

# Outlook



Washington  
University in St. Louis

SCHOOL OF MEDICINE

WINTER 2019-20

## Up in smoke

Vape crisis reverses progress  
on nicotine addiction



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**COVER** According to data from the Centers for Disease Control and Prevention, 1.5 million adolescents used e-cigarettes in 2017. By 2018, that number doubled to more than 3.6 million. Many are unaware of the very high nicotine levels in e-cigarettes, believing the products to be a healthy choice. See page 18.

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Researcher Anne Cross, MD, is working to change the face of multiple sclerosis care.

Timothy Yau, MD, center, an assistant professor of medicine, is an inaugural member of the Academy of Educators, which is training faculty in innovative, inspiring teaching methods. See page 12.

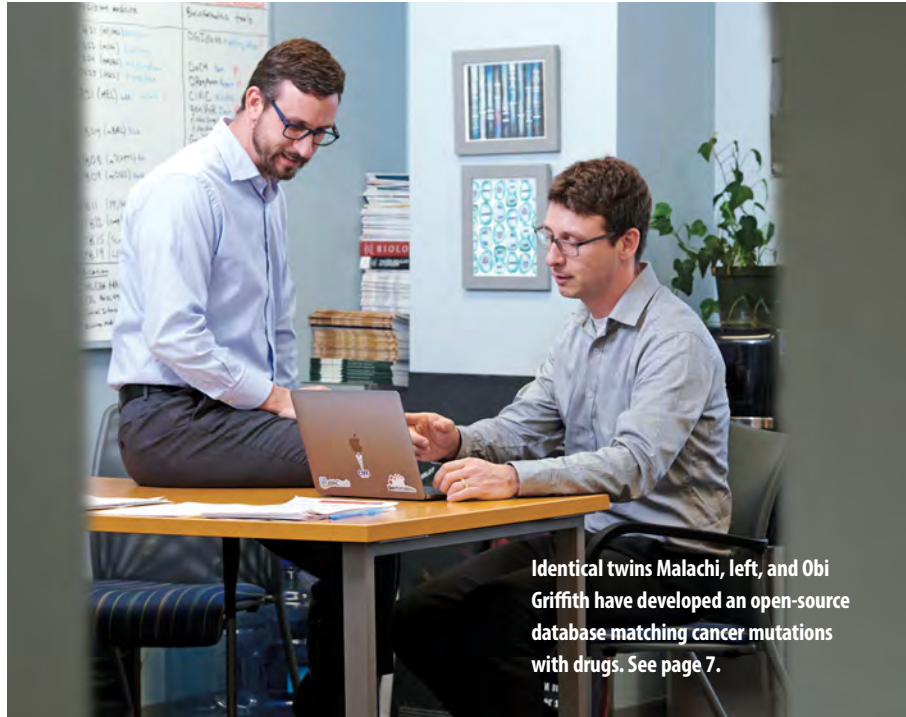


MATT MILLER

# Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU WINTER 2019-20



Identical twins Malachi, left, and Obi Griffith have developed an open-source database matching cancer mutations with drugs. See page 7.

TIM PARKER

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Anne Cross, MD, right, with her husband, DeWitte Cross III, MD, professor of radiology and neurosurgery, and son, Kevin, MD, a third-year neurosurgery resident at WUSM. See page 24.

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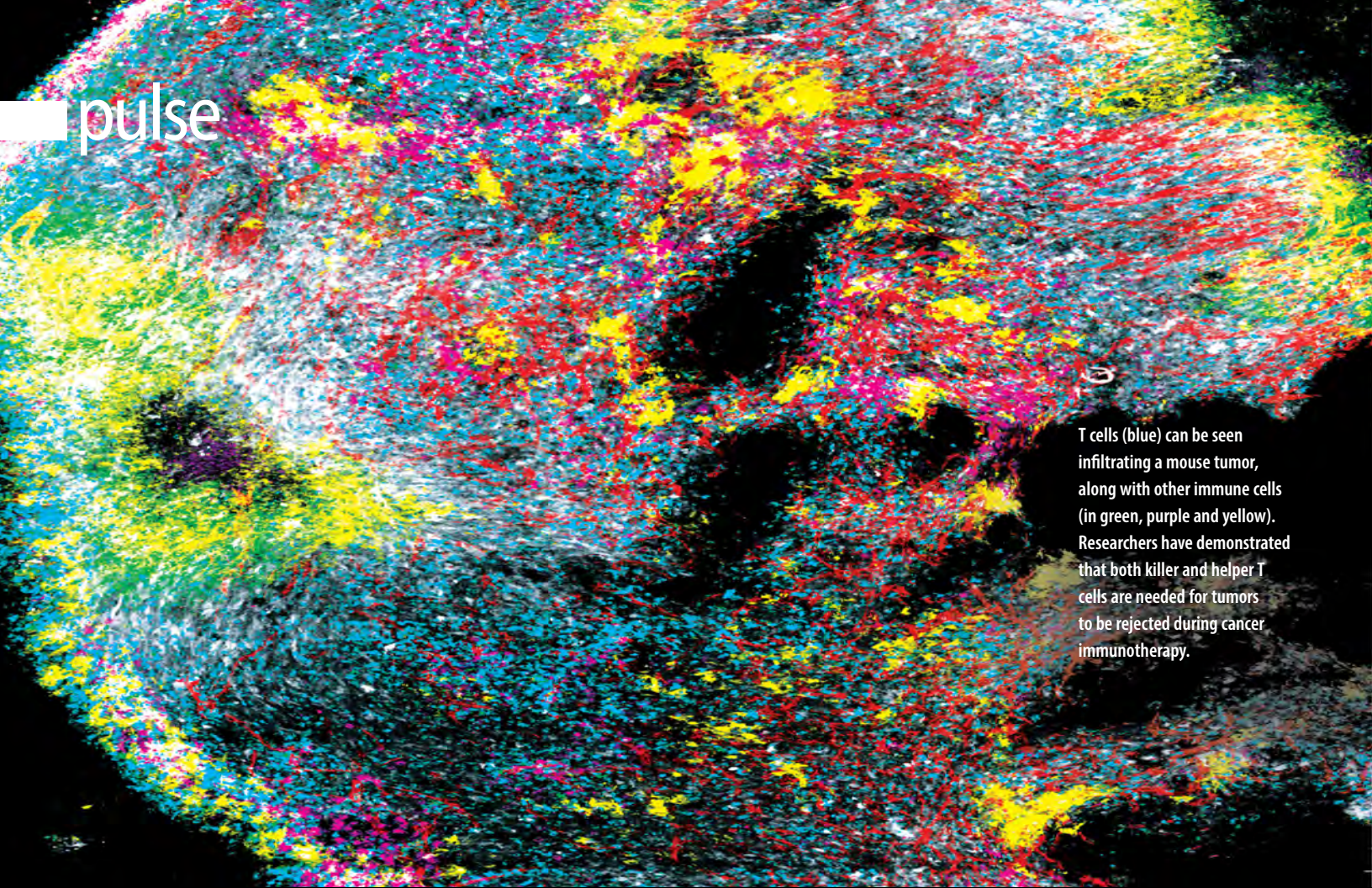
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T cells (blue) can be seen infiltrating a mouse tumor, along with other immune cells (in green, purple and yellow). Researchers have demonstrated that both killer and helper T cells are needed for tumors to be rejected during cancer immunotherapy.

# Clues to boosting immunotherapy

## Helper T cells appear vital to more robust anti-tumor response

**C**ancer immunotherapy drugs trigger the body's immune system to attack tumors and have revolutionized the treatment of certain cancers, such as lymphoma, lung cancer and melanoma. Yet, while some patients respond well to the drugs, others don't respond at all.

Immunotherapy still doesn't work for many patients, particularly for common cancers, such as breast and prostate.

A study, published Oct. 23 in the journal *Nature*, indicates a way for cancer immunotherapy to spur a more robust immune response. Such knowledge could lead to more effective cancer vaccines and immunotherapy drugs called checkpoint inhibitors. New research suggests that immunotherapy is likely

to be more effective when a vaccine is used alongside checkpoint inhibitors. The researchers studied mice with models of human cancer.

Much immunotherapy is designed to prompt immune cells called killer T cells to attack the cancer cells. But new research suggests that recruiting other T cells — called helper T cells — could boost effectiveness. Such helper T cells recognize cancer as a threat and recruit killer T cells to mount an attack. Without the helper cells, the immune system typically doesn't fully respond to fight cancer.

"This study reveals for the first time that helper T cells are essential in cancer immunotherapy," said senior author Robert D. Schreiber, PhD, who directs Washington University's Andrew M. and

Jane M. Bursky Center for Human Immunology & Immunotherapy Programs.

Schreiber's co-authors, including Maxim N. Artyomov, PhD, an associate professor of pathology & immunology, developed a computer program that can predict which mutant proteins — or antigens — on a patient's tumor will specifically activate helper T cells. This sort of predictive software is well-established for activating killer T cells. But until now, this was largely impossible for helper T cells.

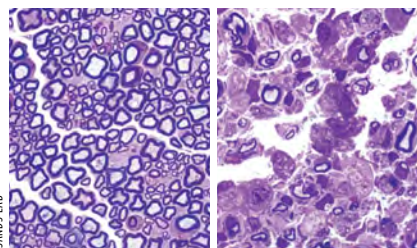
"We believe the technique that we've developed is an important step forward for harnessing helper T cells in cancer immunotherapy," said Schreiber, the Andrew M. and Jane M. Bursky Distinguished Professor.

# Cause of fatal disorder in children pinpointed

Scientists appear to have solved a decades-long mystery regarding a rare, fatal genetic disorder in children that results in seizures, developmental regression and death, usually around age 3. Studying a mouse model with the same human illness — called Krabbe disease — the researchers also identified a possible therapeutic strategy.

The research was published Sept. 16 in the Proceedings of the National Academy of Sciences.

Patients with Krabbe disease, also known as infantile globoid cell leukodystrophy, gradually lose the protective



SANDS LAB

A nerve in a normal mouse, left, and one with Krabbe disease. The disease erodes the protective layer of myelin and destroys nerves.

covering that insulates axons, the wiring of the nervous system. Scientists long have suspected that nerve insulation is destroyed because of a buildup of a toxic compound called psychosine. Patients with the inherited disorder are missing an

important protein involved in breaking down psychosine. The source of psychosine in Krabbe disease has been elusive.

“For almost 50 years, we have assumed the psychosine hypothesis was correct — that a toxic buildup of psychosine is the cause of all the problems,” said senior author Mark S. Sands, PhD, a professor of medicine.

Sands and his team, led by graduate student Yedda Li, proved the psychosine hypothesis correct by, essentially, giving the mice another genetic disease.

The scientists showed that mice harboring genetic mutations resulting in Krabbe disease and Farber disease, a lethal condition that results from the loss of a different protein, have no signs of Krabbe disease. The missing protein in Farber disease is called acid ceramidase, and when it is gone, psychosine does not build up, effectively curing Krabbe disease in mice that otherwise would have it.

The researchers gave mice with Krabbe disease a drug known to be an acid ceramidase inhibitor, modestly extending their lives. Inhibiting acid ceramidase too much, however, would cause Farber disease. Sands said he hopes researchers specializing in drug development will work toward a safe, effective acid ceramidase inhibitor for this disorder.

To learn more about stories in Pulse, go to [medicine.wustl.edu/news](http://medicine.wustl.edu/news)



MATT MILLER

**SOMETHING TO CROW ABOUT** No move would be complete without Macho, a taxidermy-preserved rooster that has held a place of honor in the Division of Nephrology for 42 years. Above, Director Benjamin Humphreys, MD, PhD, left, and Eduardo Slatopolsky, MD, professor emeritus, transport the 17-pound, formerly ornery (hence his name) rooster, to the division's new space in the McDonnell Medical Sciences Building. Over Macho's storied life, he produced powerful antibodies that were instrumental in developing a bone disease treatment for patients with kidney disease.

