do? Where in the organism does it do those jobs?

As a result, geneticists interested in studying genes linked to a specific structure or disorder — the heart, for example, or heart disease — sometimes face months or years of grinding, repetitive search and analysis to identify the specific genes they want to study.

Susan K. Dutcher, PhD, professor of genetics and of cell biology and physiology, recently developed an innovative way to quickly pick out genes of interest. Her approach combines modern computing power and millions of years of evolutionary history built into DNA to sift through thousands of genes and selectively extract many genes related to her research.

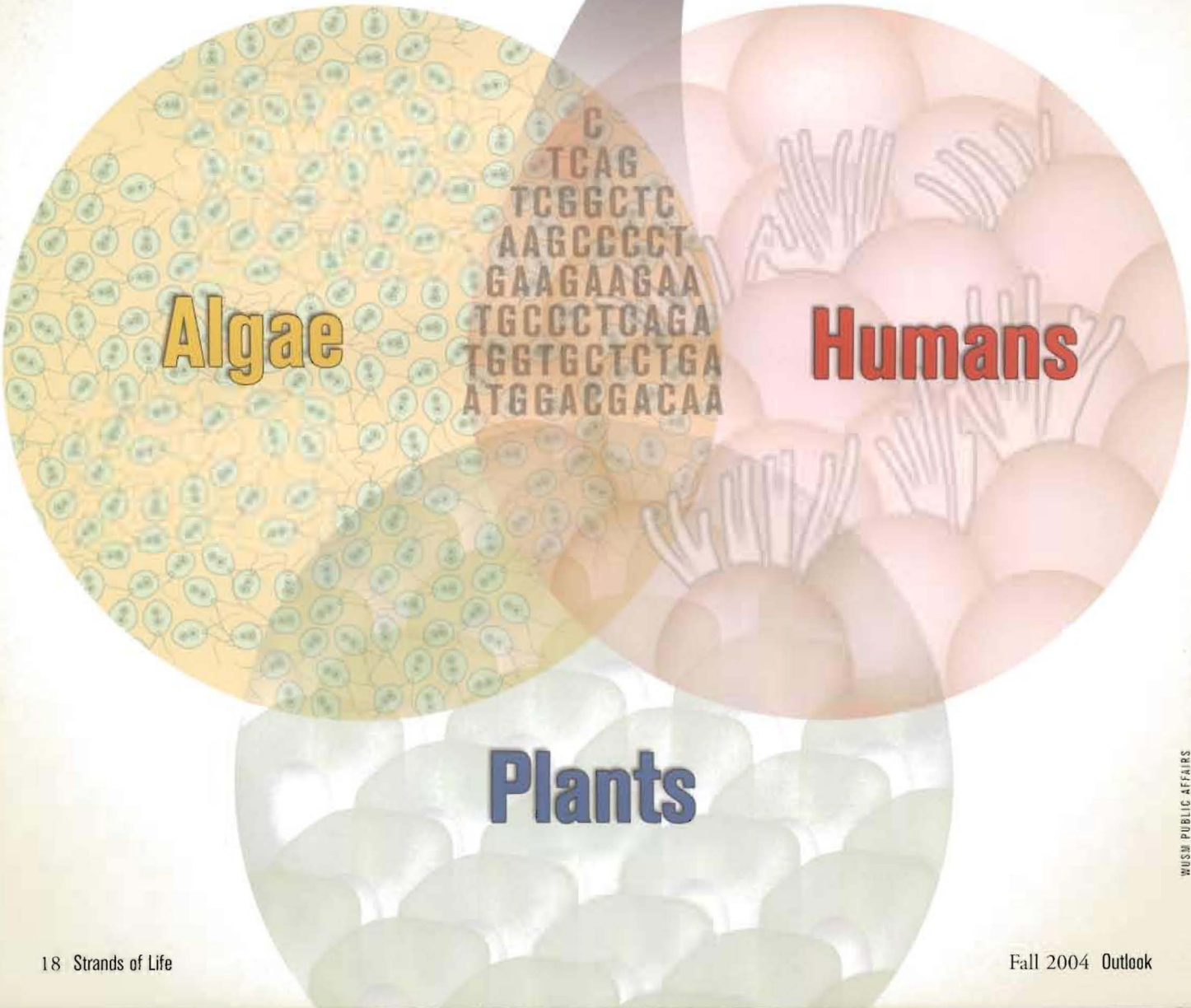
Match... eliminate... identify.

Humans and algae share many genes for basic functions and essential structures, including some genes that go into cilia and basal bodies.

CTCAGTCGGCTCAAGCCCCTAAGAGAATGCC

Cilia perform important functions in both multicellular organisms and single-celled organisms.

Scientists used a computerized comparison to identify human-algal gene matches, then eliminated all matches found in a land plant that doesn't have cilia or basal bodies.





The new approach has been spectacularly successful, quickly leading to benefits for both Dutcher's research program and for other researchers, including a group at Johns Hopkins University that used her data to identify a human disease gene.

Dutcher's new method centers on a computerized comparison of the genomes of three species: humans; a weed, *Arabidopsis*; and *Chlamydomonas*, a green alga.

Dutcher works with *Chlamydomonas* to learn more about cilia, hair-like structures on the surfaces of cells.

"Almost every cell in the human body has cilia," Dutcher says. "Cilia that are active early in development ensure that organs like the heart and stomach end up where they're supposed to be. Cilia clear away dirt and bacteria in the respiratory tract, help sperm swim and help keep fluid flowing into and out of the brain."

Problems in the cilia and basal bodies, the structures that anchor cilia to the surfaces of cells, are linked to a variety of disorders, including polycystic kidney disease and genetic disorders that affect the ear, nose, sperm, placement of internal organs, number of fingers and toes, and length of the limb bones.

Studying *Chlamydomonas* allows Dutcher's group to more easily isolate and manipulate cilia and basal bodies. Although the alga is more easily subject to experiments, its genetic material has 20,000 genes, which still left researchers like Dutcher with quite a bit of searching to do. Amid those thousands of genes, Dutcher and other scientists were seeking only an estimated 250 to 400 genes — potentially a very long and repetitive hunt.

"It had been pretty slow going," Dutcher says. "Although there are a lot of people interested in *Chlamydomonas* and in these genes, we had only identified a few of them at the time we began this genome comparison."

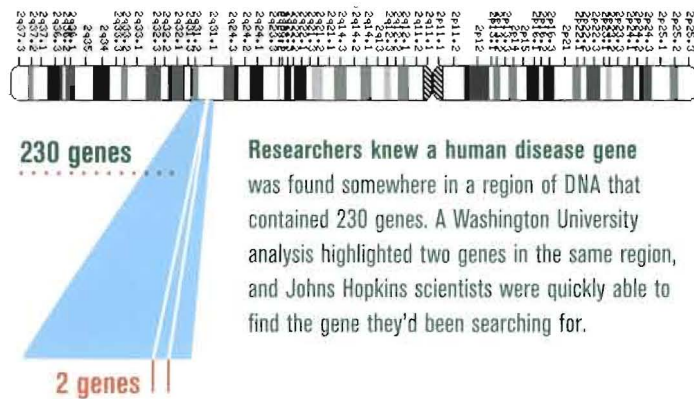
Dutcher's analysis derives its power to identify interesting genes from the evolutionary history written into the organisms' genomes. Evolution tends to retain genes that make proteins for essential cell structures and processes. Scientists call genes kept intact through the development of many different species "highly conserved," and Dutcher and others have shown that genes for cilia and basal bodies fit this description.

Significant exceptions to this principal of conservation can occur when life has to make major adjustments to its environment. In one such instance, most plants evolving to adapt from life in the sea to life on land discarded their cilia.

"If you look at any flowering land plant, it doesn't make any cilia, and it doesn't make basal bodies," Dutcher explains. "Once the idea hit me, it seemed fairly obvious: Why not have the computer look for gene matches between humans and *Chlamydomonas*, and then compare those results to a land plant and remove all the genes from the first comparison that also had matches in the land plant?"

The human-to-*Chlamydomonas* comparison would locate many of the genes for basic functions and structures those two organisms share, Dutcher reasoned, but any matching genes also found in the flowering land plant likely would have nothing to do with cilia or basal bodies.

"We thought the final result might be incredibly enriched with cilia and basal body genes," she explains.



Dutcher approached Gary D. Stormo, PhD, professor of genetics, with her idea. "My first reaction was, that's an interesting idea, but that's a lot of genes!" Stormo recalls.

A specialist in computational analyses of genetic code, Stormo is particularly interested in finding signals contained in DNA that interact with proteins to turn genes on and off.

