

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | SUMMER 2013

# PITTMED

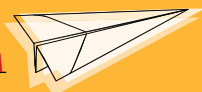


DSM 5.0  
Now Available



## A BIG UPGRADE

FOR THE PSYCHIATRISTS' MANUAL.  
MEET THE MAN BEHIND IT.



## ROCK ON

I have long considered your publication to be the *Wired* of alumni magazines because of the interesting stories, cool updates on my alma mater, layout, and very clever headlines. I felt as though I could fly like an eagle, bang a gong, and rock and roll all night (and party every day) when I read the Spring issue and identified eight song titles in an ad [see below, "Wish You Were Here"]. Combined with the other creative headlines—like "What Would Galileo Do?"—this willingness to take journalistic risks warmed my heart and soothed my soul.

You see, earlier that day, I found out that the editorial board of one of our surgical journals had changed the titles of four of my papers. For a few years now, I have tried to sneak in lyrics and titles of some of my favorite rock songs. For example, I recently published "Get on Your Boots," a paper on including professionalism in curricula.

This time, however, the editors caught on to my shenanigans. "Handle With Care" was reduced to "Incidence and Management of Adverse Events After the Use of Laser Therapies for the Treatment of Hypertrophic Burn Scars," and so on. Scientifically more accurate? I guess so. Boring? Absolutely.

So, thanks for rejuvenating my sense of humor, which provided me with more than a feeling, but also a sweet emotion. It don't come easy, but while you see a chance, take it. Just like starting over, I will stop my sobbing, pursue a renewed lust for life, and ramble on, right down the line.

Wish I were there. *Pitt Med* is the best!

Scott Hultman (MD '90)  
Chapel Hill, N.C.

## HIS AND HERNIA

I did my surgery rotation in 1973 as a third-year medical student under Mark Ravitch ["The Surgical Curmudgeon," Spring 2013]. Surgery was not a major interest of mine, and I became a pediatric endocrinologist. I did learn a lot about surgery, though, which helped during my pediatrics residency in Buffalo. The pediatric surgeons there would traditionally fire a series of questions about hernias to the residents to prove to them that they didn't know anything. After correctly answering the fourth question (the most common hernia in girls is the inguinal hernia, but almost all femoral hernias are in females), the surgeon looked up and said, "You didn't go to school here in Buffalo, did you?" I had to confess that Mark Ravitch taught me what I knew about hernias.

Daniel Postellon (MD '74)  
Grand Rapids, Mich.

## A STAPLE IN TIME

I may have been Dr. Ravitch's ["The Surgical Curmudgeon," Spring 2013] first Pitt med student. I was an acting surgical intern assigned to Montefiore in 1970 when Dr. Ravitch was working with a small house staff and his protégé, Dr. Felix Steichen. I remember him showing me the staplers—my classmates were practicing suture tying, and I was stapling. When I did my surgical internship, and then my orthopaedic residency, people thought I was crazy when I discussed stapling wounds.

Dr. Ravitch encouraged me to go into surgery. I do not recall the horrors of the morbidity and mortality conferences described in the arti-

cle, but again, I was a low man on the totem pole.

Aaron Levine (MD '71)  
Houston, Texas

## NOTICED

I got an unsolicited copy of *Pitt Med* and was quite impressed with the content.

Great job. I can tell it was written by those committed to the science of medicine. Truly uncharacteristic of similar publications and a welcome surprise.

Thomas A. Selvaggi (Res '92)  
Hackensack, N.J.

## RECENT MAGAZINE HONORS

2013 Press Club of Western Pennsylvania, Golden Quill Award, Health/Science/Environment Article or Series, Magazines (J. Miksch, "The Meaning of Life, Told With 13 Polypeptides")

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We gladly receive letters (which we may edit for length, style, and clarity).

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Mark Ravitch (center) traveling in the former Soviet Union.



## WISH YOU WERE HERE

There must be 50 ways to leave your med school. You can go your own way, ride a horse with no name, or take a midnight train to Georgia. Tell us what you've been up to: career advancements, honors you've received, appointments, volunteer work, publications. And we love to hear old Pitt memories, like: What's going on with this scene we found in Pitt's 1975 edition of *The Owl*? Let us know, one way or another. Write a message in a bottle, ring our bell at the number listed above, or friend us on Facebook at [www.pittmedfb.pitt.edu/](http://www.pittmedfb.pitt.edu/).



# PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, SUMMER 2013

VOL. 15, ISSUE 2



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40 1/2

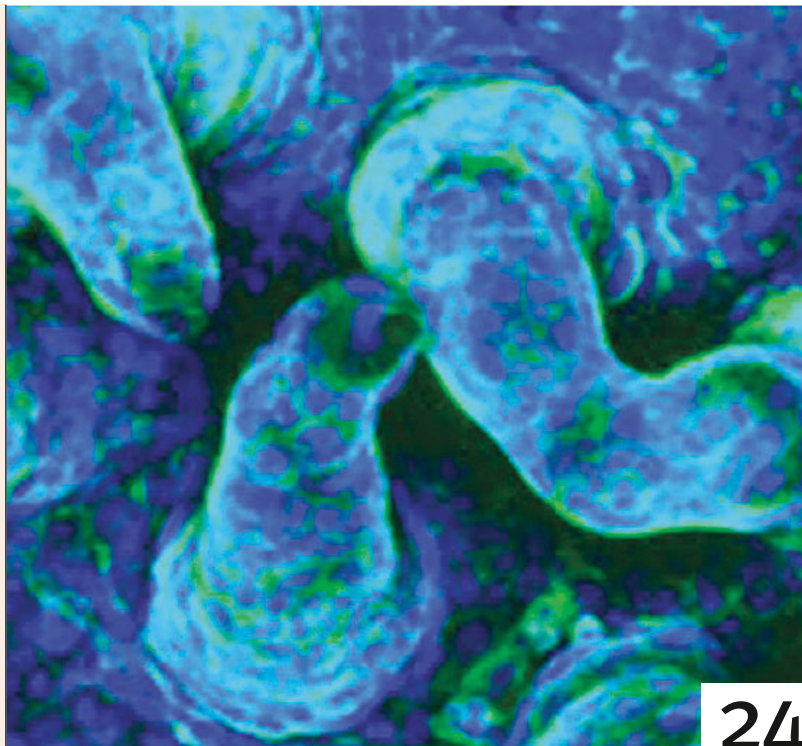
## CONTRIBUTORS

It's appropriate that **CHUCK STARESINIC** [author of "The Scourge of the NICU"], who has netted national awards for his writing, would be a champion of literacy. The director of communications for academic affairs, health sciences (and former *Pitt Med* senior editor) recently won the Chancellor's Award for Staff Excellence in Service to the Community. When his neighborhood library, the Carnegie Library of Pittsburgh-Lawrenceville, and other branches were in danger of closing, he helped reverse their fortunes. With his library saved, Staresinic is leading renovations of the nearly 120-year-old structure. "Now, with [new] air conditioning, the library will fill up when it hits 93 degrees instead of shutting down," he says.

For 25 years, photographer **JIM JUDKIS** ["Works in Progress," p. 12] worked with Fred Rogers. Last winter, after the shootings in Newtown, Conn., a photo from their very first session together in 1978 went viral on Facebook. It showed Rogers with Pittsburgh tot Tommy Paulhamus and was captioned with this Rogers' quote: *When I was a boy, and I would see scary things in the news, my mother would say to me, "Look for the helpers. You will always find people who are helping." To this day ... I am always comforted by realizing that there are still so many helpers—so many caring people in this world.* Judkis' environmental portraits have appeared in *The Washington Post*, *People*, and many other publications.

## COVER

David Kupfer describes revising the psychiatry manual that has a life of its own. (Cover: Jesse Lenz © 2013.)



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## COVER STORIES

### Works in Progress

12

He "brought up" Pitt's Department of Psychiatry from being home to a few dozen faculty members to the powerhouse it is today. He's been called the Mentor of All Mentors. And now David Kupfer would like to see the latest *Diagnostic and Statistical Manual of Mental Disorders*, psychiatry's handbook, help his field come into its own. Meet the man behind the manual.

BY ELAINE VITONE

### DSM 5.0

19

Its title is dry, but an awful lot of people care deeply about what the *Diagnostic and Statistical Manual of Mental Disorders* has to say. David Kupfer delves into the depths of crafting the latest edition, which he sees as a "living document."

INTERVIEW BY DAVID LEWIS AND  
MAGGIE MCDONALD

## FEATURE

### The Scourge of the NICU

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NEC may be the most important and confounding disease you've never heard of.

BY CHUCK STARESINIC

## PITTMED

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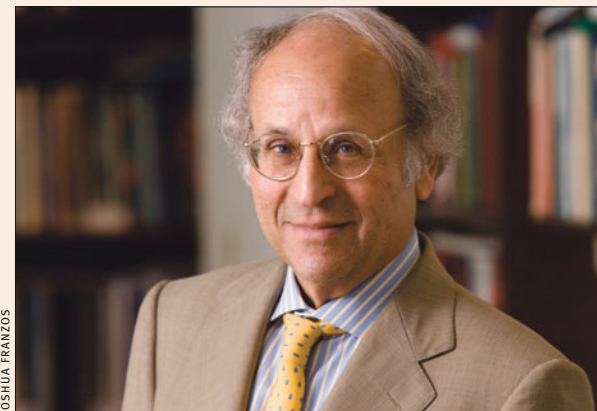


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I don't particularly care about the usual. If you want to get an idea of a friend's temperament, ethics, and personal elegance, you need to look at him under the tests of severe circumstances, not under the regular rosy glow of daily life. Can you assess the danger a criminal poses by examining only what he does on an ordinary day? Can we understand health without considering wild diseases and epidemics? Indeed the normal is often irrelevant. —Nassim Taleb



JOSHUA FRANZOS

You may be familiar with the ideas of Taleb, author of *The Black Swan* (not the ballerina film with Natalie Portman; Taleb's subtitle is *The Impact of the Highly Improbable*). In his book, he discusses how rare "shocks and jumps" have great consequence in social, political, and financial life. Incidents like the rise of the Internet or of Hitler or of a particular school of art don't fit into the normal Gaussian "bell curve" embraced by scholars of social science and economics. Yet, Taleb notes, their potential impact is almost always profound, and failing to account for the possibility of such "Black Swans," as he calls them, can lull us into believing we've tamed uncertainty.

Game-changing outliers also make themselves known in the natural world. Consider the virus that unexpectedly jumps from chicken to human, threatening a worldwide epidemic. Or how variation among species, like an addition of a lens in a trilobite's eye, is likely to happen suddenly, rather than gradually, often because of new environmental pressures. By "suddenly," I'm referring to the geologic time scale, perhaps over 50,000 or 100,000 years. Stephen Jay Gould and Niles Eldredge articulated this theory of "punctuated equilibrium" in 1972. Their proposal challenged an interpretation of Darwin's theory of evolution as a gradual progression.

As technology has progressed and allowed us to interrogate in great detail the genomes of tumors, we are seeing the same evolutionary patterns on the molecular time scale—at hyper-speeds. A recent report from a team of researchers at Cornell, Harvard, and Trento universities shows mutations in prostate tumors occurring in abrupt, periodic bursts, causing complex, often wholesale reshuffling of DNA—punctuated equilibrium in cancer! With this revolution in their genomic structure (356,000 base-pair mutations and 5,600 rearrangements among 57 tumor genomes!), the tumor cells were more likely to adapt and survive. Here again we see how "shocks and jumps" in the natural world have profound implications. It's as though cancer cells do whatever it takes to survive, and may do so very quickly. Viruses also may show "shocks and jumps." For example, HIV, in one infected person, may develop many mutations in weeks. This is why single drugs with single mutations as targets fail to overcome viral resistance, but multiple drugs with multiple targets, given simultaneously, are effective. The latest prostate story mandates combination chemotherapy, as has long been practiced with childhood leukemia and other hematologic malignancies.

Normal cells don't typically endure sudden, massive mutagenesis, or we'd quickly morph from one species to another. Yet recent reports suggest that while normal cells have a mechanism for inducing mutations in immunity genes so as to broaden their antibody repertoire when needed, this same mutagenic mechanism may, on rare occasions, turn against many of our other genes—itsself promoting cancer.

Both Taleb's ideas and the findings of the international prostate tumor team remind us of the need to welcome intellectual complexity in our approaches to treating cancer and—as we find increasingly—in health care in general.

*But in all my experience, I've never been in any accident ... of any sort worth speaking about. I have seen but one vessel in distress in all my years at sea. I never saw a wreck and never have been wrecked nor was I ever in any predicament that threatened to end in disaster of any sort.*

—E.J. Smith, 1907, Captain, RMS *Titanic*

Arthur S. Levine, MD

Senior Vice Chancellor for the Health Sciences  
Dean, School of Medicine





*Devoted to noteworthy happenings  
at the medical school*

PHOTO: CAMI MESA / MODEL: JACK MIKSCH

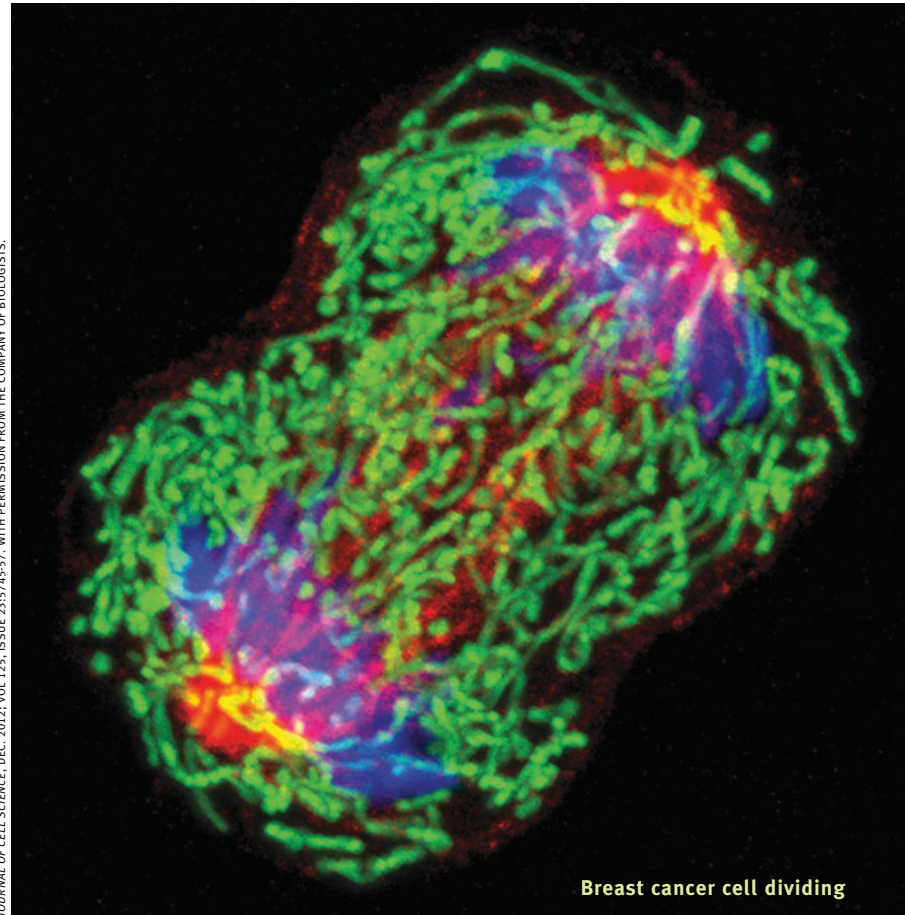


## Footnote

Word has it that Maud Menten wasn't much of a driver. Reports from the 1920s have the Pitt med prof's Model T lurching up and down Shadyside's streets. Reports from 1913, though, prove that she was one hell of a chemist. One hundred years ago, Menten, with Leonor Michaelis, crafted what has become known as the Michaelis-Menten equation. This was the first mathematical means for determining the rate of an enzyme reaction—a tool that, among other things, led to the rise of the pharmaceutical industry. The equation helps scientists figure out how to build drugs that inhibit enzyme activity.

Now you can celebrate the Michaelis-Menten centennial with a *How Inhibited Are You?* T-shirt. Not kidding: [www.zazzle.com/michaelis+menten+kinetics](http://www.zazzle.com/michaelis+menten+kinetics)

JOURNAL OF CELL SCIENCE, DEC. 2012, VOL. 125, ISSUE 23:5745-57. WITH PERMISSION FROM THE COMPANY OF BIOLOGISTS.



Breast cancer cell dividing

## Stopping the Great Divide

Cancer cells win through a process of divide and conquer. They keep dividing, making more of themselves until the host body is overwhelmed. The University of Pittsburgh's Bennett Van Houten and Wei Qian have found a way to stop this seemingly unstoppable proliferation, at least at the lab bench. They managed this while exploring the world of mitochondria (our cells' energy factories and much more).

Van Houten, a PhD and the Richard M. Cyert Professor of Molecular Oncology in Pitt's Department of Pharmacology and Chemical Biology, and Qian, a PhD and postdoctoral fellow, tried interfering with cancer cell growth by knocking down a protein that helps mitochondria divide, a process necessary for cell health.

The experiment worked. But the researchers used genetic means, which could make for a difficult leap to the clinic. So, they turned to pharmacology. An existing compound called mdivi-1, they discovered, achieved the same result as the genetic approach, but through different mechanisms.

When combined with the common cancer drug cisplatin, mdivi-1 becomes even more effective in arresting breast cancer cell growth. The potential, Van Houten says, is that a combination mdivi-1/cisplatin cocktail would allow for lower doses of toxic cisplatin while enhancing its efficacy. Also, and this is quite promising, such a cocktail kills cisplatin-resistant cancer cell lines. The breakthrough was a recent cover story for the *Journal of Cell Science*.

Van Houten and Qian are now seeking funding to further their research in animal models. —Joe Miksch



## Overheard

### A computer guy's take on personalized medicine

**Shyam Visweswaran**, an MD/PhD, began his career in neurology. But after completing graduate work in biomedical informatics at Pitt, he's more focused on the computer brain than the human one. Perhaps you're aware that the biomedical science community has an eye toward customizing care for each patient. That effort (or dream), called personalized medicine, hopes to get the right therapy to the right patient at the right time. Add "via the right model," to that line, Visweswaran, an assistant professor of biomedical informatics at Pitt, might say. He believes we should also personalize the computer model for each patient.

#### What that means—modeling for each patient

"Currently, for most risk assessments and other prediction models in medicine, a single model is developed, and that model is applied to everybody. This approach involves building a prediction model that will perform well for the average patient, but not necessarily for the current patient that the physician is seeing. What I am working on is patient-specific (or personalized) modeling, where computer programs build a prediction model for the current patient that is tailored to that patient's information, such as age, gender, blood pressure, cholesterol level, and, in the future, DNA sequence. These computer programs will, on the fly, figure out what are the important factors that should go into the model to achieve the best prediction for the current patient."