## BJC Investigators named

Carolina López, PhD, recognized internationally for her research on viral infections, and Jonathan Kipnis, PhD, a leader in how the nervous and immune systems interact in neurodegenerative, neuroinflammatory and neurodevelopmental disorders, are the third and fourth BJC Investigators, respectively.

López, an associate professor of pathobiology at the University of Pennsylvania School of Veterinary Medicine, will join the faculty in the spring of 2020. Kipnis, the Harrison Distinguished Teaching Professor and chair of the Department of Neuroscience at the University of Virginia in Charlottesville, will assume the new role July 1.

They join current investigators Helen McNeill, PhD, and Adam Kepecs, PhD.

BJC Investigators are recommended by a search committee of 42 leading School of Medicine scientists. The committee selects candidates who already have indelibly changed their fields and whose discoveries will result in new and fundamental shifts in scientific thinking. Eventually, the program will bring 10 highly regarded researchers to the School of Medicine and the life sciences ecosystem in St. Louis.



Carolina López, PhD



Jonathan Kipnis, PhD



## Fighting cancer in impoverished areas

The National Cancer Institute, part of the National Institutes of Health (NIH), has awarded \$7.6 million to Washington University to create a research center that will develop ways to implement proven cancer-control interventions among disadvantaged rural and urban populations in 82 counties in Missouri and central and southern Illinois.

The Washington University Implementation Science Center for Cancer Control will seek to eliminate cancer disparities with rapid-cycle studies that put findings into practice quickly. It will be led by a team of researchers affiliated with Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine and the Brown School on the Danforth Campus.

Rural Missouri and Illinois residents are a particular focus of the center because they have cancer mortality rates that are significantly higher than those in urban populations. Risk factors such as smoking and obesity are consistently higher for rural than for urban populations.

The region includes highly impoverished areas, all within three hours of St. Louis. In southeastern Missouri, five counties have the highest poverty rates and some of the highest cancer rates in the country. Several Illinois counties are at the bottom of the county health rankings in Illinois and nationally. Many are areas where more regular screening for breast and colon cancer, for example, could have profound impact.

The center will be co-led by Graham Colditz, MD, DrPH, the Niess-Gain Professor and director of the Division of Public Health Sciences in the Department of Surgery, and Ross C. Brownson, PhD, the Steven H. and Susan U. Lipstein Distinguished Professor of Public Health at the Brown School and at the School of Medicine.

## Scientists find timekeepers of gut's immune system

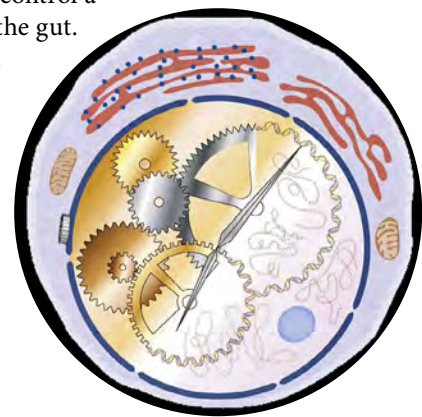
As people go through their daily and nightly routines, their digestive tracts follow a routine, too: digesting food and absorbing nutrients during waking hours, and replenishing worn-out cells during sleep. Shift work and jet lag can knock sleep schedules and digestive rhythms out of whack. Such disruptions have been linked to increased risk of intestinal infections, obesity, inflammatory bowel disease and colorectal cancer, among others.

Now, researchers have identified a type of immune cell that helps keep time in the gut. Such cells, known as type 3 innate lymphoid cells (ILC3), are responsible for keeping the intestine operating in a normal, healthy manner.

The researchers found that so-called clock genes are highly active in such cells and that the cells' production of immune molecules track with the activity of the clock genes. When the researchers eliminated a key clock gene from mice, the animals failed to produce a subset of ILC3 cells and struggled to control a bacterial infection in the gut.

"What we've found here is that circadian rhythms directly affect the function of immune cells in the gut, which could help explain some of the health issues we see, such as inflammatory bowel disease and metabolic syndrome," said senior author Marco Colonna, MD, the Robert Rock Belliveau MD Professor of Pathology and a professor of medicine.

The findings, published Oct. 4 in *Science Immunology*, suggest that targeting clock genes could affect immune cells and help counter the negative effects of erratic sleep schedules associated with intestinal illnesses.



An immune cell that helps set the daily rhythms of the digestive system has been identified by researchers. The findings open the door to treatments for digestive ailments targeting such cells.

# Protecting heart from damage after heart attack

Studying mice, scientists have shown that boosting the activity of specific immune cells in the heart after a heart attack can protect against developing heart failure.

The study could lead to therapies that reduce the risk of developing heart failure after a heart attack, severe viral illness or other cardiac injury. Damage to the heart muscle often causes progressive inflammation, a major driver of heart failure. The research was published Nov. 1 in the journal *JCI Insight*.

During a heart attack, blood supply to part of the heart muscle is cut off, starving the muscle of oxygen and leading to

the death of cardiac tissue. If the patient survives, the body's immune cells respond to the heart injury to get rid of dead tissue and begin healing.

"These specific immune cells — macrophages — eat up the dead cells damaged during the heart attack and stimulate the heart to repair itself, but if the macrophages stick around too long, they become inflammatory and drive the damage that leads to heart failure," said senior author and cardiologist Abhinav Diwan, MD, an associate professor of medicine.

The researchers have found a way to supercharge these macrophages, increasing their abilities to digest and dispose of damaged heart tissue. The key is in stimulating specialized sacs called lysosomes, which are inside immune cells. Digestion and waste disposal take place inside lysosomes.

The researchers activated a molecule — called TFEF — spurring heart macrophages to make more lysosomes. The researchers plan to investigate various small molecules as potential drug therapies.

## Division of Physician-Scientists established

**T**he School of Medicine has established a Division of Physician-Scientists to nurture the career development of physicians who treat patients and also want to conduct research.

Physician-scientists are crucial to developing approaches to diagnosing and treating disease. According to the Physician-Scientist Support Foundation, the proportion of physicians who conduct basic and laboratory research has dropped to 1.5% of the overall physician workforce.

The division will be headed by Wayne M. Yokoyama, MD, the Sam J. Levin and Audrey Loew Levin Professor of Arthritis Research. Yokoyama, also an associate dean, will continue leading the university's highly regarded Medical Scientist Training Program, which allows students to earn both an MD and a PhD in a scientific field.

The division encompasses two new programs: the Physician-Scientist Investigator Initiative and the Burroughs Wellcome Fund (BWF) Physician-Scientist Institutional Award project. It also will serve as a central resource

for other postgraduate physician-scientist training efforts across the Medical Campus.

The Physician-Scientist Investigator Initiative will target MD and MD/PhD researchers who are approaching or are already at the associate or full professor rank and have an elite track record of research contributions and funding. The School of Medicine has committed \$40 million to recruit such candidates. With seed funding from this commitment, the clinical departments will aim to attract the most talented physician-scientists in the U.S. and abroad.

Established with a \$2.5 million grant, the BWF Physician-Scientist Institutional Award program is aimed primarily at MDs as part of their initial faculty appointments to the school's clinical departments. The BWF award provides seed funding over five years that will help allow for stipends, pilot project funding, loan repayment, mentoring and enrichment activities. The School of Medicine and its departments plan to bolster the program with an additional \$6.6 million.



Wayne M. Yokoyama, MD

"A common perception is that earning an MD/PhD is the only route toward becoming a physician-scientist," Yokoyama said. "One of the goals of this new division is to show alternative routes for combining patient care and research."

The division also will endeavor to recruit, train and retain people who are underrepresented in the physician-scientist pool, including women and persons of color.



MATT MILLER

**ADDRESSING COVERAGE GAPS** School of Medicine doctors went door to door, collecting signatures to get Medicaid expansion placed on the 2020 statewide ballot. Expanding Medicaid, they say, would help deliver health-care coverage to vulnerable citizens and bring billions of Missouri’s tax dollars home from Washington.

## New round of sequencing incorporates human diversity

The School of Medicine and collaborating institutions will share \$29.5 million from the National Institutes of Health (NIH) to improve the accuracy and diversity of the reference human genome sequence. The new Human Pangenome Reference Sequencing Project will better reflect the spectrum of human diversity.

The project continues the legacy of the McDonnell Genome Institute, which played a major role in the original Human

Genome Project, completed in 2002. The institute contributed 25% of the genetic data needed to spell out — in order — all 3.1 billion units of DNA that make up the human genome.



GETTY IMAGES

“The original human genome is from a few volunteers,” said Ting Wang, PhD, the co-lead principal investigator and the Sanford C. and Karen P. Loewentheil Distinguished Professor of Medicine. “And for many parts of the reference genome, the sequence is from only one individual.

“The goal of this new round of sequencing for the human pangenome project is to incorporate human diversity,” said Wang, also a professor of genetics. The collaborators will perform whole-genome sequencing of 350 individuals from different racial and ethnic backgrounds.

## Discovery could propel universal flu vaccine

An antibody protects mice against a wide range of lethal influenza viruses, according to a study from Washington University School of Medicine, Icahn School of Medicine at Mount Sinai in New York City and Scripps Research in La Jolla, Calif. The antibody could serve as a template to aid in designing a universal vaccine that protects against all strains of the virus, and a drug to treat and protect against severe cases of flu, including those caused by pandemic strains. The research was published Oct. 25 in *Science*.



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Co-senior author Ali Ellebedy, PhD, an assistant professor of pathology and immunology at Washington University, discovered the antibody — an immune protein that recognizes and attaches to a foreign molecule — in blood taken from a patient hospitalized with flu at Barnes-Jewish Hospital in the winter of 2017.

The antibody attaches to neuraminidase, a protein essential to flu virus replication that cuts newly formed viruses free of infected cells so they can move on and infect new cells. Tamiflu, the most widely used drug for severe flu infection, inactivates neuraminidase.

Antibodies from the sample, researchers found, blocked activity in all known types of neuraminidase in flu viruses. The researchers tested the antibodies in mice given a lethal dose of influenza virus. The antibodies were effective against many strains, and one antibody — called 1G01 — protected mice against all 12 strains tested, representing all three groups of human flu virus, as well as avian and other nonhuman strains.

The researchers are developing treatments and vaccines for influenza based on antibody 1G01, which Washington University has patented.

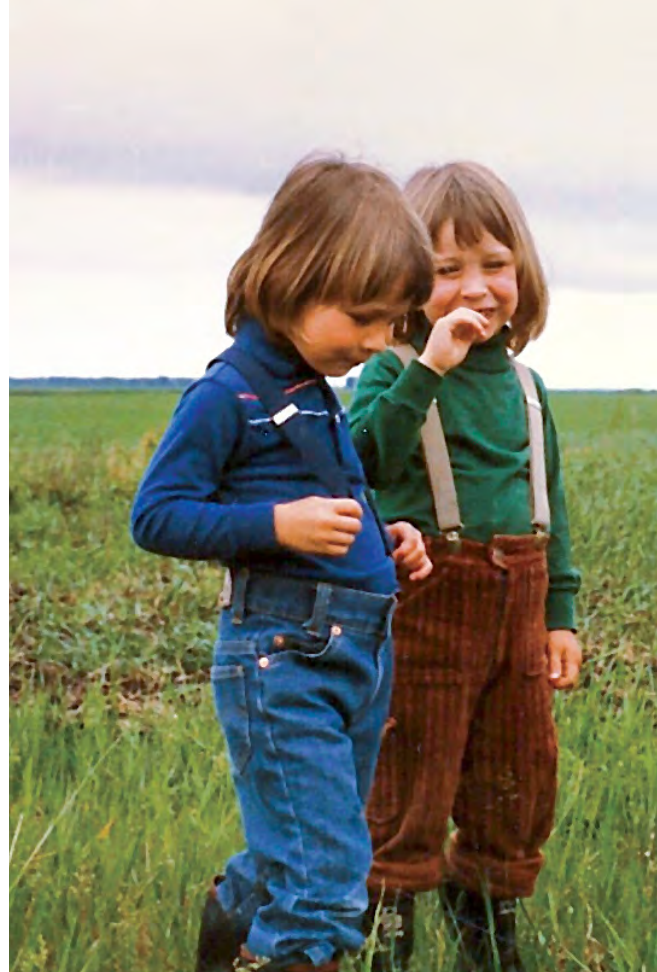


# Personal toll

**Mother's death sets twin scientists on  
journey to find precision cancer therapies**

BY JULIA EVANGELOU STRAIT

Avid explorers Malachi, left, and Obi Griffith in Peru before starting PhD studies. An earlier gap year helped them process their mother's death.



heir mother's death when they were teenagers set identical twins Obi and Malachi Griffith on a shared path to find better cancer therapies.