Stormo and Dutcher, who are married, were jointly mentoring a graduate student, Jin Billy Li, who took the lead in carrying out the comparisons. For the land plant, researchers chose to use the genome of *Arabidopsis*, a weed. (Scientists at Washington University's Genome Sequencing Center and at Cold Spring Harbor Laboratory completed mapping of the *Arabidopsis* genome in 2002.)

The human-to-alga comparison produced 4,348 gene matches. Comparing those results to *Arabidopsis* yielded approximately 3,600 matches, allowing researchers to narrow down the pool of prospective cilia and basal body genes to 688. Further comparison with the genomes of the fruit fly and the sea squirt, a small ocean-going animal, reduced the list of genes to approximately 300.

To determine how effective the screening process had been, Dutcher and colleagues first looked to see if their results had highlighted any of the cilia and basal body genes scientists had already identified in *Chlamydomonas*. They were delighted to find the comparison caught 90 percent of the genes they already knew about.

“This absolutely flabbergasted us,” says Dutcher. “We thought we’d be less successful.”

Other tests produced similarly encouraging results. Li and research assistant Lin Ya Li cut the cilia off *Chlamydomonas* and watched to see if 103 of the genes identified by the comparison became more active as the algae rebuilt the cilia. More than a third increased their activity. A follow-up experiment suggested that several genes that didn’t increase their activity when the cilia were cut off were instead involved in the construction of basal bodies.

“We don’t yet know how many of the genes we identified are completely unrelated to cilia and basal bodies, but so far the results have been very encouraging,” says Stormo. “The technique seems to have been not just a moderately good filter, but in fact a very good filter for the genes Susan is interested in.”

Dutcher then searched for matches between the genes found by the comparison and known human genes for cilia and basal bodies. She found that the research team’s results had highlighted both of the genes associated with juvenile polycystic kidney disease and five of six genes linked to Bardet-Biedl Syndrome (BBS), a rare genetic condition that causes blindness, mental retardation, severe obesity and other problems.

Dutcher became intrigued by the possibility that the comparison’s results might help scientists identify new disease genes. She learned that scientists had narrowed the hunt for a seventh BBS gene down to a large region on human chromosome 2. However, that region had approximately 230 genes, far too many for scientists to examine on a one-by-one basis.

“We contacted Nicholas Katsanis, PhD, a BBS researcher at Johns Hopkins, and he told us they had no idea where the BBS gene on chromosome 2 was,” Dutcher recalls. “We explained that our comparison had highlighted two genes in that area and suggested they might be worth checking into.”

When Katsanis, assistant professor at Hopkins’ McKusick-Nathans Institute of Genetic Medicine, analyzed the two genes in families afflicted by BBS, he found several sufferers had abnormalities in one of the genes and named it BBS5.

To confirm that the BBS5 gene was important to cilia or basal bodies, Dutcher reduced the gene’s activity in the alga.

“We see different effects depending upon how much we knock the activity of the gene down, but it looks like it actually is a basal body protein,” Dutcher says. “Our hope is that we can now take our data set and accelerate the search for genes that contribute to some of the many human disorders that involve cilia and basal bodies.”

In addition to probing those potential connections, Dutcher already has started brainstorming new genetic comparisons designed to identify genes of interest.

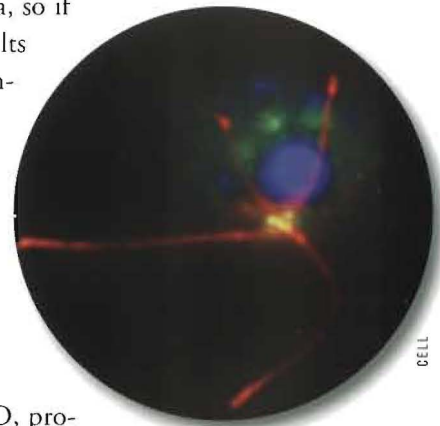
“Humans have two kinds of cilia — motile cilia, which create motion, and non-motile cilia, which respond to motion,” she says. “The microscopic worm *C. elegans* only has non-motile cilia, so if we were to take our results from this study and eliminate all the genes that have a match in the genetic code of *C. elegans*, that might let us highlight genes for proteins that create and control the movements of cilia.”

Mark Johnston, PhD, professor and head of the department of genetics, says Dutcher’s results have other geneticists excited about the possibility of using similar comparisons to identify genes that carry out important functions or contribute to human diseases.

“What’s so heartwarming about this result is how vividly it illustrates the value of basic genetic research in these model organisms,” says Johnston. “There are quite a few scientists now thinking about how we can use this approach in other contexts.” □



To test genes highlighted in computerized comparisons, researchers tagged the proteins made by some of the genes with fluorescent antibodies. Results from a mouse lung (above) and from the sea algae *Chlamydomonas* (below) confirm the proteins’ presence in cilia.



CELL



Seeking closure

Painful, debilitating:
varicose veins.
For better treatment,
turn up the heat.

BY KIMBERLY LEYDIG

SINCE HER EARLY 20s, Donna Kurowski has battled pain, swelling and pressure in her legs from varicose veins — tortuous, twisted and painful veins with poorly functioning valves.

As a staff nurse at the university's Pain Management Center, Kurowski actively works with chronic pain patients. She also has a 10-year-old son who keeps her busy. Although prolonged standing would trigger intense pressure and pain, Kurowski never let the condition interfere with life.

"I didn't let it limit my activities," she says. "I learned to make adjustments and find ways to elevate or reposition my legs. Or, I'd just deal with the pain."

Jeffrey Petersen, MD, assistant professor of medicine, wanted to help Kurowski improve her quality of life and suggested that she undergo the VNUS closure procedure to treat her varicose veins.

A fan-shaped catheter delivers radiofrequency energy to the vein wall in a minimally invasive treatment offered by Jeffrey Petersen, MD.



The innovative procedure is a minimally invasive treatment for a condition called superficial venous reflux, which causes pain, swelling and varicose veins.

The condition can be precipitated by genetics, age, pregnancy, traumatic injury and can occur in people with professions — nurses, chefs, waitresses, hair stylists — that require prolonged standing.

The NIH estimates that nearly 25 million people in the United States suffer from complications of prolonged venous reflux. Studies reveal that 41 percent of American women may have varicose vein disease by the time they reach their 40s and 50s.

Symptoms include pain, fullness, heaviness, aching, visibly enlarged veins, swelling, skin discoloration and ulcers around the ankles.

Normally, veins carry blood from the extremities toward the heart. In varicose veins, the blood flows backward, resulting in pooling of impure and acidic blood that contributes to multiple medical pathologies.

"People mistakenly think the procedure is cosmetic, but many patients are very unhappy due to the pain and discomfort," says Petersen, who now performs about 20 closure procedures monthly. "Patients often don't realize it's a medical condition that's usually covered by insurance."

The VNUS procedure uses radiofrequency or laser heat placed directly into the wall of the saphenous vein, which runs from the ankle to the groin. Over time, faulty valves in the saphenous vein can result in unattractive, bulging and painful varicose veins. The radiofrequency or heat causes the vein wall to collapse, cutting off the source of blood.

The VNUS procedure became available in the United States in 1999 as an alternative to traditional vein stripping, the surgical removal of veins from the leg. Vein stripping usually requires general anesthesia, an extended hospital stay and a long recovery, and it causes significant swelling, bruising and pain.

Kurowski had vein-stripping surgery in 2001. "Recovery from the procedure was really painful, and

Nearly 25 million people in the United States suffer complications of prolonged venous reflux

I was very bruised," she says. "By nighttime I was exhausted from the pain and pressure, and I couldn't go back to work for two weeks."

Last year, a study in the *Journal of Vascular Surgery* compared vein stripping and the VNUS closure procedure by evaluating procedure-related complications, overall patient recuperation and quality-of-life issues. In every measurable category,



Post op: Less pain, more attractive.

patients who underwent the closure procedure had better outcomes.

"There's a dramatic difference," Kurowski says. "A week after the closure procedure most of my bruising was gone, and the pain and pressure in my leg was considerably better."

Petersen says that European studies have shown that more than 91 percent of legs treated with the VNUS procedure were free of venous reflux, the underlying cause of varicose veins, two years later.

"There is little, if any, pain with the closure procedure — most patients don't require oral sedation for relaxation," he says. "They can get up and walk out of the office after the procedure."

Petersen performs the closure procedure at Washington University's Center for Dermatologic and Cosmetic Surgery in West County.

