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Outlook

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AUTUMN 2014



Washington
University in St. Louis

SCHOOL OF MEDICINE

Seeing CANCER

Visualizing tumor cells
opens therapeutic horizons



Outlook Autumn 2014

outlook.wustl.edu

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Catalyst for innovation

A renovated telephone factory adds a prime St. Louis location to commercialize research technology, a place where students and trainees can engage creatively with businesspeople and investors in biomedicine. This office and lab facility at 4240 Duncan Ave., dubbed @4240, provides space for established and start-up companies. The Office of the Vice Chancellor for Research and other university tenants anchor this new \$73-million facility, located in the CORTEX bioscience district just east of Washington University Medical Center.

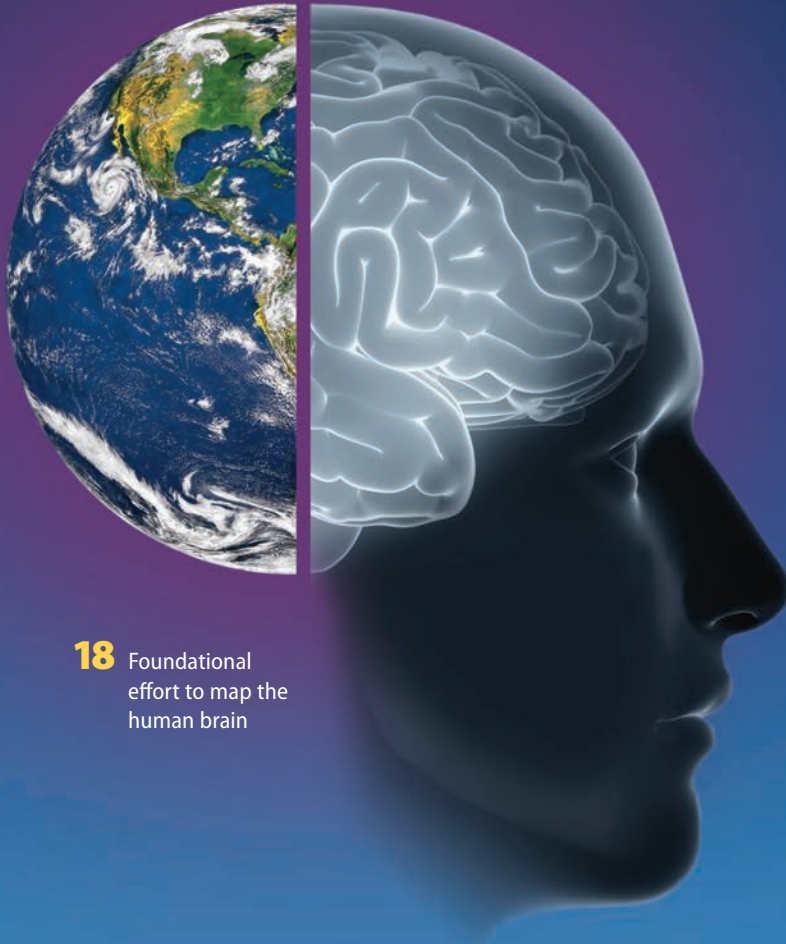
Outlook

Washington University School of Medicine

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COVER High-tech glasses are making it possible for surgeons to visualize cancer cells in real time. To learn more, turn to page 14.

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A Bangladeshi mother holds her malnourished child. The dark spot placed on his head is said to ward off evil spirits.

Microbes & malnutrition

Problem affecting millions of children may be rooted in underdeveloped gut communities

New findings may help explain why millions of malnourished children suffer from stunted growth and fail to thrive after treatment with nutrient-rich therapeutic foods.

Studying healthy and malnourished young children in Bangladesh, a team at the School of Medicine found that malnutrition has persistent detrimental effects on the vast community of microbes living in the gut. These “friendly” microbes typically aid in extracting nutrients and calories from food, and perform many other vital functions.

The results suggest that the long-term consequences of childhood malnutrition, such as stunted growth, cognitive problems and weakened immune systems, may be rooted in lingering, underdeveloped gut microbes that can’t fully harvest energy and calories from food, said senior author Jeffrey I. Gordon, MD, director of Washington University’s Center for Genome Sciences & Systems Biology.

In healthy children, the researchers identified features associated with normal development of the gut’s community of microbes. In comparison, they noted that malnourished children carried communities of gut microbes that did not mature along a normal trajectory. These immature bacterial collections could not be restored to good health with standard treatments of therapeutic foods.

The research, conducted in collaboration with colleagues at the International Centre for Diarrhoeal Disease Research in Dhaka, Bangladesh, is published online in *Nature*.

These immature bacterial collections could not be restored to good health with food-based interventions.

“Although therapeutic food-based interventions have resulted in a significant decline in deaths from malnutrition, many children never fully recover,” said first author Sathish Subramanian, a Washington University MD/PhD student. “We found that children who were malnourished had gut microbial communities that were not consistent with their chronological ages. The severity of a child’s malnourishment was tied closely with the degree of immaturity of his or her gut microbial community, and this immaturity could not be durably repaired with standard treatments.”

The researchers are following up their research in animal models colonized with immature gut microbe communities from malnourished children. They are seeking to determine whether giving therapeutic foods for longer periods of time or administering beneficial mixtures of naturally occurring human gut microbes can repair this immaturity and improve health.

How gene-lifestyle interactions affect cardiovascular disease

\$8 million grant a first for scale and scope

School of Medicine researchers have received an \$8 million grant to investigate the genetic and environmental roots of cardiovascular disease risk factors. The four-year grant supports the first large-scale, multiethnic statistical analysis of risk factors for cardiovascular disease that looks at lifestyle interactions with genes.

The investigators will use existing data from more than 30 studies, which include detailed genetic data, measures of cardiovascular risk factors — namely, blood pressure and cholesterol levels — as well as information on lifestyle, including smoking, alcohol consumption, physical activity, socioeconomic status and diet.

To carry out this type of study, large numbers of subjects are needed to have sufficient power to detect interactions of genes and lifestyle.

The study represents a massive international collaboration that brings together data on more than 300,000 subjects from diverse ethnicities. The multiethnic approach allows a broad view of interactions and how they play out in populations with different genetic and cultural histories.

“This study is unprecedented in many ways,” said principal investigator D.C. Rao, PhD, professor of biostatistics, genetics, psychiatry and mathematics and director of the Division of Biostatistics.

“We have compelling preliminary data that highlight the potential of these investigations,” he said. “We found, for example, several novel genes associated with high blood pressure that were not previously known until the interactions with alcohol consumption or education were brought in.”

Considering lifestyle factors in the context of a genetic analysis offers the possibility of identifying novel genes and may provide clues to intervention points.



Investigators Ingrid Borecki, PhD, and D.C. Rao, PhD

STEVE DOLAN



CLEM SPALDING

Uncommon monkey Researchers at The Genome Institute at Washington University and at Baylor College of Medicine have decoded the genome of the common marmoset. A look at its DNA begins to explain the animal’s frequent twin births; most primate species have single births. Unlike humans, marmosets consistently give birth to twins without any medical issues. Marmoset gene changes associated with twinning perhaps act as a critical switch between multiple and single pregnancies. Findings could shed light on multiple pregnancies in humans.

Earhart named PT program director

Gammon Earhart, PhD, professor of physical therapy, now is director of the Program in Physical Therapy at the School of Medicine. She succeeds Susie Deusinger, PhD, who has retired.

Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the medical school, announced the appointment.

“Gammon Earhart is an innovative thinker, a well-respected researcher and a leader in physical therapy,” Shapiro said. “She is exceptionally qualified to continue the legacy of excellence Susie Deusinger built during her 24 years as director.”

Earhart, also a professor of neurobiology and of neurology, joined the faculty in 2004. **Gammon Earhart, PhD** A 2000 graduate of the Movement Science PhD Program, she is associate director of that program. Earhart earned undergraduate and master’s degrees from Arcadia University in Pennsylvania and did postdoctoral work at Oregon Health and Science University.

Earhart’s research focuses on nervous system control of movement and examines how different treatment approaches may benefit people with Parkinson’s disease.

Under Deusinger’s leadership, the program evolved into one of the top programs in the country and consistently ranks among the best, according to U.S. News & World Report.





RAY WARKLIN

Senior prom Johanna Kaufman, medical student and leader of the Geriatrics Outreach Group, dances with Don Harper. Harper was one of about 200 St. Louis-area seniors who attended the annual prom in the 560 Music Building. The event fosters intergenerational dialogue, social interaction for seniors and is a learning opportunity for students. The prom is hosted by student volunteers from the medical school, the programs in Physical Therapy and Occupational Therapy and the undergraduate schools.

Cardiothoracic surgery chief named

Ralph J. Damiano Jr., MD, an internationally known cardiac surgeon, has been named chief of the Division of Cardiothoracic Surgery at the School of Medicine.



Ralph J. Damiano Jr., MD

The new appointment is one of several taking effect in the cardiothoracic surgery division. With his appointment, Damiano becomes the Evarts Ambrose Graham Professor of Surgery. He succeeds G. Alexander Patterson, MD, who has served as chief of cardiothoracic surgery since 2005.

Patterson, who becomes the Joseph C. Bancroft Professor of Cardiothoracic Surgery, has stepped down as division chief to devote more time to editing *The Annals of Thoracic Surgery*, the journal of The Society of Thoracic Surgeons. He is editor-elect of the journal and will become editor-in-chief early next year.

Marc Moon, MD, succeeds Damiano as chief of the Section of Cardiac Surgery.

“We have tremendous depth and breadth in the Division of Cardiothoracic Surgery,” said Timothy J. Eberlein, MD, the Bixby Professor and chairman of the Department of Surgery, in announcing the new appointments. “Our cardiothoracic surgeons are national and international leaders in developing and refining innovative surgical procedures for the heart and for pulmonary diseases. We are grateful to Alec Patterson for his many years of dedicated service in leading the division to additional prominence and look forward to Ralph Damiano continuing the long tradition of leadership in the field.”