Today, the twins, both geneticists and computational biologists at the School of Medicine, are seeking precision treatments for the disease. The Griffith Lab, driven by the twins' independent and complementary research interests, is a large team of biologists, bioinformaticians, computer scientists and software engineers.

One of the lab's key developments is a free, open-source database that matches cancer mutations found in patients' tumors with drugs targeting such genetic errors. The database, called CIViC, stands for Clinical Interpretations of Variants in Cancer. With CIViC, doctors treating unfamiliar forms of cancer can quickly comb the available medical research to find insights for their patients.

The Griffiths compare CIViC to the online encyclopedia Wikipedia, which similarly is maintained and updated by volunteers. Anyone can create an account and contribute information to the CIViC database. Experts in the field serve as CIViC editors, curating data that is incorporated into the system.

Maintaining up-to-date, comprehensive information about genetic mutations — and what those mutations may mean for patients — is a major bottleneck to improving cancer care.

“Often, doctors have some genetic information about a patient's tumor, but it's not clear what that might mean for treatment,” said Obi Griffith, PhD, an associate professor of medicine and of genetics. “Searching the scientific literature is time-consuming, and important data could be missed.

“The purpose of CIViC is to streamline and automate that process,” he added. “It's a resource that can help clinicians determine the specific type of cancer a patient has, the prognosis and, in some cases, identify a drug that has the potential to help the patient.”

CIViC users span 163 countries. Many opt to receive automated CIViC updates so they can be incorporated into diagnostic or clinical workflows.

The National Cancer Institute of the National Institutes of Health (NIH) recently provided \$3.7 million in new support for the database project.

It's easy to wonder whether the existence of a tool like CIViC could have helped the twins' mother 23 years ago.



COURTESY OF OBI AND MALACHI GRIFFITH

## Overcome by grief

The Griffiths grew up on a tree farm in Manitoba, Canada, and spent free time helping their father run his landscaping business. Their childhood and early teenage years were lived outdoors, with lots of canoeing, hiking and fishing, and attending the occasional summer science camp.

Their world was shaken during their junior year of high school, when their mother was diagnosed with breast cancer. She was treated with the standard care available at the time. The treatment was not effective, and she died just weeks before their high school graduation.

“We were in a state of shock,” said Malachi Griffith, PhD, an assistant professor of medicine and of genetics. “I think our father felt like college would be a good distraction. It was sort of a heads-down, get-to-work approach to grieving, which has pros and cons.”

Obi added, “We did well that year academically, but it was miserable.”

Relatively soon after her death, other family members were diagnosed with different forms of the disease. A cousin developed Burkitt lymphoma, a form of non-Hodgkin’s lymphoma. And a stepbrother was diagnosed with Ewing sarcoma, a bone cancer most commonly found in rapidly growing teenagers.

Cancer, although quickly fatal for the twins’ mom, was curable for their cousin and stepbrother. Why were the outcomes so different? This question would haunt them. As early undergraduates — before they had the education and skills for that question to crystallize in their minds — the brothers realized they needed a break.

“It’s hard to focus on complicated intellectual tasks, like getting a degree in biochemistry, when you’re really distracted by grief,” Malachi said. “We needed time to reset, so we took a gap year after our first year of college. As far as personal and emotional healing, the break was extremely important.”

Obi added, “A lot of adults around us questioned whether it was a good idea. But we didn’t share their concerns.”

With two high school friends, Obi and Malachi left the University of Winnipeg and drove west across Canada and north to the Yukon Territory, where they fished and hiked and canoed several hundred miles down the Teslin River. Over the next year, they made their way south down the Pacific Coast to Mexico, where they explored archeological sites and swam in the ocean.

“It was a great experience — playing chess in an orange camper van on some paradise beach in the middle-of-nowhere Mexico,” Malachi said. “But we were living on rice and beans and working odd jobs for gas money, so it didn’t take long to recognize that it was important to return to our studies. Still, for anyone dealing with traumatic loss — if you can swing it — I highly recommend that kind of reset.”

## Embracing bioinformatics

The brothers returned to the University of Winnipeg and finished their biochemistry bachelor’s degrees with what seemed to be unfortunate timing. It was 2002, and the so-called “dot-com bubble” had

*“It’s hard to focus on complicated intellectual tasks, like getting a degree in biochemistry, when you’re really distracted by grief.”*

*– Malachi Griffith, PhD*

**Far left: The twins’ mother, Rhéa, died of breast cancer the year they graduated from high school in Beausejour, Manitoba.**

**Obi, left, Malachi, center, and stepbrother, Alex, who later was diagnosed with cancer. Alex survived the disease.**



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**Today, Obi, center left, and Malachi lead a project to develop a crowdsourced cancer mutation database aimed at helping doctors match cancer patients to the best treatments for their tumor types.**

burst, flooding the job market with skilled biotechnology workers all looking for employment.

The twins began to realize they would need more education and started discussing this “new thing” called bioinformatics. After an internet search for the term, Obi zeroed in on Vancouver.

“Steven Jones was doing bioinformatics work at the British Columbia (BC) Cancer Agency,” Obi said. “So I gave him a call. He listened to my background and offered me a job. He remains head of bioinformatics there. Even now, it’s hard to find people with a specific bioinformatics background. The field is basically looking for people who understand genetics and biology and aren’t afraid of computers.”

Malachi soon got a job at the BC Cancer Agency in a similar informal fashion. In the early 2000s, at the height of the Human Genome Project’s race to sequence the complete DNA of the human genome, the fields of genomics and bioinformatics were just taking off. The Griffiths consider themselves fortunate to be among the first people hired by the BC Cancer Agency as its bioinformatics research group was rapidly expanding.

Then, cancer struck again: Malachi’s supervisor was diagnosed with a brain tumor. He managed to survive against seemingly impossible odds.

“At some point not terribly long ago, all of these cancers — breast cancer, Ewing sarcoma, Burkitt lymphoma, brain tumors — all of them were a death sentence, and many still are,” Malachi said. “We’re making progress, but still, why can we stop some tumors but not others?”

Ultimately, the question would bring them to Washington University. The Griffiths had completed doctorates in medical genetics at the University of British Columbia, Vancouver, and conducted postdoctoral research in Vancouver and Berkeley, Calif. For the Griffiths’ next move, Washington University offered three crucial advantages: cutting-edge genomics with big data sets; top computer science and bioinformatics specialists; and an affiliated cancer hospital treating patients — opening the door for new discoveries to impact patient care.

## A lifesaving clue

After joining the School of Medicine, the twins learned that a young, fellow cancer researcher, Lukas Wartman, MD, was battling a recurrence of the disease he now studies, acute lymphoblastic leukemia (ALL). In a race against time, this relapse prompted an ensemble team to harness all the tools and skills it had been building to save lives.

Wartman had been diagnosed with ALL while still a Washington University medical student. A first round of chemotherapy led to a five-year remission. He graduated in 2005 and undertook an internal medicine residency and hematology/oncology fellowships. A relapse in 2008 was treated with a bone marrow transplant from a matched donor, and that remission lasted until 2011, when he relapsed a second time.

A second relapse in adult ALL is usually incurable and quickly fatal. But Wartman joined a research protocol led by Timothy Ley, MD, the Lewis T. & Rosalind B. Apple Professor of Medicine, who was conducting genomic sequencing of patients with lymphoid cancers.

Whole-genome sequencing and the sequencing of the protein coding regions of Wartman's cancer's DNA did not reveal any routes to therapy. Sequencing of RNA — a close chemical relative of DNA — provided a clue: one protein, while normal in its sequence, was being produced by the tumor in far higher amounts than normal.

"At the time, I was trying to automate and streamline different kinds of genomic analyses, combining DNA and RNA sequencing data, along with many computational approaches for interpreting these data," Malachi said. "We wanted to look at genes that were outliers inside this tumor. I remember sending an email summary of that case around to the leading investigators. I didn't see any mutations, but there was one gene — FLT3 — that was extremely highly expressed. Tim Ley wrote back within a few minutes, saying that we should dig further — as this finding could be important."

FLT3 had never been implicated in ALL but was widely known to drive kidney cancer and other tumor types. And there was a drug to treat it. Based on this analysis, Wartman began taking the

drug sunitinib, a FLT3 inhibitor. Wartman, MD, now an assistant professor of medicine, has described the result as miraculous and lifesaving.

The result is precisely the kind of discovery that the Griffiths hope to make more common for cancer patients who have run out of options.

The early work that led to Wartman's lifesaving treatment — in automating and streamlining genomic analysis — has expanded and grown into CIViC.

More recently, the Griffiths started working with their colleagues to design personalized cancer vaccines. Using genomic analysis and bioinformatics, they are predicting which misshapen proteins (characteristic of a specific patient's tumor) will be most likely to trigger T cells to mount a powerful immune response.

"There are now seven clinical trials going on at Washington University looking at various personalized cancer vaccines, including for breast and brain cancers," Obi said.

"Expanding the CIViC knowledge base and developing cancer vaccines are two very different approaches to personalized treatments for cancer," he added, "but they both harness the genomics and bioinformatics tools that we're working to build, in an effort to help more patients." ☐

*Julia Evangelou Strait is a senior medical sciences writer in Medical Public Affairs.*

## CIViC Advancing cancer precision medicine with community collaboration



### Genetic mutations

Many cancers are driven by mutations in the genome — mistakes in the DNA — of specific cells. Increasing numbers of cancer patients have access to some kind of genome sequencing analysis of their tumors to identify mutations.



### Sequencing data

Likewise, doctors have increasing access to genetic information about the mutations in a patient's tumor, but it's often not clear what that might mean for treatment.



### Targeting drugs

CIViC is a resource that can clarify which mutations might be meaningful to a patient's care, including defining cancer type, prognosis and, in some cases, identifying a drug that could help the patient.



### Doctor to patient

This free online resource could help doctors bypass the bottleneck in maintaining up-to-date, comprehensive information about genetic mutations and their implications, so that patients can receive better care no matter where they are treated.

To learn more about the cancer variants database, visit [civicdb.org](http://civicdb.org).



# We are the academy



Teaching support, resources ramp up  
in advance of curriculum renewal

BY KRISTINA SAUERWEIN

In less than a year, the School of Medicine will debut a new curriculum — known as the Gateway Curriculum — focused on emerging technologies, integrated community outreach programs, student health and wellness, and educational instruction that incorporates research-based best practices.

The latter poses a particular challenge in revising the curriculum, said Eva Aagaard, MD, the senior associate dean for education, who is leading the effort. “Modern medical education in the U.S. faces two big obstacles: Many of those entrusted with training future doctors have little or no training in education. Secondly, the material they’re supposed to teach students and residents looks almost nothing like what they learned as medical trainees.”

Assistant Professor Kari Allen, PhD, leads first-year students in their final day of dissection in anatomy class. Allen is one of 42 inaugural members of the Academy of Educators.