#### Predicting outcomes

"Within 10 years, I anticipate, we will see a patient's DNA sequence become part of the electronic medical record. We are going to need computer programs that combine DNA sequence information with traditional clinical data to help predict well-outcomes that are of interest to the physician, such as, *Is my patient at high risk of developing Alzheimer's? What is the precise DNA sequence abnormality that is causing pancreatitis in my patient? Will my patient respond to this therapy?*"

#### Another kind of physician assistant

"The current generation of clinical-decision support systems assists the physician with simple tasks such as alerting when a vaccination needs to be done or if two medications that interact are prescribed to the same patient. We want, and hope, to build far more intelligent support systems that will assist physicians in all tasks they do, day in and day out, including better risk assessment, more precise diagnosis, more accurate evaluation of prognosis, and better selection of therapy."

—Interview by Joe Miksch

## Faculty Snapshots

**T**he University of Pittsburgh School of Medicine's Bruce Freeman and Valerian Kagan have been named fellows of the American Association for the Advancement of Science (AAAS). Freeman, PhD professor and chair of pharmacology and chemical biology, who holds the UPMC/Irwin Fridovich Chair, was honored for his career-long research into free radicals and their roles in inflammation and cell function. Kagan, professor of radiation oncology in the School of Medicine (whose primary appointment is in the Graduate School of Public Health, where he is vice chair for environmental and occupational health), was also added to the AAAS rolls. Kagan has a distinguished background in free radical biology and programmed cell death research.



Freeman



Kagan

The American Society of Neural Therapy and Repair named Pitt associate professor of radiology Michel Modo, a PhD, winner of the 2013 Bernard Sanberg Memorial Award for Brain Repair. Modo was recognized for his efforts in neurorestorative biology for TBI patients, including better use of noninvasive neuroimaging techniques to identify brain damage and developing strategies for repair. His imaging work focuses on finding ways to best monitor live cells moving through the body.



Modo



Schwartz

A Pitt team received one of the Clinical Research Forum's Top 10 Clinical Research Achievement Awards for work with brain-computer interfaces. The interfaces and the science behind the technology came out of the lab of Andrew Schwartz, a PhD professor of neurobiology. (Early clinical studies were done with support from Pitt's Clinical and Translational Science Institute.) The group's most recent triumph involved using the technology to allow a woman with quadriplegia to manipulate a robotic arm with her mind. She was able to feed herself chocolate. Jennifer Collinger, a PhD assistant professor of physical medicine and rehabilitation, was the lead author of the paper, which was published in *Lancet*.



Collinger



Arnold

Robert Arnold has long researched ways to improve communication between doctors and patients in cases where patients face life-threatening illnesses. And now the MD has received the Lifetime Achievement Award from the American Academy of Hospice and Palliative Medicine. Arnold is the Leo H. Crip Professor of Patient Care and the medical director of the UPMC Palliative and Supportive Institute. —JM



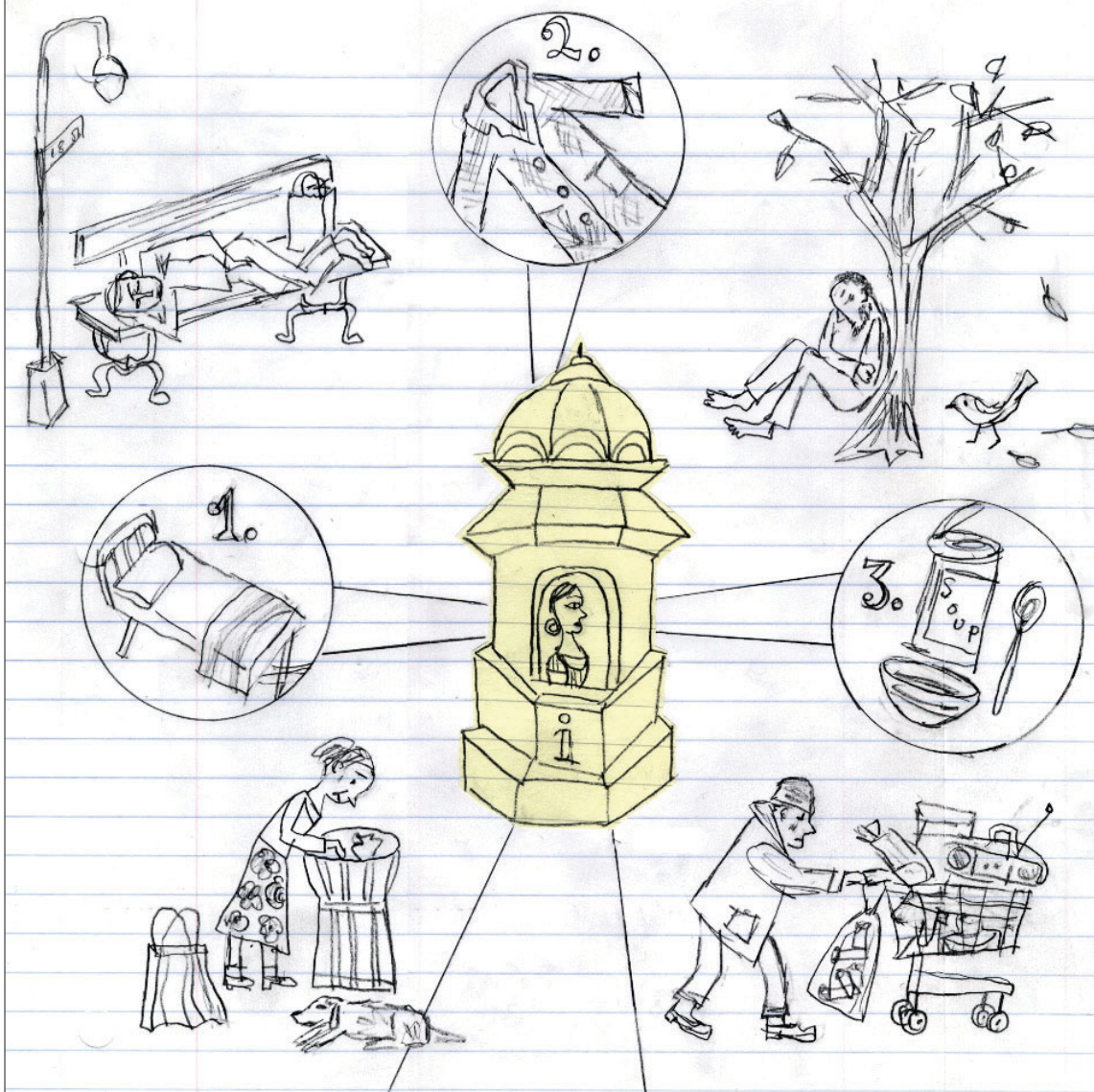
## Street Smarts

Third-year Pitt med student Gary Ciuffetelli was visiting Salt Lake City for a conference, and he toured the city's street medicine program. Ciuffetelli was impressed by how cooperative and intertwined the agencies were. From shelters to food banks to a free pharmacy, all aspects of street medicine were well-coordinated. But that seamlessness took years to develop.

"It's great that so many people want to help, but the biggest obstacle is that they don't know how," he says. "Organizations have the same problem: They don't know what others are doing or if there are opportunities for collaboration."

Hence, Serebral.org (a portmanteau of "service" and "cerebral"). The site, now in the proof-of-concept stage (Ciuffetelli and several collaborators are looking for money to go beyond that), will function as a repository of information regarding services available to underserved populations, like homeless people.

"Organizations and volunteers will have profile pages to help with recruitment and scheduling," Ciuffetelli says. "And everyone will be able to see a community map that you can filter by resource. If you're at an organization that offers clothing, and you have a client who needs food or a place to sleep, you can use Serebral to make a referral to that type of organization." And creating a community of helpers, Ciuffetelli says, will also make for more powerful grant applications, streamlined service, and a greater sense of community. —JM



## FLASHBACK

The above photo is from the 1964 yearbook of Cheltenham High School in Wyncote, Pa. See numbers 56 and 53? Neither really panned out as a hoopster, but each met with some success after leaving Wyncote. Reggie Jackson, 56, had a pretty notable baseball career. And 53, National Academy of Sciences member Peter Strick, went on to inform the world about how neural networks control voluntary movement—like dribbling balls. Among Strick's titles: Distinguished Professor and chair of neurobiology at Pitt and codirector of the Pitt/CMU Center for the Neural Basis of Cognition.

## Keeping Our Talent

From the very start, Esa Davis shared a productive dynamic with her mentor, Dennis McNamara, an MD, professor of medicine in the Division of Cardiology, and director of the UPMC Heart Failure and Transplantation Program. "We had a mutual research interest," says Davis, who's an MD, MPH, and assistant professor of medicine in the Division of General Internal Medicine.

Then the two learned they could apply for a grant to develop a research proposal. "It made us come together around the project," resulting in an arrangement "more collaborative than the traditional, 'I'm the mentor, you're the mentee'" setup, Davis says.

The duo is one of 15 mentor/mentee pairs who have completed the first year of the Promoting Academic Talent in the Health Sciences (PATHS) program, a partnership between Pitt and UPMC that seeks to retain and promote trainees from underrepresented groups within the institutions. PATHS offered the grant Davis and McNamara received.

PATHS is expanding quickly: Its next cohort will include 30 mentees from 19 departments in the School of Medicine. With continued success, the program will be implemented in, ultimately, all six schools of the health sciences. According to Paula Davis, assistant vice chancellor for health sciences diversity, "We have all of these phenomenal people, and if we can show them that they have a place at the table, we can keep them."

—Chad Vogler





## BODY EXPLORERS

Through the glass doors to Joseph Samosky's fourth-floor lab in Pitt's McKee Place, a simulated heart rhythm fills the area with emergency room-style urgency. Inside, a mannequin lies flat on a table as a projector hovers above, displaying a behind-the-skin reaction of the heart to a dose of adrenaline.

This is Samosky's evolving teaching tool, **BodyExplorer**, in action. It can show how a patient might react to various interventions, with data readouts on organ systems and, of course, sound effects. The device uses "augmented reality," placing computer-generated input and simulations onto real-world objects.

With an infrared pen, users can explore structures of the human body. (This gesture interface is a lot like using the Nintendo Wii.) Samosky, a PhD and assistant professor of anesthesiology and bioengineering, directs Pitt's Simulation and Medical Technology Research and Development Center. He's been developing the device with bioengineering PhD student Douglas Nelson (demonstrating the system above, center).

All these bells and whistles are about improving patient safety and quality of care. Samosky imagines **BodyExplorer** one day training doctors- and nurses-to-be and those who are already caring for patients. —Jeff Ihaza

## Immunology Gets New Leader

**Mark Shlomchik** has had a lengthy and impressive record as a scientific investigator. He was among the first to flesh out the roles of B lymphocytes and Toll-like receptors (both of which are key players in our immune systems) in systemic autoimmune diseases like lupus; that research recently garnered him the Lupus Insight Prize. He has also been a leader in understanding how long-lived antibody immunity develops, which is critical for understanding how vaccines function.



Shlomchik

As of July 1, Shlomchik, a PhD, formerly of Yale University, will succeed founding chair and Distinguished Professor Olivera Finn as leader of Pitt's Department of Immunology. Finn, who remains at Pitt, recently stepped down in order to focus more intensely on her research into developing peptide vaccines against pancreatic and colon cancers.

The move to Pitt, Shlomchik says, will allow him to scratch an itch he's had for some time. "It's been a great run [at Yale], but I felt like I have leadership skills and talents, and I wanted to pursue them," he says. Leading immunology at Pitt was an especially attractive opportunity. "I think the relationship between the medical school and UPMC is fantastic and enviable," he says. "The whole culture of how they work together has been instrumental in making [the School of Medicine] so successful. It has risen in an unprecedented way."

In his capacity as chair, Shlomchik hopes to find inventive ways to acquire funding (as federal dollars have declined in recent times), inspire creativity, and grow the department. —JM





## IT'S THE LITTLE THINGS

Donna Beer Stolz's main line of work isn't art photography. But the PhD associate professor of cell biology and associate director of Pitt's Center for Biologic Imaging (CBI) sometimes can't help but be taken by the beauty of the images she gathers from the lab's microscopes, even if she's peering at a pack of liver-destroying cancer cells.

Stolz's son, Ezra, graduated from Pittsburgh's Creative and Performing Arts School (CAPA) in 2012. Thinking that the school's budding creatives might have overlapping interests in art and science, Stolz recruited two CAPA students, Latia Tucker and Ben Kraemer, who were willing to look through the microscope for art's sake.

At Phipps Conservatory and Botanical Gardens, Stolz helped the teens gather samples, including clusters of pollen from coffee and princess flowers, to photograph with CBI's confocal and field-emission scanning electron microscopes.

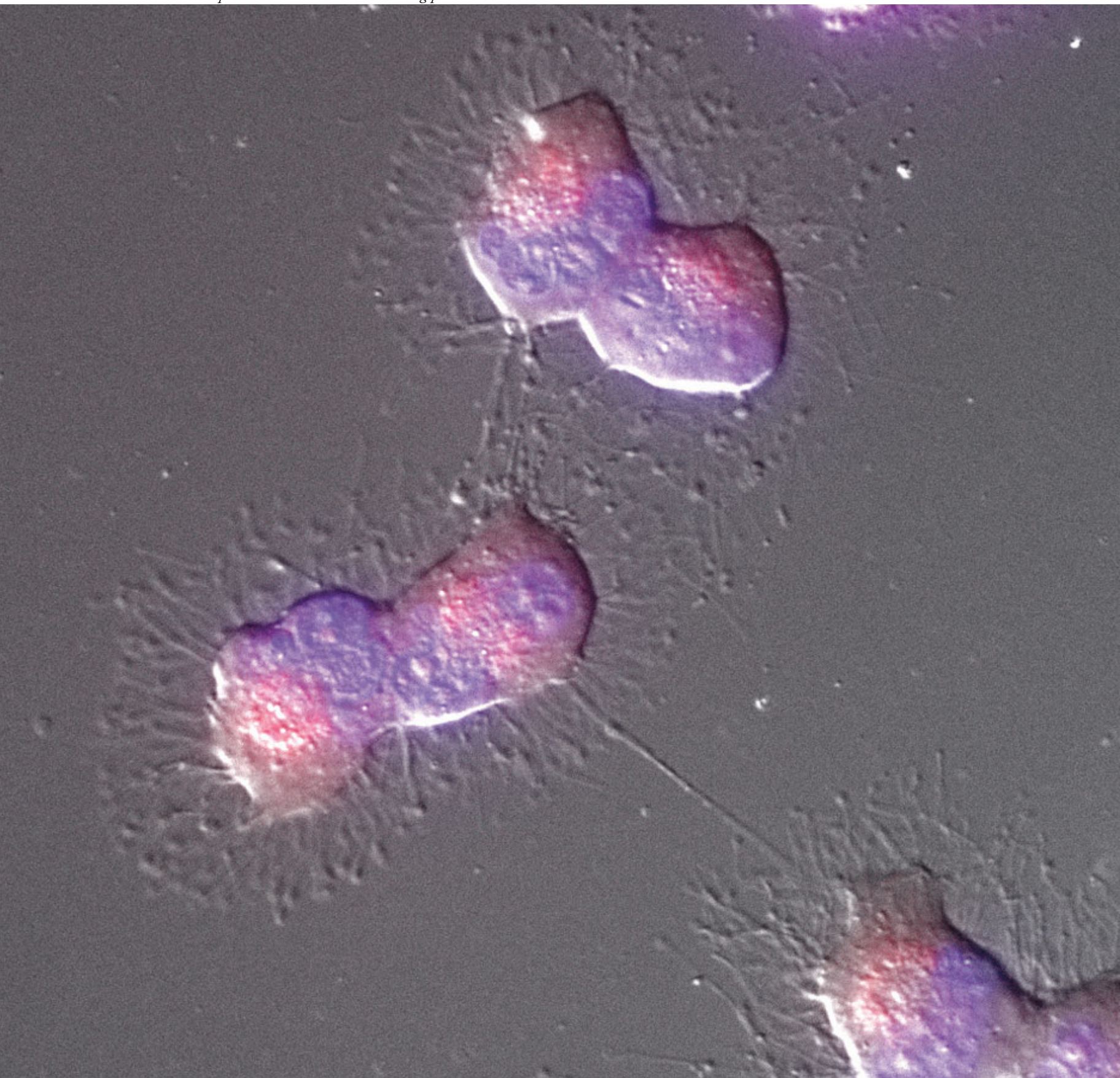
They colored and fleshed out the images from the microscopes in Photoshop. Ben says he tried to use colors that would create a connection between the scanned sample and the finished piece. "If it was a plant, I tried to use greens and yellows. One of the pieces was of a fern, and it had spores. I thought they should look like veins." (Latia was also taken with a fern; her staghorn fern is shown here.) Phipps put 14 of the pieces on display during its 2013 Secret Garden Spring Flower Show. Because the pieces had such a positive response, they will reappear at Phipps' fall flower show.

Latia, a visual arts major, says the process changed the way she looks at everyday items. "It was very bizarre to look at items we take for granted that closely. Everything, no matter how smooth it looks to the eye, has friction beneath it, and I think about that when I see everything now."

—Nick Keppler

—Microscopy by Donna Beer Stolz/Coloring by Latia Tucker





Temozolomide is used to treat glioblastoma multiforme (GBM), the deadliest form of brain cancer, but most patients become resistant to this chemotherapy drug. Here, GBM cells (their nuclei shown in blue) survive after treatment with temozolomide. Pitt scientists have identified genes that may contribute to this resistance.



# GENES OF INTEREST

NEW SUSPECTS IN CHEMORESISTANT  
BRAIN CANCER | BY DANA YATES

**G**lioblastoma multiforme (GBM) is a disease of extremes. Both the most common and the most lethal type of brain cancer in adults, it is tremendously resistant to chemotherapy. A team of University of Pittsburgh researchers, however, has identified potential weak spots within GBM—and homing in on those targets may make these tumors more sensitive to existing treatments.

Robert Sobol, associate professor of pharmacology and chemical biology and of human genetics, is senior author of a study that identified new targets for drugs that are aimed at destroying glioblastoma multiforme. The investigation, which was led by David Svilar, a PhD student in the School of Medicine's Medical Scientist Training Program, was the December 2012 cover story of *Molecular Cancer Research*.

According to the National Cancer Institute, GBM accounts for about 15 percent of all brain tumors. It's an extremely aggressive cancer with no effective long-term treatments; as a result, patients with these tumors typically survive less than 15 months after diagnosis.

The standard treatment for glioblastoma multiforme involves surgery to remove as much of the tumor as possible, followed by radiation and the chemotherapy drug temozolomide. The chemical agent damages the genome of GBM, which, in turn, prompts

the tumor cells to die.