New center aims to use immune system to fight cancer, diseases

A new center will help scientists use the power of the immune system to fight infections and cancers.

The Center for Human Immunology and Immunotherapy Programs (CHiiPs) is part of BioMed21, the university’s initiative to accelerate basic science discoveries into improved diagnosis and treatment for patients. The center is housed in the BJC Institute of Health at Washington University.

Scientists also are developing ways to restrain the immune system when it mistakenly attacks healthy tissue, leading to autoimmune disorders.

“Several very important basic discoveries in these areas have been made by Washington University faculty, but it has been challenging to move those discoveries into the clinic,” said CHiiPs director Robert D. Schreiber, PhD, the Alumni Professor of Pathology and Immunology.

Pioneering researchers at the medical school have shown that the immune system can recognize cancers and regulate their growth. The scientists also have identified ways to manipulate the immune system’s ability to destroy cancer cells. The school has been a leader in developing vaccines for emergent diseases such as West Nile virus and in identifying cells and molecules involved in autoimmune conditions.

A center laboratory will monitor changes in the immune system during clinical trials of new immunotherapies.

“Until now, faculty performing immunological clinical trials or studying unique immunologic clinical syndromes had to set up these tests in their own labs, which is a lot of work and doesn’t always produce standardized results,” Schreiber said.

The center’s leaders are recruiting faculty interested in applying immunological discoveries to clinical problems.



ROBERT BOSTON

The center’s new time-of-flight mass cytometer simultaneously detects more than 50 different structures either on the cell surface or inside the cell, providing important clues to the identity of the cells and the functions they perform. From left, center leaders Olga Malkova, PhD; Stephen Oh, MD, PhD; Michael Diamond, MD, PhD; Robert Schreiber, PhD; and Wayne Yokoyama, MD.



Before the Cardinals, there were colleges

The first phase of Ballpark Village, a mixed-use entertainment and retail district next door to Busch Stadium in St. Louis, opened for this year's baseball season. But, in the 1870s, this area was the epicenter of medical education in St. Louis — home to the two oldest medical schools west of the Mississippi:



St. Louis Medical College in the 1870s

PHIL SARGISKA • ARCHIVES AND RARE BOOKS

Missouri Medical College and St. Louis Medical College. These two colleges later would merge to become Washington University School of Medicine. To see maps, photos and learn more about these historical roots, visit bit.ly/1pu2xPx.

RADIOLOGY RESEARCH

The next generation of brain scanning

Scientists have advanced a brain-scanning technology that tracks what the brain is doing by shining dozens of tiny LED lights on the head. This new generation of neuroimaging compares favorably, while avoiding the radiation exposure and bulky magnets other approaches require, according to School of Medicine research.

The new optical approach to brain scanning is ideally suited for children and for patients with electronic implants, such as pacemakers, cochlear implants and deep brain stimulators (used to treat Parkinson's disease). The magnetic fields in magnetic resonance imaging (MRI) often disrupt either the function or safety of implanted electrical devices, whereas there is no interference with the optical technique.

The new technology is called diffuse optical tomography (DOT). While researchers have been developing it for more than 10 years, the method had been limited to small regions of the brain. The new DOT instrument covers two-thirds of the head and for the first time can image brain processes taking place in

multiple regions and brain networks such as those involved in language processing and self-reflection (daydreaming).

"When the neuronal activity of a region in the brain increases, highly oxygenated blood flows to the parts of the brain doing more work, and we can detect that," said senior author Joseph Culver, PhD, associate professor of radiology. "It's roughly akin to spotting the rush of blood to someone's cheeks when they blush."

The technique works by detecting light transmitted through the head and capturing the dynamic changes in the colors of the brain tissue.

Although DOT technology now is used in research settings, it has the potential to be helpful in many medical scenarios as a surrogate for functional MRI, the most commonly used imaging method for mapping human brain function. Functional MRI also tracks activity in the brain via changes in blood flow.

Another common method for mapping brain function is positron emission tomography (PET), which involves radiation expo-



TIM PARKER

sure. Because DOT technology does not use radiation, multiple scans performed over time could be used to monitor patients treated for brain injuries, developmental disorders such as autism, neurodegenerative disorders such as Parkinson's, and other diseases.

Unlike fMRI and PET, DOT technology is designed to be portable, so it could be used at a patient's bedside or in the operating room.

While DOT doesn't let scientists peer very deeply into the brain, researchers can get reliable data to a depth of about one centimeter of tissue. That centimeter contains some of the brain's most important and interesting areas with many higher brain functions represented.



Winning graduate students Hirak Biswas, Whitney Grither and Anurag Agarwal.

Breast cancer startup challenge

The resources required to get discoveries from bench to bedside can be astounding. Many promising innovations never reach their potential.

To reverse this trend, The Avon Foundation for Women, the National Cancer Institute (NCI) and the Center for Advancing Innovation created the Breast Cancer Startup Challenge. The initiative was aimed at bringing 10 promising breast cancer discoveries out of the lab and closer to market.

Some 200 teams of graduate students worldwide competed. Graduate students Hirak Biswas and Anurag Agarwal in the Division of Biology and Biomedical Sciences and Whitney Grither in the Medical Scientist Training Program won for their proposal to advance a therapeutic breast cancer vaccine developed by NCI researchers and patented in 2011. The team also included Gurudatta Begur Nadiger, an executive MBA student at Northwestern University, and Erik Nyre, a law student at the University of Minnesota.

The vaccine showed promise in preclinical mouse trials, but further research and development is needed. This would be the focus of the startup company. The team must negotiate an exclusive licensing agreement with the NCI's technology transfer office and raise seed funding.

School of Medicine faculty members mentored the students.



Neuro thriller Neurosurgeon Eric Leuthardt's research often has been described as science fiction brought to life. An associate professor of neurosurgery and of biomedical engineering, Leuthardt, MD, is working to develop brain implants known as neuroprosthetics that detect brain signals and relay them to a computer. He hopes to use the technology to restore movement, speech and other functions in people suffering from stroke. Experiences in the lab and the operating room inspired him to write a futuristic thriller. His

first novel, "Red Devil 4," envisions a world where brain implants permeate every level of personal and social interaction as cell-phones do today.

Could a single medication fight multiple infectious agents?

\$32 million NIH grant will fund project

School of Medicine researchers are leading a multi-institutional campaign to harness a newly recognized cellular defense against infection.

The project could lead to drugs with unprecedented versatility in fighting different infections. A \$32 million grant from the National Institutes of Health (NIH) is funding the collaborative, which also includes Massachusetts General Hospital, the Broad Institute and the University of Texas Southwestern Medical Center.

The grant creates a four-site Center for Excellence in Translational Research (CETR), which is a National Institutes of Allergy and Infectious Diseases program.

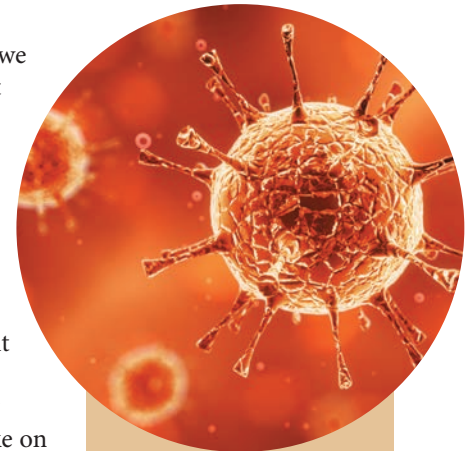
"If we're successful, we may develop drugs that allow us to treat bacteria, viruses, fungi and parasites with a single medication," said principal investigator Herbert W. Virgin IV, MD, PhD, head of the university's Department of Pathology and Immunology. "We now have drugs that can take on viruses or bacteria but nothing that can fight several types of infectious agents at the same time."

Virgin and his colleagues are investigating a newly recognized connection between a cellular waste disposal system called autophagy and the body's ability to fend off infections.

Scientists already knew that autophagy proteins clean out cellular debris. But researchers recently have started to link the proteins to infection control, suggesting that the disposal system may not only take out the trash but also help identify unwanted cellular houseguests — such as bacteria, viruses, fungi or parasites — and destroy them.

Other proteins involved in autophagy may fight infection in different ways, indicating that this pathway is a versatile tool used by the body to fight a range of infections.

The researchers will identify proteins involved in autophagy, explore the roles the proteins play in waste disposal and immunity, and attempt to develop drugs that engage the autophagy process in fighting infections.



Using a newly recognized cellular defense system to fight infection



TECHNOLOGY

'Printing' a new arm for Sydney

Thirteen-year-old Sydney Kendall had one request for the students building her robotic prosthetic arm: Make it pink.

Kendall Gretsch, Henry Lather and Kranti Peddada, 2014 seniors studying biomedical engineering in the School of Engineering & Applied Science, accomplished that and more, with guidance from School of Medicine faculty.

Using a 3-D printer, they created a robotic prosthetic arm out of bright-pink plastic. Total cost: \$200, a fraction of the price of standard prosthetics, which start at \$6,000.

"Currently, prosthetics are very expensive, and because kids keep growing, it is too costly for them to have the latest technology," said Sydney's mother, Beth Kendall.

While 3-D printers can cost about \$2,500, they are capable of producing artificial limbs at a relatively low individual cost.

Sydney lost her arm in a boating accident at age 6. She learned to write with her left hand, but found most tasks difficult to accomplish with her prosthetic arm. Sydney said her new arm is easy to manipulate. By moving her shoulder, she can direct the arm to throw a ball, move a computer mouse and perform other tasks.

The students developed the robotic hand as part of an engineering design course with Joseph Klaesner, PhD, associate professor of physical therapy at the medical school. Charles A. Goldfarb, MD, and Lindley Wall, MD, orthopedic hand surgeons and associate professors of orthopaedic surgery, served as mentors.