MATT MILLER

**E**nter the Academy of Educators, an inaugural cohort of 42 faculty members exemplifying high achievement in education. Formed earlier this year through the Office of Education, the academy will strive to build a community of physician and science educators, as well as train faculty in new, innovative and inspiring ways to teach in an academic medical setting. The academy supports faculty engaged in all aspects of education on campus — those teaching MD students, graduate students, residents and fellows, and trainees in the programs in Physical Therapy, Occupational Therapy and Audiology and Communications Sciences.

“Faculty professional development is a critical component of curriculum renewal,” said Aagaard, also the Carol B. and Jerome T. Loeb Professor of Medical Education. “Since the last curriculum update 20 years ago, the medical field has been transformed by technology and scientific discovery.

“At the same time, research-backed knowledge about how best to teach physicians-in-training has increased significantly. All of these changes have come at us rapidly and drastically. The academy will help us keep pace with the changes while also positioning us at the forefront of medical education.”

The current curriculum requires students to learn basic sciences in classroom or observational settings for the first two years and hands-on patient care in the last two. But with technological advances and research extolling the benefits of immersion learning, a better scenario may be integrating science and patient care all four years — requiring a significant educational shift.

“Change isn’t always easy, but support from leadership, faculty and students has been amazing,” Aagaard said. “They *want* to innovate. They *want* to learn. They *want* to change.”

Several years under development, the academy’s purpose isn’t just to support the curriculum revision, but also to exist as a vital, ongoing professional resource. The academy is implementing pathways for faculty at every stage of the career: foundational skills for teachers starting out, more advanced skills for those who are further developing as educators, and



**Mary Klingensmith, MD**

leadership skills for those who want to help shape the school’s educational mission.

The academy offers something for everyone — from those who would like to brush up on tips, to those who want to take a deep dive in educational research and instructional design. Options include faculty certificate training programs in education, workshops and seminars on pedagogy, mentorships and networking opportunities, award and recognition ceremonies and, by early 2020, small grants for medical education research or pilot projects.

Leading the academy is Mary Klingensmith, MD, the Mary Culver Distinguished Professor and vice chair for education in the Department of Surgery. Klingensmith has achieved national distinction for nearly 30 years of work in medical education and innovation at Washington University and as president of the Association for Surgical Education and as chair of the American Board of Surgery, among other roles.

“The Academy of Educators lets me focus on one of my greatest passions: medical education,” Klingensmith said. “As the medical field continues to evolve with technology, scientific advancements and other factors, our students and trainees have an enormous amount to learn. By having a network of faculty who can provide instructional development to other faculty, we expect to see more innovative teaching methods across the medical school campus.”

One academy member is Justin S. Sadhu, MD, MPHS, an assistant professor of medicine in the Cardiovascular Division and co-director of a cardiovascular course for medical students. He is applying what he’s learned to revamping curriculum on the electrocardiogram (EKG), a low-cost, widely available diagnostic and screening test. National studies have shown that medical students struggle with EKG interpretation, he said.

“The academy represents a bold commitment to recognize and promote excellence in medical education as an integral part of the School of Medicine’s academic mission,” he said.

## Teaching Scholars Program

Sadhu recently completed the academy’s Teaching Scholars Program. This yearlong certificate program, launched in fall 2018, is geared toward established faculty who want to develop as future leaders in health-care education. Topics include curriculum and instructional design, educational





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program evaluation, educational research and scholarship, and leadership/change management in education. Participants attend twice-monthly seminars, complete a project under faculty mentorship and give a capstone presentation. The program launched its second class in fall 2019.

“The program has been invaluable and transformative,” Sadhu said. “We have learned so much from each other as we discussed innovative approaches to curriculum and academic instruction. The academy’s programs inspire us to be better educators.”

Steve Taff, PhD, associate professor of occupational therapy and of medicine, directs the Teaching Scholars Program. Physicians are experts in their field, he said, but that expertise may not translate into excellence as an educator.

“There is a critical need to prepare faculty at all stages of their career to be effective educators. Not only are these faculty learning new concepts and skills, they have also created a community of learners where they can discuss innovations in teaching, challenges in leadership roles and vet ideas for educational scholarship.”

## Foundations in Teaching Skills

A certificate program, Foundations in Teaching Skills, is geared toward junior educators who are one to five years out of medical training. Launched in fall 2019, the yearlong program includes a retreat and workshops examining successful teaching strategies. Participants receive mentorship and feedback on their teaching skills after being observed in the learning environment five times.

“For faculty starting their careers as educators, learning foundational skills can help launch their careers in medical or health sciences education,” said Dominique Cosco, MD, program director and an associate professor of medicine.

“What may be more important, though, is connecting to fellow faculty who are interested in and focused on education,” Cosco said. “This encourages them to support one another, share teaching methods and collaborate on innovations and projects. In turn, the academy offers mentorship and guidance to faculty beginning their careers in medical education.”

**Thomas De Fer, MD, professor of medicine and associate dean of medical education, is an inaugural academy member helping to foster a culture of educational excellence. Here, he teaches third-year medical students.**

The Gateway Curriculum website is continuously updated: [sites.wustl.edu/gatewaycurriculum](https://sites.wustl.edu/gatewaycurriculum).

For more information about the academy and related programs, visit [education.med.wustl.edu](https://education.med.wustl.edu).



# New design studio undergirds curriculum

Kenan R. Omurtag, MD, uses the studio's light-board to explain the diagnosis and treatment of infertility. The tool allows instructors to face viewers while writing on the board.

**N**ear-empty lecture halls increasingly greet faculty at medical schools nationwide. And while much hand-wringing has occurred about the growing number of students and trainees who prefer digital learning, the School of Medicine is embracing it.

In September, it debuted the Instructional Design Studio. Located in the lower level of Bernard Becker Medical Library, the 700-square-foot space includes a formal sound-proof video-recording studio with greenscreen technology, as well as a smaller do-it-yourself studio. The studios support high-quality, faculty-directed video resources to enhance student engagement with course materials.

"Video-based education flows seamlessly into our curriculum renewal plans," said Eva Aagaard, MD, the senior associate dean for education. "Not only has technology transformed our instructional capabilities, but it has been an integral part of most students' lives from an early age.

"Instead of focusing on how to get the students to attend in-person lectures and courses, we want to meet the students where they are today," she added.

A 2017 report by the Association of American Medical Colleges found that about one-quarter of

the 1,347 second-year medical students surveyed acknowledged "almost never" attending lectures — a trend that increases each year.

"There are some topics where it makes sense for students to focus their time and energy on using video as their primary learning resource," said Carolyn Dufault, PhD, assistant dean for educational technology and innovation in the Office of Medical Student Education.

This also could enable faculty to use their expertise in more effective ways. "By flipping content that was previously a one-way push of information into a more efficient, shorter video-based format, the goal is to have faculty available to work directly with students in active learning sessions," Dufault said. "Active learning is going to be key in our new curriculum."

Educational leaders are systematically going through the curriculum looking for ways it can be enhanced through dynamic, clinically relevant videos, and encouraging faculty members to think about similar opportunities.

"We are just at the beginning of a critical transformation of how and why we deliver parts of our curriculum through video resources," Dufault

*“Instead of focusing on how to get the students to attend in-person lectures and courses, we want to meet the students where they are today.”*

*– Eva Aagaard, MD*

said. “While more medical schools realize that students choose to watch videos rather than attend lectures, few have a studio and dedicated resources to develop and produce educational videos.”

The team — including Matt Rice, a veteran videographer, and Erin Morris, an educational specialist and instructional designer — has worked with faculty on videos already in use.

One is a second-year course called Clinical Topics in Otolaryngology, taught by Joseph P. Bradley, MD, an assistant professor of otolaryngology. With the studio’s guidance and resources, Bradley helped transform an auditorium lecture presented with a standard slide deck into a video that includes examples of a real-life patient with his occupational therapist discussing age-related voice changes.

The video also shows an audiologist administering a standard hearing test and evaluating hearing aids, which students would have learned abstractly as it is impractical for 125 students to observe the procedure in an audiology testing booth.

“Students can see what really happens during a hearing test instead of listening in a detached manner,” Bradley said.

Another is a second-year course on infertility taught by Kenan R. Omurtag, an associate professor of obstetrics and gynecology. “The videos supplement assigned readings and allow me to deliver content that is more attuned with the ways content is consumed these days,” he said.

The studio team will build a video repository that broadly appeals to many learners,

incorporating clinical skills demonstrations, standard protocols and refresher material.

“In the not-so-distant future, I envision video resources being available for just-in-time learning or re-learning,” Dufault said. “For example, if first-year students see a video related to performing an abdominal exam, the hope is that they will watch it again, as needed, in later years when they are on clinical rotations and that information is newly relevant.”

The library will grow and change in real time with the curriculum. Tracking analytics will allow ongoing improvement.

“Our analytics capabilities are going to be a game changer,” Dufault said. “Are students watching the full video? Skipping sections? If so, we can look to see what was happening there. Likewise, if we see large numbers of students re-watching a given segment of video, we may have evidence of an area that needs clarification or unpacking.

“The goal is to expand the depth, meaning and dimension of the already outstanding educational experience we provide students.” □

*Kristina Sauerwein is a senior medical sciences writer in Medical Public Affairs.*



MATT RICE

The Instructional Design Studio includes a sound-proof recording studio and greenscreen technology that makes it easier to import backgrounds. Studio team members are helping faculty elevate presentation materials.



# E-cig epidemic

**Addictive vape products surge in popularity  
among teenagers**

BY RICHARD H. WEISS, SALLY J. ALTMAN AND DEB PARKER

Pediatric pulmonologist Thomas Ferkol, MD, had long been suspicious of the safety claims made for electronic cigarettes. But until a few years ago, vaping had not riveted his attention. Ferkol's focus is on children, and he assumed the devices were for adults trying to kick their addiction to combustible (tobacco) cigarettes.

"I did not truly understand the problem until I was talking with the mother of a child with asthma," recalled Ferkol, the Alexis Hartmann Professor of Pediatrics at the School of Medicine. "I asked if anyone in the family had been using e-cigarettes. The mother was surprised by the question, saying I was the first physician who had ever asked."

The mother reported no one in the family used the devices but added that she was a teacher in a suburban school district and that e-cigarettes were a huge problem in her class. She had a drawer full of devices she had confiscated from her students.

Afterward, Ferkol began to review the medical literature and made a stark realization: "We were in the midst of a growing epidemic of nicotine addiction in children and adolescents," he said. "We did not fully grasp what these products were doing to their lungs, and no one was talking about it."

In international advocacy roles, pediatric pulmonologist Thomas Ferkol, MD, has been sounding the alarm again and again about the youth vaping epidemic.



MATT MILLER

**F**erkol was not the first to recognize the problem. But because of his prominent role in the American Thoracic Society and his relationship with other professional organizations worldwide, he knew he had a better opportunity than most to warn others about the threat e-cigarettes posed to teenagers.

That was four years ago. Since then, Ferkol has spoken frequently about the growing epidemic of e-cigarettes with youths, sounding the alarm again and again. On behalf of the Forum of International Respiratory Societies (FIRS), a collaborative of global respiratory disease experts, he was first author on a position statement about the threat of e-cigarettes to adolescents.

Ferkol and other School of Medicine physicians are aghast at how quickly vaping has taken hold among adolescents after a charmed decade when young people were turning away from combustible cigarettes.

“What we are hearing now is really alarming,” said Patricia Cavazos, PhD, an associate professor of psychiatry. She has studied the impact of e-cigarette marketing on youth as part of addiction research supported by the National Institute on Drug Abuse.

According to data from the Centers for Disease Control and Prevention (CDC), 1.5 million adolescents were using e-cigarettes in 2017. By 2018, that number more than doubled to 3.6 million. “The data show that one in five middle schoolers and one in three high school students are vaping,” Cavazos said.