During the procedure, a mixture of intravenous saline solution, lidocaine (a local anesthetic) and

epinephrine (a drug that contracts blood vessels) helps reduce blood loss and postoperative bruising while providing anesthesia. First, Petersen inserts a thin catheter in the damaged vein through a small incision. Using an ultrasonic guide, the catheter is manipulated up the vein, and radiofrequency energy is delivered to the vein wall, causing it to heat, collapse and seal shut.

Once the diseased vein is closed, healthy veins take over, and normal blood flow returns to the leg, allowing the swelling, pain and discoloration to noticeably improve.

After the procedure, a compression garment is worn for several weeks to aid healing. Patients can resume normal activities in one to two days but must refrain from strenuous activities, prolonged standing and heavy lifting for a few weeks.

Just days after her procedure, Kurowski felt considerably less pressure and pain in her leg. And while she didn't undergo the closure procedure for cosmetic reasons, she was certainly happy to see bulgy veins and pigment discoloration disappear. □

The solution has legs: VNUS procedure works for varicose veins and ulcers

In addition to eliminating unsightly and painful varicose veins, the VNUS procedure provides relief for venous leg ulcers, painful lesions that result from varicose veins and can cause eczema, other inflamed skin conditions and permanent scarring.

Standard treatment for leg ulcers is compression bandaging combined with anti-bacterial dressings over a period of 12 to 24 weeks. However, many patients fail to respond and end

up undergoing multiple costly therapies in an attempt to alleviate symptoms.

Petersen is researching the use of the VNUS procedure to treat both ulcers around the ankles and venous changes to the leg. The study aims to stop those changes from occurring and to decrease the frequency of ulceration.

Petersen's research reveals that patients who receive the closure procedure for ulcers experience an 80 to 90 percent reduction in ulcerations.

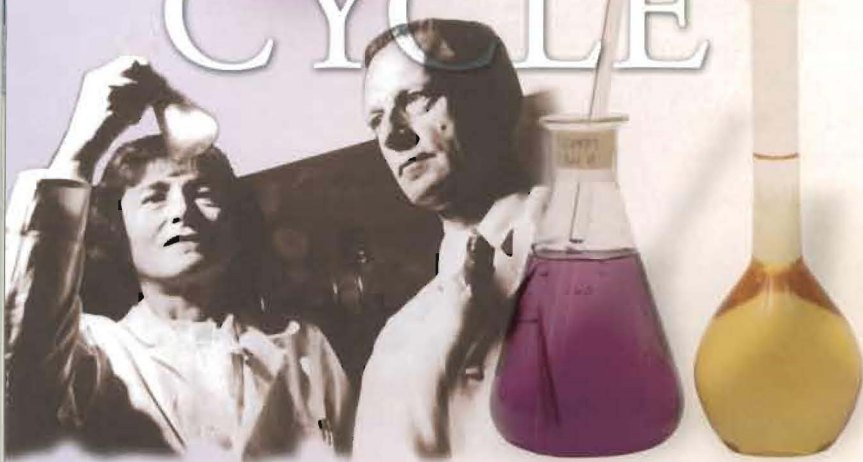
Before and during the procedure, ulcer patients wear a device called an Unna boot which presses on the skin and helps keep the wound closed.

"Many of these patients have dealt with chronic leg ulcers for five to 10 years and are very unhappy," Petersen says. "We can resolve this condition with VNUS closure, and many times patients will not need to see a physician for further treatment, which makes it very rewarding."

Historic Outlook

THE CORI CYCLE

**Complementary
in marriage
and medicine:
The legacy of
Carl and
Gerty Cori**



Carl Cori and Gerty Radnitz shared much in common.

Both were born in 1896; both came from families that were Austrian in origin but had lived in Prague for generations. When they met in their first year of medical school, they found other things they had in common: a love of research and an enthusiasm for mountain climbing.

The two first met in 1914 — at the beginning of World War I — when they entered Carl Ferdinand University in Prague to study medicine. In 1916, Carl was drafted into the Austrian army. His experiences in a barracks that served as a hospital for infectious diseases left him gloomy about the ability of doctors to control disease. He wrote, “the influenza epidemic, with its high mortality rate among the poorly nourished soldiers and civilians and the inability to be of any help, came as a great shock to me.”

At the end of the war, Carl and Gerty were reunited. They received their medical degrees in 1920. That same year the young couple was married in Vienna, where they were pursuing postdoctoral studies. Carl wrote many years later that “life in Vienna had its compensations,” but in fact it also had its deprivations, and Gerty developed symptoms of xerophthalmia, a condition caused by vitamin A deficiency. Because of the difficulty of life in Europe and because Gerty, as a Jew and a

woman, had trouble finding an academic position, the Coris decided to emigrate to the United States.

Carl accepted a position as a biochemist at the State Institute for the Study of Malignant Disease in Buffalo NY in 1922. Gerty joined him six months later, taking a position as an assistant pathologist. The two were never apart again professionally. At the beginning of their tenure there, the Coris encountered opposition to their working together. Gerty was told she would lose her job if she strayed from her laboratory in the pathology department. Soon, however, their colleagues came to understand and respect the Coris’ wish to work together.

In 1931, Carl was offered the chairmanship of the pharmacology department at Washington University School of Medicine. In 1946, he switched departments, becoming chairman of biological chemistry. The years in St. Louis were productive and rewarding for the Coris. They were able to collaborate on research, doing seminal work in the mechanism of glycogen utilization. And they liked St. Louis, so much so that they turned down prestigious offers from Harvard, Berkeley and the Rockefeller Institute. The Coris were supportive of the many scientists who flocked to their laboratory in St. Louis to study and work with them. All were invited to take part in the daily brown bag lunches in the library, where the conversation included current research interests but also might touch on a raft of non-scientific subjects.

Most visitors were impressed by the depth of their interests and

knowledge. The Coris had many friends in St. Louis, a modern house and a garden in which they divided the labor (she grew the flowers; he raised the vegetables). The Coris also read widely. Gerty was interested in history, biography and modern fiction, while her husband was knowledgeable in archaeology, poetry, and art. Carl was also a poet and fluent in German, French, Italian, and English.

It was a truly collaborative relationship, as relatives and former colleagues testify. David M. Kipnis, MD, Distinguished University Professor of medicine and of molecular biology and pharmacology, says: "They were a remarkable pair. Gerty would have flights of fancy. She'd come up with extraordinary ideas. Carl had the ability to put them into concrete questions to answer. And therefore, as a team, they were extraordinary."

Their son Tom says his mother had the ideas; then they both would go into the laboratory to execute the idea or disprove it.

Carl summed up the nature of their partnership in his remarks at the 1947 Nobel banquet: "Our collaboration began 30 years ago when we were still medical students at the University of Prague and has continued ever since. Our efforts have been largely complementary, and one without the other would not have gone as far as in combination."

Celebrating the Cori legacy: Washington University in St. Louis Chancellor Mark S. Wrighton accepts a plaque designating the former Cori laboratory as a National Historic Chemical Landmark. The official recognition, which took place on Sept. 21, 2004, was bestowed by the American Chemical Society.

Cori research illuminated metabolism

Carl and Gerty Cori spent more than three decades exploring how the human body metabolizes glucose. It was known in the 1920s that faulty sugar metabolism could lead to diabetes, and it was also known that insulin kept the disease in check. The effect of insulin on blood sugar levels had been observed, but scientists did not understand the biochemical mechanism behind insulin's effect or how carbohydrates were metabolized.

Sugar metabolism supplies energy for life's activities. The human body is unable to make the slightest muscular movement without burning sugar. In the 19th century, the great French physiologist, Claude Bernard, discovered glycogen, the starch-like substance found in muscles and the liver. Glycogen is the polymeric storage form of glucose, and when energy is needed, glycogen is converted by the body into glucose. This mechanism keeps the glucose level in the blood constant even though the supply is uneven.

The interplay between glucose and glycogen is at the heart of what is known as the "Cori cycle." The Coris found that insulin increased the oxida-

tion of glucose and its conversion to glycogen in muscle, as well as in the liver. Epinephrine, or adrenaline, worked in reverse, decreasing muscle glycogen and liver glycogen. Since other researchers had established that muscle glycogen does not contribute significantly to blood glucose, the Coris concluded that muscle glycogen must form an intermediate substance that then circulates through the blood to the liver. The Coris theorized — and eventually demonstrated — that this intermediate was lactic acid and was integral to the "cycle of carbohydrates," or the "Cori cycle."