"They brought their engineering expertise, and we shared our practical experience with prosthetics and the needs of children," Goldfarb said. □



PHOTOS BY ROBERT TOSTON

Paving the road to **RESIDENT**

Every summer, at teaching hospitals across the country, newly minted MDs formally begin introducing themselves as “doctors.”

Despite years of preparation, it’s a steep learning curve — going from student, observer and helper, to being an on-call resident, writing orders and managing high-acuity patients through long nights.

Given significant changes in U.S. residency training — and reduction of hospital duty hours — residents are facing new challenges. Nationally, medical schools are thinking beyond the four-year experience and trying to offer more seamless transitions to residency. To help graduating students hit the ground running, School of Medicine faculty created “Capstone,” a four-week, robust hands-on course.

“We are convinced it makes an impact at the outset of internship,” said course co-founder L. Michael Brunt, MD, professor of surgery. “This is an important first step leading to more specialized curriculum development that will better prepare our students for residency training.”

Through morning didactic sessions and afternoon procedure workshops, students cover many of the situations they soon will encounter in real life. Theoretical lectures are replaced

with practical application, taking students’ accumulated knowledge — from first-year anatomy to third-year clerkships — and putting it all together.

Here, they begin thinking like independent physicians, focusing on day-to-day tasks and in-the-moment decision-making, such as juggling multiple patients or choosing the right medication dosages. The students refine technical skills — suturing, placing a central intravenous line, or inserting a chest tube — procedures that, in some cases, they’ve only observed. Specialty-specific breakout sessions further reinforce essential clinical competencies.

Capstone course builds confidence in critical decision-making, hones hands-on skills of tomorrow’s physicians

PHOTOS BY
ROBERT BOSTON



Theory put into practice: facilitators L. Michael Brunt, MD, Julie Woodhouse and Thomas M. De Fer, MD

CY/



Students practice inserting chest tubes into racks of ribs. This procedure is used in patients with a pneumothorax (collapsed lung).

SYNTHESIS





CAPSTONE, created three years ago as a two-week elective by Brunt and Thomas M. De Fer, MD, professor of medicine, continues to evolve based on student and faculty feedback. “Capstone provides a ‘just-in-time’ learning experience for medical students who are a few months away from being an intern,” DeFer said. “That’s always been anxiety-provoking, but, until courses like this, it was just something that they had to work through as best as they could and hopefully not make too many mistakes along the way.”

“Our students do get a lot of these educational elements earlier in the curriculum, but it’s always a challenge to retain it all. This course provides practical information in one fell swoop at a time when they need it the most and are most receptive.”

As part of the core curriculum in 2014–15, the four-week session will run twice, with each of the many procedural workshops offered multiple times, to accommodate the entire medical class. Hundreds of faculty and house staff members from many disciplines are involved in the program. Coordination is a year-round logistical challenge headed by Julie Woodhouse, assistant director of the Howard & Joyce Wood Simulation Center.

“Capstone is one of our success stories. The whole school comes together and contributes to it,” said Michael M. Awad, MD, PhD, associate dean for medical student education.

APPLICATION



CAPSTONE topics address the curricula of modern medicine — patient safety, emergency management, end-of-life care, informed consent, ethics, working in a team, communication, and sign-outs and handoffs, among many others. In addition, the class gives students tips to manage their personal wellness (dealing with stress, time management and sleep deprivation).

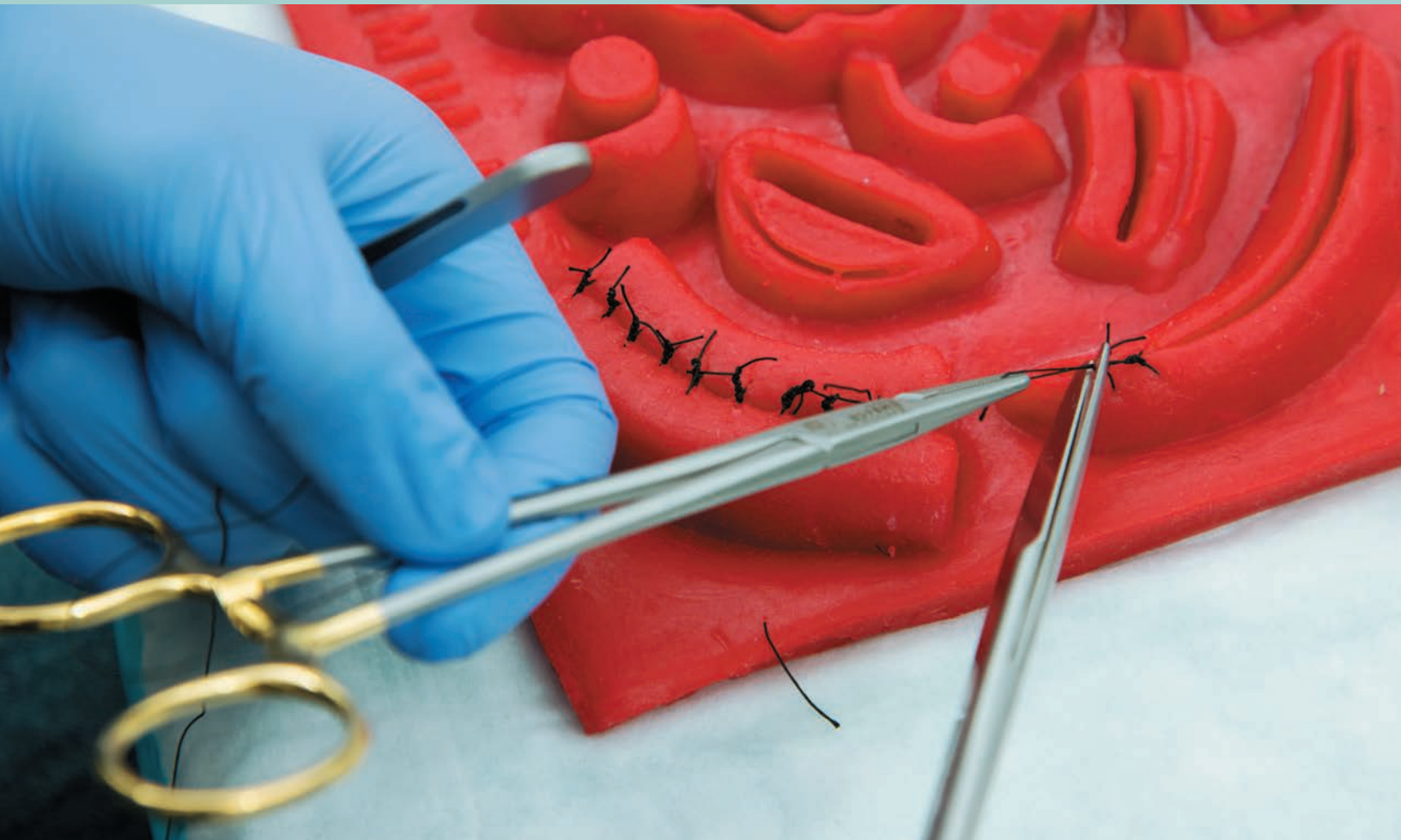
Rated particularly high among students are the “mock page” sessions. Nurses call in a scenario, i.e., “the patient had surgery yesterday and is now running a fever,” and students are forced to think through the next steps.

Capstone students recently completed pre- and post-course questionnaires assessing their ability to handle clinical problems, procedures and patient-care tasks. In all categories, students rated their abilities markedly higher post-course.

“The thing many of us felt the most apprehension about was getting that call in the middle of the night about a patient who wasn’t doing well,” said Linda Jin, MD, now a first-year surgical resident at Barnes-Jewish Hospital. “Even through fourth year, most of our education is focused on understanding pathophysiology and knowing what is in the literature.

“Capstone helped us synthesize our knowledge so we can apply it in a practical way. It was also so useful to have a forum to practice saying things like ‘I’d like a chest X-ray, CBC and BMP now’ in a safe environment. One week into my intern year, I said those exact things. I’m glad I had a chance to do a practice run.” □

— Deb Parker





Ca

Ability to see glowing cancer cells opens doors to precision treatments BY JIM GOODWIN

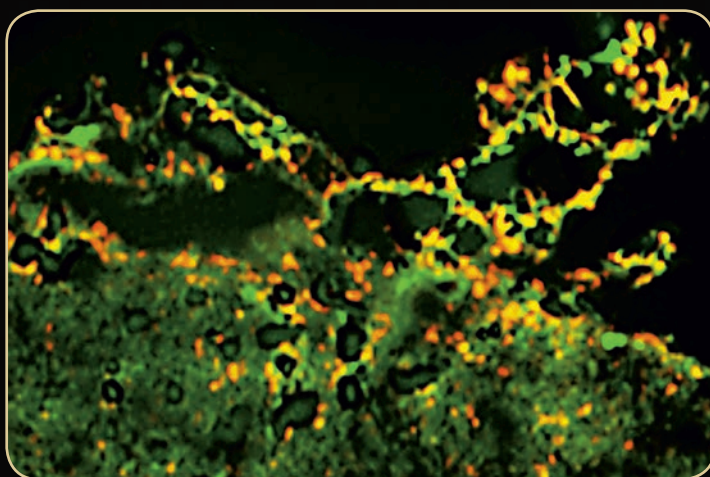
ncer VISION

CANCER CELLS ARE NOTORIOUSLY difficult to see, even under high magnification. Until now, it's been nearly impossible for operating surgeons — using only static MRIs and X-rays as a guide — to tell where the tumor ends and healthy tissue begins.

After hearing a group of doctors discuss this frustration in 2009, Samuel Achilefu, PhD, a professor of radiology at the School of Medicine, had an idea: Could night-vision goggles used by the military also work in the war against cancer?

Achilefu's mission was to design wearable technology for surgeons, helping them distinguish cancer cells from healthy cells in real time — perhaps reducing the need for additional surgeries and subsequent stress on patients.