*\*CDC statistics, as of December 2019.*

Concern began to rise with reports of mysterious lung infections that were sending young people to emergency rooms. The CDC has linked vaping to 2,291\* cases of lung damage illnesses and 48 deaths. While the cases are still being investigated, doctors nationally are suggesting that the injury pattern and tissue damage resemble a chemical burn or toxic chemical exposure injury. The condition is now known as EVALI (e-cigarette, or vaping, product use-associated lung injury).

People also use e-cigarettes to smoke marijuana, and black-market products containing tetrahydrocannabinol (THC) have emerged as a primary suspect in the injuries. In November, the CDC reported vitamin E acetate as a chemical of concern in EVALI. The sticky additive is used as a thickening agent in THC vaping products.

The cannabis issue aside, researchers say that it may take 20 years to fully discern the effects of inhaling heated e-cigarette liquids.

The battery-operated devices include a reservoir for holding liquid that typically contains nicotine, a heating element or an atomizer, and a mouthpiece. It heats the liquid into an aerosol that is inhaled by the user.

The enormous variability in the product category — with differing chemicals, devices and nicotine levels — makes public health recommendations challenging.

E-cigarettes do contain far fewer toxins than combustible cigarettes. However, Ferkol said, electronic cigarette aerosols are not simply

“harmless water vapor,” but contain noxious and potentially harmful ingredients, including ultrafine particulates, volatile organic compounds and heavy metals, such as nickel, tin and lead.

“Other reports have shown that these products can be contaminated with bacterial and fungal toxins. It is quite possible that recent respiratory complications are related to existing or newer chemicals or flavorings, some known to be injurious to the lung,” he said.

Still, the number of people vaping is increasing markedly — and not because of the original intent: to wean adult smokers off combustible cigarettes. Youth and young adults use e-cigarettes more than any other age group.

An e-cigarette brand called JUUL launched in 2016 with a novel nicotine formulation, assorted flavors and a stealthy device. Sales among young people soared. JUUL now owns half the e-cigarette market.

Before JUUL’s launch, e-cigarettes relied on bottled liquid containing nicotine, flavorings and a humectant such as vegetable glycerin or propylene glycol. JUUL introduced pre-filled, pocket-sized pods that are fueled with a nicotine-salt formulation.

A single pod delivers as much nicotine as a pack of 20 cigarettes. Depending on usage, a pod (about 200 puffs) typically can last from one half-day to more than one week. The brand’s commercial success, with its high nicotine concentration, is generating copycat products.

Nicotine salts are known to produce a smoother, more pleasant hit. “It’s easier to

inhale nicotine-salt vapor than other e-liquids or tobacco products, which can be quite harsh,” Cavazos said. “So, it becomes easier for non-smokers to ingest these newer products.”

Adolescents identify flavoring as a prime reason they experiment. A November 2019 NIH analysis suggests teens prefer mint and mango as their vaping flavors of choice.

Amid rising concerns, manufacturers now are significantly limiting flavors, and a number of states are enacting bans on vaping flavors. At one point, e-liquids came in more than 7,000 flavors, among them cotton candy, bubble gum, gummy bear and cherry crush.

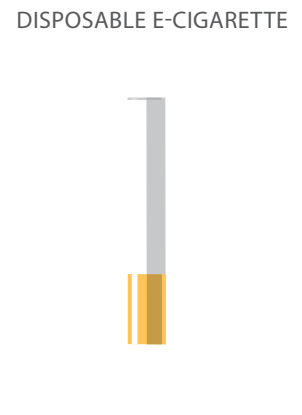
The JUUL device, which looks like a USB flash drive, is sleek and discreet, and can be easily hidden from teachers and parents. Perhaps this is why 10% of middle and high school students in a recent survey cited the “cool factor” as a reason they started experimenting with e-cigarettes. Students routinely vape during class, as nicotine salts do not generate a huge plume of smoke.

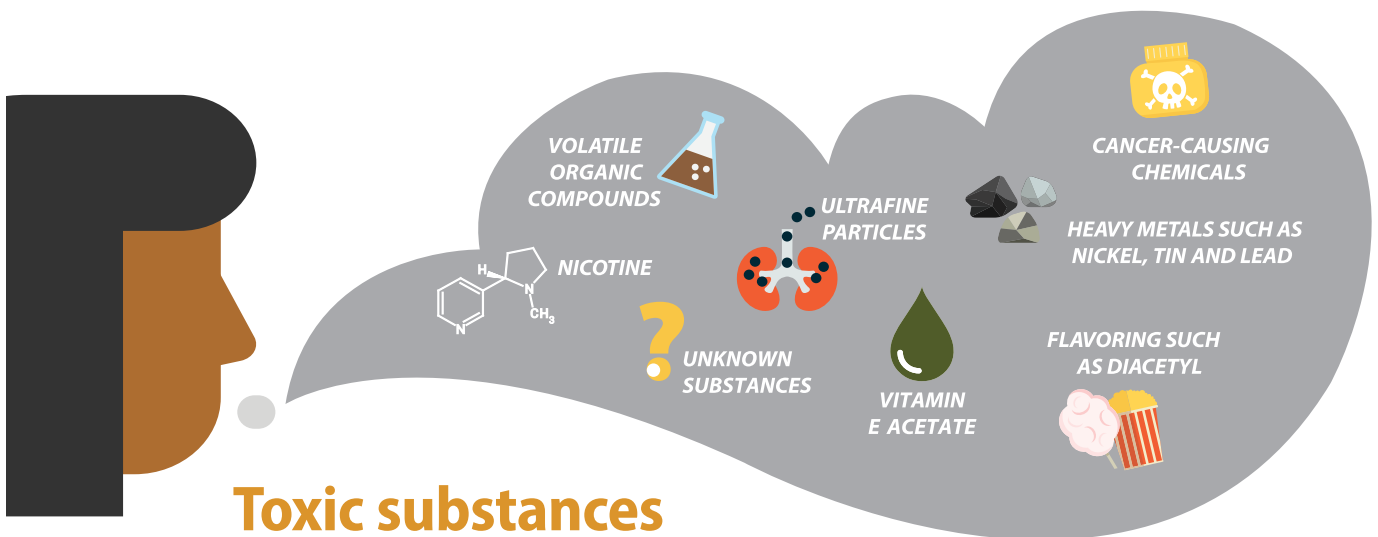
E-cigarette companies market the devices through Twitter, Facebook, YouTube, mobile and TV ads, and even use scholarship offers as a way to recruit youth users.

Sarah Garwood, MD, associate professor of pediatrics and adolescent medicine, sees adolescents from across the region in her practice. She estimates that a quarter have tried vaping or are doing it regularly. Most weren’t smoking cigarettes, so they had no need to use a device touted for properties that would help a user kick the combustible habit.

## Electronic cigarette products

SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION





SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION

## Toxic substances

E-cigarette aerosol is NOT harmless “water vapor.” The e-cigarette aerosol that users breathe from the device and exhale can contain harmful and potentially harmful substances, including nicotine, ultrafine particles that can be inhaled deep into the lungs, flavorings such as diacetyl, a chemical linked to a serious lung disease, volatile organic compounds, cancer-causing chemicals, and heavy metals such as nickel, tin and lead.

### Susceptibility to addiction

In fact, combustible smoking rates, alcohol use and illicit drug use among youths have been going down for 20 years. “We have had a great public health success by reducing combustible cigarettes among adolescents,” said Laura Bierut, MD, the Alumni Endowed Professor of Psychiatry, who also sits on the FDA Tobacco Products Scientific Advisory Committee.

Cavazos questions whether e-cigarettes might negatively impact this progress. “The rapid uptake of e-cigarettes has taken us by surprise,” she said.

One substance that concerns both investigators is marijuana. As marijuana continues moving into the mainstream, the new technology of e-cigarettes has given young people more ways to consume it.

Vaping THC (the primary psychoactive ingredient in marijuana) does not produce the telltale smell associated with smoking a joint or blunt — potentially allowing users to escape negative stereotypes and detection. Users consume even higher THC concentrations when they vape rather than smoke, which means greater exposure to the drug’s mind-altering and addictive ingredient. Also, the drug often is purchased through less-than-reputable sources.

“The implicated vaping products were marijuana products. And marijuana use is increasing in adolescents,” Bierut said.

Marijuana, she added, has been linked to increased risk for mental illness, including psychosis/schizophrenia, depression and anxiety. With vaping, the health risks of e-cigarettes and cannabis compound each other.

“Adolescent brains are more susceptible to the addictive qualities of a substance,” Bierut said. “Once addicted to one substance, it is easier to become addicted to another substance, such as alcohol and marijuana.”

For those who aren’t already smoking combustible cigarettes, e-cigarettes potentially could become a pathway to nicotine addiction.

In the report Ferkol delivered for FIRS, he and his co-authors highlighted concerns about repeated nicotine exposure in youths: “The central nervous system undergoes structural and functional adaptations, such that the brain requires nicotine to function normally . . . . Several lines of evidence indicate that nicotine exposure during adolescence may have lasting adverse consequences for brain development.”

Researchers say they need more data about nicotine’s impact on the developing brain. “Especially for young people, their brains are developing at a very rapid pace,” Cavazos said. “It’s possible that nicotine use can change the wiring of young people’s brains, and could lead to problems with cognition, learning, memory and other mental health issues. We need to better understand the negative consequences.”



Smoking, with its addictive qualities, has been around for a very long time. For tobacco manufacturers, the goal was to get people to try the product. That initial impression — that first drag of a cigarette — might not be so wonderful. But if peers are doing it, and if marketing suggests that it's glamorous (in the 1940s), cool (in the 1950s) — and at one point touted as healthy and safe — people might smoke until they're hooked.

When the surgeon general's report arrived in 1964 saying that cigarettes "could be hazardous to your health," many Americans decided to "kick the habit." That proved to be difficult, so difficult that it eventually created another market for devices that would help.

Does using e-cigarettes help people quit smoking? Evidence is limited. Current research, in fact, confirms dual usage of e-cigarettes and combustible cigarettes in all age groups, from young users to adults. This suggests that people may be using the products interchangeably, supplementing — not replacing — tobacco smoking with vaping.

Yet, some committed adults are successfully using e-cigarettes to wean themselves from combustible cigarettes. "The American Cancer Society has a good policy statement on this," Bierut said. "If you are a combustible cigarette user, you should quit. If you choose not to quit, have a harm-reduction approach; the standard e-cigs are safer than combustible cigarettes.

"Simply put, vaping can be helpful if you quit combustible cigarette smoking and can be dangerous if you use rogue products."

The FDA has urged the public to avoid using THC-containing vaping products or products obtained off the street. The agency's Forensic Chemistry Center is working closely with federal and state partners to identify substances that may be causing illnesses.

The FDA now stipulates that buyers must be 18 years of age and present a photo ID.

## Mitigating a menace

The question is whether any of the current regulations and restrictions are effective. And the answer is: not very. Ferkol has found vendors employ weak verification measures. "It's almost laughable," he said. In some cases, internet sites simply ask a consumer to fill in the year he or she was born. "If a student doesn't know how to dodge that verification step it suggests a failure of the American education system," he joked.

Ferkol wants to see much stronger measures: regulating nicotine-delivery systems in the same way as tobacco products; barring the sale of e-cigarettes to adolescents, while also providing rigorous enforcement; regulating advertising; eliminating flavorings; and conducting ongoing studies to better understand the threat that e-cigarettes pose to youth.

In the meantime, parents and physicians need to help mitigate the menace to public health. Studies show that many adolescents don't believe e-cigarettes are dangerous, and some assume they are comprised mostly of flavoring.

"There is speculation that e-cigarettes are healthier than regular cigarettes because they don't burn tobacco, but they are by no means healthy," Cavazos said. "Too many youths believe these products are healthy."