In the 1930s, the Coris found a new intermediate of glycogen breakdown, which they demonstrated to be glucose-1-phosphate, known as the "Cori ester." Working with Sidney Colowick, the Coris established the compound's structure and discovered the enzyme that catalyzed its formation, which they named phosphorylase. In addition, the Coris demonstrated that the reversal of the phosphorylase-catalyzed reaction produced glycogen, the first time a biological macromolecule had been synthesized in a test tube. The Coris, in collaboration with Arda Green, crystallized the enzyme glycogen phosphorylase from muscle and investigated its chemical properties.

The Coris' path-breaking research resulted in their sharing the Nobel Prize in Physiology or Medicine in 1947 with Bernardo Houssay of Argentina. The Nobel committee cited the Coris "for their discovery of the course of the catalytic conversion of glycogen" and Houssay "for the discovery of the importance of the anterior pituitary hormone for the metabolism of sugar."



Highlighting the accomplishments of students, medical graduates, current and former house staff, and faculty who embody the School of Medicine's unbroken tradition of excellence.

Man of many passions

John Crane, MD 64, and his wife, Carol, have lived in a pre-Civil War stone house on a small farm near Washington MO (population 14,000) since he opened his practice there in 1975. After psychiatry residency at the University of Iowa and Washington University, Crane served two years as a captain in the U.S. Air Force, then spent five years on the staff of a large multispecialty clinic. Living in a semi-rural area had more appeal to the Cranes; Carol had grown up near Washington, and they decided to move there.

A Distinguished Fellow of the American Psychiatric Association, Crane has a solo practice in Washington, is medical director of Family Wellness Clinics in Union and St. Peters, and consults monthly at the nearby Emmaus Home for the developmentally disabled. "I'm one of very few shrinks in this area," Crane says, "so by need I see almost anyone who comes through the door... this kind of practice has been very gratifying. I love to hear the stories people have to tell, and you never know what's coming next."

Crane participates in medical missions with the Washington Medical-Dental Construction Brigade and has made three trips to Honduras, serving the very poor. The first time he was "on the construction crew, mainly carrying heavy stuff. The next two trips I was a general medical doc... we generally saw more than 1,000 patients on a 10-day trip."

**John Crane, MD 64,
with his wife, Carol.**

He describes the experience as "tremendously rewarding... life changing."

He is passionate about his woodworking hobby: "I've done carvings of small birds, larger abstracts of wildlife, built model boats, etc. For the sculptures, I use 'found wood' from the farm... walnut, oak, wild cherry, apricot. They're fun, but I felt like I was 'coming home' when I went to the WoodenBoat School in Maine last year... I'm currently building a 12-foot sailboat of western red cedar strips over oak ribs, keel and stem. It's my first major project, thus a learning experience, and a whole lot of fun. I think it will float, and maybe even sail, when done!"

The Cranes met and married while he was in medical school and she was a nurse at Barnes Hospital. They have three sons: John II, an optometrist and faculty member at the University of Missouri-St. Louis; David, an emergency room physician; and Christopher, a computer engineer.

An outstanding student

In 2002, the year he started medical school, Kyle Eash was one of only 20 students in the country named to the *USA Today* All-USA Academic Team. That led to his selection as one of 200 outstanding students from 40 countries to participate in the American Academy of Achievement's 2003 International Achievement Summit in Washington DC. The four-day annual gathering brings together the brightest youth with leaders in politics, science, history and art (the likes of Colin Powell, Sandra Day O'Connor, Desmond Tutu, Herman Wouk). Eash says it felt "surreal to be interacting on a personal level at meals and social events with people I usually only saw on TV." He was especially impressed by Dr. Francis Collins, director of the National Human Genome Research Institute.

Eash is spending this year as a Howard Hughes Research Fellow, learning whether he prefers the "accomplishment of discovering something new that could eventually lead to better patient care for many patients,





Kyle Eash, WUMS III

Before medical school he held a research internship at Praecis Pharmaceuticals, Inc., in Massachusetts. He first experienced the “satisfaction of a successful experiment, the frustration of a difficult one, and the rewards of seeing my work published,” in the organic chemistry lab at Illinois Wesleyan University, where he majored in business and biology.

He was also a three-year football letterman, quarterback and co-captain of the 2001 College Conference of Illinois and Wisconsin co-championship team and member of the track team, and he received the 2002 Walter Byers Postgraduate Scholarship from the National Collegiate Athletic Association. The \$25,000 award is given annually to one male and one female student “who has combined the best elements of mind and body to achieve national distinction...and promises to be a future leader in his chosen field.”

A leader in student community service groups, Eash has coordinated the Saturday Neighborhood Health Clinic and the Community CPR group and taught public school students in the Drug Education Project, the Reproductive Health Education Project, and STATS (Students Teaching AIDS to Students).

Advocating for health

It might be said that, as a psychiatrist, Margaret Kitchell, MD 74, focuses on heads and, as an environmentalist, focuses on feet. Either way, she expresses her dedication to improving health.

A specialist in geriatric psychiatry and a Distinguished Fellow of the American Psychiatric Association, Kitchell is a staff psychiatrist with Compass Health, a network of mental health service clinics north of Seattle. She is also secretary of the board of Feet First, a member organization of America Walks, a coalition of local pedestrian advocacy groups. She co-chairs the Environment

or the accomplishment of using already discovered knowledge I have learned to improve the health of individual patients I come in contact with.” In 2003, he was a summer research student at the Siteman Cancer Center, supported by grants from the Center and the American Cancer Society.

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and Health Committee of Washington Physicians for Social Responsibility and was a lead organizer for the Transportation and Global Warming Conference held in Seattle in May 2004, which drew nearly 300 attendees. Her interest in environmental issues was kindled at Reed College in Portland OR, where she earned a BA in philosophy. As a medical student at Washington University, she participated in the St. Louis Medical Committee for Human Rights activities concerned with lead poisoning and Vietnam War issues.

Kitchell specialized in psychiatry because she “liked getting to know people’s stories with the longer visits that psychiatry allowed.” While completing her psychiatry residency and fellowship in geriatric psychiatry at the University of Washington, she lived in a collective house, also the home of a business in solar and alternative energy. Later, her concerns that the United States’ dependency on oil embroiled us in the first Gulf War led to her increasing involvement in transportation issues, “hoping to encourage walking, bicycling and transit as cleaner, sustainable and more efficient modes.” Such lifestyle changes, she says, help reduce health threats that range from global warming to the current epidemic of obesity.

Kitchell takes the bus to work (her clinic is in Lynnwood), often rides her bike for transportation, and usually walks at least one or two miles a day. She and her husband, Jack Buchans, a video producer and part-time transit operator, own a hybrid Toyota Prius and have days when they don’t drive at all.

Their daughter graduated recently from Fairhaven College of Western Washington University and has a position with Americorps, working with youth. Their son is a senior at the University of Oregon, majoring in geography.

Margaret Kitchell, MD 74



Faithful stewardship

Pediatric immunologist devotes self to children, university

William T. Shearer, MD 70, PhD, speaks with admiration as he recalls the valiant struggle of his patient David Vetter, the well-known boy who was born without an immune system. David spent 12 years in a plastic bubble and never knew human contact.

But in his world of isolation, David's spirit touched many.

"He was a wonderful, cheerful child who had a 'go get 'em' attitude," Shearer recalls. "And the whole world learned immunology from this boy."