The goggles evolved from an effective but clunky prototype (left), into a more streamlined version for testing in the O.R. (middle). The version currently in development (right) provides a clear view of the surgical field and the ability to visualize cancer cells (highlighted here in orange). The goggles are modeled by Suman Mondal, a PhD candidate in biomedical engineering, who is coordinating research efforts toward clinical translation of the technology.



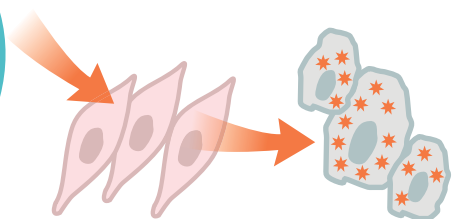
To care for patients, surgeons today remove the tumor and neighboring tissue, which may or may not include cancer cells. The samples are sent to a pathology lab and viewed under a microscope. If the surrounding tissue contains cancer cells, a second surgery is performed to remove even more tissue, which also is checked for the presence of cancer. About 20 to 25 percent of breast cancer patients who have lumps removed require a second surgery. It's a balancing act — surgeons don't want to remove too much or too little surrounding tissue.

“No one wants unnecessary surgery — not surgeons, not nurses and certainly not patients or their families,” said Achilefu, also a professor of biochemistry and molecular biophysics and biomedical engineering. “Our goal with these glasses is to eliminate follow-up surgery by removing all cancerous cells the first time.”

Targeting cancer



Removing a tumor and minimal surrounding tissue is rarely straightforward; typically the exact boundaries are unclear.



Researchers have developed dye agents that can pass through healthy cells but remain trapped within cancer cells.

As the dye fluoresces in infrared energy, the goggles aid in seeing the boundary between tumor and healthy tissue.

Technology UNVEILED

Achilefu dedicated five years to the project. Initially, people were skeptical that his idea could be realized. He carried out his research using discretionary funds from the Mallinckrodt Institute of Radiology and support from the Department of Defense Breast Cancer Research Program. Achilefu assembled a multidisciplinary team, including engineers and video game specialists, who worked together to further refine and miniaturize the glasses. Over time, Achilefu successfully demonstrated the technology in mice, rats and rabbits, and, in 2012, the team received a \$2.8 million grant from the National Institutes of Health (NIH).

Major collaborators include Viktor Gruev, PhD, associate professor of computer science and engineering, and Ron Liang, PhD, associate professor of optical sciences at the University of Arizona (UA). Washington University graduate students Suman Mondal, Shengkui Gao and Yang Liu and UA postdoctoral fellow Nan Zhu also played key roles.

On Feb. 10, 2014, the high-tech glasses were used during surgery for the first time at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. Surgeon Julie Margenthaler, MD, operated on 67-year-old breast cancer patient Karen Clodfelter.

In this procedure, an FDA-approved, commonly used contrast agent, indocyanine green, was injected into the patient's tumor. When viewed with near-infrared light, the cancerous cells glowed blue. Lighter shades of blue indicated higher concentrations of cancer cells.

Margenthaler was heartened by the technology, which enabled her to see the tumor, as well as the bordering malignant cells. (Tumors generally do not form in perfect circles, but instead have tentacles that branch out in different directions.)

“We're certainly encouraged by the potential benefits for patients,”

said Margenthaler, an associate professor of surgery at the School of Medicine. “Imagine what it would mean if these glasses eliminated the need for follow-up surgery and the associated pain, inconvenience and anxiety.”

So far the technology only has been used on patients with breast or skin cancer. Given the success of the initial nine surgeries — four breast and five melanoma — more are planned.

“The distinction between normal and cancerous tissue is not always clear to the naked eye,” said melanoma surgeon Ryan Fields, MD, a Washington University assistant professor of surgery who also has used the goggles. “Often, we're relying on how something looks or feels. Even CT scans and MRI images can fail to detect microscopic cancer.”

In a study published in the *Journal of Biomedical Optics*, researchers noted that tumors as small as 1 mm in diameter (the thickness of about 10 sheets of paper) can be detected.

Could such technology curtail follow-up surgeries?



The ongoing refinement of the goggles, shown in their latest concept (left), involves cross-disciplinary scientific collaboration. Some of the project contributors are pictured here, from left: Ron Liang, PhD, Nan Zhu, Viktor Gruev, PhD, and Shengkui Gao. Inset, top: Samuel Achilefu, PhD, and Julie Margenthaler, MD.

Theoretically, the technology could be used to visualize any type of cancer in the operating room.

Video components in the glasses allow surgeries to be recorded. As only a small number of observing medical students can fit into an operating room, the recordings could serve as a useful teaching tool in a larger auditorium. There also may be applications that could help guide physicians practicing in remote areas.

Achilefu has worked with Washington University's Office of Technology Management and has a patent pending for the technology.

Revolutionizing TREATMENT

Achilefu, who also is co-leader of the Oncologic Imaging Program at Siteman Cancer Center, is seeking FDA approval for a markedly improved contrast agent, LS301, he is helping develop. This agent, injected into the bloodstream, selectively enters cancer cells anywhere in the body and stays there longer, up to a week, in some cases.

It appears to be the first contrast agent to mark cancer cells universally — breast, prostate, liver, brain, colon, leukemia and lymphoid cancers, even metastatic cells. The cells glow under infrared light.

Achilefu is optimistic — pending FDA approval for a pilot study — that human clinical trials will begin soon. For now, his research group — partnering in a study with the University of Missouri School of Veterinary Medicine — will be removing cancerous tumors in dogs, providing treatment hope for the pets' owners.

If approved for use in humans, this targeted agent potentially could someday act not only as a marker, but also as a way to deliver drugs directly to cancer cells, sparing healthy tissue and eliminating some surgeries. The agent also may shed light on how tumors are responding to chemotherapy.

Another mission is born.

"Our goal is to make sure no cancer is left behind," Achilefu said. □

Future targets

Success of the cancer targeting agents could lead to further innovations. For example, it might be possible to inject the targeting agent along with a cancer therapy, thereby identifying and destroying cancer cells even before tumor development begins.

The Human

Effort to relate brain connectivity to individual capabilities

WHAT MAKES US THINK, FEEL AND REMEMBER? Why do people behave differently or have varied learning styles? What makes people unique? The answers can be found in the neural networks firing within our brains.

The Human Connectome Project (HCP) is a \$30-million, five-year effort to comprehensively map human brain circuitry — and its variability — in 1,200 healthy adults using advanced, noninvasive neuroimaging methods. Washington University, the University of Minnesota and Oxford University are leading a 10-institution consortium involving more than 100 investigators and staff.

The project is gathering and analyzing data, and making its results freely available to the scientific community, in the hope of sparking future discoveries — shedding light on healthy brain function and, ultimately, informing doctors' ability to diagnose and treat disorders, such as ADHD, schizophrenia, Alzheimer's, autism and many others.

BY THE NUMBERS

\$30 million

5 years

1,200 healthy adults

300 twin pairs & non-twin siblings

10 institutions

100 investigators

THE EVOLUTION OF WORLD CARTOGRAPHY



1630
MERCATOR/
HONDIUS



1855
MITCHELL
BOOK ATLAS



2003
LANDSAT 5



2014
USGS/GOOGLE



Connectome

ilities will establish a new baseline for future studies

It took centuries to arrive at today's detailed views of Earth as speculative imaginings yielded to exploration and technology. While cartographers only had one Earth to map, HCP collaborators are creating maps that may be useful in understanding billions of human brains. Researchers are exploring the similarities and differences that make us who we are, giving us all our unique mix of personality quirks, mental traits and individual identities.

In short, the HCP is conducting the most complex and ambitious mapping ever attempted: charting the intricacies of the living, working human brain. Co-principal investigator David Van Essen, PhD, appreciates the challenges as well as the limits of this historic endeavor.

"In comparison with our historical efforts to chart the Earth's surface, the HCP will, in effect, take us from an 18th-century representation of the cortical landscape to a 19th-century representation," Van Essen said.

BY MICHAEL C. PURDY

PROJECTED DATASET

1 petabyte

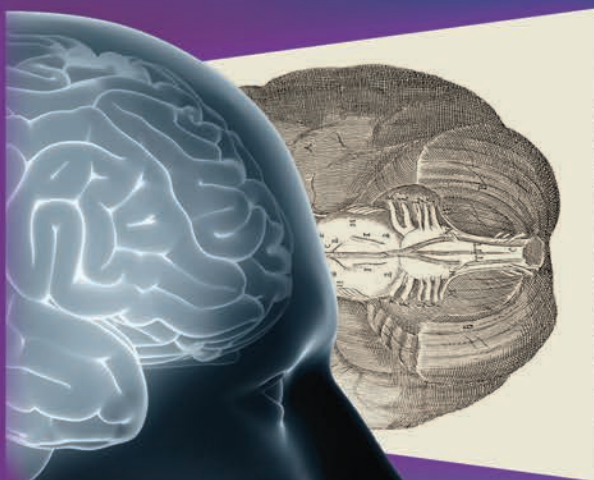
EQUIVALENT TO

1 million gigabytes, or
58,000 DVD movies

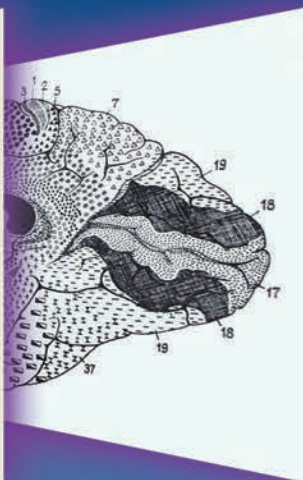
Open access

Freely available worldwide

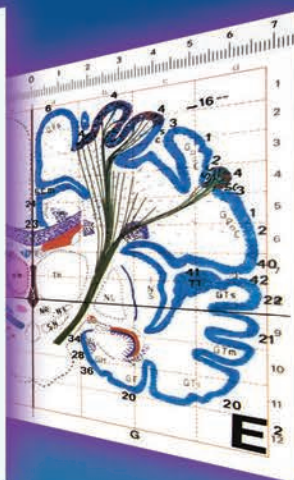
THE EVOLUTION OF BRAIN MAPPING



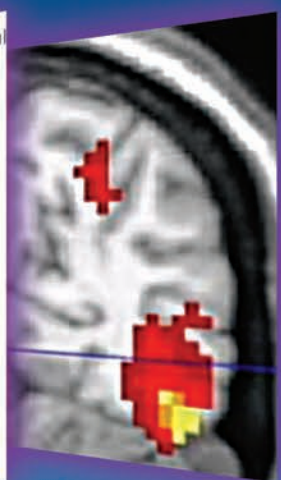
1664
WILLIS



1909
BRODMANN



1988
TALAIRACH
BOOK ATLAS



2005
MRI STUDIES

Left and right hemispheres

Holding bookends that model the human brain: Washington University HCP lead investigators Deanna Barch, PhD, the Gregory B. Couch Professor of Psychiatry and chair of the Department of Psychology, and David Van Essen, PhD, the Alumni Endowed Professor of Neurobiology. The HCP's co-principal investigators are Van Essen and Kamil Ugurbil, PhD, a professor at the University of Minnesota.