When an adolescent is discovered with a vaping product, parents should get a health professional involved to educate about the risks, and, if necessary, prescribe smoking cessation medication or counsel about nicotine addiction.

Every health-care provider should ask young patients whether they or anyone in their home are vaping. "I talk to all of my patients about the risks whether or not they are vaping or smoking other substances," Garwood said.

Garwood strongly advises patients to quit immediately or to set goals for quitting — perhaps by cutting back and picking a quit date. That's when the patient is instructed to remove vaping products and substitute a healthier habit.

Looking ahead, Ferkol said he cannot predict whether e-cigarettes will be legislated out of existence. He acknowledges that some believe e-cigarettes could be a useful tool for smoking cessation in adults who are committed to quitting. However, with the surge of respiratory illnesses, he "truly hopes our policymakers recognize the threat and address this public health issue much more carefully.

"I'd like to think in time we will come to a general consensus as to what their place is in society. But until we understand the short- and long-term deleterious effects of e-cigarettes, they need to be closely regulated and kept out of the hands of children." □

*Richard H. Weiss is a freelance writer who worked as a reporter and editor at the St. Louis Post-Dispatch for 30 years. Sally J. Altman, MPH, is a journalist specializing in public health and racial equity issues. Deb Parker is editor of this magazine.*

## Vaping flavors

Teens say flavors are the No. 1 reason they use e-cigarettes. Thousands of vape flavors are on the market. Federal flavor bans are at the center of debate.



**Blueberry**  
DONUT



**Strawberry**  
CHEESECAKE



**Chocolate**  
ICE CREAM



**Gummy**  
BEAR



# Fighting MS

**MS researcher Anne Cross is working to change the face of multiple sclerosis care**

BY GAIA REMEROWSKI

During his freshman year of college, Brian Phillips came home one day to find his parents unexpectedly already there. With tears in his eyes, his dad, a former Marine, put his hand on his son's shoulder and asked him to sit down. "I'll never forget it," Phillips said. "I'd never seen my dad cry before."

The test results were in. At age 19, Brian had just been diagnosed with multiple sclerosis.

He had known something wasn't quite right for a while. Tennis had always come easy to him. But when he challenged a friend to a game, he played so badly that he completely missed many of the shots. Following some tests, including an MRI brain scan, he received the diagnosis.

Brian Phillips, a patient with MS, receives an infusion of rituximab, a drug that depletes B cells and has been shown to slow the progression of the disease in certain patients.

## A multifaceted disease

Multiple sclerosis, or MS, is a chronic, often disabling disease in which the immune system attacks the myelin, the fatty substance that insulates axon nerve fibers and makes up the brain's white matter.

The multiple forms of MS present with variable symptoms depending on the individual. These may include impaired motor function, lack of coordination, blindness, neuropathic pain, bladder and bowel issues, extreme fatigue and more.

Further from the equator, disease rates are higher. This suggests a link to a lack of vitamin D, which the skin makes in response to sunlight, but this has yet to be proven as a definitive cause.

In the U.S., over 600,000 people live with the disease — 70% of whom are women. The age at diagnosis ranges from 20 to 60 years old.

After encountering three colleagues and many patients with MS during her medical training,

neurologist Anne Cross, MD, made it her life's work to study and treat patients with the disease. "As a resident, I saw a lot of MS patients. They were predominantly young women my age and there was really nothing we could do for them," she said.

## Expanding the arsenal

With few drugs available, Cross, now director of the John L. Trotter MS Center at Washington University, decided she wanted to help discover treatments through research. Even though she had no research experience, she was accepted into a fellowship working with two highly respected MS researchers at the National Institutes of Health: Dale McFarlin, MD, and Henry McFarland, MD.

"They really took a chance on me. I had not done any research before that. I didn't even know how to hold a pipette," said Cross, the Manny and Rosalyn Rosenthal–Dr. John Trotter MS Chair in Neuroimmunology. The work she did there was similar in scope to a PhD program, she added.

Cross completed two more fellowships before being recruited to the School of Medicine with her husband, DeWitte Cross III, MD, a professor of radiology and of neurosurgery. They moved to St. Louis with their young son (now a third-year neurosurgery resident) and daughter.

It was here she met John Trotter, MD, one of the first neuroimmunologists, thanks to his unique training at the time in both neurology and immunology. Trotter, who died unexpectedly in 2001, cared for half the patients with MS in St. Louis at the time of his death.

## B vs. T cells

Trotter ran a lab at Washington University and Barnes-Jewish Hospital that focused on identifying oligoclonal bands of antibodies in spinal fluid. Oligoclonal bands are present in over 90% of people with MS, making them valuable in diagnosing the disease. Increased antibodies in spinal fluid also implicate B cells in the disease process, as B cells make antibodies.

Trotter asked Cross to co-author a textbook chapter summarizing the literature on B cells and antibodies in MS. This prompted Cross to think about how B cells might be involved with MS.



Anne Cross, MD

MATT MILLER

# How B cells may be involved in MS

At the time, T cells were believed to be the main player in MS. Researchers already knew that it took T cells, not B cells, to generate the animal model of the disease, Experimental Autoimmune Encephalomyelitis (EAE). To activate this disease process in a mouse, researchers had to immunize the animal with myelin oligodendrocyte glycoprotein (MOG). This would induce autoimmune T cells to lead the attack on the mouse's own myelin.

Additionally, T cells are more abundant than B cells in areas of demyelination in MS tissues. "Everybody was interested in T cells," Cross said. "So, I thought: 'Let's look at B cells.'"

To better understand the role of B cells in MS, Cross and her postdoctoral fellow at the time, Jeri Lyons, PhD, (now at the University of Wisconsin-Milwaukee) found mice that had been genetically altered to lack B cells. These mice would allow the researchers to test a hypothesis: that without B cells, the mice would be unable to develop EAE.

When they tried to induce an autoimmune response in the B-cell deficient mice by immunizing with MOG, the mice remained healthy. But when they performed the same MOG immunization in mice with B cells, those animals developed EAE. This clearly implicated B cells as critical cells for EAE development in mice.

"It was one of the most dramatic experiments I've done," Cross said.

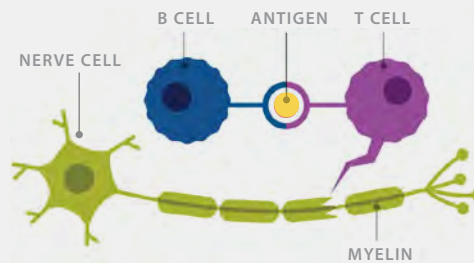
Using these exciting results, Cross and her team decided to test the idea that B cells were contributing to MS.

Rituximab, a drug that depleted B cells, had recently been approved by the FDA for non-Hodgkin's lymphoma, a B cell cancer. Cross convinced Genentech, the company that made rituximab, to allow her to use the drug for the first time in a clinical trial looking at patients with MS. Her results were encouraging. MRI activity in the patients went down by 88% after treatment with rituximab.

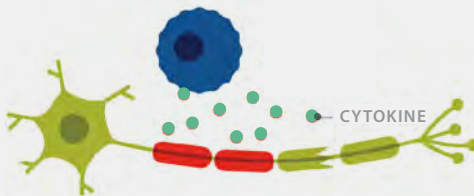
Rituximab is a monoclonal antibody that targets the molecule CD20 on the surface of B cells. CD20 is only found on B cells, so the drug can selectively eliminate B cells, while other cells remain unaffected.

Genentech subsequently developed ocrelizumab, a similar, second-generation version of the drug rituximab, for use in people with MS.

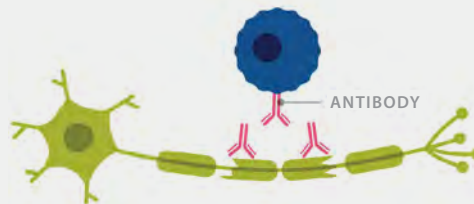
Critical to healthy immune function, B cells are constantly watching for foreign proteins, known as antigens, and present these to T cells, which work to destroy intruders. B cells further mount an immune response by secreting inflammatory chemicals and antibodies. In MS, these processes often go awry. Research points to several ways B cells attack the protective myelin coating that surrounds the nerve cells in the brain and spinal cord.



In MS, B cells mistakenly may process and present myelin proteins to the T cells as foreign, and T cells become autoimmune, attacking the body instead of intruders. The T cells multiply and become more inflammatory. Together, the B and T cells (and possibly other cells) then attack the myelin.



In MS, B cells also may release abnormally high amounts of chemicals called cytokines that stimulate inflammation and may lead to tissue injury in the brain and spinal cord.



B cells also can produce antibodies that attack the myelin directly in MS. These antibodies also may recruit other immune cells and prompt additional attacks and damage to myelin.

## Targeting B cells in MS



B cells at a certain stage in their development have the molecule CD20 on their surfaces. The drug ocrelizumab is an antibody that targets CD20 on the B cell surface so that the cell is eliminated.

GENENTECH, A MEMBER OF THE ROCHE GROUP

The most common form of MS, relapsing remitting MS, is characterized by debilitating attacks on the central nervous system, alternating with periods of remission. Primary progressive MS is less common — affecting only about 10 to 15% of patients — and is characterized by a progressive worsening of neurologic impairment with no remission. Many with relapsing remitting MS will develop secondary progressive MS, which presents initially as relapsing and remitting, but then becomes progressive.

Cross was Washington University's site lead in a study looking at ocrelizumab's effects on patients with primary progressive MS. The study showed that those taking ocrelizumab had a slower progression of disability compared with a placebo. In 2017, ocrelizumab became the first FDA-approved drug for this form of MS.

## Expanding the field

"B-cell therapy in MS is the fastest growing therapy we have," said Robert Naismith, MD, professor of neurology and director of the Clinical Trials Program at the John L. Trotter MS Center. Naismith analyzed MRI scans of patients in the rituximab trial, serving as the "blinded" investigator, meaning he did not know which patients received the drug.

Imaging advances have dramatically changed the field of MS, as MRI scans now can enable physicians to diagnose the disease sooner. Cross also has been actively involved in researching new imaging techniques to advance the study of MS.

Typically, MS is diagnosed through MRI scans of the brain and spinal cord, which can detect lesions in the white matter, indicating loss of myelin. If the lesion is "active," meaning there is inflammation in that area, it can pick up a contrast or dye called gadolinium that appears as a bright spot on an MRI. As the disease progresses, lesions may appear as "black holes," which indicate more severe damage to the underlying axons or nerve fibers.

Around the time the rituximab study was starting, Cross formed a collaboration with Sheng-Kwei (Victor) Song, PhD, professor of radiology. They became among the very first to use a novel MRI scan called Diffusion Tensor Imaging, which measures the diffusion of water through tissue, to better image the demyelination process in MS.

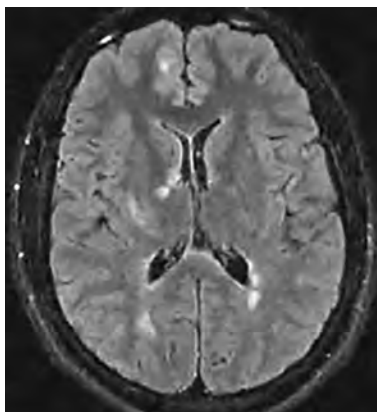
Naismith has since expanded his role, now overseeing more than 12 MS clinical trials that look at everything from new imaging techniques and drug therapies to the effects of intermittent fasting on MS.

No drugs are risk-free, and those available for the milder forms of the disease, while less risky, are often not very effective. For patients who have not had luck with the weaker treatments, Naismith said drugs like rituximab and ocrelizumab have still shown relatively few side effects and are convenient since they are given intravenously twice a year.