But some genes in the tumor repair the damage; other cells soldier on no matter what is thrown at them, says Sobol.

So, with funding from the National Brain Tumor Society, the National Institutes of Health, and a NYSTAR James D. Watson Investigator Program Award, the research team set out to stop the genome-repair process. Along the way, the researchers discovered that a supplementary treatment—one that could act as a powerful ally of temozolomide—may do the trick.

The team treated tumor cells with temozolomide, but only enough to cause a small

activities in the cancer cells, including metabolism, protein synthesis, and cell division. These proteins, therefore, could potentially serve as druggable targets. For example, an accompanying drug therapy could be developed to affect these specific proteins, inhibiting them from doing their jobs and ultimately improving a patient's response to temozolomide.

Now Sobol's team is investigating the genes of interest and their attendant proteins in greater detail. The goal: sleuth out exactly what is happening in the genes and pinpoint the precise functions that are governed by the proteins. It may take years to develop a new drug to support temozolomide, Sobol says,

**The genes of interest oversee 12 broad categories of cell activities. And while the actions vary greatly, each one appears to be critical to helping the tumor survive the onslaught of treatment.**

percentage of the cells to die. Using siRNA—small RNA molecules that interfere with gene function—the researchers then tested more than 5,200 genes derived from GBM. The idea was to determine which ones helped temozolomide work better and whether there were additional genetic components that could be targeted to improve treatment response.

Eventually, from the original collection of 5,200 genes, the researchers were able to identify 125 “genes of interest”—that is, those that produce proteins that bind tightly with small molecules in order to spur various important

but he is hopeful that his detective work at the molecular level will one day make a major difference in the clinic for those with the deadliest form of brain cancer.

The genes of interest oversee 12 broad categories of cell activities. And while the actions vary greatly, each one appears to be critical to helping the tumor survive the onslaught of treatment.

“This demonstrates the complexity of the cellular response when exposed to temozolomide. Cells respond in a multitude of ways,” says Sobol. ■

# BIG DATA BIG HELP

## MAKING SENSE OF A POSTGENOMIC WORLD

BY LILY DAYTON

**A**nsuman Chattopadhyay was a biochemistry postdoc at Vanderbilt University in the 1990s—a time when cloning was hot and Dolly the sheep dominated the headlines.

“Everyone wanted to compare gene sequences, but they needed computer software,” he says. “I had no formal training, but I saw the need. I started playing with [data-analysis] tools.”

He was a molecular biologist by day, and by night, he became his peers’ go-to guy for questions about how to harness the ever-growing amount of genomic data to ask biological-research questions.

Soon after he completed his postdoc, Chattopadhyay went to work for a start-up software company, where he began his training in bioinformatics—the branch of science that connects biology with information science and computer science. The start-up did not survive the dot-com collapse, but something else awaited Chattopadhyay. In 2002, the University of Pittsburgh’s Health Sciences Library System (HSLS) was looking for someone with his knowledge and skill set to lead one of the first bioinformatics programs in the country, the Molecular Biology Information

Service (MBIS). Chattopadhyay came aboard and built the service from scratch, drawing from his own experience as a young researcher in a postgenomic world. He put himself in the shoes of Pitt scientists and asked, *What do they need?*

When Chattopadhyay held his first library workshop for scientists, the demand was so high he had to triple the number of programs offered. Demand continues to increase as more genomic, proteomic (the full set of proteins encoded in genomes), and other genetic information becomes available. In this information tsunami, it can be difficult for researchers to find the information they need, let alone the tools to process it.

Chattopadhyay and colleague Carrie Iwema, an information specialist in molecular biology, advise researchers at various stages of their projects—whether they’re searching for a particular gene, deciphering the structure of a protein, or trying to find the underlying cause for complex disorders like cancer or schizophrenia.

“We don’t analyze data for them,” says Chattopadhyay. “We train them and give them tools so they can do it themselves.”

Between workshops and graduate and

undergraduate courses, the two MBIS specialists trained 844 researchers in 67 hands-on bioinformatics sessions in 2012. They also offered one-on-one consultations to 431 researchers last year.

Researchers are not only trained in how to use leading commercial software programs in their research, but they are also given free access. The license for many of these packages costs around \$10,000—a high price for most labs. With 1,353 registered users last year, the HSLS program saved Pitt researchers more than \$6.2 million in licensing fees. The HSLS site ([www.hsls.pitt.edu/molbio](http://www.hsls.pitt.edu/molbio)) also hosts videos, tutorials, and search engines to locate software, databases, and other resources.

Pitt’s approach has proven so successful that it’s been used as a model for other molecular library programs cropping up across the country, including those at the University of Southern California, the National Institutes of Health, the University of Rochester Medical Center, and the University of Florida.

“We train people to navigate the human genome—the ultimate blueprint for finding disease,” says Chattopadhyay.

“Everything is there; the question is how to find what you want to know.” ■





# SCRATCHING THE SURFACE

THE EMERGING NEUROBIOLOGY OF ITCH

BY ELAINE VITONE

Pain and itch have an interesting relationship. If you are bitten by a mosquito, you can ease the itch by scratching your skin. And if you take a dose of a powerful painkiller like morphine, you're likely to itch. The interrelatedness of these two experiences has made deciphering the neurobiology of itch—the least understood of our somatic senses—a real head scratcher for scientists. Many have reasoned that the circuits must be the same for both itch and pain.

But Sarah Ross, a PhD assistant professor of neurobiology at Pitt, points out that we experience pain and itch very differently. Pain can happen anywhere in the body, but itch is only on the skin. And we react completely differently to these two sensations: Your hand flies away from the hot skillet, and right at the mosquito bite.

As a postdoc at Harvard, Ross studied a protein called *Bhlhb5*—a transcription factor known to play a key role in healthy development of the nervous system. She developed a mouse that lacked *Bhlhb5* and found that it rubbed little bald spots in its coat. “It looked like it was suffering from itch,” she says. She compared the sensory-stimuli responses of these mice to those of normal mice and found that the mutants had a heightened response to itch—but not to pain.

Next, she began looking at more selective removal of *Bhlhb5* from the components of the nervous system. She found that a *Bhlhb5*-free brain produced a normal mouse. A *Bhlhb5*-free system of primary sensory neurons (where we first encounter sensation) in the mouse's body didn't have any effect either. But when she removed *Bhlhb5* only from the spinal cord, the mice had a heightened itch response. She then examined what had gone wrong in the spinal cords of these mice and found that they lacked a particular population of inhibitory neurons—nerve cells that dampen the sensation of itch. They'd been wiped out by the loss of *Bhlhb5*.

“In retrospect, the spinal cord seems like a logical place to look,” she says. “Because primary sensory neurons convey their information to the spinal cord, and that's the first place that the information is processed and modulated.” A failed brake system there would send itch signals firing through the body willy-nilly.

Ross tagged this special population of inhibitory neurons, which she dubbed B5-I, in normal mice, providing the first molecular handle on the circuits that have eluded neurobiologists for so long.

Her studies are the first to offer a model of

chronic itch as a loss of neurological inhibition (loss of inhibition also underlies chronic pain, interestingly). Her team published these findings in *Neuron* in 2010. Last fall, her grant application to continue her work received a perfect score from the National Institutes of Health.

Now, Ross's team is beginning to draw the circuit for itch in the spinal cord. “And, eventually, we'll trace that circuit further up into the brain.” She adds that one exciting thing about this project is the mystery of it: Nobody knows which neurons in the brain give rise to the experience of itch or how the brain distinguishes itch from pain. Lots of things can cause either itch or pain (certain chemicals, for example), yet people tend to experience one or the other, not both. How the nervous system tunes such sensory input isn't clear.

Ross hopes her work might eventually lead to better, more targeted treatments for people who have chronic itch, an underappreciated problem that can devastate quality of life.

“But we're not stopping with itch,” she says. “We're going to use the same approach . . . to look at other types of sensation, as well. And this is going to have broad implications for pain, which is another huge problem for people worldwide.” ■





DAVID KUPFER WANTS THE *DSM-5*  
TO HELP HIS FIELD COME OF AGE  
BY ELAINE VITONE

# WORKS IN PROGRESS

I n the last few years, if you've read anything about the *Diagnostic and Statistical Manual of Mental Disorders*, the psychiatrist's manual (some would say "bible"), it probably hasn't been good. The pharmaceutical industry isn't making new drugs for psychiatric illness, say the blogs, because they can't find targets, and that's the *DSM's* fault. The normal range of human emotion is getting all mushed up with disease and causing overprescription of potentially toxic treatments, say the editorials, and that's the *DSM's* fault. The response around the latest version, *DSM-5*, is even less popular.

"Did you see that one in *The New York Times*? They're blaming [higher rates of ADHD diagnosis] already on *DSM-5*. It hasn't even been published!" says David Kupfer, sitting in his office on the second floor of Western Psychiatric Institute and Clinic on a late afternoon in April 2013, just weeks before the culmination of the massive document-revision effort that he has tended to, round the clock, "like an emergency physician," since 2006.

PHOTOGRAPH | JIM JUDKIS

Kupfer, 72, is tall and wiry with a warm smile, a welcoming presence, and, typically, a sharp suit. It's fitting that, in a 2004 story about the process of applying for competitive federal research funding, *The Wall Street Journal* characterized this MD as a "salesman," even though that's not a word you'd expect to hear when the subject is a professor. But this particular academic's claim to fame is building the once-minuscule research herd of the University of Pittsburgh's Department of Psychiatry into one of the largest and most prominent in the country—a feat that took no small amount of combined persuasive power and business smarts.

Well, his claim to fame until seven years ago, that is.

"So I put in a very brief letter to the editor that came out yesterday," he says. "And I sent it to two of my children who read *The New York Times*. And they said, 'That looks fine, Dad, but why didn't you quote us?'" (He'll use any excuse to talk about his kids.)

It's not that Kupfer is making light of the implications of revising the *DSM*. Weighing heavily on his mind, and on the minds of the 160 members of the task force and work groups whom he led through the revision process, is the fact that the diagnosis criteria listed in the *DSM* are the bases for Medicare and Medicaid reimbursements. There are financial implications, treatment implications, and social implications. Hence, Kupfer made the revision process of the *DSM-5* more transparent than any of its predecessors, putting the draft out to the public three times. Some 13,000 comments were posted online, and the task force and work groups read every one.

There has been tremendous outcry from patient advocacy groups, the pharmaceutical and insurance industries, the media, and the public. Members involved in drafting the previous *DSM* edition have written scathing commentaries and made the rounds of talk shows. At times, it's gotten pretty ugly.

"He listens extremely well," says James Scully Jr., medical director of the American Psychiatric Association, which publishes the *DSM*. "He's calm in the face of everybody lighting their hair on fire.

"He reminds me of General Eisenhower."

Many of the concerns are well intentioned: What of the Asperger's community?

These people have fought hard for acceptance and understanding. Now Asperger's is being stricken from the manual altogether? What of the bereaved, who are no longer explicitly excluded from the criteria for clinical depression? Will we be doling out antidepressants to everyone who loses a loved one, medicalizing a natural reaction to a horrible life event? (For more on these issues, see p. 19.)

It's complicated. But that should be no surprise. The brain is the most complicated organ in the body. It's arguably the most complicated thing on earth.

Psychiatry is still in an adolescent stage. For all the promising research—in genetics, imaging, cognitive neuroscience—scientists are still grasping for biologically based diagnostic measures they can use with sensitivity and specificity.

Kupfer says that when he started this process he honestly thought the *DSM-5* would have a firmer foothold in science. Alas, the science isn't there yet. But he's confident that is coming. His hope is that the new *DSM* will help to nudge psychiatry, finally, into its rightful place—as a branch of medicine

**Think of it as "DSM 5.0," he says, because, from here on out, more frequent,**

grounded in understanding, in evidence, in measurable outcomes.

This has been an obsession of his for more than 40 years.

**K**upfer grew up in New York, graduated from his Long Island high school at 17, and was voted "most likely to succeed." Yet a guidance counselor discouraged him from applying to Yale University—he is Jewish and there were still quotas. But he got in. He studied economics, history, and architecture, graduating a year early there, too. And he stayed at Yale for med school.

In the first half of his MD program, he thought he was going to be a urologist. He experimented with kidney-transplantation surgery in the animal lab. (Thomas Starzl, now Distinguished Service Professor of Surgery at Pitt, was just beginning to perform the first successful kidney transplants on humans at the time.) And then, Kupfer discovered something he found even more intellectually challenging: psychiatry.

Here was an area that was utterly bereft of understanding at the biological level. Mental illness was still seen in terms of psychological constructs, and psychoanalysis was very much the rule of the day. Then came the advent of the first psychopharmacological treatment, the bipolar medication lithium. Kupfer was absolutely fascinated. In an age so fixated, to borrow a Freudian term, on the art of caring for the mind through talk therapy, here was the first glint of the science of healing the brain.

He grew curious about the circadian clock and all its quirks that varied from person to person. The overachieving Kupfer realized he himself had always had "gobs" of energy without needing much sleep at all. And neither, he learned, did Yale-New Haven Hospital's psychiatry chief, a quintessential European gentleman by the name of Thomas Detre, who became his mentor. The pair hit it off. Detre was Hungarian. Kupfer's father's family was Hungarian. The two started putting in late nights writing papers together in Kupfer's third year of med school.

Kupfer graduated, and, after his first year of residency with Detre in New Haven, he

accepted an intramural research fellowship at the National Institute of Mental Health.

"I had innocently applied, not realizing only four out of 500 applicants got these positions," he says. (He says "innocently" a lot.) He assumes it was the transplant surgery that set him apart. At the NIMH, Kupfer spent a year running a clinical psychiatry lab, then another year conducting sleep research.

Before neuroimaging, sleep was one of the only things that gave us any real information about what was going on in the brain, Kupfer explains. He examined electroencephalography (EEG) in people with depression and found that certain patterns of activity could be used to separate these patients into subgroups. For example, if a person had an early onset of his first REM period and most of his REM in the first half of the night, that was a bad sign. These findings offered the basis for one of the first biological measures used to understand, classify, and predict long-term outcomes for people with mood disorders. Kupfer landed a paper in *Lancet* in 1972. "I was way ahead of myself in terms of how much undeserved



notoriety I had," he says.

By the time Kupfer returned to Yale to complete his training, he was convinced his path would be in academia. He won an NIMH career development award and set out to challenge a pervasive notion that distressed him to his core: That psychiatry was different, or even lesser than, the rest of medicine.

For instance, what's with the intake interview? Before you see a doctor for any other reason, while in the waiting room, you sit with a clipboard, dutifully filling out pages of forms. *Do you exercise? No/Yes, and how much? Do you smoke? No/Yes, and how much? Do you drink? No/Yes, and how much?* And before the physician says so much as, "How are you today?" you're in the exam room, with your chart filled out by an RN, documenting weight, blood pressure, reason for your visit, and on and on. These metrics are carefully recorded and tracked over time. If your blood pressure spikes dangerously high from one visit to the next, your doctor notices and does something about it.

But when you go to see a psychiatrist, what do you do in the waiting room? Skim *Reader's*

see him in action now, Kupfer was shy back then, by his own admission.

Kupfer was advisor to two med students that year: Rosenbaum and also Charles Reynolds, an MD, the UPMC Endowed Professor of Geriatric Psychiatry, and director of the Pitt/UPMC Aging Institute. Reynolds recalls, "One of [Detre's] fundamental critiques of American culture in general was that Americans are often afraid to take appropriate risks to achieve great things. If he weren't willing to take risks, Detre would have never left the security of Yale."

But, in the spring of 1973, leave he did, to head to Pittsburgh's Western Psychiatric Institute and Clinic (WPIC) and chair Pitt's Department of Psychiatry. His very first recruit was Kupfer, whom he chose to direct research. Kupfer was 31. "It was a very easy job because there was no research here. It was a no brainer." Ten years later, when Detre became Pitt's senior vice chancellor for the health sciences and president of UPMC, Kupfer would succeed him as head of the Department of Psychiatry. (Kupfer was also named Thomas Detre Professor of Psychiatry in 1994.)

Jim Harris, a Johns Hopkins professor of psychiatry and behavioral sciences and a friend of Kupfer's for some 25 years, says, "[Kupfer] has been uniquely connected in both the psychotherapy side and the neuroscience side of research in mood disorders."

Jack Barchas, chair of psychiatry at Weill Cornell Medical College, raves breathlessly about both Frank and Kupfer, alternately calling them "incredible," "brilliant," and "remarkable" and pointing out that they are one of only two couples ever to have won the prestigious Institute of Medicine's Rhoda and Bernard Sarnat International Prize in Mental Health. He says, "They are without a doubt one of the greatest couples ever in the field of psychiatry."

**K**upfer (and Detre) didn't move to Pittsburgh right away. Every two weeks, they'd come work for two days—two *18-hour* days—and this went on for six months. According to Pitt lore, one night, an administrator was leaving WPIC and saw the lights still on in both their offices, and joked to a colleague, *It's 5:30, and they're*

**partial updates will be released as the science evolves. This may well be the last print edition.**

*Digest.* Your overall mental health, diagnosis, and treatment options are all assessed solely on the basis of one of your conversations with your psychiatrist.

"I think that's the most ridiculous waste of time," says Kupfer. "While you're waiting, you should be filling out a bloody [huge] amount of information, which I will then be able to see before I see you."

Kupfer put the idea to Detre, and he was game. Through many late nights, they developed a series of forms together—questionnaires for patients to self-report their symptoms—which they called the KDS, for Kupfer Detre System. It was one of the first attempts at evidence-based assessments of mental disorders in the clinic.

He was "quite a research geek back then," recalls Jerry Rosenbaum, professor of psychiatry at Harvard University, who first knew him in 1972, when Kupfer was his MD thesis advisor. Rosenbaum recalls often finding Kupfer surrounded by reams of computer paper—stacks of KDS data printouts all over his office. And, though you'd never know it to

When the two Yalies first came to Pitt, Detre hired a writer named Ellen Frank, and among the first projects the three of them worked on together was a book about the initial diagnostic interview, *The First Encounter*.

"It was like a seminar in psychiatric diagnosis with two teachers and one student," says Frank.

The book was never published, but on the bright side, it resulted in Frank going to graduate school and, a couple of years later, in a marriage. Kupfer and Frank, who is now a PhD and Pitt Distinguished Professor of Psychiatry, celebrate their 38th anniversary this summer.

Kupfer pursued his interest in sleep and depression. He then focused on major depression and bipolar disorder and their treatments. Frank and Kupfer became collaborators and went on to make significant contributions to the design of randomized clinical trials for mood disorders. Theirs were among the very first such studies of the treatment of recurrent depression—and not just of one treatment versus another, but also, more importantly, of any drugs at all versus psychotherapy.