ROBERT BOSTON

Understanding complexity Scientists admit the human brain remains a mystery. Each human brain, weighing about 3 pounds, contains about 85 billion neurons, or nerve cells — more than 12 times the number of people on Earth — which transmit information across roughly 150 trillion cell-to-cell connections known as synapses. In nearly all brain disorders, there's something wrong with these connections, though, in most cases, scientists don't yet know exactly what has gone awry.

In the last two decades, an explosion of new brain imaging methods has yielded vast amounts of information.

Functional magnetic resonance imaging (fMRI), developed in the 1990s, opened the door to direct observation of cognitive activities. By detecting changes in blood oxygenation and flow, fMRI produces activation maps showing which parts of the brain are involved in specific mental processes. Using fMRI, researchers are scanning participants while they perform tasks and at rest.

Diffusion MRI gives insight into how regions of the brain are physically wired together into networks that communicate electrical signals through the white matter.

Structural MRI scans clearly show the physical features of the participants' brains; these features vary greatly among individuals.

See "Making connections" on page 21 to learn more about how HCP data is being gathered from the human test subjects.

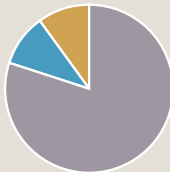
Why this study is so challenging

Researchers seek to interpret data with respect to the human brain's organizational features and structural dimensions. However, the size, function and connectivity of the parts vary so greatly among individuals that making comparisons and establishing averages becomes a key challenge. Each critical area may connect with dozens of other areas and the connection strengths differ over many orders of magnitude.

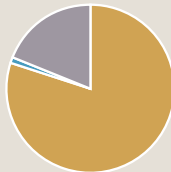
Anatomical STRUCTURES



Distribution of TISSUE



Distribution of NEURONS



The outer **cerebral cortex** (gray), occupies about 80% of brain volume but contains only about 20% of the brain's 85 billion neurons. Its convoluted surface has 150–200 critical areas of study, which vary in size twofold or more across the normal adult population.

Some 80% of the neurons reside in the **cerebellar cortex** (gold). This region of the brain also varies highly among individuals.

Subcortical structures (blue) occupy the remaining approximately 10% of brain volume but contain only about 1% of the neurons.

Wrinkles unraveled Much of the brain's uniqueness is found in the cerebral cortex, the wrinkled outer layer of the brain often known as the gray matter.

"The cortex is like a sheet that is crumpled and folded up to fit inside the skull," Van Essen explained. "This folding pattern varies from one person to another, and that makes it really hard to just look at a brain and say, 'okay, how is it organized?'"

Scientists already knew that the wrinkles, or folding patterns, of the cerebral cortex are what they call "partially heritable." A glance at the brains of a pair of twins reveals major differences, but closer study uncovers structural elements that strongly suggest common genetic influences.

Prior to the Connectome, Van Essen was a leader in the application of visualization techniques that effectively inflate the crumpled sheet into a spherical beach ball, making it easier to match up significant features from one brain to the next.

Through the advanced scanning and data-analysis techniques developed and applied by HCP, scientists have created another tool for standardizing these comparisons: maps of myelin, the protective white material that wraps many nerve cell branches. Connectome scientists devised ways to use aspects of this material like the mountains, rivers and other landmarks that helped earthly mapmakers get their bearings.

Making connections

HCP researchers are studying twins and their non-twin siblings, a total of 1,200 subjects, to better understand how genes affect the wiring of the brain: What aspects of circuitry are inherited and what aspects are shaped by experience?

To reflect the true normal range of brain connections, study volunteers come from all racial, ethnic, economic and educational backgrounds.

Study volunteers spend about four hours over two days in a customized MRI, sometimes lying quietly and sometimes performing tasks. All the while, the machine is recording patterns of brain activity. A participant might move her right hand, for instance, and a section of the left motor cortex lights up. The testing is replicated in hundreds of subjects. For something more complicated, such as a working memory test, several brain regions in the front and back light up together, working in a coordinated way.

“We are trying to understand which parts of brains are active when people are processing information, doing math or remembering things,” explained Deanna Barch, PhD, lead investigator, who is coordinating data collection at Washington University.

In addition to the brain scans, research volunteers undergo a battery of cognitive, physical fitness and psychological tests. They spend about six hours participating in wide-ranging activities — from tasting mysterious liquids on a cotton swab to running around traffic cones in a corridor. These tests, which look at intelligence, sensory abilities and emotional state, among other aspects, bring added dimension to the imaging data. For instance, do differences in brain circuits have any bearing on high or low IQ?

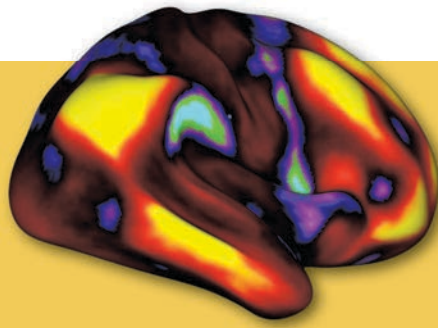


PHOTOS BY ROBERT BOSTON

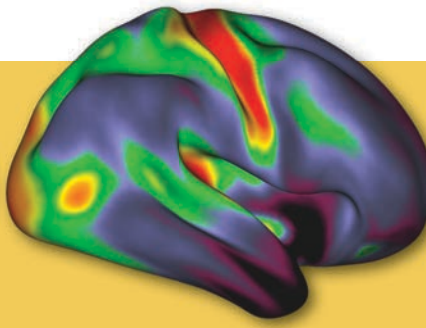


Tucker Hartley and Owen Footer, HCP research assistants, perform some behavioral tasks used by the HCP to measure each subject's abilities, such as gait speed (top), odor identification (middle), and taste (bottom). At right, Footer prepares Hartley for a functional MRI scan in which the subject indicates choices with a button box.

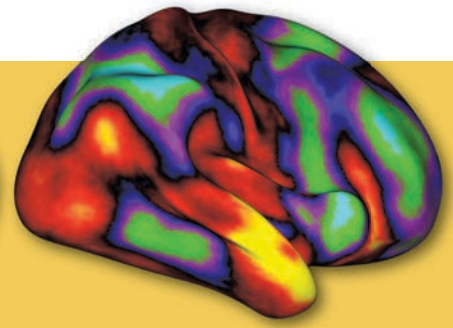




At rest Average functional connectivity is collected on subjects while at rest in the MRI scanner. Yellow regions are functionally connected to a “seed” location in the right hemisphere, whereas regions in blue and purple are weakly connected or not connected at all.



Myelin Red and yellow regions have high myelin content compared to other colors. Mapping the myelin on the cortex indicates functionally distinct brain regions — an important step toward understanding how brain networks form dynamically to do tasks.



Story vs. math Participants are asked to listen attentively to either a story or a calculation (e.g. “16 minus 5 plus 18 equals”) and answer a question about what they heard. Stories activate yellow and red regions, whereas math affects green and blue regions.

“We think there are about 150 to 200 cortical areas — analogous to the political subdivisions of Earth’s surface — that are critically important for understanding brain function and connectivity,” Van Essen said. “Myelin maps give us markers for an interesting subset of this mosaic of areas. We can see these markers in individual subjects and watch how their location jumps around from one subject to the next.”

One of Van Essen’s MD/PhD students, Matthew Glasser, is leading an effort to create a new master map of the cortex based on combining myelin maps with other HCP data. They expect to unveil the map this year.

Future implications HCP scientists made their fourth large data release earlier this year, doubling the data they have made available to the public.

The release included scanning, demographic and behavioral data from more than 500 subjects. The information is organized in a web-accessible database called ConnectomeDB. A software application, Connectome Workbench, allows users to view and compare many types of

imaging data, both produced by HCP and by other labs.

“These maps are going to have a major impact on our understanding of the healthy adult human brain, and that impact is already starting to be felt,” Van Essen, said. “Not only have we published many papers on what we’re learning about the brain from the data-gathering process, there also already have been a handful of independent investigators who have published papers based on HCP data. We weren’t expecting that this early in the process.”

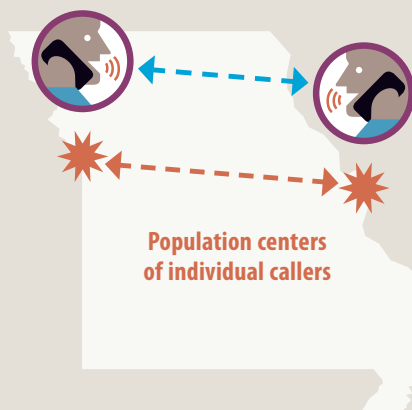
“We’re approaching the point where we have enough data to really sink our teeth into these questions and are starting to do some serious science on what factors influence the folding of the cortex,” he said.