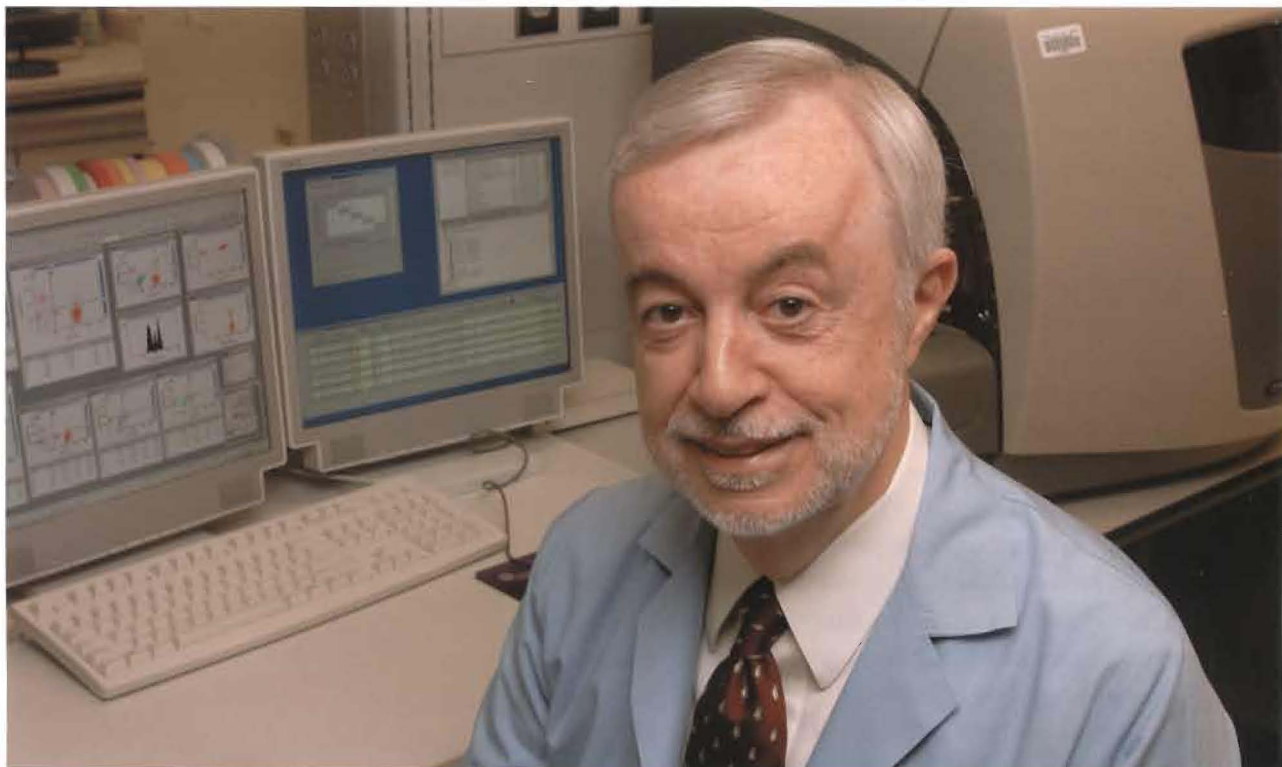
Shearer provided National Institutes of Health scientists with transformed cells

that were involved in the discovery of the gene defect David had.

"It was a unique experience, and I was fortunate to be involved," Shearer says, adding that watching the field of immunology explode has been extraordinary. "Scientists now have identified 100 gene defects."

David was a special patient, but only one of thousands who have benefited from Shearer's skill as a doctor. He has been professor of pediatrics and immunology at Baylor College of Medicine in Houston and chief of the Allergy and Immunology Service at Texas Children's Hospital since 1978.

William T.
Shearer,
MD 70, PhD



JASON BRYANT

Shearer also directs the HIV/AIDS Research Center at Baylor and has made enormous contributions to the field of immunoglobulin gene activation in HIV infection. Nationally, he is a member of the Leadership Group of the Pediatric AIDS Clinical Trials Group, an 18-center research group devoted to the study of antiretroviral and immune-based therapies in children with HIV.

"Bill wrote more published papers as a pediatric resident than many good doctors produce in their careers," says James P. Keating, MD, the W. McKim O. Marriott Professor of Pediatrics, who trained Shearer at St. Louis Children's Hospital. "His intellectual and expository skills have allowed him to rise to positions locally and nationally where his influence has been of great value to younger physicians and colleagues."

At the School of Medicine, Shearer says he learned to look beyond the immediate facts to get to the heart of the matter. "I also learned to push myself to the extent of my knowledge," he says.

In gratitude to the School of Medicine, Shearer and his wife, Lynn Des Prez, have made a bequest to endow the William T. Shearer and Lynn Des Prez Professorship in Pediatrics. They also have established the William T. Shearer and Lynn Des Prez Underrepresented Minorities Scholarship.

Lynn Des Prez, who resides in Philadelphia, is the administrative director of the American Board of Allergy and Immunology.

"The way Washington University has risen to the top is astonishing, and the world has recognized it," says Shearer. "To be part of Washington University is very important to us."

Shearer grew up with a brother and two sisters in a middle-class family in Detroit. Later, his parents sent him to Passionist Preparatory Seminary in St. Louis, a large Catholic high school that stood where the University of Missouri—St. Louis is located today.

"Sometime in high school, I decided I wanted to be a doctor," Shearer says. "It was very appealing to me because the profession seemed to have few boundaries."

After majoring in chemistry and biology at the University of Detroit, Shearer decided to pursue an MD/PhD at Wayne State University. He went to medical school there for one year and then pursued a PhD in immunology, which he earned in 1966. He chose to finish medical school at Washington University School of Medicine.

When Shearer told then-registrar William Parker of his interest in immunochemistry, Parker introduced Shearer to his son, Charles W. Parker, MD 53, PhD, an assistant professor of medicine at the time and allergist and immunologist. The meeting produced serendipitous results — Shearer then worked for Charles Parker during his fourth year of medical school and during a postdoctoral fellowship in pediatric allergy and immunology.

Shearer specialized in pediatrics for a number of reasons, one of which was the honesty of children. "Pediatrics is fun," he says. "You're treating people who have no pretense."

He also jokes that he chose the specialty because he has six children — a biological daughter and five adopted sons — between the ages of 34 and 46.

"The way Washington University has risen to the top is astonishing, and the world has recognized it."

WILLIAM T. SHEARER, MD 70, PHD

After clinical training at St. Louis Children's Hospital and Barnes Hospital, Shearer joined the Washington University faculty in 1974. He was promoted to professor of pediatrics in 1978 before leaving for Baylor.

Not long after Shearer moved to Houston, the AIDS epidemic hit. Under his guidance, Baylor was one of the leading hospitals in decreasing mother-to-infant disease transmission by giving babies the drug AZT. Shearer also conducted trials to prove that protease inhibitors could help children with HIV.

Shearer serves as a member of the Washington University Medical Center Alumni Association and received a Washington University Distinguished Alumni Award at Founder's Day in October. He has been active through the years in alumni leadership roles in Houston.

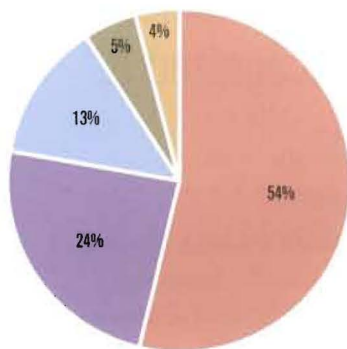
Philanthropist Robert S. Brookings and others, Shearer says, inspire him in his commitment to Washington University. "Brookings gave most of his fortune to the university, and look at how many times that has multiplied in helping people who want to do good in the world," he says. "I know that whatever I can leave to the university is going to live on forever."

Alumni Association hears from students

Although alumni activities, by definition, imply a graduation date, this year's alumni association meetings more often than not featured input from those whose degrees are still a work in progress.

Medical students made pitches to the Washington University Medical Center Alumni Association to garner funding for their favorite community service programs. Months later, they reported on these and other activities, painting a picture for the Executive Council of the myriad outside interests juggled by this year's students.

WUMCAA Fund Allocation 2003-2004 Total: \$295,982



- Distinguished Alumni Scholarships
- Farrell Learning and Teaching Center
- Eleven student organizations and community service projects
- Other student-related activities
- Primary care preceptorships

Throughout the discussions, fourth-year class president Jason Stephenson, an ex-officio member of the Executive Council, voiced the student perspective.

By the end of its term, the 2003-2004 Executive Council had allocated more than \$295,000, all of it addressing students' needs in some way. A longstanding commitment to scholarship support continued, some \$160,000 this year.

A payment of \$70,000 brought the Executive Council closer to fulfilling its 10-year, \$750,000 commitment to the Farrell Learning and Teaching Center, which will upgrade the spaces for students to learn, study and gather.

Primary care preceptorships received funding, as did a graduation reception and other efforts designed to round out the medical school experience.

Led by President Brent T. Allen, MD 79, the Executive Council set its sights on outstanding alumni, selecting candidates to receive alumni achievement awards and identifying others after whom to name scholarships.