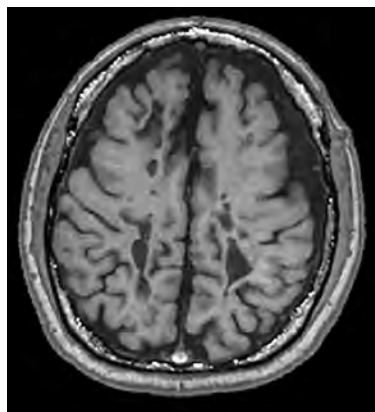
Naismith and Cross are investigating other MS therapies, including a B-cell depleting drug that can be taken subcutaneously, as well as oral medications. They also are planning studies with more personalized therapies that would modify a patient's own immune cells to fight the disease. He added the next frontier of MS therapy involves researching drugs that may help with remyelination and possibly even axon regeneration.

This year, Cross received the prestigious John Jay Dystel Prize for MS Research, an award that recognizes outstanding contributions to research in the understanding, treatment or prevention of MS. She won this primarily for her role in demonstrating the importance of B cells in MS.

## MRI scans of patients with MS



The bright white areas on this MRI scan are abnormal, and suggest inflammation in the myelinated white matter or at the gray matter/white matter junction.



The darker spots on this MRI scan are called "black holes," which appear when the nerve cells underneath the myelin have died.



MATT MILLER

“It is the prize in MS recognizing career achievement,” said Jack Antel, MD, professor of neurology and neurosurgery at McGill University and past president of the International Society of Neuroimmunology.

“Anne is recognized as a very distinguished, caring and competent physician. She is a true physician-scientist.” He added that she has a knack for translating therapies from the experimental phase to the clinic and vice versa. “If she gives a clinical opinion, you respect it. If she presents research, you respect it. If she gives advice on how an organization should run, you respect it.”

Cross said that when she first started in the field, there were few to no viable MS treatments. “Now we have so many medications it makes it hard to choose,” she said. “We have MS treatments that don’t just treat the symptoms, they actually slow the disease.”

But physicians like Cross still struggle with determining which patient should receive which drug, since it is not yet clear who will develop a more aggressive form of MS that might need a more aggressive, but riskier, drug and who will

not. There are some people with MS who were diagnosed early, began therapy and decades later you wouldn’t even know they had the disease, Cross said. “While with others, we can try almost every drug available yet they still go downhill,” she added.

Cross’ patient, Brian Phillips, said he feels fortunate and tries to maintain a positive attitude. Shortly after his diagnosis in 1998, he had a Gaelic saying tattooed on his ankle: “To the valiant heart, nothing is impossible.”

While he is legally blind and cannot drive, he walks unassisted and generally goes about his daily life, which includes working and spending time with his wife and two children. Over the years, he has been on a number of MS drugs and is currently taking rituximab, which he started three years ago. “I haven’t had a relapse in 12 years,” he said. “I feel like I’m in a good place.” □

*Gaia Remerowski is a senior content strategist in Medical Public Affairs.*

**Cross chats with her patient, Brian Phillips, during one of his twice-yearly infusions of the B-cell depleting drug rituximab, which Cross has studied extensively. Phillips has had MS for 22 years and has largely been able to manage the disease through medication.**

Joan Luby, MD, observes a parent and child through a one-way mirror and, using a microphone and earpiece, coaches the parent on how to help keep the child's emotions under control. The intervention helps relieve symptoms of clinical depression in young children.



MATT MILLER

# Nature vs. nurture

Studying adversity's effects  
on children's brains

**C**ompelled by the potential to improve the lives of vulnerable children, emeritus trustee Walter Metcalfe and his wife, Cynthia, have committed nearly \$4 million through outright and estate gifts to support the work of Joan L. Luby, MD, a highly regarded child psychiatrist.

Luby and her colleagues have linked adversity, including poverty and neglect in the first years of life, to changes in brain anatomy. These changes increase the risk of learning difficulties, clinical depression and behavioral problems that affect a child's well-being.

Their research also demonstrates that, by contrast, extensive nurturing from parents and supportive early therapeutic intervention can limit, or even eliminate, the impact of adversity on the developing brain.



**W**ith support from the Metcalfes, Luby is expanding a project to gauge the effects of environmental stress on brain development and overall health in children by recruiting their mothers while they are still pregnant. Luby will measure stress and adversity experienced during pregnancy and after the children are born. The study, funded by an \$11.6 million grant from the National Institute of Mental Health (NIMH), will follow 370 children in the St. Louis area from before birth to age 3.

Luby, the Samuel and Mae S. Ludwig Professor of Child Psychiatry and director of the school's Early Emotional Development Program, will assess emotional and behavioral development. Meanwhile, co-investigators Christopher D. Smyser, MD, associate professor of neurology, will use MRI to track brain development, while professor of pediatrics Barbara B. Warner, MD, examines the impact of environmental stress on the children's gut microbiome and immune systems.

The study will include an expanded focus on epigenetics. Described as the interface of nature and nurture, epigenetics investigates the influence of environment on gene expression.

The researchers will collect saliva samples from infants at birth and 12, 24 and 36 months of age to analyze genetic information. They are looking for any changes that might appear throughout the genome and are storing the DNA from the children for further analysis should patterns emerge. The eventual plan is to learn how gene-environment interactions influence brain development and emotional and behavioral health.

Luby's team has demonstrated poverty's negative effects on the developing brain. In previous work, the researchers found that a type of interactive therapy that helps parents be more nurturing, and teaches them to enhance their child's emotional development, can reduce rates of childhood depression and other mental health problems. Although these problems present particular problems for poor children, they also affect children across the income spectrum.

"Dr. Luby's work on childhood depression has been groundbreaking, including an entirely new strategy for effective therapeutic behavioral intervention," said David H. Perlmutter, MD, executive vice chancellor for medical affairs, the George and Carol Bauer Dean of the School of Medicine and the Spencer T. and Ann W. Olin Distinguished Professor. "Her continuing efforts to understand the negative effects of poverty and neglect on the young brain, and developing

therapies to combat those effects, is critically important and inspirational. We are so fortunate to have the vision of the Metcalfes to invest in and support research like Joan's that is innovating in this most challenging area of medicine."

## Influencing public health

The new gift is one more way Walter and Cynthia Metcalfe have supported Washington University over the years. "We see this as an investment in Washington University, in St. Louis and, most importantly, in children and their mental health," said Cynthia Metcalfe.

Walter Metcalfe, like his parents before him, attended Washington University; he earned a bachelor's degree in history in 1960. Several family members also are alumni, including Cynthia Metcalfe's father.

"The power of the research is that it could really have an impact on public policy and funding for programs that make a difference early on," Walter Metcalfe said. "I don't know of anything that's more important than helping children lead productive, healthy lives."

A member of the School of Medicine's National Council since 2007, Walter Metcalfe is chair emeritus of Bryan Cave Leighton Paisner LLP, an international law firm that doubled in size under his leadership. He has served on Washington University's Board of Trustees and the Washington University Law National Council. The Metcalfes also are sustaining charter members of the Danforth Circle Chancellor's Level of the William Greenleaf Eliot Society.

Luby said she is grateful for the Metcalfes' generosity, which will allow her to immediately build on the existing NIH-funded study and more rapidly influence public health.

"It will give my research team the freedom to explore and innovate in areas with a very high potential public health payoff that would take many years to launch through the typical federal grant system," Luby said.



**Cynthia and Walter Metcalfe**

*Information for this story provided by Jim Dryden, Tricia Hendricks and Channing Suhl.*

## Find your friends.

Classnotes are organized first by year of degree/training completion and then in alphabetical order.

## How about you?

Share your news via the online form at [wumcnews.org/classnotes](http://wumcnews.org/classnotes). Submissions will be printed in a subsequent issue of Outlook magazine as space allows. Photos are welcome.

## 1960s

### Steve Fredman, LA '58, MD '62,

a practicing gastroenterologist for 40 years, retired in 2010. He hopes some of his fellow WUSM graduates will add their stories and observations about how health care has changed in their lifetimes to his evolving digital online book: [savingobamacare.com](http://savingobamacare.com).

**David Bray, MD '66**, is retiring after 40 years in otolaryngology and facial plastic surgery practice.

**Robert Porter, MD '67**, retired from nephrology practice in 2017 and from Federal Aviation Administration aviation medical examiner duties in June 2019. He volunteers weekly at the Abilene & Smoky Valley Railroad as a trainman/engineer. Porter is also a volunteer "grandpa" at the Children's Palace, a preschool for homeless children in Topeka, Kan.

**Earl Hearst, LA '66, MD '69, HS**, and his wife, Sherrie Sushner, continue to divide their time between winters in The Villages, Fla., and summers in Silver Spring, Md. Hearst plays senior softball and doubles table tennis. He won a bronze senior Olympics medal in Florida for men's double

table tennis and a silver senior Olympics medal for mixed table tennis doubles in Maryland this past year.

**Wallace B. Mendelson, MD '69**, completed his residency in psychiatry in 1974 and served as assistant professor of psychiatry at WUSM in 1974-1975 before joining the Intramural Program of the National Institute of Mental Health in Bethesda, Md. He has published prolifically since leaving WUSM, including hundreds of peer-reviewed papers, abstracts, book chapters, letters and reviews. Mendelson also has authored or co-authored seven books, most recently "Understanding Medicines for Anxiety" in 2019.

## 1970s

**Bruce Fisher, MD '70**, was awarded mastership in the American College of Physicians. Masters must have made a notable contribution to medicine, including, but not limited to, teaching, clinical medicine, preventive medicine, improvements in health-care delivery and/or the medical literature. As noted in the ACP's convocation program, Fisher's publications include articles and abstracts on opportunistic infections and on historical aspects of tuberculosis and other infectious diseases. Fisher is clinical

professor of medicine at Rutgers Robert Wood Johnson Medical School (RRWJMS), and he is on staff at Hackensack Meridian Health Jersey Shore University Medical Center in Neptune. His colleagues at Muhlenberg Regional Medical Center, where he was chief of infectious diseases from 1979 to 2001, established the Bruce Fisher Award. This award, presented annually since 2002, honors the graduating student or students at RRWJMS who best represent the ideals of scholarship and humanism in medicine. He also received the Gold Humanism Honor Society's Leonard Tow Humanism in Medicine Award. He has been married to his wife, Doris, since 1974 and has a son, a daughter, two granddaughters, and a granddog.

**Barry Bernfeld, GR '73, MD '77**, has retired from a 34-year career in general surgery and as a longstanding cancer liaison physician for the Commission on Cancer. His wife, **Wendy Eider, MD '76**, died from pancreatic cancer in 2016. Their three children continue to bring him joy. Jessica is in the Office of the Colorado State Public Defender near Denver. Sean is a third-year internal medicine resident at the University of Utah and will be chief resident at its veterans hospital next year. Lynsey is a first-year resident on the internal medicine-primary care track at the University of Washington, Seattle.

**James L. Vacek, MD, HS '77-82**, has been presented with the 2019 Exemplary Leadership Award by the Kansas City Medical Society. Vacek is a professor of medicine at the University of Kansas Medical Center. The award recognizes a medical society member-physician for outstanding leadership and service. Vacek has been a leader in patient care, teaching and research in the field of cardiology in Kansas City. He helped design patented technology that contributed to the development of today's radiofrequency ablation catheters used to treat heart arrhythmias.



**Kansas City Medical Society President Mark D. Brady, MD, left, presents James L. Vacek, MD, with the 2019 Exemplary Leadership Award.**



**Timothy Ley, MD '78, HS**, was recognized by the National Academy of Sciences for distinguished and continuing achievements in original research.

Membership is a widely accepted mark of excellence in science and is considered one of the highest honors that a scientist can receive.

## 1980s



**Steven Perlmutter, MD '80, HS '84**, recently published "High Times Ahead: Products Liability in Medical Marijuana" in *Health Matrix: The Journal of Law-Medicine/Case Western Reserve*

University School of Law. The paper won the Ross-Blakley Law Library Award for Exemplary Student Research at the Sandra Day O'Connor College of Law at Arizona State University.