Lead investigator Barch said that to comprehend how structural or functional connectivity goes awry, researchers must first establish the parameters of normal connectivity.

“You need a baseline to work from,” she said. “Down the road, the HCP will become a benchmark enabling us to see how abnormalities contribute to or result from disease. It will suggest better ideas about disease prevention or the means of early intervention.” □

INFORMATION PROVIDED BY JENNIFER ELAM, PHD, OUTREACH COORDINATOR, HCP

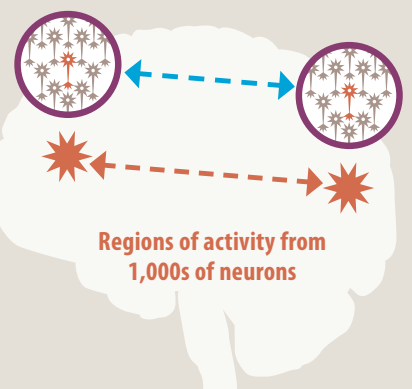
The ‘state’ of the art in brain mapping



Population centers of individual callers

Imagine mapping population centers

by tracking telecommunications activity — say, grouping at least 100,000 phone calls from one location to another. This would reveal Kansas City and St. Louis as two hot spots in Missouri, but would not identify individual callers. HCP mapping, somewhat similarly, monitors the overall activity of more than 100,000 neurons at a time. This allows researchers to better understand the brain’s functional hot spots and their connectivity, providing the most detailed and accurate whole-brain portrait yet developed.



Regions of activity from 1,000s of neurons



What we can do for
CANTU

**The world's only clinic
explores the science
behind a rare syndrome**

BY MICHAEL C. PURDY

At the Cantu clinic,
Cole Eggemeyer shows
he's got what it takes.

For seven years, Randall and Rachel Lamfers struggled to get a diagnosis for their son, Noah, who was born prematurely, had problems with pulmonary hypertension and needed a breathing tube. In November 2013, analysis of Noah's DNA finally gave them a diagnosis: a rare condition called Cantu syndrome.

An Internet search quickly led them to Washington University. And this summer, the Lamfers, who live in South Dakota, brought Noah to St. Louis.

In June, researchers and physicians at the School of Medicine and St. Louis Children's Hospital hosted the world's only medical clinic for patients with Cantu syndrome, providing some treatment options and support for families, who, until this time,

may have never met others with the disorder.

A scientific symposium was held in conjunction with the clinic.

Medical literature reports only about 50 people with Cantu, but many more now are being identified by genetic analysis, and the researchers already are following six patients in the St. Louis area, indicating that the syndrome may be significantly more common than first realized.

Cantu syndrome causes excessive hair growth, bone abnormalities, swelling in the legs, problems with heart function and a range of other symptoms that researchers are just beginning to quantify.



Dorothy Grange, MD, examines Riley Dyck during the Cantu clinic.

A major focus of the Cantu syndrome clinic has been in-depth study of the cardiovascular abnormalities associated with the condition. This June marked the second time the clinic was held at the St. Louis campus.

Dorothy K. Grange, MD, professor of pediatrics in the Division of Genetics and Genomic Medicine, created a registry for Cantu syndrome patients; in August 2013, she organized the first clinic, along with professor Gautam K. Singh, MD, instructor Mark D. Levin, MD, and assistant professor Beth A. Kozel, MD, PhD, all in the Department of Pediatrics.

"We've been waiting a long time for this," Rachel Lamfers said. "We're excited to be able to introduce Noah to other children with Cantu syndrome, and we want to hear the stories of other families who have children affected by this condition."

At the first clinic, Tracy Buerck-Eggemeyer's son, Cole Eggemeyer, then 12, was fearful of having his blood drawn.

"He asked me, 'Mom, is having my blood drawn going to help other people who have Cantu syndrome in the future?'" recalled Buerck-Eggemeyer. "When I told him yes, he said, 'I want to do it.'"

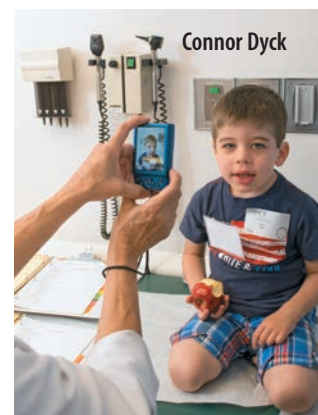
Bench-to-bedside link

The Cantu clinic and collaborative research efforts came about when roads covered for two different groups at Washington University Medical Center.

At St. Louis Children's Hospital, Grange and Singh, professor in the Division of Pediatric Cardiology, were treating a family with multiple cases of Cantu syndrome. The researchers were the first to suggest that Cantu is caused by a defect in a potassium channel gene that affects the cardiovascular system.

Meanwhile, Colin Nichols, PhD, the Carl Cori Professor in cell biology and physiology and director of the Center for Investigation of Membrane Excitability Diseases (CIMED), had linked potassium channels — openings in the surfaces of cells that let in charged potassium particles — to neonatal diabetes. To understand the role of a related channel, he had mutated the underlying gene in the cardiovascular system in mice.

In late 2012, the two groups realized that their investigations were linked. The CIMED scientists discovered their mice models with mutated



Connor Dyck



Cantu syndrome can cause heart chamber enlargement, low blood pressure and fluid build-up. Ultrasound provides a detailed view of Noah Lamfers' heart in motion (inset). Gautam K. Singh, MD, discusses the care recommendations with Noah's mother, Rachel.

potassium channels had Cantu-like symptoms. At about the same time, the clinicians' genetic studies, conducted in collaboration with a group of Dutch researchers, led them to a gene called *ABCC9*.

"That's not the same gene we were studying; we had mutated a gene called *KCNJ8* in our mice," Nichols said. "But we knew that proteins from each of these two genes come together to form a single potassium channel, and we now know that mutations in either gene can cause Cantu syndrome."

Due to these mutations, the potassium channels remain open, making it harder for blood vessels to contract, a step that helps the circulatory system increase blood pressure when needed.

CIMED, a BioMed 21 interdisciplinary research center, specializes in studying these kinds of changes. Problems with these channels can lead to neurological and psychological disorders, cardiac arrhythmias, cystic fibrosis, diabetes and myriad other conditions. Nichols and the members of CIMED — which now include Grange and Singh — focus on improving therapies for these diseases.

Moving forward

Nichols said he believes the Cantu group is on the verge of significantly alleviating the marked lifestyle and clinical problems from which these patients suffer, and is gearing up for trials of a targeted drug therapy.

"Until now, Cantu syndrome patients have been treated solely on the basis of their symptoms, and what we're learning now about the actual causes of those symptoms suggests that there may be better ways to treat them," Nichols said.

"For example, even before the link to Cantu syndrome was identified, we were finding evidence that the mutation we were studying in mice causes blood vessels to relax," Nichols added. "That can explain why the ductus arteriosus, a vessel that redirects blood flow during fetal life, fails to close

normally after birth in many Cantu patients. It may also help us find new ways to close off this blood vessel in other situations."

Based on what they've learned from studying Cantu syndrome patients, Washington University researchers now know more about how drugs such as Rogaine or minoxidil stimulate hair growth.

"Because of the gene mutation they carry, these patients are experiencing the equivalent of a chronic overdose of minoxidil," Nichols said.

The clinic's discoveries may not only help develop appropriate treatments for the cardiovascular problems and excess hair growth seen in Cantu and in other conditions, but also aid in the search for improved drugs that promote hair growth.

"The advances in our knowledge about Cantu syndrome have been incredible in the last two years," Grange said. "I am optimistic we will have effective therapy for our patients in the near future." □

Hold tight! Colin Nichols, PhD, measures Riley Dyck's ability to maintain his grip for up to two minutes. Such measures will establish a baseline for Riley's condition and allow physicians to accurately gauge future changes and benefits of therapy.



BioMed 21

Dedicated to speeding the transformation of basic science discoveries into advances in the clinical diagnosis and treatment of disease.

The Center for Investigation of Membrane Excitability Diseases (CIMED)
cimed.wustl.edu





A LEGACY OF GRATITUDE

BY RICK SKWIOT

The commitment of one family has made a profound difference.

Breakthroughs in developing leukemia therapies, in treating osteoporosis and childhood asthma, in fighting viruses that cause blindness, and in understanding Alzheimer's disease — these and countless other advances have come about with the aid of one St. Louis couple, the late Alan A. and Edith L. Wolff. Together they donated more than \$70 million to the School of Medicine to fight cancer and other diseases and to support the scientists and physicians responsible for the medical breakthroughs.

“The power of philanthropy to change people's lives and improve the well-being of future generations is undeniable,” said Chancellor Mark S. Wrighton. “Patients here at the Medical Center and around the world have benefited from the generosity of supporters such as Alan and Edith Wolff — through improved patient care, new treatments and a deeper understanding of the causes of diseases.

“Through their gifts, which continue to fund the work of world-renowned physicians and researchers, the Wolffs have left a lasting legacy by advancing medicine and science. In the process they have earned the gratitude of us all.”

Thanks to the far-reaching vision of the late Alan A. and Edith L. Wolff, countless lives are changing through improved patient care, breakthrough research and student mentorship. The couple's estate has endowed 20 professorships in perpetuity at the School of Medicine.



THE WOLFF LEGACY ENDURES

Alan and Edith Wolff lived a quiet life, according to those who knew them, remaining in the same unassuming home despite their growing wealth. But their dynamic work as civic benefactors and philanthropic leaders over the years has helped Washington University excel in medical science, enabling its researchers and physicians to make

advances that benefit patients worldwide and continue to propel new, life-saving discoveries.