WUMCAA Officers and Members 2004-2005

PRESIDENT	Edward P. Rose, MD 71
James W. Fleshman Jr., MD 80	Marlys E. Schuh, MD 79
PRESIDENT-ELECT	Donald A. Skor, MD, HS 84
Janet M. Ruzycski, MD 81*	Garry S. Tobin, MD 85, HS 90
VICE PRESIDENT	Alice W. Trotter, MD 69
Jeffrey L. Thomasson, MD 82*	OUT-OF-TOWN MEMBERS
TREASURER	Susan Bennett, MD, HS 91, Washington DC*
Marlys E. Schuh, MD 79*	Mark J. Lucarelli, MD 91, Madison WI*
PAST PRESIDENTS	Colin McDonald, MD 93, Boston MA*
J. William Campbell, MD 77	Jon Morris, MD 92, San Diego CA*
Carlton S. Pearse, MD 78	William T. Shearer, MD 70, Houston TX*
Brent T. Allen, MD 79	EX-OFFICIO MEMBERS
LOCAL COUNCIL MEMBERS	Ian Dorward, Fourth-Year Class President
Elliot E. Abbey, MD, HS 80*	W. Edward Lansche, MD 52
Edward F. Berg, MD 64	Larry J. Shapiro, MD 71, Dean
Kim D. Colter, MD 78*	Emily L. Smith, MD 88
Mark E. Frisse, MD 78	Morton E. Smith, MD, HS 64
James W. Forsen Jr., MD 88*	Alison J. Whelan, MD 86, HS 89
James M. Goldring, MD 86	
J. Michael Hatlelid, MD 77*	
Katherine L. Kreusser, MD, HS 82	
Amy Sullivan Nordmann, MD 99	
Timothy C. Philpott, MD 94*	

* Newly elected

Distinguished Alumni Scholarship Honorees

Sidney Goldring, MD 47	Donald Sessions, MD 62
Maurice Lonsway, MD 50	Larry J. Shapiro, MD 71

A legacy of learning New WUMCAA president

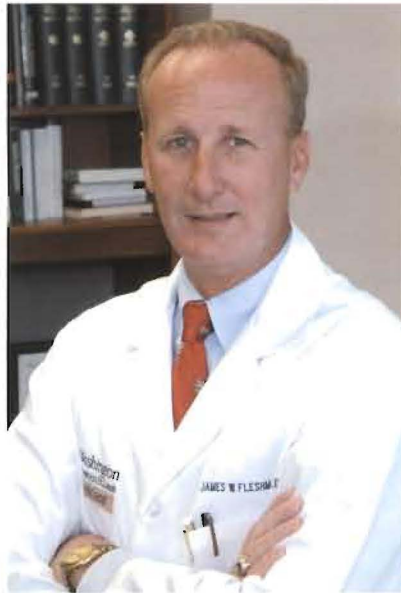
As the new president of the Washington University Medical Center Alumni Association, James W. Fleshman Jr., MD 80, notes that paying for medical school gets more challenging with each passing year.

“To date myself, the tuition during my first year of medical school was \$5,000, and I thought that was going to break the bank,” Fleshman says. “I could mow yards or work in a lab and come up with income to get my education covered.”

Today’s students rely on scholarships and financial aid, provided in large part by alumni.

“In the best of all worlds, I think tuition to medical school would be free, and we would all owe something back to society to pay for that education,” Fleshman says. “But it may not happen in my lifetime.”

Leaving nothing to chance, Fleshman, professor of surgery at the School of Medicine and chief of the Section of Colon and Rectal Surgery, leads alumni activities, supports Scholars in Medicine, and encourages other graduates to get involved.



James W. Fleshman Jr., MD 80

A New Orleans native, Fleshman earned a bachelor’s degree in biology from Washington University, graduating *summa cum laude*. After medical school, he completed an internship, residency and fellowship in surgery at what was then Jewish Hospital, serving as chief resident in 1985–86. A fellowship in colon and rectal surgery at the University of Toronto followed. He joined the School of Medicine faculty in 1987.

Fleshman specializes in treatments for colon and rectal cancer, inflammatory bowel disease and Crohn’s disease and has published more than 90 articles on topics including minimally invasive colon and rectal surgery. When he travels for committee meetings, he notices that representing Washington University brings instant recognition.

“I really enjoy seeing the value of my diploma go up every year, and I think the alumni association has helped that,” he says. “We attract the best medical students, no question. Our scholarship programs have made a difference.”

To Fleshman, teaching and mentoring medical students and residents are valuable pursuits.

“The only way to really see that you have succeeded in your profession and your career is to actually duplicate yourself—to leave a legacy of people you have trained or helped through their education,” says Fleshman. “That’s the motivation behind the academic side of my life and why I volunteer for the Eliot Society and alumni association.”



Scott Drost

Drost named annual giving director

If you receive mail from the School of Medicine, odds are Scott Drost now has something to do with it. As the school’s new director of annual giving, Drost works with volunteers like the Annual Fund chair to “get the word out” to thousands of alumni and Washington University School of Medicine supporters — often through the mail.

“Connecting the dedication of our volunteers and the enthusiasm of the WUSM community is a recipe for success,” says Drost. “I feel fortunate to be part of the equation.”

Drost also works closely with each year’s reunion gift chairs as well as supporting the efforts of the School of Medicine Eliot Society’s membership committee.

A resident of University City for more than 15 years (his wife, JoAnne, is an alumna of the School of Art), Drost joined the Office of Medical Alumni and Development Programs in 2003. He holds a bachelor’s degree in English and a certificate in writing from the University of Missouri–St. Louis.

A banner year!

Annual Fund

Alumni Results by Program

PERCENT PARTICIPATION JULY 1, 2003–JUNE 30, 2004

MD Alumni	42%
Physical Therapy	32%
Health Administration	31%
Nursing	29%
Occupational Therapy	24%
Former House Staff	21%

Thanks to the generous support from alumni, former house staff, and friends, the School of Medicine's annual fund drive ended as one of the most successful years on record! From July 1, 2003 to June 30, 2004, more than \$2.7 million was raised from 7,159 donors, supporting important programs throughout the School of Medicine.

The year would not have been such a success without two special annual fund challenges:



In February, an anonymous donor offered the Fives Challenge — matching all gifts that came in during the last five months of the academic year with \$500 (or \$1000 for Eliots), up to \$500,000. More than 1,900 individuals participated in this challenge (with gifts ranging

from \$5 – \$10,500), surpassing the goal of the \$500,000 match. In the end, \$500,000 in matching funds were directed to the Farrell Learning and Teaching Center.



Charles C. Norland, MD 59

In honor of his 45th medical reunion, Chuck Norland, MD 59, issued a special challenge to his class, matching each percent of participation with \$100 of his own. The Class of 1959 ended the year with a 75 percent participation rate — the highest among this year's reunion classes.

Reunion 2004

More than \$2.6 million was raised from classes celebrating reunion in 2004 (including both restricted and unrestricted gifts). The classes of 1954, 1964, 1969, and 1974 continued their efforts to raise additional funds for their endowed class scholarships. The Class of 1979 launched an effort to establish an endowed scholarship in honor of its 25th reunion. Under the leadership of Brent Allen, MD 79 and Jeffrey Cichon, MD 79, the Class of 1979 raised nearly \$18,000 in gifts and \$49,000 in pledges toward the project.

Records and highlights

- The Eliot Society (gifts of \$1,000 or more) set a record in new and renewed members: 216 and 602 respectively. The previous records were 182 new members in 1998 and 573 renewed members in 2003.
- MD alumni annual giving surpassed \$1 million for the second consecutive year.
- Former house staff participation and dollars were at a four-year high: 20.9 percent and \$243,933.
- Health Administration Program alumni set a new record for generosity to their Annual Fund, making nearly \$46,000 in gifts!
- Three hundred forty-three nursing alumnae made gifts this year — a record participation rate.
- The Program in Occupational Therapy increased its participation rate from last year.

Newest alums make a difference

- The MD Class of 2004 established a gift to accompany each year's Resident/Fellow of the Year Awards for the next five years. Nearly 50 percent of the class participated.
- The Program in Physical Therapy's Class of 2004 continued the young alumni gift effort begun by the previous class — perhaps launching a new tradition.

Class Notes

20s **Carl Rosenbaum, MD 27**, was featured in an article in the *Arkansas Democrat-Gazette*, noting that he celebrated his 105th birthday on May 18, 2004, at Presbyterian Village in Little Rock. Members of Grace Presbyterian Church there honored him at a luncheon and his family hosted a party in his honor. Rosenbaum retired from his private surgery practice in Little Rock at age 70. He commented that his family is blessed with longevity and that he has a cousin who is now 107.

30s **Benjamin Milder, MD 39**, has a new book of verse, *The Zoo You Never Gnu, a Mad Menagerie of Bizarre Beasts and Birds*, published by Time Being Books. Milder's zoo includes xiphias, hackee, zebu and urubu, animals presented in the form of a poetic palindrome with names ranging from A to Z and back.

40s **Stanley S. Kahn, MD 43 (March)**, is the author of a paper on the late Dr. Ralph Major, a prominent medical historian, published in the Winter 2004 issue of *Pharos*, the journal of Alpha Omega Alpha. Kahn practiced internal medicine and endocrinology in Birmingham AL for many years before he and his wife moved to California to be near their children. Both are active in volunteer work, and he is serving his third year on the Berkeley City Health Commission.