*still not done with their work? These guys are never gonna make it.*

But in the first 10 years, the department shot up to third in NIH funding, and the faculty grew from a few dozen to some 150. The WPIC staff tripled to 1,200.

How did that happen?

Kupfer says he has always been interested in the psychology of motivation: How do you get people to perform beyond what even they believe to be their capacity? "That fits into the rhythm of what I've innocently done with my own kids," he says. "My son told me once, 'Dad, you're nothing but a professional coach.'"

He thought of the department as one big laboratory, a place to test out his ideas about motivation. For his test subjects, he used a cadre of faculty he enlisted from what he saw as the most exciting new subfields of psychiatry. When he first arrived in the '70s, the hot new thing was pharmacology and pharmacokinetics. Over time, he would recruit experts in basic science, neuroscience, neuroimaging, and the translational science of psychiatry.

Kupfer says that the department has been, and continues to be, “a department of kids,” a term he uses often and without condescension. His long-held appreciation for the new and novel has yielded a menagerie of relatively newly minted PhDs.

“They encouraged any warm body,” says Frank, “including a first-year graduate student like me, to apply for research funding.”

Investigators who are yet a little “unformed,” Kupfer says, are more willing guinea pigs for the favorite experiment in the Kupfer Laboratory, a.k.a. the Department of Psychiatry (which has been chaired by David Lewis since 2009)—interdisciplinary collaboration.

Kupfer developed his own formula for the proper care and feeding of researchers: Give them the seed money they need to fund their work. Give them credit when their hard work pans out. Promote them, sometimes at a rate

Within a year of their arrival, Kupfer and Detre also started a long-standing policy of issuing rewards to investigators in proportion to the amount of federal-research funding they brought in. It might sound unseemly to some—kind of like corporate culture, says Daniel Buysse, professor of psychiatry and of clinical and translational science, director of the Neuroscience Clinical and Translational Research Center, and codirector of the Sleep Medicine Institute at Pitt. (Buysse is also a Kupfer mentee dating back to 1983.) But he means that as a compliment. “Science is business, and David realized that before a lot of people did. It’s just a reality.” Kupfer operates in a strategic, systematic way, says Buysse. He delegates. He pays attention not only to whether a study is worth doing, but also to whether it can be paid for.

The Research Review Committee makes

something missing.’ It took me two years to find out that he was right.

“He has this ability. He can sense the people who have talents he can elicit. And he can also make the judgment on the other side, which is sometimes harsh. But I think that ability—to actually understand where people are coming from, what their talents are, and how to use them—is really remarkable. And to have it in a person who’s as good a scientist as he is, is really amazing. ... All you have to do is look at the quality of the Pittsburgh faculty. People used to say that if you go to Pittsburgh and David says you have talent, you are gonna stay in Pittsburgh.”

What’s the secret? Kupfer is sure it’s a gift, something that may not be teachable. There are certain attributes Kupfer tends to notice and file away as he gets to know people: birth order, handedness, and the like. (He estimates some

**“The profession has got to decide that it needs some measurable outcomes. And it can’t be my saying, ‘Well, I think you’re doing a little better.’ Then somebody else in New York says, ‘Well, hmm. I think you’re doing terribly.’ See? What the heck is that?! It’s not sufficient.”**

that might surprise outsiders. But the Pitt lot gets away with this, if history is any indication, because it happens in an environment where people feel safe trying out untested ideas.

But they can’t do that alone.

“David often says we’re like real estate agents,” says Lewis, an MD who is also UPMC Professor of Translational Neuroscience, medical director of Western Psychiatric Institute and Clinic, and among a long list of people who came to Pitt as young pups and grew into research giants. “The three most important things are mentoring, mentoring, and mentoring.”

Very soon after Kupfer arrived at Pitt, he set up the Research Review Committee, which is still active and which he has led since he stepped down as department chair. It’s an internal grant-review process designed to be every bit as stringent as that of the NIMH, if not more. Some 200 faculty now participate, a few of whom are from outside the department and most of whom have served on federal grant-review committees. Grant writers get their feedback within a week. (When the program began, turnaround time was 48 hours. “People dropped everything to read” new proposals, says Frank.)

sense from the standpoint of fostering a collegial, collaborative environment. In reviewing one another’s grant drafts, researchers network with people in their department.

Another way to get people to share new ideas, Kupfer says, is to make them share other things, too. Instead of setting up, say, several different sleep labs for schizophrenia, for depression, for children, and so on, make one big sleep lab and throw all of the researchers together.

Of course, not every excellent scientist is cut out for a place like Pitt. For all their brilliance, some people just aren’t good mentors. And some, if asked to share and share alike, just will not like that *at all*. But Kupfer has a remarkable gift for spotting such people—and for reading people in general—and can do this very quickly. Many of Kupfer’s close friends have stories like this:

“I was working with someone once, and she is quite brilliant,” says Helena Kraemer, professor emerita of biostatistics in psychiatry at Stanford and professor of psychiatry at Pitt. “David met her and talked to her for about 15 minutes. And then he said to me, ‘You know, she’s not going to make it.’ And I said, ‘Why do you say that?’ And he said, ‘There’s just

30 to 40 percent of the department’s faculty are lefties. Kupfer himself is a southpaw, too.)

“There’s some anecdotal stuff that happens to be true, which is that people who don’t share, well, are not likely to share!” he says with a laugh. “In the early days, when we used to recruit people from Yale and take them out for dinner, I would find out whether they would be willing to share their food. Just a little taste.”

When he reviews a CV, Kupfer pays special attention to a candidate’s list of publications. When doctors don’t have a history of sharing authorship, they’re not likely to share other important things. And, perhaps most importantly, he asks, *What has this person done in the way of mentoring?* “Somebody who hasn’t mentored is not a good team player, even if they’re very young. It doesn’t matter who they’ve mentored. It could be a younger sibling.”

In addition to his people-reading skills, he’s famous for his team-building, both at Pitt and beyond. “He is the consummate scientific *shadkhen*” (that’s “matchmaker” in Yiddish), says Laurence Steinberg, PhD, Distinguished University Professor of Psychology at Temple University.

As a result of all this careful people picking and pairing, the Department of Psychiatry’s



research efforts cover just about every aspect of psychiatry and brain science that you can shake a stick at: diagnosis, neurobiology, psychobiology, cognitive neuroscience, biological treatment, policy. From pediatrics to geriatrics. It's all there.

"Very few departments are that broad," says Barchas. "There's almost no area of research that NIH funds that there isn't someone at Pittsburgh working on. It's just plain astounding."

Though the department is welcoming to newbies, a sizeable percentage of its faculty are not "kids," in fact. Many are original Detre/Kupfer recruits from decades ago. You've got to wonder how common that must be.

"I don't know if it's like that at other places, because I've never been anywhere else," Buysse says, laughing.

Posed with the same question, Lewis gives the same answer.

**K**raemer says people—even a lot of psychiatrists—tend to use the terms *disorder* and *diagnosis* interchangeably. But the disorder is what's ailing you—the quirk of the organ that is your brain, the fact that your striatum fails to activate in response to a reward stimulus, or whatever. And the diagnosis is someone's *opinion* of what's ailing you.

"From my perspective," she says, "the crucial thing about *DSM-5* is that we're trying to bring diagnosis one step closer to the disorder."

In the absence of biological measures, psychiatrists and others have made their best guesses at diagnosis using the only tools they've had: symptoms. In fact, in previous editions of the *DSM*, symptoms were the only criteria that were *allowed*. This is one of those things that has kept psychiatry out in the wilderness, different from the rest of medicine. As Buysse puts it, you wouldn't lump together any other kind of diseases based on how they look in the clinic, would you? If you put, say, all conditions that cause you to cough up blood into one category, you would be blindly lumping together bronchitis, tuberculosis, and cancer.

"When we say people have depression, it's kind of like the bloody sputum of psychiatry," Buysse says.

Diagnosis has always been challenging, because the scientific community has known so little about disorders. And yet without accurate diagnosis, scientists can't understand the disorder any better, because they can't trust the

reliability of the research.

But if scientists ever want to begin to understand the individual quirks of the organ that is the brain—and to help it heal—they have to start somewhere.

Kupfer's solution: While previous editions have been named with Roman numerals, (*DSM-III*, *DSM-IV*), he decided the fifth edition should be titled with an Arabic number. Think of it as "*DSM 5.0*," he says, because, from here on out, more frequent, partial updates will be released as the science evolves. This may well be the last print edition. Gone are the days of waiting 15, 20 years to start from scratch. He calls the new *DSM* a "living document."

One aspect of the revision that was utterly ignored by the media in the buildup to the release of the latest edition, but which means a great deal to task force members, is the manual's "meta-structure." Essentially, the book has been reorganized, and the chapters have been reordered. Disorders that now appear to share common biology have been put right next to one another. For example, ADHD, schizophrenia, bipolar disease, anxiety, and depression are now together because they've recently been found to have genes in common.

So how does this help patients?

Alan Schatzberg, professor and former chair of psychiatry at Stanford and former president of the American Psychiatric Association, says, "It helps them in that anxiety and depression seem to be quite related. One seems to presage the other," for example.

And it helps because, if your physician realizes that certain disorders share biology, she might view your family history differently. "We still have distinctions of disorders," Schatzberg says, "but there are commonalities in terms of how they run in families. . . . A schizophrenic kid will have a bipolar father or grandfather."

Within the chapters, the diagnostic criteria will be very different. In *DSM IV*, physicians were presented with checklists—if the patient has five of these seven psychiatric symptoms, he has disorder X. But the science is telling us that it doesn't always work that way.

Which is what has led to what are often called "wastebasket" diagnoses, not otherwise specified (NOS). That's where people just outside of the criteria end up. Previous *DSMs* have led to overflowing waste bins—in autism spectrum disorders, famously, among others.

So, in 5.0, diagnosis is not so all-or-nothing, you-have-it-or-you-don't. Now, it's about severity of symptoms. A continuum. A spectrum. The evolving understanding of the underlying biology of disorders is teaching psychiatrists to focus more on the similarities between disorders than their differences—or, rather, what is *perceived* as their differences.

Because they've found that often they've been wrong.

Disorders psychiatrists thought *weren't* related really *are*. Like autism. In *DSM-IV* there were four distinct diagnoses thereof (Asperger's and so on). But the science to justify all this hairsplitting just isn't there. So in 5.0, it's one big autism spectrum.

Alternatively, disorders that people think *are* related really *aren't*, says Kupfer. To illustrate, he points his finger at each of the swiveling, black-leather Eames chairs around the low, white marble table in his office.

"Let's say we have [several] people sitting here," he says. "All of them have clinical depression. The person next to you, you know, that person is suicidal but also has clinical depression. This person over here also meets the criteria for clinical depression, but he's psychotic—he has delusions. And what about this person? This person's had all kinds of panic attacks. The person next to me has a drug problem. And this person on the other side of you? It's his first episode, and he may never have another episode. All right? They all meet the diagnosis of clinical depression, but we treat them differently."

Nobody here is suffering from just depression, Kupfer says, and that's where the term *comorbidity* comes from. But the evidence is showing scientists that that comorbidity is the rule rather than the exception—and 5.0 says as much, for the first time in *DSM* history.

"Comorbidity may simply mean that we've got the wrong diagnosis." That is, maybe, for each of the imaginary patients at the table, there is a different disorder that cuts across several different clusters of symptoms. But psychiatrists will never recognize these cross-cutting clusters unless they start measuring and tracking symptoms in a systematic way.

In the new *DSM's* Section III—an appendix of sorts where the task force has included items that are in need of further investigation—is a return to the Kupfer Detre System. (Remember those reams of papers that surrounded Kupfer in his office in 1969?) It's a

computer-based questionnaire patients can fill out in less than 15 minutes, an inventory of general measures of mental health status: level of depression, anxiety, sleep, substance abuse, and so on—mental health counterparts of blood pressure and heart rate.

Kupfer hopes professionals in the field of psychiatry will take this tool and run with it. Perhaps it will stimulate new ways of thinking about disorders. “Maybe you can begin to divide your subgroups differently, like we do with the rest of medicine.” In other words, maybe psychiatrists can start to get past the bloody-sputum kind of thinking. “And once we get *there*, we can start making some progress.”

Such an inventory could be helpful in the clinic, Kupfer says. “I’d sit down with you and go over these things as part of my getting to know you. You get into things a lot quicker, and I think you do a much more accurate evaluation.

“The profession has got to decide that it needs some measurable outcomes. And it can’t be my saying, ‘Well, I think you’re doing a little better.’ Then somebody else in New York says, ‘Well, hmm. I think you’re doing terribly.’ See? What the heck is that?! It’s not sufficient.”

Also in Section III is a tool clinicians can use for something the task-force folk call “dimensional diagnosis.” It’s a way to assess symptoms along a spectrum—not whether or not a patient has depression, but how much?

Reynolds says this new emphasis on dimensionality could lead to better prospects for patients diagnosed as NOS—not only in terms of getting them out of the wastebasket diagnoses, but also to improving their outcomes.

“Many people live with subsyndromal, sub-threshold symptoms, for example, of depression,” he says. “It’s important to recognize that. Because many such persons are at risk of going on to develop frankly clinical expressions, for example, of depression or schizophrenia.

“I think the *DSM-5* will also assist with the further development of prevention science within psychiatry. This is a very important aspect of *DSM-5*.”

Reynolds, who chaired the work group on sleep-wake disorders for *DSM-5*—a work group Kupfer chaired for *DSM-IV*—is proud to point out that this section includes, for the first time in *DSM* history, biological measures with proven diagnostic use, as well as epidemiologic studies, all written right into the

official diagnostic criteria.

“We had not been allowed to include biological measures in *DSM-IV*,” Reynolds says. “That was just not part of the spirit of the times. It has been a long journey, a journey not without quite a bit of controversy along the way. David was never afraid of the controversy, never afraid to take risks and to try to push the field forward.”

**O**n a chilly morning in April 2013, Kupfer welcomes this *Pitt Med* writer who has come to crash his party. “Have some breakfast—you’re too skinny anyway,” he says, channeling my mom.

It’s the start of an intensive, five-day course for bipolar-disorder-research “kids” from around the world—this year, from Poland, Chile, and Colombia, as well as across the United States. Kupfer started this semiannual course eight years ago, bothered by the stagnation in bipolar disorder research. (“Lithium was something that was being used . . . in the late ’60s,” he says. “We don’t have a better drug to treat bipolar disorder 45 years later. There’s something wrong. Radically wrong.”)

More than a decade ago, Kupfer and Schatzberg founded the Career Development Institute for Psychiatry, a similar mentoring program for physician-scientists in all areas of psychiatry. A collaboration between Pitt and Stanford, the institute has since been revised and expanded as a long-distance mentoring program, offered year-round. The idea is to try to figure out how to change the nature of mentoring, or lack thereof, in other places and “influence or pollute their own environment back home—not in an antagonistic way, but to help them on their home turf,” Kupfer says. “Because not everybody is gonna move to the six or seven places where we would say there’s good mentoring.”

Two years ago, the American College of Neuropsychopharmacology presented Kupfer with the Julius Axelrod Mentorship Award. (Kupfer knows its namesake as “Julie,” who consulted for Pitt’s department many years ago.) The morning of the award ceremony, he looked around the room and realized that among the 200-some people there, he’d probably mentored a quarter of them. When he came home, Pitt gave him a T-shirt emblazoned with “Mentor of All Mentors.”

These are the kinds of things Kupfer does to keep himself “off the street,” he says. Another

is an international conference on bipolar disorder. The first one, which took place 15 years ago, was a small affair in Pitt’s student union. The last couple have drawn more than a thousand attendees from 25 countries.

“His energy is frightening,” jokes Frank, of her partner the night owl.

As the participants take their seats at this spring’s crash course, Kupfer encourages them to relax. Here, he lives up to his reputation as a “consummate schmoozer,” as *The Wall Street Journal* called him. “The dress mode is as casual as you are comfortable with,” he says—he’s dressed business-casual today. “We want you to enjoy yourself and work with the faculty colleagues”—many of whom are alums of this program, he notes, and all of whom have come here, pro bono. (Mentoring, mentoring, and mentoring.)

And it does seem cozy, or as cozy as it can be for a group of young investigators in the presence of one of the most influential academic psychiatrists in the world.

Kupfer has the mentees go around the room, introduce themselves, and talk about what challenges they face in doing what they want to do. The mentor faculty then do the same. They commiserate over many shared frustrations: work/life balance, clinical-work/research-work balance, departmental politics, getting published. Kupfer interjects often with advice. (“When my children ask me what they need to get ahead in life, I say, ‘There are only, really, two or three things, and one of them is that you’ve really got to learn how to write.’”)

And then it’s Kupfer’s turn. He says his biggest challenge, now that the *DSM-5* is coming out, will be to gradually extricate himself from those efforts, which have kept him on call 24/7 for seven years, and get back to his real passion, mood-disorder research—bipolar-disorder research in particular. “The real problem for me is the question of how many of these involvements should be where I commit myself as principal investigator—which is something like five years, 10 years—versus helping other people attain their PI status. . . . That’s something I’ve always been comfortable doing.”

Then, a faculty member asks, “If you knew then what you know now, would you have done the *DSM-5*?” and a chuckle spreads through the room.

“Absolutely,” he says. “No question about it.” ■



# DSM 5.0

A CONVERSATION WITH DAVID KUPFER  
ON REVISING THE PSYCHIATRY MANUAL  
WITH A LIFE OF ITS OWN  
INTERVIEW BY DAVID LEWIS  
AND MAGGIE MCDONALD



DSM 5.0  
Now Available



**I**n case you missed it, there's been a bit of an uproar about the new *Diagnostic and Statistical Manual of Mental Disorders (DSM)*.

*DSM* is the go-to guide for diagnosing mental disorders; it's published by the American Psychiatric Association (APA). The manual contains descriptions of mental disorders, symptoms, and other criteria to support consistency and accuracy in diagnosis; it has also been the basis for reimbursement followed by health care providers, insurance companies, and Medicare.

How could something with a title so dry and a purpose so seemingly utilitarian cause such a fuss?

Much of the fuss came before the manual was even released. And that explains some of it.

Yet the *DSM* often informs how clinicians, researchers, policymakers, and the public interpret mental health conditions and diagnoses, so its impact on treatment and funding decisions can be profound. The manual's latest revision has been an arduous, contested process. One measure of how salient the *DSM* is: During three open comment periods in the revision process, the APA received 13,000 comments and 12,000 e-mails and letters from clinicians, researchers, and patient advocates.

ILLUSTRATION | JESSE LENZ

The gargantuan task of revision was led by David Kupfer, who is the Thomas Detre Professor of Psychiatry at the University of Pittsburgh and chair of the APA's *DSM-5* Task Force. (See p. 12 to learn more about the man behind the manual.) Kupfer, with vice chair Darrel Regier, executive director of the American Psychiatric Institute for Research and Education and director of the APA's Division of Research, directed the task force's efforts to revise the retiring *DSM-IV*, which had served as the gold standard since 1994.