The Wolffs found success developing subdivisions and shopping centers in Missouri, Illinois and Kansas. But they created a lasting legacy through their efforts to help those in need and those striving to advance medical care.

“The 20 endowed professorships that the Wolffs have established in perpetuity enable us to recruit and retain world-class talent dedicated to continuing our cutting-edge biomedical and translational research,” said Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

After Alan Wolff’s death in 1989, Edith Wolff took over Wolff Construction Co. and its subsidiaries, successfully expanding its assets. She also expanded the family’s philanthropic efforts.

In 2007, she made a \$20-million commitment to Washington University School of Medicine to establish the Alan A. and Edith L. Wolff Institute, underwriting promising biomedical research and serving as the principal support for the university’s BioMed 21 initiative. Other multi-million-dollar gifts went to fund cancer research and to endow an interest-free loan fund for medical students.

Shapiro said that informed, thoughtful and targeted philanthropy like the Wolffs’ significantly influences medical science.

“Such philanthropic support is vital as federal research budgets tighten, and at a time when we are on the verge of so many new discoveries thanks to the explosion of knowledge in genetics and molecular biology,” Shapiro said. “Our ongoing quest to understand, diagnose and treat disease depends in large part on people like the Wolffs.

“The Wolffs’ impact is immeasurable,” Shapiro said.

But in some ways the Wolffs were unlike many other successful people, according to their longtime attorney James L. Fogle.

“Mr. Wolff was particularly quiet about the extent of their wealth, and they were rather quiet about their generosity as donors when he was alive. But then Edith increasingly took a higher-profile leadership role in order to encourage others to give as well,” Fogle said.

“They didn’t have children. Edith focused on helping people who couldn’t take care of themselves and to supporting people aspiring to do great things,” he said. In addition to medical research, many community organizations benefitted from Edith Wolff’s generosity.

She died in 2008 at age 93.

Although the Wolffs’ relationship with the Medical Center dates back to when Edith, at age 16, volunteered at the original Jewish Hospital, they were first inspired to support Washington University by the late I. Jerome Flance, MD, professor emeritus of clinical medicine.

Flance, a close friend and their personal physician for more than 50 years, fueled their interest in the medical research being done at the School of Medicine and helped guide them in their initial contributions to the university.

“Our ongoing quest to understand, diagnose and treat disease depends in large part on people like the Wolffs.”

— Larry J. Shapiro, MD

From left: Wolff Professors Daniel C. Brennan, MD; Chyi-Song Hsieh, MD, PhD; and Daniel S. Ory, MD.





BOB BOSTON



BOB BOSTON



JOE ANGELES



BOB BOSTON

Wide-ranging impact

A gallery of Wolff Professors in action — clockwise from top: Urologist Arnold D. Bullock, MD, advises a resident in the operating room; geriatrician David B. Carr, MD, assesses driving skills in older adults; Daniel C. Link, MD, studies the genomics of leukemia; and Mario Castro, MD, MPH, listens to the lungs of a patient with asthma.



THE WOLFF PROFESSORS

Wolff Professors are leaders in many disciplines at the School of Medicine. Following is a list of professors and dates of installation. Five more professors will be added, bringing the total to 20.



William A. Peck, MD
Alan A. and Edith L. Wolff
Distinguished Professor of Medicine
SEPT. 9, 2002



Daniel C. Link, MD
Alan A. and Edith L. Wolff
Professor of Medicine
JULY 1, 2009



L. David Sibley, PhD
Alan A. and Edith L. Wolff Distinguished
Professor of Molecular Microbiology
AUG. 10, 2011



Daniel C. Brennan, MD
Alan A. and Edith L. Wolff
Professor of Renal Diseases
AUG. 8, 2013



Chyi-Song Hsieh, MD, PhD
Alan A. and Edith L. Wolff
Professor of Rheumatology
AUG. 13, 2013



Daniel S. Ory, MD
Alan A. and Edith L. Wolff
Professor of Cardiology
AUG. 15, 2013



Lee Ratner, MD, PhD
Alan A. and Edith L. Wolff
Professor of Oncology
SEPT. 23, 2013



Mario Castro, MD, MPH
Alan A. and Edith L. Wolff Professor of
Pulmonary and Critical Care Medicine
DEC. 12, 2013



Richard K. Wilson, PhD
Alan A. and Edith L. Wolff
Distinguished Professor of Medicine
MARCH 20, 2014



Todd P. Margolis, MD, PhD
Alan A. and Edith L. Wolff Distinguished
Professor of Ophthalmology and Visual Sciences
APRIL 4, 2014



Arnold D. Bullock, MD
Alan A. and Edith L. Wolff Distinguished
Professor of Urology
JUNE 18, 2014



David B. Carr, MD
Alan A. and Edith L. Wolff
Professor of Geriatric Medicine
AUG. 14, 2014



John Turk, MD, PhD
Alan A. and Edith L. Wolff
Professor of Endocrinology
SEPT. 4, 2014



Lilianna "Lila" Solnica-Krezel, PhD
Alan A. and Edith L. Wolff Distinguished
Professor of Developmental Biology
NOV. 3, 2014



Aaron DiAntonio, MD, PhD
Alan A. and Edith L. Wolff
Professor of Developmental Biology
DEC. 11, 2014



IN THEIR OWN WORDS

Below, in their own words, meet three Alan A. and Edith L. Wolff Distinguished Professors. They discuss the role of philanthropy in advancing medical science and the impact of the Wolff legacy on the School of Medicine.

A lasting impact **William A. Peck, MD**

“Jerry Flance, a great internist and Washington University clinical professor, introduced me to Edith, his patient and close friend in the 1990s. I had the privilege of visiting with Edith frequently thereafter. When her husband, Al, passed away, Edith’s deft leadership continued to advance his flourishing real estate business. Al’s estate included funds to be held for the support of medical research and Edith was able to use her own funds and estate for the same purpose.

“With the advice of Jerry Flance, Edith proceeded to provide funds for multiple outstanding Washington University scientists. Edith had a passion for excellence and ‘invested’ accordingly.

In addition to supporting the research, Edith’s funds have established multiple endowed chairs at our institution, enhanced by actual research support.

“Forgetting about me, excellent scientists and department heads have been so honored, including leaders in a wide variety of missions from geriatrics to genomics.

“Edith knew the impact that these investments would have over the lasting lifetime of our institution: support for leadership and research, enabling the recruitment and retention of outstanding faculty and enhancing their productivity. This incredibly creative philanthropy is likely to yield an enormous positive impact worldwide.”



William A. Peck, MD, director of the Center for Public Health, was the first Wolff Distinguished Professor, named in 2002, when he served as dean of the School of Medicine and executive vice chancellor for medical affairs. A noted clinician and researcher in bone and mineral metabolism, he served as founding president of the National Osteoporosis Foundation.

ROBERT BOSTON



THE WOLFF LEGACY ENDURES

Building excellence **Todd P. Margolis, MD, PhD**

“The amount of NIH [National Institutes of Health] support has been shrinking for the past 15 years. The core modular grant of \$250,000 hasn’t changed, it’s much harder to get a grant, and the buying power has decreased dramatically.

“If a researcher doesn’t get a grant, it takes nine months to turn around another submission — and so who covers the research in that interim? Even the best scientists in the world don’t always get the grant, and even if they do, it’s not going to cover the costs of research. So the way we need to do this is through philanthropy.

“My attitude about philanthropy is this: Whenever patients get a good result, they thank the physician. But what they are really thanking

are the physician’s skill and training and the research that allowed him or her to use the most modern methods — all of which need to be supported in one way or another.

“Philanthropy in medicine is absolutely critical. Institutions used to be able to make up the money from clinical services, but those days are pretty much gone. It’s very hard to do that the way insurance has gone and where health care is going.

“Endowed professorships and research funds — such as the ones the Wolffs established — allow us to offset some of the costs and recruit the best people and allow us to have funding for pilot projects and interim funding — bridge funding — for individuals, and it gives us some flexibility.”



Earlier this year, Todd P. Margolis, MD, PhD, was named chair of the Department of Ophthalmology and Visual Sciences and ophthalmologist-in-chief at Barnes-Jewish Hospital. Former president of the world’s largest eye and vision research organization, the Association for Research in Vision and Ophthalmology, his own research focuses on the herpes simplex virus and blindness. He was named a Wolff Professor in April.

ROBERT BOSTON



ROBERT BOSTON

Opening new avenues **Lilianna Solnica-Krezel, PhD**

“Philanthropic support for research is particularly important currently for many reasons. Number one is that we are witnessing an unprecedented potential for biomedical sciences right now. There are many technologic breakthroughs that allow us to ask questions that we were not able to ask before. They allow us to study diseases and now recognize the genetic codes of diseases that we were not able to do previously, and not at the rate we can do now.

“From the perspective of the Department of Developmental Biology, there are entire areas that relate to adult stem cells and embryonic stem cells that really open completely new avenues to study and understand birth defects, and to study aging and ameliorate the effects of aging. We are living in times of absolutely remarkable potential for biological sciences.

“We are witnessing financial limitations because federal funding for research is going down in all practical terms. This fiscal tightening in biomedical research discourages many young people from choosing science as a calling.

“Philanthropic support — such as the two endowed professorships in our department — becomes more crucial as the only means to provide support for imaginative high-risk, high-potential-payoff investigations that can transform the way we understand, diagnose and treat disease.

“Philanthropic support touches our department and all departments of Washington University. It is truly welcome — and we are so grateful for our donors — because it allows us to retain the most talented faculty and also allows these faculty to have freedom of investigation, to ask the most important questions and not be limited by the current fiscal constraints.”

Lilianna Solnica-Krezel, PhD, head of the Department of Developmental Biology, will be installed as a Wolff Distinguished Professor in November. Using advanced imaging and genetic techniques, she studies embryonic development in zebrafish models to better understand similar processes in human development.

1940s

William Anderson, MD 42, is retired in Williamsburg, Va., and enjoys reading and attending movies, plays and shows.