**Timothy Caruso, PT '82**, founded The Kids Equipment Network (TKEN), a not-for-profit that provides medical equipment to children with special needs at no cost. Since its 2005 inception, TKEN has provided more than 2,000 pieces of equipment and paid it forward to a number of other charities in the U.S. and around the world.

**Mitchell Strominger, LA '82, MD '86**, moved recently to Reno, Nev., where he is building the pediatric ophthalmology and neuro-ophthalmology division at Renown Medical Center and the University of Nevada, Reno School of Medicine. In his spare time, he hopes to produce wine as he discovered a small vineyard on his property.

**Stephen Brown, MD, EN '77, GB '79, HS '88**, was honored with the 2019 Wyoming Physician of the Year and also the 2019 Natrona County Physician Service awards. He has practiced child psychiatry in Casper, Wyo., since 1990.

**Merri Johnson, PT '88, DPT '11, NCS**, accepted a faculty position at Texas Woman's University Program in Physical Therapy, Dallas campus.

## 1990s

**Jeffrey Grills, MD '90**, is now working in the pediatric emergency department at Arkansas Children's Hospital Northwest in Springdale, Ark.



**Melissa Piasecki, LA '87, MD '91**, recently took on an expanded role as executive associate dean at the University of Nevada, Reno School of Medicine (UNR Med). She will oversee institutional

vision, stability, growth and excellence. Piasecki will continue to lead the school's accreditation process, clinical partnerships and conflicts of interest. Additionally, Piasecki will oversee UNR Med's Office of Continuous Institutional Assessment, Office of Statewide Initiatives and the Savitt Medical Library.

**Julie Miller, MD '96**, is enjoying life as an endocrine surgeon in Melbourne, Australia, where she lives with her husband and three teenage children. Miller was elected president of Australia and New Zealand Endocrine Surgeons and of the Asian Association of Endocrine Surgeons — the first female to hold either of these titles. She reports trying not to work too hard, though, and enjoy the kids while they are still home. Miller encourages any classmates heading to Australia to get in touch — "We love visitors!"

## 2000s

**Gregory Janicki, PT '02**, received a U.S. patent on a multipurpose fitness and rehabilitation device.

**Katherine King, MD/PhD '03**, was awarded the 2019 Presidential Early Career Award for Scientists and Engineers.



**David J. Parks, MD '88**, was profiled in *The Guam Daily Post* as he celebrated 20 years of providing eye care services on Guam and surrounding Micronesian islands that would be unavailable otherwise. In July 2010, Parks opened an office full-time on Guam that allows him to provide high-level surgical care for his patients. He has been named a top doctor by *U.S. News & World Report* and *Castle Connolly Medical Ltd.* for more than 15 consecutive years. Parks is a board-certified ophthalmologist and remains committed to providing care to these populations for many years to come.



**Giancarlo C. Xavier Oliveira, PhD '03**, is the coordinator of the Graduate Program in Applied Ecology, the reference graduate program in the area of environmental sciences in Brazil.



**Sukanya Pyne, DPT '06**, founded ReJenga in 2018. It is a nonprofit organization with a mission to educate, equip, engage and empower people with disabilities in rural areas,

while establishing permanent access to orthopedic rehabilitative services in developing countries, and maintaining long-term relationships. ReJenga envisions

sustainable rehabilitation supporting people with disabilities in rural areas by involving the families and community health-care providers.

**Oluwadamilola “Lola” Fayanju, MD ‘07, MPH ‘11**, has been named a 2019 Emerging Leader in Health and Medicine Scholar by the National Academy of Medicine in Washington, D.C. Fayanju is one of a class of 10. She is an assistant professor of surgery and population health sciences at Duke University School of Medicine, surgical lead for the Inflammatory Breast Cancer (IBC) Clinic at the Duke Cancer Institute, and director of the Breast Clinic at the Durham VA Medical Center.



**Sara Reardon, LA ‘04, DPT ‘07, OCS**, lives and works in her hometown of New Orleans, with her husband and two sons. She opened NOLA Pelvic Health in 2018, the first privately owned pelvic health physical therapy practice in New Orleans, and launched a telehealth platform, The Vagina Whisperer, which provides online

pelvic health and wellness sessions to women across the country. Reardon gave a TedX talk on “Rethinking Postpartum Care” at TedxLSU in March 2019 and was awarded the 2019 Program in Physical Therapy Alumni Achievement Award and the 2019 Gambit Magazine’s top 40 under 40 (young people doing great things in the New Orleans area).



**Ashley Steed, MD/PhD ‘08**, received a 2019 Career Award for Medical Scientists from the Burroughs Wellcome Fund, a nonprofit organization dedicated to biomedical science through research and education. Steed is instructor of pediatrics at the School of Medicine.



**Shandiz Tehrani, MD/PhD ‘08**, recently was promoted to associate professor of ophthalmology at Oregon Health & Science University.

## 2010s



**Brynn Rooney, DPT ‘10**, recently opened a private physical therapy practice in Downers Grove, Ill., after teaching at Northern Illinois University’s physical therapy program for six years. She provides

comprehensive and holistic physical therapy services across the life span for orthopedic, sports and pelvic health conditions. Rooney is board-certified in sports physical therapy and is trained in pelvic health, which allows her to treat people looking at integrative movement and function.

**Hyekyeng Lyn Kim, OT ‘11**, is one of 20 Emerging City Champions (ECC) fellows selected by 880 Cities and the Knight Foundation. The ECC fellowship funds young leaders from around the U.S. to develop and implement innovative ways to address public space, mobility, and/or civic engagement. Her project will be in Charlotte, N.C.

**Jessica Garcia Wood, OTD ‘12**, is a practicing occupational therapist in pediatric and adult acute care at the University of New Mexico (UNM) Hospital, a public teaching hospital and Level 1 trauma center. Wood assists with the UNM School of Medicine OT Graduate Program neurological practice lab and received the Distinguished Preceptor Award in spring 2019.

**Samuel Nemanich, MSCI ‘16, PhD ‘16**, recently was selected as a 2019-2020 NIH StrokeNet Fellow at the University of Minnesota.



**Jonathan R. Brestoff, MD, PhD, HS ‘19**, an assistant professor of pathology and immunology at WUSM, received a 2019 Career Award for Medical Scientists from the

Burroughs Wellcome Fund, a nonprofit organization dedicated to biomedical science through research and education.



**Brian DeBosch, MD/PhD ‘08**, assistant professor of pediatrics, **Andrew Kau, MD/PhD ‘06, HS**, assistant professor of medicine, and **Philip Budge, MD, PhD**, assistant professor of medicine, have received a 2019 Clinical Scientist Development Award from the Doris Duke Charitable Foundation. These three physician-scientists at the School of Medicine are among 16 across the U.S. receiving the awards, which provide \$495,000 over three years to each investigator. The Clinical Scientist Development Award funds physician-scientists at the early stages of their careers.



**John Oscar Eichling**, a longtime professor at Mallinckrodt Institute of Radiology and Washington University's first radiation safety officer, died Monday, July 22, 2019. He was 82.

Eichling, who completed a PhD in radiation biophysics at Washington University, joined Mallinckrodt Institute of Radiology in 1963. He was hired to oversee the installation and operation of the first cyclotron to be used at a U.S. medical facility, a 20-ton, 10-million electron volt Allis-Chalmers accelerator at the Washington University Medical Center. There, he continued working as a researcher, professor and radiation safety officer of the university.

He served as the director of the Division of Radiation Hazards, which spanned the then-largest Nuclear Regulatory Commission medical licensee covering Barnes-Jewish Hospital North and South campuses, St. Louis Children's Hospital, Barnes-Jewish Hospital Heart Care Institute, and more than three cyclotrons, five clinical chemistry groups, 160 diagnostic X-ray units, 900 labs and 1,500 people. He retired in 2000.

Eichling was the author or co-author of more than 50 highly cited research papers, guest speaker at numerous radiology conventions and international symposiums, and patent holder for a radiolucent breast implant filler.

Eichling was as happy on a tractor as he was in the lab. He enjoyed wildlife and would do his best to care for an animal in need. While living in Marthasville, Mo., he and his wife were caretakers to more than 100 rescued animals including dogs, cats, horses, birds, and a monkey. He spent countless hours renovating and researching the history of the early 1800s log cabin there as well, becoming an expert in Warren County history and settlements.

He is survived by his wife, Carol Eichling, and one son, Daniel Eichling (Hannuo), and other relatives and friends.

## 1940s

**Virginia Bastian Copp**, NU '47; Feb. '19

**Aileen M. Dohm**, NU '47; July '19

**Don L. Fisher**, MD '43; March '19

**Mary M. Grassel**, NU '47; April '19

**Ruth Jane Imel**, NU '48; April '19

**Sarah Bales Krainess**, NU '47; June '19

**Donald M. Moore**, MD '42; Aug. '19

**Clifford G. Neill**, DE '46; Feb. '19

## 1950s

**James R. Davidsmeyer**, DE '54; Aug. '19

**John L. Denman**, MD '52; July '19

**Edward H. Forgotson**, MD '57; July '19

**Griffith R. Harsh**, HS '54; Sept. '19

**James Richard Harte**, MD '54; March '19

**Joan A. Johnson**, NU '54; July '19

**Herzl Katz**, MD '55; Aug. '19

**Betty Hahneman Kolb**, HS; July '19

**Maurice J. Lonsway Jr.**, LA '46, MD '50;  
June '19

**Mary L. Mendelson-Scripp**, OT '53,  
MSOT '84; July '19

**Wade H. Shuford**, HS '53; July '19

**Dixon F. Spivy**, LW '51, MD '57; Aug. '19

**Joyce Treffinger**, NU '50; July '19

**Frank Tull III**, MD '55; Aug. '19

**Miles C. Whitener**, MD '55; June '19

**Homer D. Wright Jr.**, DE '57; Sept. '19

## 1960s

**Gerhard W. Cibis**, LA '63, MD '68; Sept. '19

**Jan Thomas Goff**, HS '65; Aug. '19

**Carl Roerig Hartrampf Jr.**, HS '62; June '19

**John R. Hogan**, HS '64; July '19

**William Benjamin Horner**, MD '67; June '19

**Russell James Keizer**, HS '66; June '19

**Alice Nouhan**, NU '62; Aug. '19

**Edward Okun**, HS '62; June '19

**Joseph A. Sisson**, MD '60; Aug. '19

**H. Anthony Tarrasch**, DE '66; June '19

**Merlyn B. Thompson**, HS '68; May '19

**Richard Frank Ulrich**, HS '65; April '19

## 1970s

**Paul T. Coleman**, DE '73; June '19

**Arthur D. Earl**, MD '73; April '19

**Lawrence Daniel Hafner**, DE '75; July '19

**Elsie F. Meyers**, HS '71; June '19

**Linda G. Peterson**, MD '74; July '19

**Robert W. Sindel**, LA '69, MD '75, HS '77;  
June '19

## 1980s

**Michael Wayne Christensen**, MD '86,  
HS '90; April '19

**Gilbert Roger Hart**, DE '82; July '19

**Michael Choate Molleston**, LA '82,  
MD '86, HS; May '19

## 2000s

**Brian C. Brauer**, HS '01; Sept. '19

**For full obituaries, visit:**  
[medicalumni.wustl.edu/  
alumni/](http://medicalumni.wustl.edu/alumni/)





# Inauguration Day

Andrew D. Martin, PhD, the 15th chancellor of Washington University, and his daughter, Olive, 11, are welcomed by the medical school community on Inauguration Day Oct. 3. Martin delivered official remarks in the Eric P. Newman Conference Center. Afterward, Dean David H. Perlmutter, MD, engaged in a lighthearted Q&A with the new chancellor.

MATT MILLER PHOTOS



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