Long overdue, *DSM-5* itself was 14 years in the making; it represents the scientific input of more than 500 experts from the United States and abroad. It takes into account developments that could barely have been imagined 20 years ago.

Shortly before unveiling *DSM-5* at the APA's 2013 Annual Meeting in San Francisco in May, Kupfer spoke with UPMC Endowed Professor in Translational Neuroscience David Lewis, who succeeded Kupfer as Pitt's chair of psychiatry and is Western Psychiatric Institute and Clinic's medical director and director of research, and also Maggie McDonald, who worked as a science journalist specializing in psychiatry in the 1970s and '80s. McDonald is Pitt's associate vice chancellor for academic affairs, health sciences. She also holds appointments as assistant professor of epidemiology in the Graduate School of Public Health and of psychiatry in the School of Medicine.

These edited conversation excerpts give a glimpse behind the scenes of the revision process, *DSM's* move towards criteria based on emerging biological research, and the future of the manual. Number 5 is the first online *DSM*, and Kupfer imagines that it may be the last print version. He sees it as *DSM 5.0*—a more agile, living document that will adapt as the science behind psychiatry progresses. —*Introduction by Josie Fisher*



Kupfer

Lewis

everything was up for grabs in terms of looking at every diagnosis. On the other hand, the thresholds and standards we used for change were quite high.

Another is that we espoused the position that development needed to be thought of across the entire lifespan. So we removed the first chapter of *DSM-IV*, which dealt with all of the disorders of what I would call childhood. Instead, we would work to ingrain the whole continuum of both age and development within each major cluster of disorders.

Another principle: The *DSM*, since it is primarily to be used by clinicians for clinical assessment, would be [designed for ease of use by these practitioners], although its [consistent application] would inform research across various fields.

Another principle was to move *DSM-5* closer to the rest of medicine . . . to say that whether you had a psychiatric condition or a medical condition, it was all on the same axis. Furthermore, we felt that we could do a better job of aligning the *DSM* to the next edition of the *ICD*, the *International Classification of Diseases* (which covers all of medicine and psychiatry), developed by the World Health Organization.

**MM:** Have there been particular advances in neuroscience that have broadened the base of evidence that have allowed you to bring the psychiatric disorders closer to the medical diagnostic model?

**DK:** The optimism was that by the time we finished *DSM-5*, we would have enough information for some of the major disorders—whether from genetics, neuroimaging, or cognitive neuroscience—to apply some of



McDonald

**Maggie McDonald:**

You have been working on *DSM-5* since 2006. We're here to talk about this journey.

*DSM-II* [published in 1968] was a thin, half-inch-thick book of definitions made up by prominent psychiatrists of the time. Then, *DSM-III* [which came out in 1980] was the first criterion-based system. It was really a sea change in defining psychiatric illnesses. How does *DSM-5* differ substantially from the previous version, *DSM-IV*?

**David Kupfer:** To put it in perspective, *DSM-IV* did not differ much from *DSM-III*. So we're really talking about what substantial changes have taken place since 1980 that need to be incorporated into *DSM-5*. *DSM-III* was influenced by a group at both Washington University and Columbia, and it represented the consensus of the research and diagnostic criteria of that time and from the early to mid-1970s. *DSM-5* constitutes a much wider group of individuals involved and very different procedures used to arrive at changes.

**David Lewis:** What principles guided the process?

**DK:** The first was that [after 30 years]



these biological variables as diagnostic criteria or to enhance diagnostic criteria in existing categories. We haven't gotten where we would like to get.

The chapters are reorganized so that they are more neuroscience compatible. [For example], chapter one is neurodevelopmental, which has autism and ADHD. Chapter 2 is schizophrenia and other psychoses. And chapter 3, standing by itself, is bipolar disorders.

Only in a very few disorders have [scientists pinpointed] a biological variable—for example, in narcolepsy. We have some of that in the neurocognitive areas. But not very much of it. Hopefully, we'll get there soon.

That leads me to our changing the Roman numeral V to the Arabic 5. *DSM-5* can be a living document. We don't have to wait 20 years for the next version. And so, hopefully, in three or four years, changes in a

reflect more of a dimensional way of thinking about how [patients] got to where they are.

[Dimensional assessments rate the presence and severity of symptoms in increments such as “very severe,” “severe,” “moderate,” or “mild.”]

**DL:** Some changes in *DSM-5* have attracted controversy. Could you speak to one or two examples, and what you think about the basis for the controversy?

**DK:** So, let's take a couple of them. One of the major areas of public discussion and clinical discussion was around autism. The data suggested that there weren't such fine differences between Asperger's, pervasive developmental disorder, and autism. For years, people have talked about putting these together and calling it autism spectrum disorder. We'd look at the major symptom clusters in a dimensional way and, therefore, be able to grade different levels of severity and need, using a label called

obstetricians, and gynecologists. According to *DSM-IV*, in essence, if somebody were in the early phase of bereavement (within two months of having a loss), it was not permissible to diagnose clinical depression.

So, it made some interesting assumptions: One is that everybody would always be confused about making that diagnostic differentiation and would assume that even if someone were, quote, “severely depressed and suicidal,” you shouldn't do anything for the first two months. We were told [by a number of groups] not to get rid of the bereavement exclusion because that would be permission for, say, gynecologists and obstetricians to immediately give everybody antidepressants. . . . If, for example, a couple had lost a child at birth, when they really needed grief counseling.

So we've gotten rid of that exclusion; it's not part of the criteria of major depression anymore. [Instead] we put in two different

**One measure of how salient the *DSM* is: During three open comment periods in the revision process, the APA received 13,000 comments and 12,000 e-mails and letters from clinicians, researchers, and patient advocates.**

version 5.1 or 5.2 might include [specific biological] variables relating to psychosis and schizophrenia to diagnose, say, 20 percent of the people who have psychosis in a more objective fashion than we can now. And 5.1 doesn't have to affect all diagnoses. Updates to specific sections can be made to the online *DSM* as needed.

[Regarding moving the *DSM* closer to the medical model:] One thing we did is we reconsidered conceptually somatic disorders . . . as conditions due to . . . or associated with medical conditions. We assumed that there may be an etiology related to both a psychiatric disorder and a medical disorder.

This assumption of comorbidity relates to a discussion of categories versus dimensions in the *DSM*. We need categories because we need the code to be reimbursed. However, in the world of psychology and science, most of us think in dimensions. We think about continuous measures. And so, *DSM-5* reflects graded levels of severity in many diagnostic areas. And some diagnoses are grouped to

autism spectrum disorder.

We decided that if we [presented the autism spectrum diagnosis early on in the revision process], hopefully studies in the field would follow that would allay what some people feared might happen [if the previous four diagnoses went away]. People feared that the prevalence of these disorders would dramatically change [either through lack of diagnosis or overdiagnosis in light of the new classification]. Some feared that educational institutions and other institutions would deny benefits for children if they were, quote, “not diagnosed with Asperger's” or one of the specific [previous diagnoses]. What we've discovered is that the diagnosis of autism spectrum disorder seems to work well. The scientific literature, as well as major associations of advocacy groups and advocacy/scientific groups like Autism Speaks, have, in general, endorsed the change.

Another [area of controversy is the] so-called bereavement exclusion. Let's think about it in terms of primary care physicians,

notes, carefully crafted, explaining the difference between sadness, grief, and clinical depression. One note is included right with the criteria set in the short version of the *DSM* that people keep on their desks. In the [longer] text is a further explanation. Now, having done all of those things, there is still a great deal of furor about what we've done.

**DL:** In *The New York Times* and *The Wall Street Journal*, and in the scientific literature, we continue to read about advances in imaging the human brain. President Obama has initiated a new process to map the human brain. To what extent does *DSM-5* incorporate findings from brain imaging, or, if not, when do you think that will become part of the psychiatric diagnostic criteria?

**DK:** Some of us would have hoped that [even] without the new brain initiative coming up, that we would have had enough data to [include brain imaging and other biologically based evidence] in the actual [diagnostic] criteria sets.

There is mention within the text of spe-

cific disorders of some major things going on from a genetic and imaging point of view. And for the first time there are references in the *DSM* (online version), linking to the actual journal articles.

**MM:** You mentioned that one of the issues with a new classification system is its association with reimbursement for care. How are the *DSM-5* and the American

was, basically, insurance companies. Now, with *DSM-5* coming out, obviously all of us are going to have to deal with those two constituencies.

We will likely see that some of the changes that we've made will facilitate the use of both pharmacologic and nonpharmacologic agents in mental disorders. But the second thing that we may see is that we may have made

words "behavioral health." Do you think that change has helped or hurt our understanding of the root causes of these disorders?

**DK:** I'm not sure. I do think that we're still dealing with a certain level of stigma, no matter what you call it, that pervades all of medicine and therefore is also driven by the decisions that we have made as a society—which relates to reimbursement, which

**All of medicine needs to understand more about mental disorders. And the root causes [of those disorders] are going to be found to have a lot more common etiological features than we ever suspected.**

Psychiatric Association working with the insurance industry to be sure that people who need to be reimbursed don't suffer from the changes?

**DK:** In the development of the *DSM-5*, and appointing of the work groups and all of the members, there were two constituencies that were purposely left out. They represented a level of bias that we did not want. One of them, not surprisingly, was the pharmaceutical industry, and the second

some quote, "changes in reimbursement," which represent opportunities for the insurance industry to change the level of coverage for certain mental disorders and psychiatric conditions. We are already working with clinicians and physicians to explain the coding for *DSM-5* and the coding to use for reimbursement.

**MM:** Over the last decade or so, there seems to have been a transition from the use of the word "psychiatry" to the use of the

relates to much of the separation of mental and addictive disorders from other medical disorders, which did not work out, I think, to the advantage of patients and their families. And by doing so, we don't understand that we're dealing with patients who have a chronic psychiatric condition and another medical disorder.

It's not an accident that I have a strong interest, since 50 percent of the patients who have serious bipolar disorder, my own specialty area, have metabolic syndrome. We are

## WHAT IT REALLY SAYS

So what are psychiatrists saying around water coolers these days? Particularly those in the know on the *DSM-5*? In addition to Pitt's David Kupfer, who served as the task force chair, several other Pitt people helped shape the new manual. We asked Pitt *DSM* work-group-and-task-force-folk if they could tell us, very briefly, what the big take-aways are from their respective chapters. Here's what we learned.  
—Sidebars by Josie Fisher

For more detail:  
[www.psychiatry.org/dsm5](http://www.psychiatry.org/dsm5)

## FEEDING AND EATING DISORDERS

"One of the major changes is the addition of a new disorder, binge eating disorder, characterized by persistent and recurrent binge eating without the compensatory behaviors (e.g., purging, overexercising) seen in bulimia nervosa," says Marsha Marcus, a PhD, professor of psychiatry and psychology in the School of Medicine, and chief of Western Psychiatric Institute and Clinic's Behavioral Medicine Program. Marcus was a member of the Feeding and Eating Disorders Work Group. She notes that binge eating disorder differs substantially from common overeating: It is much less common, far more severe, and associated with significant physical and psychological problems. In addition, *DSM-IV's* "feeding disorder of infancy or early childhood" is now "avoidant/restrictive food intake disorder," because the condition is not limited to early childhood.



Marcus



dealing with major medical problems and major psychiatric problems in the same individual all the time.

It's not perhaps an accident that the first commentary I wrote for *JAMA* [related to the new manual] was why all of medicine needs the *DSM-5*. And I guess it is timely that the [April 24 issue] of *JAMA* had a viewpoint which is basically *DSM-5*: The future has arrived.

All of medicine needs to understand more about mental disorders. And the root causes, as you put it, are going to be found to have a lot more common etiological features than we ever suspected. ■

## NEUROCOGNITIVE DISORDERS

The label “neurocognitive disorders” refers to a cognitive impairment that’s a defining feature of a condition and acquired, rather than present from early childhood, says Pitt’s Mary Ganguli, an MD, MPH, professor of psychiatry, neurology, and epidemiology. Ganguli was a member of *DSM-5*’s Neurocognitive Disorders Work Group.

She says the chapter describes major neurocognitive disorder, which encompasses the likes of “dementia” in geriatrics and “neurocognitive disorder” in other circumstances (e.g., young people with severe impairment from head trauma). In a move away from Alzheimer-centric criteria, depending on the cause of the impairment, “the domains that are impaired in neurocognitive disorders do not necessarily include memory,” says Ganguli.

Newly introduced is mild neurocognitive disorder, in which a person is less severely impaired. The patient still functions independently, albeit with greater effort and often relying on lists, reminders, and other compensatory mechanisms. This diagnosis has been criticized by some as medicalizing normal variation. In fact, psychiatrists have long recognized the condition though it was lumped into the “not otherwise specified” category in *DSM-IV*, Ganguli says. “With increasing focus on early detection and intervention, we need to be able to recognize and appropriately classify mild impairments.” She adds that it’s important to note that “mild” is not synonymous with “early”—the impairment may be a sign of further deterioration ahead, may stay as is, or it may even be reversible.

The chapter also offers further guidance on diagnosing underlying conditions—like HIV infection, cerebrovascular disease, or Alzheimer’s or Parkinson’s disease—that may be causing a given cognitive disorder. The scale at which this task was undertaken (with colleagues in general medicine, neurology, etc.) is unique to this edition of the manual, notes Ganguli, and a huge contribution.

## SLEEP-WAKE DISORDERS



Reynolds

A sleep-wake disorder can be a risk factor for certain mental conditions and a warning sign for serious medical issues, such as congestive heart failure, osteoarthritis, and Parkinson’s disease. To draw attention to this, *DSM-5* criteria ask clinicians to list coexisting psychiatric and medical diagnoses, says Charles Reynolds III, an MD and the UPMC Endowed Professor in Geriatric Psychiatry who also directs the UPMC/Pitt Aging Institute. Reynolds chaired the *DSM-5* Sleep-Wake Disorders Work Group and was a member of the *DSM-5* Task Force. He says Sleep-Wake Disorders incorporate laboratory-based measures for diagnosis of breathing-related sleep disorders (such as obstructive sleep apnea) and narcolepsy with hypocretin deficiency. The manual also now describes restless legs syndrome, REM sleep behavior disorder, and advanced sleep phase syndrome.

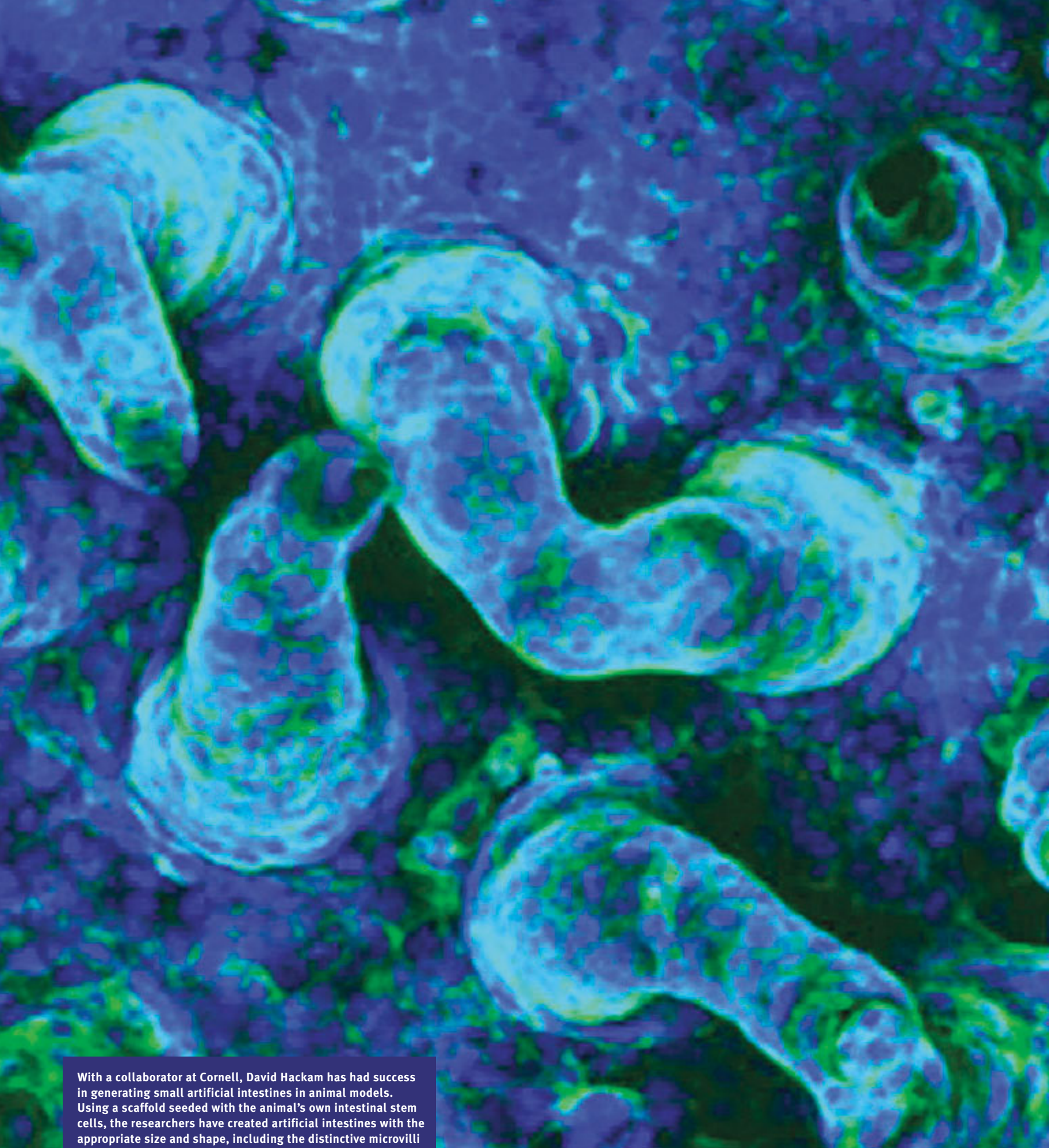
## MOOD DISORDERS



Frank

Pediatricians should know about the newly described disruptive mood dysregulation disorder in children. It’s characterized by extreme, persistent emotional outbursts many times a week, lasting at least a year, across multiple situations—at home, in school, at play, etc. Unlike normal temper tantrums, these episodes seriously impair functioning and, in between outbursts, the child is markedly sad or irritable, says Pitt’s Ellen Frank, a PhD and Distinguished Professor of Psychiatry and Psychology. Frank was a member of the *DSM-5* Mood Disorders Work Group. She hopes that the newly articulated disorder will reduce misdiagnoses of childhood bipolar disorder—and the mismedication that goes along with it—and jumpstart effective treatment. Epidemiologic evidence shows that these kids grow up to have depression or anxiety, *not* bipolar disorders, says Frank. Bipolar and Related Disorders is its own chapter in *DSM-5* (separate from Depressive Disorders), in part because neuroscience and genetic evidence suggest that bipolar disorder aligns more closely with schizophrenia and other psychotic disorders than with unipolar depressive disorders. Further, bipolar disorder criteria now urge clinicians to ask upfront about a patient’s changes in energy/activity levels, in addition to asking about elevated, euphoric, or irritable moods. Data show that increased activity is an equally important marker, says Frank.