Clayton Manry, MD 44, is retired and living in Redwood City, Calif. His hobbies include gardening and orchid culture.

1950s

Irving Kushner, MD 54, is professor emeritus of medicine at Case Western Reserve University and served as a medical expert for the Social Security disability system. He spends his free time writing and reading and has published several articles recently.

Richard Aach, MD 59, and his wife are happy to have returned to St. Louis. In addition to attending Lifelong Learning Institute classes through University College, Aach enjoys photography, gardening and visiting the Saint Louis Art Museum. He was inducted into Clayton High School's Alumni Hall of Fame in May.

1960s

Gabriel Zatlin, MD 60, has retired from patient care and teaching medical students and residents. He and his wife, Jan, now enjoy spending time at their Connecticut home, watching the fauna and growing vegetables.

John Bigger, MD 64, is an active volunteer with local arts groups in South Carolina, including serving as president of the North Augusta Arts Council and as treasurer of the Arts and Heritage Center. He and his wife have 12 grandchildren.

1970s

James Hudson, MD 75, was the 2013 recipient of Alton Memorial Hospital's prestigious Chairman's Award. After more than 34 years, he has retired from the practice of ophthalmology in Alton, Ill., and now enjoys spending time with his four young grandsons.

Pamela McLain, MD 77, is symposium director for the North American Young Rheumatology Investigator Forum. Now in its eighth year, the forum promotes mentoring and networking with rheumatology fellows across North America. She is proud to note that fellows from Washington University have attended, presented their research and been given the best abstract award.

1980s

Chandlee Dickey, MD 89, is director of the Harvard South Shore Psychiatry Residency Training Program and assistant professor at Harvard Medical School. Since switching into education, she enjoys mentoring the residents and creating innovative teaching experiences.

Ellen Reynolds, MD 89, is medical director of the Department of Children's Surgery at St. Luke's Regional Medical Center in Boise, Idaho. In her free time, she is a swimmer, and holds national and world records for her age group with U.S. Masters Swimming.

1990s

Melissa Piasecki, MD 91, is the senior associate dean for academic affairs and a professor of psychiatry at the University of Nevada School of Medicine.

Grant Hoekzema, MD 94, was named chair of the Council of Academic Family Medicine for 2013-14. He recently completed a three-year term as president of the Association of Family Medicine Residency Directors. Hoekzema is program director for Mercy Family Medicine in St. Louis.

2000s

Kenisha Campbell, MD 04, is assistant professor of pediatrics, medical director of Adolescent Primary Care & Family Planning Services, and co-director of Adolescent Medicine Outpatient Rotation at Children's Hospital of Philadelphia.

She enjoys spending time with her son, staying active at the gym and playing tennis.

Elliott Weiss, MD 10, has been selected for the Penn Fellowship in Advanced Biomedical Ethics. He will work toward a Master of Science in Medical Ethics at the University of Pennsylvania while continuing his neonatology fellowship at the Children's Hospital of Philadelphia.

IN MEMORY

Rebecca Kay Acquisto, OT 99

Acquisto, 55, of Longmont, Colo., died Saturday, April 5, 2014, at the age of 55 from complications of a brain tumor. She attended Texas Women's University, where she graduated with honors before receiving a master's degree from Washington University. In her free time, Acquisto enjoyed beekeeping, backpacking, watercolor painting, gardening and knitting. Through her work and her personal life, she loved helping people, cherished her friendships and will be dearly missed. She mentored and supported many women over her lifetime.

Karen Arnold, MD 68, HS 69

Arnold, 72, of Mechanicsburg, Pa., and formerly of St. Louis and Belleville, Ill., died Monday, April 28, 2014. After attending the University of Notre Dame and receiving a medical degree from Washington University, Arnold proudly served in the U.S. Air Force as a physician. Afterward she returned to St. Louis where she was a general and vascular surgeon before retiring in 2002. Arnold then worked at FairCode Associates for more than eight years until her death. She was a faithful member of Saint Katharine Drexel Catholic Church where she served on the Women's Council and attended daily Mass.

Terrell Covington Jr., LA 40, MD 43

Covington died Sunday, April 13, 2014, at 95. After graduating from WUSM, he undertook a rotating internship as a second lieutenant in the U.S. Army Corps, eventually training as an officer following World War II. He went to North

Carolina to serve as a ward physician of a 1,200-bed temporary hospital overseen by the Jefferson Medical College treating the sick and injured soldiers from the Pacific Theatre. After nine months, he was transferred to Fort Belvoir in Virginia and became chief of medicine and headed the dispensary. In 1950, Covington moved to Tulsa where he dedicated his life to community development and projects related to health-care needs. He practiced at St. John Hospital for almost 50 years where he became chief of staff in 1971. Covington retired at the age of 80. He was very proud to watch his granddaughters, Emily, LA 12, and Anna, LA 12, receive their white coats in August 2013 as they began as WUSM students.

Eugene Crews III, MD 70, HS 74

Crews, of Atlanta, died Sunday, Feb. 23, 2014. He earned a medical degree and completed a psychiatric residency at WUSM. After service in the U.S. Navy, he was associate professor of psychiatry at the University of Alabama in Birmingham (UAB) and director of UAB Psychiatric Residency Training. Crews was inducted into the Missouri Athletic Hall of Fame in 1962 for shot put as a University City High School senior. He also was a Mystical Seven scholar-athlete at the University of Missouri-Columbia and inducted into its Hall of Fame in 2000.

Paul Cummings, MD 93

Cummings, of Portland, Ore., died Thursday, Feb. 13, 2014, of gastric cancer. He attended Willamette University studying science, math and humanities before pursuing training as a physician. After completing a medical degree, Cummings was awarded a fellowship at the University of Witwatersrand in South Africa, practicing both rural and inner-city medicine. He then completed an internal medicine residency at the University of Washington in Seattle. Cummings later worked for Legacy Health and focused on effective and best practices for patient care. He is remembered for his love of the outdoors, strong sense of family and one of his favorite sayings: "solvitur ambulando" (it is solved by walking).

Jack F. McKemie, MD 43

McKemie died Monday, April 29, 2013, at 95. After graduating from WUSM, he completed an internship at Barnes-Jewish Hospital and a residency at Children's Medical Center in Dallas before serving in the U.S. Army. He was a longtime pediatrician, first serving in Corpus Christi, Texas, and then at the Santa Rosa Hospital emergency room in San Antonio.

Charles Miller Jr., MD 52

Miller died Saturday, Oct. 19, 2013. After graduating from Washington University, he proudly served the Kirkwood community as a physician for 42 years.

Richard H. Morrow Jr., MD 58

Morrow of Baltimore died Saturday, Aug. 17, 2013, at 81 from pancreatic cancer. A professor in the Johns Hopkins Bloomberg School of Public Health since 1991, Morrow was a pioneer in the field of international public health. Prior to joining Hopkins, he established public health programs in Africa, taught at Harvard School of Public Health, and directed a tropical disease program at the World Health Organization in Geneva, Switzerland. He earned a bachelor's degree in economics from Swarthmore College, a medical degree from WUSM and a master's degree in public health from Harvard University. Morrow completed a residency at the Strong Memorial Hospital in Rochester, N.Y. He received the 2006 Lifetime Achievement Award from the American Public Health Association's International Health Section.

C. Barber Mueller, MD 42

Mueller died Thursday, Feb. 13, 2014, after a brief illness. He attended Blackburn College, graduated from the University of Illinois and received medical education at Washington University. He was a decorated World War II veteran, having served in the South Pacific. Mueller was in the first class of Markle Scholars, a Distinguished Fellow of the American College of Surgeons and chairman of surgery at the Upstate Medical Center in Syracuse, N.Y. Additionally, he was the founding chairman of the Department of Surgery at McMaster Medical Centre, and was always devoted to the cause of medical education.

David W. Talmage, MD 44

Talmage died Thursday, March 6, 2014, at the age of 94. Born in Korea to missionaries and spending his young life there, Talmage came to the U.S. and graduated from Davidson College in 1941 before attending Washington University for medical school. From 1945-47, he served as a medical adviser to the Korean government for the U.S. Army. He later served two internships, one at Georgia Baptist Hospital and the other at Barnes Hospital where he then completed a residency and fellowships between 1949 and 1951. Talmage had a distinguished career at the University of Colorado Health Sciences Center (UCHSC), the University of Chicago and the University of Pittsburgh. He served in many roles at these institutions, including professor, department chairman, associate dean of research affairs and dean of the faculty at UCHSC. He was elected to the National Academy of Sciences in 1976. Other awards include the Bonfils-Stanton Foundation Award, the Sandoz Prize for Immunology and two honorary Doctor of Science degrees. He also was a member of Phi Beta Kappa and Alpha Omega Alpha.

Ljubinka "Louise" Vojcanin, NU 50

Vojcanin died Thursday, March 6, 2014, at 86. Born in St. Louis, she graduated from Cleveland High School before attending the Washington University School of Nursing. Vojcanin served as a registered nurse at Barnes Hospital, Anheuser-Busch, Holy Cross Hospital, Nabisco Brands and in private practice. She was a past president of Holy Trinity Orthodox Church Choir, national secretary and historian of the Federation of Serbian Sisters Circles, and member of the Sisters Circles of the Myrrh-bearing Women of St. Sava Monastery, St. George (Schereville), St. John the Baptist (Bellwood), and Holy Trinity (St. Louis).

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



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No small achievement

Four-year-old Ian Rimer accepts a medical degree on behalf of his dad, Ryan, from Dean Larry J. Shapiro, MD, during the May 15 Commencement ceremony. Ryan, who has wanted to be a physician since he was 10, earned his long-awaited degree after previously working as a Nevada firefighter-paramedic. He remains in St. Louis for a diagnostic radiology residency at Barnes-Jewish Hospital. A father of four, he is married to Jamie Rimer, a postdoctoral researcher at the university.

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