George Prothro, MD 45, was honored with the Leadership Award from the Retired Senior Volunteer Program of Tulsa OK at a dinner on May 14, 2004. Prothro, who retired from his position as medical director of the Tulsa City-County Health Department in 1978, recently retired from teaching at the University of Oklahoma College of Medicine, where he developed a system for training medical students in public

health. He still serves on the Health Department's Food Advisory Council, which oversees restaurant and food-processing licenses. An advocate for older people, Prothro was the first chairman of the Tulsa County Medical Society's Concerns of Older Tulsans Committee, which started a drug recycling program through which unused prescription drugs from nursing homes are made available to the poor.

Frank B. Norbury, MD 48, represented Washington University at the inauguration of Axel D. Steuer, PhD, as the 13th president of Illinois College, Jacksonville IL, on April 17, 2004.

50s **Muriel Kreyling MacKallor, OT 53**, of Mililani HI writes that she is "retired and enjoying Oahu. The local alumni group recently had a terrific program."

60s **Joshua Grossman, MD 65**, writes that he "served as visiting professor in the Department of Surgery on April 15, 2004, at the University of Tennessee Knoxville — Surgery Grand Rounds — Surgery Tall Tales." Grossman is a member of the clinical faculty of East Tennessee State University in Johnson City.

70s **Robert J. Langlais, MHA 75**, president and CEO of the Cheshire Medical Center in Keene NH, has been awarded Life Fellow Status by the American College of Healthcare Executives. He has been a member for more than 30 years. This is a special recognition for exemplary leadership in health care, advancing the profession through published articles and lectures, and public service. Langlais plans to retire in November 2004 and relocate to Arizona.

Pamela F. Gallin, MD 78, has authored her second book, *How to Survive Your Doctor's Care*, published in 2003 by LifeLine Press. The book

advises patients on the workings of medical facilities and how to navigate today's medical maze to receive the best medical care. Gallin practices and teaches at Columbia Presbyterian Medical Center and Columbia University College of Physicians and Surgeons, where she is director and associate professor of pediatric ophthalmology at the Edward S. Harkness Eye Institute and also associate professor of pediatrics at Children's Hospital of New York. Gallin's earlier book was titled *The Savvy Mom's Guide to Health Care*.

80s **Raymond J. Tesi II, MD 82**, has joined Cellarant Therapeutics, Inc., in Palo Alto CA as executive vice president of clinical development and medical affairs. Tesi will lead the development of cell-based therapies for autoimmune diseases and cancer. He is known for his work in solid organ transplantation and has been active clinically in kidney, pancreas, liver and small bowel transplantation. His earlier positions have included senior vice president of clinical development and medical affairs at SangStat Medical Corporation and associate professor of surgery and director of the extra-renal transplantation program at Tulane Medical School in New Orleans.

Jeffrey L. Thomasson, MD 82, and **Ronald R. Townsend, MD 82**, were inducted as Fellows in the American College of Radiology (ACR) at the formal convocation ceremony during the ACR's annual meeting in Washington DC in May. Thomasson is affiliated with St. Johns Mercy Medical Center and St. Louis University School of Medicine, and has served as president of the St. Louis Metropolitan Medical Society. Townsend has affiliations with the Denver Health Medical Center and the University of Colorado Health Sciences Center in Denver, where he received the 2003 John C. Stears

Class Notes

Outstanding Faculty Teaching Award. He has served as president of the Rocky Mountain Radiological Society. Only about 10 percent of the ACR members are selected for Fellowships, based on service to organized medicine, accomplishments in radiology, radiation oncology or medical physics, outstanding teaching and reputation among colleagues.

Michael P. Joyce, HA 87, assumed his duties as president of HCA's Southeast Division in Atlanta GA on July 1. He has operational responsibility for 19 hospitals and 12 outpatient surgery centers in Georgia, South Carolina and North Carolina. A Fellow of the American College of Healthcare Executives, Joyce has been with HCA for 17 years.

90s Stanley L. Hazen, MD, PhD 92, HS 94, has been appointed head of the Section for Preventive Cardiology and Rehabilitation at The Cleveland Clinic, where he has been on staff since 1997 in the Departments of Cell Biology and Cardiovascular Medicine. His research has helped to identify new markers for inflammation in patients with heart disease and mechanisms of inflammation in airways of subjects with asthma. Hazen is professor of molecular medicine in the Department of Medicine of The Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and adjunct professor in the Departments of Chemistry and Biology at Cleveland State University. He lives in Pepper Pike OH with his wife, **Jackie Hazen, MD 89**, a pediatrician, and two daughters.

Russell Holman, MD 92, was installed as treasurer of the Society of Hospital Medicine (SHM) at the annual meeting held last April in New Orleans. Holman is associate medical director for hospital services at HealthPartners Medical Group & Clinics (HPMG&C) in Minnesota

and assistant professor of medicine at the University of Minnesota, where he did his residency in internal medicine and where he won the Department of Medicine's "Teacher of the Year" award in 1997. Since starting the HPMG&C hospitalist program in 1997, Holman has expanded it to 30 physicians across four hospital sites. He also founded and directs the HealthPartners Fellowship Program in hospital medicine. In 2002, he was the recipient of the SHM award for "Outstanding Service in Hospital Medicine."

Julie Lundberg Freiner, DT 94, writes that she and her husband, Tim, welcomed their second son, Tyler Jack, born April 15, 2004. He joins big brother Troy, who was born June 19, 2001. Freiner is a certified hand therapist who is co-owner of Rehab 1- Hand Therapy Network of St. Charles County. The family lives in Lake St. Louis MO.

Karen Good, PT 98, recently earned her orthopaedic clinical specialist certification from the American Physical Therapy Association. She works at the Kennedy Krieger Institute in Baltimore MD.

Amy Malecki Rogers, MD, PhD 99, writes "Finally, I have returned to work at least part-time. In the spring semester I taught at California State University (Sacramento), picking up a microbiology and a molecular biology lab class. Yes, I can still do a miniprep! Our move to CA last summer was a success, and we are happy here."

00s Rieke Baize, HA 00, has been asked to serve on the Healthcare Executive editorial board for a term ending March 2007. In April, she received the Certified Healthcare Executive credential from the American College of Healthcare Executives, and in May she was the recipient of the 2004 Early Career Healthcare Executive Award presented at the annual meeting of the New Jersey Hospital Association. Baize lives in Maple Shade NJ.

IN MEMORY

Richard Y. Sakimoto, MD 33, HS, of Honolulu HI died April 26, 2004, at the age of 98. He was Hawaii's first board-qualified obstetrician/gynecologist and had delivered more than 12,000 babies. A native of Japan, he completed his residency at Barnes Hospital before opening his practice in Honolulu in 1938. During his career he served on the faculty of the John Burns School of Medicine at the University of Hawaii and was chief of obstetrics and gynecology at The Queen's Medical Center. In 1983, he received a Distinguished Service Award from Washington University's Medical Center Alumni Association. Survivors include his wife, Edna, a daughter, Eda, and a son, Richard.

William S. "Bill" Curtis, MD 40, HS 48, of Boulder CO died April 1, 2004, at the age of 88. He was a radiologist who had worked at Boulder Medical Center and the University of Colorado Student Health Center. During World War II he served in the U.S. Army. A member of the American College of Radiology, Curtis was a past-president of both state and local medical societies. His wife, Frances Elmer Curtis, died on April 8, 2004, at the age of 85. Their survivors include two sons and a daughter.

Robert B. Dickerson, MD 41, died April 20, 2004, in Lompoc CA at the age of 92. He retired as a colonel in the U.S. Army Medical Corps, having served as chief of cardiology at Walter Reed Medical Center and Consultant to the Surgeon General in Cardiovascular Diseases. During his military career he invented the "Dickerson needle" which is still used in performing catheterizations. Among his survivors are his wife of 63 years, three sons and a daughter.

Samuel E. Schechter, MD 41, died May 24, 2004, at the age of 87 after a long illness. He practiced in Clayton MO for many years and was an associate

professor of clinical medicine at Washington University. He interned in internal medicine at Jewish Hospital, then served in the Army Air Force during World War II, following which he completed a fellowship in gastroenterology at Michael Reese Hospital in Chicago. In 2001, Schechter endowed the Samuel E. Schechter Professorship in Medicine at Washington University. He also endowed the Rena Schechter Memorial Lectureship in Cancer Research in honor of his first wife, who died in 1995, and the David Joel Schechter and Leslie Schechter Memorial Fund for Research in Depression in memory of two of their children, as well as two scholarships in Arts and Sciences in honor of his daughters Miriam and Kay, who survive. Also surviving is his wife, Norma Bonham, whom he married in 2002. Memorials may be designated to provide scholarships for students at Washington University School of Medicine.