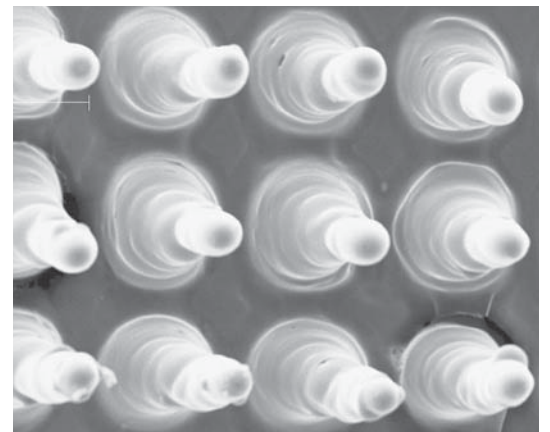
With a collaborator at Cornell, David Hackam has had success in generating small artificial intestines in animal models. Using a scaffold seeded with the animal's own intestinal stem cells, the researchers have created artificial intestines with the appropriate size and shape, including the distinctive microvilli that are the hallmark of the intestine. The team is now working to ensure that the artificial intestine can actually absorb food and have appropriate motility.



NEC MAY BE THE MOST IMPORTANT AND  
CONFOUNDING DISEASE YOU'VE NEVER HEARD OF  
BY CHUCK STARESINIC

# THE SCOURGE OF THE NICU

Expectant parents spend a great deal of time imagining the arrival of their baby, but they rarely expect major medical complications. While everyone knows that childbirth comes with risks for both mother and child, parents typically anticipate a pregnancy that lasts nine months (or close to it) and ends with a healthy mother holding and nursing a healthy newborn. Nevertheless, every year in this country, more than half a million babies arrive prematurely (before 37 weeks of gestation). That's around 12 percent of babies who are, to some extent, small, underdeveloped, and/or facing challenges; this is especially true of those born as early as 24 to 25 weeks, at the outer edge of viability. Capitalizing on scientific discoveries, new drugs, and greater understanding of the needs of these smallest of humans, specialists in neonatal intensive care units (NICUs) have become increasingly skilled at negotiating these challenges throughout the past few decades. The result is that many babies who would have died within hours or days of birth now regularly clear the hurdles of their first few weeks outside the womb.



Bioscaffolds used to grow cells into fingerlike projections that mimic those of the intestinal lining

They may begin to gain weight and breathe without support. Parents are able to see their child's face free of oxygen tubes and adhesive tape for the first time; perhaps they allow themselves to think beyond just the next few hours.

In what seems to be a rather cruel bit of timing, this is often the moment when symptoms of NEC, a life-threatening intestinal disease that affects 12 percent of preemies, first appear. NEC rhymes with "heck," a term that's mild compared to the words it often elicits from parents and care providers. NEC is short for necrotizing enterocolitis. Simply put, it is an inflammation and dying off of the intestine.

"If you ask neonatologists or pediatric surgeons, 'What's one of the most challenging and frustrating diseases in the NICU?' they will immediately say, 'NEC,'" says David Hackam, a surgeon-scientist at Children's Hospital of Pittsburgh of UPMC and the Watson Family Professor of Surgery at the University of Pittsburgh. "It's challenging, because early on it's hard to diagnose. And there's no specific treatment. It's frustrating, because our success hasn't improved in the last 30 years."

The early signs of NEC can be subtle—feeding intolerance, lethargy, temperature

When asked to describe how he approaches the parents of a very sick child with NEC, Hackam sighs. "I'm very honest with the parents," he begins. "I'm also purposefully hopeful, but not falsely so. Because, if you have to choose between being optimistic and pessimistic, then you choose optimism—but be realistic. I tell them that it's not their fault. It's a consequence of early delivery, which they had no control over.

"At first it's hour-by-hour as to whether the [babies] will even survive. And if they make it through one hour, then they have hope for the next hour. And then, generally, if they make it through the night, they can say, 'We made it through 12 hours. We can make it through another 12 hours.' Then, after a few days, I tell them it's day-by-day. And that can be a huge relief, because a few days ago it was hour-by-hour. If I come and tell *you* it's day-by-day, that sounds like a death sentence. But not in the NICU, where one hour has huge consequences.

"So I'm as honest as I can be. But I hope for the best."

Hackam traces his commitment to treating NEC to one particular patient. We'll call him Kevin. He was born at about 26 weeks of gestation. He was small at birth and destined for a stay of several weeks in the NICU, but by

four children under 10, he is familiar with the joys and the fears of parenthood and the journey a family takes through pregnancy and childbirth. Hackam is friendly and talkative in a calming way, as Kevin's parents discovered in their many conversations with him.

"I got to know his parents," says Hackam. "They were a little bit older. They'd had kind of a tough journey to get pregnant. They were neat.

"But it was a typical story—their kid was born early and was a little sick. Then, within 24 hours, he was dying. There was no option but to operate, and most of his intestines were dead. And a few days before, he had been fine. It was that dramatic."

Kevin survived his bout with NEC, but he was left with a condition called SBS, or short bowel syndrome, which is common in kids who survive NEC. With insufficient intestine for normal digestion, he relied entirely on intravenous fluids for nutrition. For reasons that aren't completely understood, this can lead to liver disease, and that is what happened to Kevin. Before he could reach his first birthday, he was on the liver transplant waiting list. He died waiting for an organ to become available.

Ever since getting to know Kevin's family, Hackam has been driven to fix the problem of NEC. He is motivated, in part, by the frustration of having a surgical fix that is an imperfect

## **"If you ask neonatologists or pediatric surgeons, 'What's one of the most challenging and frustrating diseases in the NICU?' they will immediately say 'NEC.'"**

instability—but they can rapidly progress to include vomiting bile and the appearance of blood in the stools. X-rays may show blockages and pockets of gas in the intestines, and this is when a pediatric surgeon gets involved.

Hackam operates on babies with NEC to remove dead and dying sections of intestine. It's impossible to know the extent of the problem until the intestine can be seen. At that point, Hackam says, it's obvious to even someone who isn't a doctor. Healthy tissue is pink. Diseased tissue is turning black. In the worst cases, the toxic stew in the abdomen sets off a cascade of inflammatory reactions from which the child cannot recover. Between 20 and 30 percent of infants with NEC do not survive, with sepsis and multisystem organ failure often contributing to death. In some survivors, not enough intestine remains to support normal digestion, and the child will require intravenous nutrition for the foreseeable future.

the time he was 2 weeks old, he was gaining strength. When Kevin became ill, Hackam was the surgeon who met with the parents.

The family was at a hospital other than Children's Hospital of Pittsburgh of UPMC. It was a local hospital that Hackam and some of his colleagues covered at the time. The location did not affect treatment or prognosis, but there was a subtle difference in how Hackam went about his job. He wasn't with the large team of nurses, residents, and fellows that is ever-present in a large pediatric teaching hospital. At each step in the process, it frequently came down to him, the parents, and the baby.

While nobody can understand the emotional roller coaster parents go through in the NICU without having lived through it themselves, Hackam can relate to his patients on many levels. But for the surgical scrubs and white coat, he could be just another bespectacled new dad in the NICU. As a father of

fix. To really address Kevin's problem, a radically different solution was required—something like an artificial intestine. In addition, Hackam is drawn to the biological mystery of what causes NEC in the first place. What happens inside the gut of a preemie at 2 weeks of age to set off this terrible cascade of inflammation and cells bent on self-destruction? Why does it happen in preemies and not full-term babies? If doctors knew what was happening at the cellular level, could we turn it off?

NEC is exactly the sort of conundrum that Hackam had been trained to investigate. Years earlier, as a surgical resident at Toronto General Hospital, he had begun to feel that his medical education was missing something. Every disease, he realized, was essentially a failure of cells to work properly. But the art of surgery was practiced at the level of organs, organ systems, vessels, and layers of tissue. With his MD from the University of Western Ontario and a few





(Clockwise from top left) For Austin, life with short bowel syndrome involves large shipments of intravenous nutrition to his home. ♦ In 2012, Hackam hosted Austin at Children's Hospital so that the boy could meet the research team and see the work that Austin's Cupcake Fund was supporting. Shown from left to right are Thomas Prindle, Hongpeng Jia, Chhinder Sodhi, Austin, Hackam, Maria Branca, and Shahab Shaffiey. ♦ When news of Austin's Cupcake Fund made the local newspaper, Austin was thrilled to see his photo on the front page while at the grocery store. ♦ While visiting the Hackam lab and Children's Hospital, Austin brought his piggy bank to treat Hackam to popcorn, one of the few foods the boy can eat.

years of surgical training, he was on a career path that would allow him to perform surgical procedures to improve the health of his patients. Yet he found that he often lacked a complete understanding of what was wrong with them at the cellular level. He decided to pursue a PhD in cell biology.

Taking a leave of absence from his surgical residency, Hackam spent three years in the lab of a renowned cell biologist named Sergio Grinstein, a PhD senior scientist in the Hospital for Sick Children and a professor of biochemistry at the University of Toronto. Grinstein is internationally recognized for elucidating mechanisms underlying the immune response of white blood cells (in particular macrophages and neutrophils) against microbes. At first, Hackam was a fish out of water in Grinstein's lab—a surgeon among basic scientists. He felt like he and his colleagues were speaking different languages and didn't have much in common. But that didn't last long. Between 1996 and 2001, Hackam was a coauthor with Grinstein on a dozen scientific publications exploring the basic mechanisms of the immune system, including articles in *Proceedings of the National Academy of Sciences*, *Journal of Biological Chemistry*, and *Journal of Experimental Medicine*.

Following the completion of his doctorate and a subsequent year as chief surgical resident in Toronto, Hackam arrived in Pittsburgh in 2000 for fellowship training in pediatric surgery. He was drawn to Pittsburgh by what he describes as an unparalleled pediatric surgical training program led at the time by Eugene Wiener and Henri Ford (then chief of Pitt's Division of Pediatric General and Thoracic Surgery and now a vice dean of medical education at the Keck School of Medicine of the University of Southern California). Ford had trained at Pitt himself, completing a research fellowship in immunology in 1989 and pediatric surgery fellowship in 1993 and, after joining the faculty, conducting laboratory research into the cellular mechanisms behind NEC. Hackam was heavily influenced by Ford, as well as the surgeon who recruited him to Pittsburgh—Timothy Billiar, George Vance Foster Professor and chair of surgery. Billiar is widely known for his investigations into the cellular mechanisms of trauma and inflammation, especially the role of nitric oxide.

When Hackam arrived, the division included two pediatric surgeons running their own research laboratories in addition to pursuing clinical work. While it's not unusual for

a major academic medical center to have surgeons who do basic science research, pediatric surgeons who do so are more of a rarity. Some centers have one, but most have none. Having multiple pediatric surgeons with NIH-funded labs, as Pittsburgh did then and still does, is practically unheard of. Far from being a fluke, the Division of Pediatric General and Thoracic Surgery includes four such labs today. (The division chief is George Gittes, who studies embryonic blood flow and organogenesis, particularly of the pancreas.)

The base of operations for these surgeon-scientists is the John G. Rangos Sr. Research Center, established in 1990 and moved to new quarters in 2008 alongside the new Children's Hospital of Pittsburgh of UPMC. Working closely with the University's Center for Biologic Imaging, the division has created a shared, top-notch imaging facility just steps away from the hospital. The proximity of the hospital to these labs is a great boon to the work of these surgeon scientists. When Hackam, who holds a secondary appointment in cell biology, leaves the operating theater at Children's, he simply walks down a few flights of stairs, along the covered walkway past families playing and eating in the courtyard

outside the cafeteria, and into the Rangos building. If he has tissue samples obtained during surgery, it takes just a few minutes to begin to examine them in the lab. One confocal microscope includes an incubator—a sealed chamber where researchers can control pressure, temperature, humidity, and other variables while viewing samples under magnification. Across the room is a microscope linked to a large video screen. When a sample of tissue is displayed on the monitor, researchers might draw on the screen with a stylus, encircling, for example, a single intestinal stem cell. A laser traces the same line in the tissue sample, making a precise cut so that the cell drops out of the tissue ready to be used in experiments on regenerating intestinal tissue. These facilities (supported, in part, with funding from Pitt's Clinical and Translational Science Institute) are critical to the work Hackam is undertaking to cure NEC and treat its survivors. In his office, with views of the rolling green hills of the Allegheny Cemetery and its raucous flocks of crows, Hackam shows pictures of NEC in action: tiny infants with swelling bellies, blackened and dying

the process might go wrong in NEC. Just as Hackam was beginning to ask questions about NEC in the early 2000s, revolutionary discoveries about innate immune mechanisms that responded to the presence of bacteria were being published. A 2011 Nobel Prize would recognize the discoveries that elucidated aspects of the innate immune system, including the discovery of toll-like receptors (TLRs), molecules that span the membrane of the cell and react to the presence of bacterial products.

There are several TLRs in humans. One, TLR4, piqued the interest of Hackam and colleagues because it recognizes gram-negative bacteria, a large and diverse group of bacteria common in the gut and the environment. The investigators theorized that TLR4 was in the gut and learned that something went wrong with it in NEC. They successfully demonstrated that it was present in the gut and learned that in preemies the expression of the molecule sometimes seemed to get turned up really high.

In 2007, he and colleagues reported in the *Journal of Immunology* that expression of TLR4 was increased in patients with NEC, making it

on intestinal cells, amniotic fluid no longer had a protective effect.

"It appears that EGF in amniotic fluid is able to shut off TLR4 activity and prevent NEC," Hackam says. "Perhaps if we one day banked amniotic fluid after premature delivery, we could give it to newborns at risk for the problem. We also could identify a drug that inhibits TLR4 activity to try to save these babies."

Hackam's group contacted Peter Wipf, Distinguished University Professor in Pitt's Department of Chemistry, Kenneth P. Dietrich School of Arts and Sciences. The team told him they were looking for a ligand for TLR4—a molecule that would fit the receptor like a key in a lock and shut it down. Thanks to computational tools, chemists like Wipf can search enormous databases of chemical structural information in order to identify candidates. The total number of chemicals in the databases Wipf searched is around 50 million.

After several rounds of narrowing the list based on cost and likely toxicity, Hackam's lab ordered 67 compounds and started the painstaking work of experimenting in mice. The mice had TLR4 highly expressed and were exposed

**"Hi, Dr. Hackam. My name is Austin. I have short gut.  
My biggest wish ever is to get a new tummy. Work very hard! Bye."**

intestinal tissue.

"I'm going to show you in a minute that we have a treatment for [NEC], in mice, that works," he says. "That's the first step. It works in piglets, too—second step. And that is just one step away from humans." Though he is clearly optimistic, he also cautions that the FDA approval process of a new drug has many, many steps of its own.

When he and his colleagues started this work, they had no idea what even caused NEC. They knew that it was seen in association with bacteria—not in association with a particular pathogen, like salmonella. But bacteria were needed in the gut for NEC to occur. An important clue was the age at which an infant typically developed NEC—around two weeks. "You come out sterile," explains Hackam, of newborns. "After about two weeks all the bugs [bacteria] are there that you are going to have pretty much for life, though they change a little bit. That's when NEC develops."

At the time, it wasn't even known how the gut recognized bacteria, let alone how

a likely target for treatment. Continuing this line of research, the Hackam lab published a potential breakthrough in *PNAS* in July 2012. Noting that healthy, full-term infants have relatively low levels of TLR4 in the gut, the researchers posited that something goes wrong with the TLR4 response when premature infants get colonized with normal gut flora.

"One big difference between a 34-week-old baby developing in its mother's uterus and one in the neonatal intensive care unit is that the first one is floating in and swallowing amniotic fluid," Hackam says. "Early delivery means that exposure to the fluid is over, so we speculated that components of the fluid could help prevent NEC by keeping TLR4 in check."

In the study, the researchers showed that injecting small amounts of amniotic fluid into the intestine of premature mice, or feeding the fluid to them, stopped NEC from developing. That's because the fluid is rich in epidermal growth factor (EGF), a wound-healing protein; when the researchers removed it from the fluid or blocked or removed the EGF receptor

to bacterial compounds known to trigger NEC. Working with Simon Watkins, PhD professor of cell biology and physiology, as well as of immunology, and director of Pitt's Center for Biologic Imaging, the team was able to make the intestinal tissue of the mice glow when TLR4 was active. If a drug silenced TLR4, it stopped glowing.

"One of the compounds was almost perfect," says Hackam. Compound 34, as it was randomly called, is a type of saccharide—part of a family of molecules found in breast milk. Though no one has specifically looked for Compound 34 in breast milk, Hackam says it is likely present.

"I think the compound continues to have good properties," Wipf says. "The scientific data from David's lab are very encouraging, very interesting. But at this point we have about 5 percent of what it takes to put together a package that would allow us to move toward phase 1, which is the first kind of clinical trial—[it's] where you first ask the question about toxicity and dosing in humans. That's how strenuous that road really is. A lot of the data are easy to get, but nonetheless, they have to be collected."



In yet another groundbreaking scientific paper just going to press in *PNAS*, Hackam and several Pitt colleagues, including surgery chair Billiar, have elucidated new details on the mechanisms that cause infants to develop NEC. Based on these discoveries, the authors suggest additional therapeutic strategies. This line of research began with the theory that the death of intestinal tissue in NEC was related to inadequate circulation of blood. Collaborating with Mark Gladwin, professor of medicine, chief of the Division of Pulmonary, Allergy, and Critical Care Medicine, and director of Pitt's Vascular Medicine Institute, the Hackam lab demonstrated that TLR4 activation in blood vessels led to impaired blood flow to the gut, causing or contributing to NEC. Trying to determine why breast milk prevented NEC, the team discovered that breast milk contains sodium nitrate, which gets converted to the vasodilator nitric oxide and improves blood flow. To test whether sodium nitrate was breast milk's active ingredient preventing NEC, they added sodium nitrate to the infant formula fed to the mice. The supplemented formula was protective; the researchers were able to measure improved blood flow and show that NEC did not develop in these mice. Hackam and Gladwin are now planning a clinical trial to administer a similar therapy in infants at risk for NEC.

In December 2011, Hackam opened his e-mail to find a link to a video. When he clicked "play," he saw a chipper 5-year-old in front of a Christmas tree say, "Hi, Dr. Hackam. My name is Austin. I have short gut. My biggest wish ever is to get a new tummy. Work very hard! Bye."

Austin, who lives in Butler County, suffers from short bowel syndrome. Although it's not the result of NEC, he faces the same problems as many NEC survivors. He gets a great deal of his nutrition intravenously, though he can eat carbs and proteins. He spends about 17 hours each day connected to an IV line. No matter how thirsty he gets, he can't drink water, juice, or any liquids other than his medication. As if that isn't torture enough for a child, he also is not allowed sweets, including fruits, candies, and cakes.

One day at bedtime, Austin watched his little brother take sips of water after brushing his teeth. He broke down sobbing that he hated himself and hated having short gut; he just wanted to



Austin, shown here at age 4, has been inspired by many doctors.

drink water like his brother and other kids. Austin's mother told him about Hackam's research, which she had just learned about. The next day, he insisted on making the video.

In 2010, Hackam was at a conference organized by the Hartwell Foundation. Hartwell has a goal of putting together innovators who are working on high-risk, high-reward studies to collaborate on applied biomedical research projects with potential to benefit children. And that is exactly what happened with Hackam and a bioengineer from Cornell University named John March.

The collaboration was born at a Hartwell conference. The way Hackam tells it, he was at one end of the bar talking about obstacles to building artificial intestine: He knew how to grow intestinal stem cells in a dish, but he had no way for them to grow into a structure that mimicked the complex shape of the human intestine—which, thanks to its folds and tiny fingerlike projections lining every inch of its interior, has roughly the same surface area as a tennis court. At the other end of the bar, the biophysicist and engineer March was talking about how he had developed techniques for making bioscaffolds with unique features, but seeding them with stem cells and coaxing complex structures to life were beyond his expertise. Somewhere between the two ends of the bar that night, a scientific collaboration was born. March and Hackam put their proposal for an artificial intestine together in 2011, news of which eventually prompted Austin's family to get in touch.

When Austin's family woke up on Christmas Day, they had an e-mail from Hackam, promising Austin that he would not rest until he could help him and other children who need "a new tummy." Austin has less than 10 percent of his intestines. The five-year mortality rate for children who are as sick as him is 20 percent. But in May 2012, he celebrated his sixth birthday. He told his parents that, instead of presents, he wanted to raise money to support Hackam's research. The family started a Facebook page, and when donations began pouring in, he decided to name his fund Austin's Cupcake Fund ([www.facebook.com/AustinsCupcakeFund](http://www.facebook.com/AustinsCupcakeFund)), hoping that one day he could eat lots and

lots of cupcakes. The fund has since raised more than \$70,000 to support the artificial intestine work.

It turns out that several groups around the world are working on an artificial intestine. Nanotech centers at many universities are busy creating scaffolds that mimic many anatomical structures for growing cells; they typically use a process called laser etching, which works well for detailing very small features. However, laser etching can't quite mimic the high aspect (width to height) ratio of the intestinal microvilli. (A skyscraper has a much higher aspect ratio than a pyramid; and in this respect, microvilli are more like skyscrapers.) March's secret to overcoming this challenge is to form the scaffold using a mold, which is then dissolved, leaving only the scaffold.

Viewing images of March's scaffold under a microscope, Hackam says, "It doesn't have cells on it, but that looks like a native intestine. This has been a major barrier in clinical medicine—to have a scaffold that looks like the intestine."

The team's scaffolds are made from an FDA-approved material—a compound similar to elastin and collagen naturally found in intestinal tissue. Their first experiments with it involved implanting it into the fatty abdominal tissue of mice. As the researchers hoped, the presence of the implant stimulated the growth of blood vessels, which are needed to feed and sustain the implant. Since then, the team has been able to implant and sustain artificial intestines in mice. Hackam and March have not yet published this work in a peer-reviewed journal.

Austin's Cupcake Fund allowed Hackam to hire dedicated staff and push the timetable for important experiments forward.

"If you had asked me six months ago how long it would take to do this—to take these cells and culture them on a scaffold and then have success in animals—I would have said maybe a year, and maybe more. But we've done it in the last six months really because of the funding we've had."

Austin recently visited Hackam at Children's; the boy arrived with his piggy bank. He wanted to treat his hero to some popcorn from the hospital snack bar. The two also stopped to admire the array of brightly colored candy treats in the gift shop. That day, they just looked, but both are determined to tear open some candy wrappers together someday and enjoy the sweet fruits of their labor. ■

*People and programs  
that keep the school  
healthy and vibrant*



MAGEE-WOMENS RESEARCH INSTITUTE AND FOUNDATION

Sylvia Bernassoli with Magee colleague Anthony Wakim, medical director of assisted reproductive technology.

## TO HEAL HEARTACHE NURSE GIVES TO IVF RESEARCH BY JOE MIKSCH

**S**ylvia Bernassoli, a nurse anesthetist for nearly six decades, had just finished preparing five patients for in vitro fertilization (IVF) procedures when she called this writer. She was driving home to McMurray, Pa., from Magee-Womens Hospital of UPMC. “I should have waited to call,” she says. “But I really wanted to talk to you about this.”

The “this” Bernassoli refers to is a donation to Magee-Womens Research Institute (MWRI), intended to give IVF—first undertaken in the United States in 1981—an even greater likelihood of success. (About 150,000 IVF procedures take place annually in the United States. For women under 35, 40 percent of these procedures result in birth.)

Bernassoli is 79. She works full-time, administering anesthesia to women about to undergo egg-retrieval surgery. She has no children and is not married. And after 57 years in her profession, she finds herself in a position to lend a hand.

She has arranged to donate, over the ensuing years, at least \$500,000 for Pitt/UPMC docs to research infertility and other reproductive health issues. The gift is the largest individual planned gift to Magee in the past decade. The donation will draw from Bernassoli’s individual retirement accounts

and a life insurance policy, which names Magee as the beneficiary.

“I see these [couples] so upset that they can’t have a baby,” she says. “People may say they should adopt, but they want this so much.”

Infertility is a real medical problem, she says. “It just doesn’t get the attention. Cancer does, other things do, but fertility doesn’t.”

Yoel Sadovsky, the Elsie Hilliard Hillman Professor of Women’s and Infants’ Health Research in the Department of Obstetrics, Gynecology, and Reproductive Sciences in the University of Pittsburgh School of Medicine, is also MWRI’s director.

Naturally, he’s thrilled by the gift. The money, he says, will chiefly be used to advance research in the field of reproductive endocrinology and infertility, promoting translational and clinical research, as well as patient care in the area of female and male fertility. A particular research goal, he says, is to find ways to restore fertility after chemotherapy for cancer and other conditions.

Bernassoli has vague plans to retire. Her contract runs out June 30, 2014, but, she says, she would be more than happy to stick around for a while afterward to help her successor. She’ll be 81-and-a-half when that time comes, but “I’m still enjoying this, so why not?” she explains.

Bernassoli’s generosity has been featured on *NBC Nightly News* and, locally, on WPXI-TV and in print media. But it’s not the attention that drives her.

“I think of these families, and I’m honored to help,” she says. ■



COURTESY UPMC

## BOOSTER SHOTS

**A**lbert Lexie is a shining star. The Monessen, Pa., resident has been shining shoes since 1957. In 1982, Lexie, who plies his trade at Children’s Hospital of Pittsburgh of UPMC, decided to donate every penny he received in tips to the Free Care Fund at Children’s Hospital. As 2013 rolled around, Lexie calculated that he had donated more than \$200,000 to the fund. Even if your brogans don’t need a \$5 polish, you can help support “Albert’s kids,” as he calls them, by visiting [www.givetochildren.org](http://www.givetochildren.org).

To make a gift to the School of Medicine or an associated program, contact Jen Gabler at 412-647-3792 or [jag188@pitt.edu](mailto:jag188@pitt.edu).





## IMAGINATION UNLEASHED


**A**s traditions go, the University of Pittsburgh School of Medicine's Scholarly Project is relatively new. When it was initiated in 2004, this concept of a mandatory, multiyear, research-driven, limited-only-by-the-bounds-of-the-imagination undertaking was also novel. Fast-forward to today, and scholarly projects are becoming a rite of passage at other med schools, including Harvard's.

That doesn't surprise David Hackam, an MD/PhD, associate dean of medical student research, Watson Family Professor of Surgery, and associate professor of cell biology. He's been overseeing the program since 2010. (To learn about this prof's promising breakthroughs from his other roles as a pediatric surgeon and scientist, see p. 24.) For Hackam, the goal is simple: "We want our students to look beyond textbooks and develop critical-thinking skills and the ability to test hypotheses."

Students choose individual topics that interest them and then, in most cases, begin research over the summer between their first and second years so that they can officially begin their Scholarly Projects by sophomore year. By graduation, Hackam asserts, they become experts in their areas of research and, as a result, are highly sought after for residencies. That fact has not gone unnoticed by aspiring physicians. According to Hackam, "Informal surveys indicate that a significant number of our students are coming here because of the Scholarly Project."

—Compiled and written by  
Barbara Klein and Joe Miksch

—Illustrations by Michael Lotenero



The **144** students who marched to the strains of “Pomp and Circumstance” this spring represented just the sixth graduating class to complete Pitt’s Scholarly Project course.

Among the topics? Students researched the “feasibility of a text-message-based behavioral intervention to reduce sexual risk behaviors in young adults that present to the emergency room,” explored the “effects of glucocorticoid receptor neural progenitor cells on cerebral cortex development,” and investigated “attitudinal predictors of water-pipe smoking in U.S. college students.”

## TALKING THE TALK

As if med school weren’t time-consuming enough, these grads also played roles in **234** national and international presentations.

## WRITES OF PASSAGE

This year’s crop of Scholarly Projects produced **134** published articles—with **43** boasting first authorships. Those journals included *Archives of Internal Medicine*, *The Journal of the American Medical Association*, *Hepatology*, and *Annals of Surgery*.

## NEAR AND FAR

Science knows no borders, and a few projects were international in scope (like “the dry season prevalence of Tungiasis in the rural communities of Beira, Mozambique”) while others stayed closer to campus (“the development of a health resources guide for older adults in Braddock, Pa.”). Others managed to merge global and local (“barriers to health care utilization among newly resettled Bhutanese refugees in Pittsburgh”).

## THANK YOU, THANK YOU VERY MUCH

The class of 2013 took home **39** national awards (for example, the CDC Experience Applied Epidemiology and the Doris Duke Clinical Research fellowships), as well as **39** local awards (like Pitt’s Clinical Scientist Training Program Research Fellowships).



# OH, O'MALLEYS!

Bert O'Malley (BS '59/MD '63) is one of the University of Pittsburgh School of Medicine's many success stories. His honors include winning the National Medal of Science and membership in the National Academy of Sciences. O'Malley is credited with establishing the field of molecular endocrinology and now chairs the Department of Molecular and Cellular Biology in the Baylor College of Medicine, where he is the Thomas C. Thompson Professor of Cell Biology. In 2010, he and his wife, Sally (whose '59 degree is in education from Pitt),

created the **Bert and Sally O'Malley Awards** for Outstanding Medical Student Research to recognize lesser-known success stories. The award, which comes with a \$500 stipend, honors a select few who excelled in their Scholarly Project research while pursuing their MDs at Pitt. We present the 2013 O'Malleys . . .



**Colby Croft** found an opportunity to augment Pitt med's curriculum related to the health of lesbian, gay, bisexual, and transgender (LGBT) people. His O'Malley-winning Scholarly Project—under the guidance of Pitt mentor Melanie Gold—resulted in an improved workshop on gender identity and sexual orientation for incoming med students, the creation of a standardized patient case featuring a same-sex couple, and an expanded workshop on human sexuality for the reproductive biology course.

**Past life:** Croft's interest in curriculum development grew at Pitt. But since high school there was never a time that he did not want to become a physician. During his undergrad years, he volunteered as an emergency department scribe and in triage at a free clinic. "[These experiences] opened my eyes to the exciting challenges and rewards of patient care," he says.

**What's next:** A continued focus on LGBT issues and curriculum development and a psychiatry residency at the University of California, San Francisco. Afterward, on to a career in academic medicine, working to promote the health of LGBT youth.



Something goes wrong with the colon. It becomes inflamed. At the same time, the bladder shows signs of dysfunction, but there are no obvious signs of disease in that organ. **Jocelyn Fitzgerald** set out to understand why. Under the guidance of Pitt's Chet de Groat, she implicated the mast cell (an immune cell of the bladder and colon), an enzyme it produces, and the proximity of mast cells to the sensory nerves of these pelvic organs in this disorder, called "pelvic organ cross-sensitization." Her rats with irritated colons had significantly increased bladder activity, and she found that blunting both the mast cell and its downstream targets can reverse the inflammation and calm the overactive bladder.

**Past life:** Fitzgerald became interested in science and women's health issues in high school. Then she was a double major in biology and women's studies at Penn State's Schreyer Honors College. She combined these interests in her honors thesis, which drew from the Tremin Research Program on Women's Health, an almost 80-year-old generational study of women's health throughout the lifespan.

**What's next:** A residency in obstetrics and gynecology at Johns Hopkins Hospital and further research into chronic pelvic pain, which she calls "an undertreated and debilitating problem with a significant void in both research and providers."



Some of us use Nintendo's Wii gaming system to lose to our nephews in various Mario Brothers games.

**Kellie Middleton** suspected that the gaming system might have a higher calling. Her project found that, as the title states plainly, "Playing the Nintendo Wii improves non-dominant handedness in surgically naive student performance on a virtual-reality surgical simulator." (So a little time with Super Mario Bros. might not be a waste of time for an aspiring surgeon.)

**Past life:** Crushing softballs. Middleton played varsity ball at Notre Dame and the University of Georgia, and she played professionally with the Akron Racers. While with the Racers, she worked in public policy in Berkeley, Calif., and cofounded a non-profit to provide opportunities for underserved girls through athletics.

**What's next:** A residency in orthopaedic surgery at UPMC and continued research in orthopaedics, surgical education, and public health.



Traumatic brain injury (TBI)—whether suffered on the battlefield or the football field—is a hot topic. **Thomas Phelps**, in the lab of Pitt's Anthony Kline, used his Scholarly Project to find out whether the antipsychotic drug aripiprazole might be an effective treatment for TBI. (Many antipsychotics currently used to treat TBI impair motor and cognitive recovery.) Aripiprazole, Phelps found, did no harm to his rats' cognitive abilities, and it improved their spatial-learning ability and memory. "If aripiprazole is found to improve spatial learning and memory in humans, it may have further rehabilitative potential to improve cognitive recovery in TBI patients," Phelps says.

**Past life:** Phelps served in the Army and was deployed to Iraq as an M1A1 tank commander. This experience helped mold his medical interests. "TBI has become a signature injury for the war in Iraq . . . As a result, many young men and women, while lucky to be alive, must now learn to cope with long-lasting disabilities," he says.

**What's next:** After his emergency medicine residency at Case Western Reserve University and Cleveland Clinic, Phelps plans to continue his Pennsylvania National Guard service as a medical corps officer.



## Rachel Orler Reid

recognized that it's not always easy to determine which docs provide the best care in clinic. Over the course of her Scholarly Project, which included work at RAND Corp.—in conjunction with Ateev Mehrota, MD associate professor of medicine—Reid explored the relationship between the information people use to select doctors and clinical quality. The work led her to delve deeper into the relationships between perception, cost, and quality of care while at the U.S. Centers for Medicine & Medicaid Services. A related paper was published in *The Journal of the American Medical Association* in January 2013.

**Past life:** Rowing. Lots of it. She was the assistant captain of Harvard women's lightweight crew. And before college, what was then the Governor's School program in Pitt's School of Medicine helped solidify her career path.

**What's next:** An internal medicine residency at Brigham and Women's Hospital in Boston and further investigations of how cost and information are related to the choices we have to make about health care.

**A SHOUT OUT** Mentors, by their very nature, provide support, guidance, and experience, as well as the occasional dose of tough love. Scholarly Project mentors take on a three-year commitment to individual students. For the first time, graduates returned the favor by nominating their mentors for special recognition. And the Excellence in Medical Student Research Mentoring Awards went to **Giselle Hamad**, an MD and associate professor of surgery; **Brian Klatt** (MD '97, Res '02), assistant professor of orthopaedic surgery; **Ateev Mehrotra**, an MD/MPH and associate professor of medicine; and **Vu Nguyen**, an MD and assistant professor of plastic surgery.

# MATCH RESULTS

## CLASS OF 2013

### ANESTHESIOLOGY

Cobb, Benjamin  
Hospital of the University of Pennsylvania  
Esquenazi, Jacob  
Montefiore Medical Center/Albert Einstein College of Medicine, N.Y.  
He, Amy  
Loyola University Medical Center, Ill.  
Hui, Cyrus  
University of Washington Affiliated Hospitals  
Patel, Dev  
University of Virginia Hospital  
Scholl, Jonathan  
West Penn Allegheny Health System, Pa.  
Tseng, Lisa  
Barnes-Jewish Hospital/Washington University, Mo.  
Xu, Ying  
Penn State Milton S. Hershey Medical Center, Pa.

### DERMATOLOGY

Ho, Chin  
UPMC/University of Pittsburgh, Pa.  
Johnson, Luke  
Texas Tech University Health Sciences Center

### EMERGENCY MEDICINE

Bautz, Joshua  
Vanderbilt University Medical Center, Tenn.  
Depp, Timothy  
Palmetto Health/University of South Carolina  
\*Franco, Vanessa  
UCLA Medical Center, Calif.  
Goodmanson, Nicholas  
UPMC/University of Pittsburgh, Pa.  
Lai, Jeffrey  
University of Massachusetts  
Levine, Rebecca  
Vidant Medical Center/East Carolina University, N.C.  
Mazariegos, David  
Scott & White Healthcare/Texas A&M University  
Ownbey, Micah  
Maine Medical Center  
Paccione, Kimberly  
UPMC/University of Pittsburgh, Pa.  
Perry, Steven  
West Penn Allegheny Health System, Pa.  
Peterson, Alanna  
UPMC/University of Pittsburgh, Pa.  
Phelps, Thomas  
MetroHealth/Cleveland Clinic/  
Case Western Reserve University, Ohio  
Quigley, Meghan  
McGaw Medical Center of Northwestern University, Ill.