Ewald W. "Bud" Busse, MD 42, a pioneer in understanding the human aging process, died March 8, 2004, at his home in Durham NC at the age of 86. After completing a psychiatry residency at the University of Colorado in 1948, he served on the faculty there before moving to Duke University. At Duke he was the J.P. Gibbons Professor of Psychiatry and also served as dean of the School of Medicine. He chaired the Department of Psychiatry there from 1953 to 1974, establishing the nation's first Center for the Study of Aging and Human Development, which he directed for 13 years. He was the author of more than 200 scientific papers and the editor of a number of books on gerontology. In 1985, Duke University named the gerontology building the E.W. Busse Building in his honor. Busse was a member of the Institute of Medicine and a past president of the American Psychiatric Society, the American Geriatrics

Society, the Gerontological Society of America and the International Association of Gerontology. He is survived by his wife, Ortrude "Ort" Busse, and four children.

Frederick W. Klinge III, MD 42, died June 23, 2004, in St. Louis at the age of 87. He was a general surgeon in Collinsville IL for many years and also had a strong interest in preventive medicine and physiology. Survivors include four sons and five grandchildren.

James C. Lowe II, MD 56, died May 4, 2004, at age 72. He had been a physician at Henry Ford Hospital in Detroit and West Bloomfield MI for 38 years, had headed the divisions of preventive medicine, internal medicine and executive medicine and served as president of the hospital's medical board. As the hospital's representative, he had a 36-year association with the Detroit Tigers. After residency, Lowe served in the U.S. Army Medical Corps in Frankfurt, Germany. He was a Fellow of the American College of Physicians. A world traveler who had visited all 50 states and more than 50 countries on six continents, he was also active in his home community. He was a talented musician and played clarinet in Washington University's concert band as an undergraduate student. Survivors include his wife, Margaret, an alumna of Washington University's School of Arts and Sciences, two daughters and two sons.

Johann Heinrich Joist, MD, PhD, HS 66, died February 13, 2004, at his home in St. Louis after a yearlong battle with mesothelioma. He was 69. A native of Germany, Joist came to this country in 1964 as a research fellow at Washington University, served as an assistant professor of medicine at the School of Medicine and later directed the hemostasis and thrombosis laboratory at Barnes-Jewish Hospital. He then became director of the division of hematology and oncology at St. Louis University School of Medicine, where,

from 1982 until his death, he was also a professor of medicine and pathology. As director of the Adult Hemophilia Treatment Center in St. Louis, he initiated a program linking the center with a hospital in India, improving diagnosis and treatment there. The World Federation of Hemophilia honored him with an award in 2001. In 2004, he received the St. Louis University Hospital Caring Physician Award. Joist was married to Nancy Lee Maxeiner, who survives, along with three daughters.

James T. Shaw, MD 71, was killed in a hunting accident as he was turkey hunting in Gasconade County MO on April 22, 2004. He was 58. He had been a family physician in Hermann MO for nearly 28 years, sharing an office with his uncle, Dr. George Workman, and was on the staff at the Hermann Area District Hospital. He was a lifetime member of the American Medical Association and the American Academy of Family Physicians. Shaw is survived by his wife, Kristen, two sons and a daughter. Tragically, Shaw's death mirrored that of his father, Dr. Carvel T. Shaw, who was shot and killed in a hunting accident on Thanksgiving Day in 1967.

Craig Roberts, MD 83, an emergency physician at Tillamook County General Hospital in Tillamook OR, died December 27, 2003, at age 46 when his van was struck head-on by a drunk driver. His family survived. Roberts was a nationally recognized birder, having identified more than 800 North American birds. He taught birding at several Oregon colleges and universities, often organized and led birding trips, and had organized the field trips for the 2003 meeting of the American Birding Association. Survivors include his wife, Crisanne, and three children.

A winning strategy for your year-end tax and gift planning

Find out how you can help yourself and the University through a Life Income Plan

Consider a gift of appreciated securities or real estate — begin planning to:

- Make a life income gift.
- Receive a valuable charitable income tax deduction for 2004.
- Transfer appreciated property to a life income plan and receive significant capital gains tax savings.
- Turn low-yielding assets into attractive income through a gift annuity or charitable trust.

Gift Annuity Sample Rates of Return	Single life		Double life	
	age	rate	age	rate
	60	5.7%	60 & 60	5.4%
	65	6.0%	65 & 65	5.6%
	70	6.5%	70 & 70	5.9%
	75	7.1%	75 & 75	6.3%
	80	8.0%	80 & 80	6.9%
	90	11.3%	85 & 85	7.9%

Looking for fixed payments? Consider the gift annuity.

If you are age 72 and create a \$10,000 gift annuity with cash, you will receive the following benefits:

Fixed rate of return	6.7%
Fixed annual income for life	\$ 670
Tax-free income portion	\$ 403
Taxable income portion	\$ 267
Immediate federal income tax deduction	\$4,159

(Your deduction may vary.)

You may also fund a gift annuity with appreciated securities.

Do you own appreciated real estate?

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

For further information or to request a personalized example, please call 314-935-5848 or 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>


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



“Charitable gift annuities represent an important part of my personal program of giving back to Washington University,”

says Sally Burtram, PhD, HA 72.

“It’s a win-win.”

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A winning strategy for your year-end tax and gift planning



I am age 60 or over. Please send me a personalized, confidential calculation using the following information to illustrate the very attractive benefits that I will receive from a Washington University Charitable Gift Annuity or Charitable Remainder Unitrust.

Value \$ _____ In the form of:
 Cash Real Estate (\$ _____) (_____)
COST BASIS ACQUISITION DATE
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COST BASIS ACQUISITION DATE

First Beneficiary **Second Beneficiary**
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 Relationship _____ Relationship _____



I would like information on planning my year-end giving.

I wish to become a Robert S. Brookings Partner. I have included Washington University in my estate plan through my: ___ will or trust ___ other
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This information is strictly confidential.

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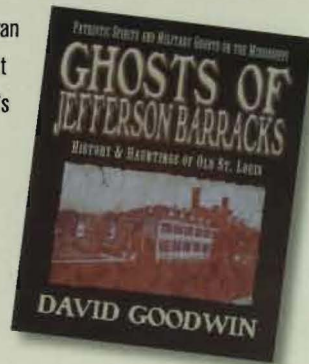
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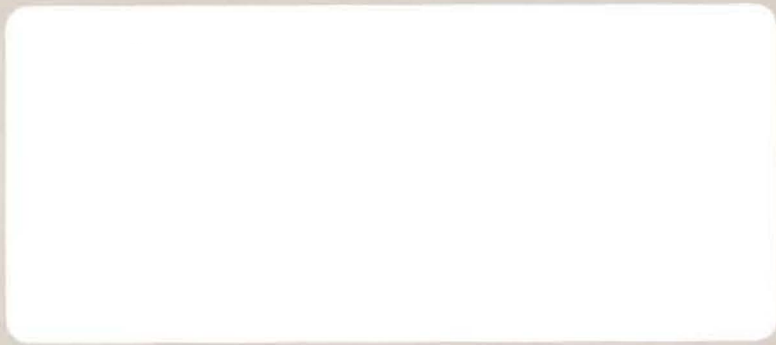




TIM PARKER

Ghostly glow David Goodwin, a seven-year veteran of the School of Medicine Protective Services Department and now a commissioned police officer on the university's Hilltop campus, relaxes in Jefferson Barracks cemetery. He is at the grave of one of the ghosts featured in *Ghosts of Jefferson Barracks*, a history of the supernatural at the military post. Goodwin, a National Guard reservist, is now deployed to Iraq.





Interviews: Kenneth Ziegler, second-year medical student.



LIVE! Satellite trucks at Bernard Becker Medical Library.



JOE ANGELES



Student reactions: Laurel Barrett and Karla Fredricks

Facing America On October 8, 2004, a presidential debate on the hilltop campus put the candidates — and the university — in the national spotlight. The School of Medicine chapter of the American Medical Student Association hosted a remote telecast in Moore Auditorium, with featured speaker Larry J. Shapiro, MD, executive vice chancellor for medical affairs and WUSM dean.



Comparisons: Dean Shapiro on medicine and science policy.

TIM PARKER



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