### FAMILY MEDICINE

Dang, Kaohimanu  
Heritage Valley Health System, Beaver, Pa.  
Doepker, Byron  
Group Health Cooperative, Wash.  
Garcia, Michelle  
Maine-Dartmouth Family Medicine  
Mokaya (Tucci), Diana  
O'Connor Hospital, San Jose/Stanford University, Calif.  
Spingarn, Russell  
University of Minnesota

### INTERNAL MEDICINE

\*Agrawal, Vineet  
Johns Hopkins Hospital, Md.  
Bahar, Runalia  
University of California Davis Medical Center, Sacramento  
Bou-Abboud, Carine  
University Hospitals Case Medical Center/  
Case Western Reserve University, Ohio  
\*Chao, Yvonne  
UPMC/University of Pittsburgh, Pa.  
Countouris, Malamo  
UPMC/University of Pittsburgh, Pa.  
Hanna, Reem  
UPMC/University of Pittsburgh, Pa.  
Klimenko, Maria  
Emory University, Ga.  
Liu, Jia  
Boston University Medical Center  
Nuzzo, Erin  
Beth Israel Deaconess Medical Center/  
Harvard University, Mass.  
Obaidi, Adam  
San Antonio Military Medical Center,  
Fort Sam Houston, Texas  
Patchett, Nicholas  
Boston University Medical Center  
Rhinehart, Zachary  
UPMC/University of Pittsburgh, Pa.  
Riley, Craig  
UPMC/University of Pittsburgh, Pa.  
Spada, Neal  
UPMC/University of Pittsburgh, Pa.  
Sprague, Benjamin  
UPMC/University of Pittsburgh, Pa.  
Steinbrink, Julie  
University of Michigan Hospitals  
Stoyak, Samuel  
Fletcher Allen/University of Vermont  
\*Xu, Lai  
University of Iowa Hospitals and Clinics  
Zhang, Yilin  
University of Washington Affiliated Hospitals

### INTERNAL MEDICINE — PEDIATRICS

Davidson, Carolyn  
Rhode Island Hospital/Brown University, R.I.  
Metter, Robert  
Georgetown University Medical Center,  
Washington, D.C.  
Meza, Benjamin  
Jackson Memorial Hospital/University of Miami, Fla.  
Thant, Mamie  
University of Minnesota

### INTERNAL MEDICINE — PRIMARY

Liu, Tao  
Yale-New Haven Hospital, Conn.  
McNamara, Margaret  
Rhode Island Hospital/Brown University, R.I.  
Orler Reid, Rachel  
Brigham & Women's Hospital/Harvard Univ., Mass.

### MAXILLOFACIAL SURGERY

Parker, David  
UPMC/University of Pittsburgh, Pa.  
Paterson, Brian  
UPMC/University of Pittsburgh, Pa.

### NEUROLOGICAL SURGERY

\*Faraji, Amir  
UPMC/University of Pittsburgh, Pa.  
Harrison, Gillian  
Langone Medical Center/New York University  
Iyer, Aditya  
Stanford University Programs, Calif.  
Shin, Samuel  
UPMC/University of Pittsburgh, Pa.

### NEUROLOGY

Gregg, Nicholas  
McGaw Medical Center of Northwestern University, Ill.  
Gupta, Anoopum  
Brigham & Women's Hospital/Harvard Univ., Mass.  
Gusdon, Aaron  
NewYork-Presbyterian Hospital/  
Weill Cornell Medical Center  
\*Samarasinghe, Ranmal  
UCLA Medical Center, Calif.

### NEUROLOGY — CHILD

Fridinger, Sara  
Children's Hospital of Philadelphia/  
University of Pennsylvania

### OBSTETRICS/GYNECOLOGY

Fitzgerald, Jocelyn  
Johns Hopkins Hospital, Md.  
Haney, Alyssa  
Duke University Medical Center, N.C.  
Kelly, Adia  
St. Luke's-Roosevelt, N.Y.  
Malczewski, Katherine  
Tulane Medical Center and Affiliated Hospitals, La.  
Nayak, Shridha  
Johns Hopkins Hospital, Md.  
Raw, Alexander  
Southern Illinois University & Affiliated Hospitals, Ill.  
Rhinehart (Horning), Erin  
UPMC/University of Pittsburgh, Pa.  
Sarin, Rohini  
Ohio State University Medical Center

### OPHTHALMOLOGY

Huang, Jason  
University of Texas Southwestern Medical Center  
Parikh, Vishal  
Cole Eye Institute/Cleveland Clinic/Case Western Reserve University, Ohio

### ORTHOPAEDIC SURGERY

Divi, Srikanth  
University of Chicago Medical Center, Ill.  
Li, Ryan  
University Hospitals Case Medical Center/  
Case Western Reserve University, Ohio  
Middleton, Kellie  
UPMC/University of Pittsburgh, Pa.  
Mock, Brady  
UPMC/University of Pittsburgh, Pa.





There comes a time, young medical student, when you must leave the stressful and demanding crucible of medical school for the stressful and demanding crucible of residency. For Pitt med's Class of 2013, the location of Crucible the Second was discovered on March 15, Match Day. (These grads-to-be marked the singular occasion with T-shirts that read, in the hashtag parlance of Twitter, "YOMO," or "You Only Match Once.")

Pigott, Matthew  
University of Michigan Hospitals  
Prodromo, John  
Hahnemann University Hospital/  
Drexel College of Medicine, Pa.  
Tetreault, Matthew  
Rush University Medical Center, Ill.

### OTOLARYNGOLOGY

Tint, Derrick  
Temple University Hospitals, Pa.  
Yu, Jason  
Hospitals of the University of Pennsylvania

### PATHOLOGY

Ferreira, Pamela  
Orlando Health, Fla.  
Olevian, Dane  
UPMC/University of Pittsburgh, Pa.

### PEDIATRICS

Antonetti, Callah  
Children's Hospital of Pittsburgh of UPMC/  
University of Pittsburgh, Pa.  
Asante, Peter  
University of Washington Affiliated Hospitals  
Baeder (Hoyson), Katherine  
Montefiore Medical Center/Albert Einstein College of  
Medicine, N.Y.  
Barone, Amanda  
McGaw Medical Center of Northwestern University, Ill.  
Bujnicki, Heather  
Johns Hopkins Hospital, Md.  
Gavigan, Patrick  
University of Tennessee  
Giwa, Adebola  
University of Chicago Medical Center, Ill.  
Hall, Christine  
UPMC/University of Pittsburgh, Pa.  
Hill, Elaise  
Duke University Medical Center, N.C.  
Kumthekar, Rohan  
North Shore-LIJ Health System, N.Y.  
Littleton, Kailey  
University Hospitals Case Medical Center/  
Case Western Reserve University, Ohio  
Mantell, Benjamin  
Cincinnati Children's Hospital Medical Center, Ohio  
Michel, Hilary  
Children's Hospital of Pittsburgh of UPMC/  
University of Pittsburgh, Pa.  
Parikh, Divya  
University Hospitals Case Medical Center/  
Case Western Reserve University, Ohio  
Proud, Lindsay  
Children's Hospital of Pittsburgh of UPMC/  
University of Pittsburgh, Pa.

Saint Georges Chaumet, Maureen  
Children's Hospital Los Angeles/  
University of Southern California  
Zhan, Yan  
University of California, San Diego Medical Center

### PHYSICAL MEDICINE & REHABILITATION

Clanton, Samuel  
Rehabilitation Institute of Chicago/McGaw Medical  
Center of Northwestern University, Ill.  
Kole, Amanda  
Sinai Hospital of Baltimore, Md.  
Pan, Jason  
Hospitals of the University of Pennsylvania  
Wilson, Meghan  
University of California, Irvine Medical Center

### PLASTIC SURGERY

Chavanon, Vincent  
Mount Sinai Medical Center, N.Y.  
Roh, Daniel  
Brigham & Women's Hospital/Harvard Univ., Mass.  
Rozak, Phillip  
University of Texas Medical Branch, Galveston

### PSYCHIATRY

Chan, Tiffany  
Cambridge Health Alliance/Harvard University, Mass.  
Croft, Colby  
San Francisco General Hospital/University of  
California, San Francisco  
Flores, Inti  
San Francisco General Hospital/University of  
California, San Francisco  
Grubisha, Melanie  
UPMC/University of Pittsburgh, Pa.  
Kalinowski, Agnieszka  
Stanford University Programs, Calif.  
Leathers, Samantha  
New York University  
Milgrom, Olga  
UPMC/University of Pittsburgh, Pa.  
Proosaselt, Yuliya  
San Diego Medical Center/University of California  
Sturman, David  
Massachusetts General Hospital/Harvard Univ., Mass.

### RADIATION ONCOLOGY

Choi, Serah  
Mt. Zion Medical Center and Moffitt/Long Hospital/  
University of California, San Francisco  
Leeman, Jonathan  
Memorial Sloan-Kettering Cancer Center, N.Y.  
\*Shukla, Gaurav  
Thomas Jefferson University Hospital, Pa.  
Wang, Kyle  
University of North Carolina Hospitals

### RADIOLOGY — DIAGNOSTIC

Ali, Rukya  
Ohio State University Medical Center  
Champlin, Jay  
University of Washington Affiliated Hospitals  
Hsu, Michael  
Boston University Medical Center  
Kannan, Neeta  
University of Chicago Medical Center, Ill.  
Kosaraju, Vijaya  
University Hospitals Case Medical Center/  
Case Western Reserve University, Ohio  
Leung, Alan  
University of Washington Affiliated Hospitals  
McLaughlin, Joseph  
University of Texas Southwestern, Dallas  
Parr, Anthony  
Indiana University

### SURGERY — GENERAL

Corbitt, Natasha  
Vanderbilt University Medical Center, Tenn.  
Kirk, Katherine  
UPMC/University of Pittsburgh, Pa.  
Lee, Suzie  
Vanderbilt University Medical Center, Tenn.  
Moore, Alexander  
Louisiana State University, New Orleans  
Moore, Carolyn  
Morehouse School of Medicine, Ga.  
Sho, Shonan  
University of California, Los Angeles Medical Center  
Tano, Zachary  
New York Medical College—Metropolitan  
Hospital Center  
Wyman, Anne  
Henry Ford Health System/  
Wayne State University, Mich.

### TRANSITIONAL MEDICINE

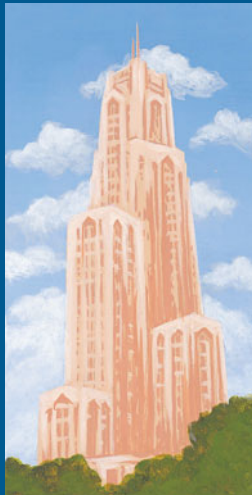
Hickey, Sergio  
Navy Medical Center, Portsmouth, Va.

### UROLOGY

Rodríguez, Joseph  
University of Chicago Medical Center, Ill.  
Uy, Jamie  
UPMC/University of Pittsburgh, Pa.

\* December 2012 graduate





## CLASS NOTES

### '50s

**Russell L. Anderson Jr.'s** (MD '54) late father was proud to receive his BA, MA, and PhD from Pitt (in 1920, 1928, and 1930, respectively), but was denied admittance to the medical school because of that era's quota system, he was told—and the same would have been the case for Anderson Jr. if not for a stellar recommendation letter. Quotas for African Americans and other minorities were still common in med schools across the country as he came of age. (By 1970, Pitt was recruiting Black students in nationally unprecedented numbers.)

Anderson Jr. became an orthopaedic pathologist in 1961 under the guidance of Pitt's Albert Ferguson and practiced for 30 years in D.C., New York, and Florida. Russell Sr. got his MD from Howard and pursued academic medicine.

At one point, father and son volunteered together in the depressed swamp communities of Tallahassee. "We delivered babies for nothing. For chickens," Anderson says. And now, history repeats itself. For 13 years, he has worked as the only pro bono orthopaedist in Riviera Beach, the poorest area of Palm Beach County. Last year, the county health department presented him with the C.L. Brumback Volunteer of the Year Award.

### '70s

**Carl Fuhrman** (MD '79, Radiology Resident '83), Pitt's chief of thoracic radiology and professor of radiology, is a veritable Johnny Appleseed of Golden Apple Awards—he's won eight of them, as well as the President's Distinguished Teaching Award, the highest teaching honor at Pitt med. In April, the American Alliance of Academic Chief Residents in Radiology named him Outstanding Teacher of the

Year. Fuhrman also serves as president of the Alliance of Medical Student Educators in Radiology. And as an associate editor of Case-based Online Radiology Education (CORE), MedU's virtual-patient program, he's helping to address the need to standardize medical education. In schools where the radiology curriculum is lacking, this new tool fills a critical need, he says. Now in its third year, the program has 35 schools subscribed.

### '80s

The FDA approved the AAA Stent Graft System just in time for former Bethel Park mayor Reno Virgili, who suffered an abdominal aneurysm in 2008. Luckily, his doc, **Michel Makaroun** (General Surgery Resident '85)—professor and chief of the Division of Vascular Surgery at Pitt and codirector of the UPMC Heart and Vascular Institute—was among the first in the United States to use a new minimally invasive system to fix dangerous bulges in the aorta. Recently, Makaroun completed a clinical trial of AAA, in which nearly all treated aneurysm sacs decreased or remained stable two years out.

African American men account for only 2 percent of all physicians in the United States, notes **William Simmons** (Pediatric Critical Care Fellow '86, Pediatric Anesthesiology Fellow '87), a Pitt clinical associate professor of anesthesiology, as well as president of Gateway Medical Society (GMS), an organization devoted to promoting the health and welfare of underrepresented groups in Southwestern Pennsylvania. In 2009, to plant the seeds of scientific curiosity in tomorrow's Black men, GMS began Journey to Medicine, a mentorship program led by **Morris Turner** (MD '73), assistant professor of obstetrics, gynecology, and reproductive sciences at Pitt, with his son, Morris Turner Jr. Each year, 15 sixth-grade boys are selected to join in the fun, suturing cow hearts, practicing CPR on simulators at Pitt's WISER Institute, and pairing up with physician mentors. The program, which the students will continue through

grade 12, is on track to have 120 Pittsburgh-area students enrolled by 2015. Last year, Journey to Medicine won a Distinguished Achievement Award from the Pittsburgh Board of Education.

### '90s

**Anil Nanda** (Microneurosurgery, Cranial Base Surgery Fellow '90) is professor and chair of neurosurgery at Louisiana State University Health Sciences Center at Shreveport. Last year, Nanda, who recently received his Master of Public Health degree from Harvard University, helped pass the Louisiana Youth Concussion Law, requiring all schools, clubs, and other organizations to provide young athletes and their parents with information about concussions and the potential long-term effects of playing after a head injury.

"Raised in Southern California, came back to Southern California," says **Ronald Navarro** (Shoulder, Arthroscopy, and Sports Medicine Fellow '96). His first gig after Pitt was at the same center that treated his thumb fracture when he was a child. Now, as the newly appointed regional coordinating chief of orthopaedic surgery for Southern California Permanente Medical Group, Navarro oversees some 200 orthopods at 13 medical centers.

If a baby has a lazy eye, her brain will favor the eye that does see well. Without early treatment, her visual system will never form correctly. **Joshua Brumberg's** (PhD '97) Pitt mentor, neurobiology professor Dan Simons, developed an animal model for this kind of neurological reorganizing: a simple whisker trim, which is just as brain-shaping for a young rodent (though it's painless—"like a haircut," Brumberg says). Now, as professor of psychology and neuroscience at Queens College, Brumberg is beginning to uncover the mechanisms of the "use it or lose it" rule of cortical circuitry. He's shown differences in the animals' dendrites, glia, extracellular matrixes, and myelination—changes affecting cellular structure, conductivity, and adaptability. The good news is that his preliminary studies show that certain enrichment activities (e.g., playtime with pet toys) may reverse some of the damage.

Prostate cancer is one of the most common forms of cancer in American men, with nearly 240,000 expected new cases in 2013. **Badrinath Konety** (Surgery Resident '94, Urology Resident '98) hopes to help bring that figure down. He investigates the role of triptolide Hsp70 inhibitor in preventing the growth of prostate cancer, as well as gene therapy studies of the cancer. He also studies novel diagnostics and the outcomes of bladder cancer. After his residency at Pitt, Konety became an American Foundation for Urologic Disease research scholar and received the Ferdinand Valentine fellowship at the University of Pittsburgh Cancer Institute. Konety also completed his MBA in Pitt's Katz Graduate School of Business. Today, he's chair of urology at the University of Minnesota.

**Sandi Kwee** (MD '96) is a nuclear medicine specialist at the Queen's Medical Center in Honolulu, and an associate professor of clinical sciences and cancer biology at University of Hawaii Cancer Center. His research interests center on the development and evaluation of small-molecule radiopharmaceutical tracers for PET imaging of cancer. Kwee is the principal investigator of three National Cancer Institute-funded clinical trials evaluating a tracer





Kwee with his daughter, Erika, in Tokyo during cherry blossom season, 2013

used to image hepatobiliary tumors as well as the assessment of patient response to chemotherapy or hormonal therapy in cases of advanced prostate cancer. Kwee's efforts are part of an emerging discipline involving the customization of cancer treatment using molecular imaging studies of tumor metabolism.

## '00s

Celiac disease is the most common genetically related food intolerance in the world. **Kimberly Newton** (MD '00), assistant adjunct professor of pediatrics at University of California, San Diego and director of the Pediatric Celiac Disease Center at Rady Children's Hospital—San Diego, is working to better understand why. She is creating a comprehensive database for pediatric celiac disease patients, which she hopes will help to further our understanding of genetic, environmental, and immunologic causes of the disease. —Jeff Ihaza, Katie Martin, and Elaine Vitone

## MATTHEW WILSON

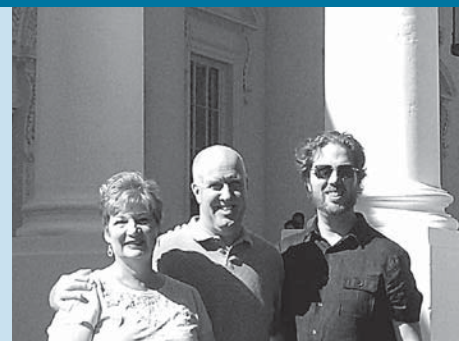
### CULTIVATING STEM SEEDLINGS

**W**hen Matthew Wilson (Biochemistry & Molecular Genetics PhD '04) was a postdoc researching breast cancer epigenetics at the University of California, San Francisco in the mid-2000s, he and his fellow lab staffers took turns leading discussions about current literature at their monthly meetings. One day, when it was his turn, he picked two papers about new techniques for harvesting embryonic stem cells. The topic was way outside of the group's expertise, but that didn't matter. Instead of focusing on the work itself, Wilson wanted to talk about the ethical and policy implications of these new technologies. "It was the most fun I'd ever had at a lab meeting," says Wilson.

After a great discussion, one of his colleagues said, "You know, there are actually jobs for doing these kinds of things." It got him thinking.

In 2008, Wilson won an American Association for the Advancement of Science fellowship with the National Science Board (NSB), the National Science Foundation's policy-making board, which also functions as an independent advisor to the president and Congress. In 2011, Wilson landed a full-time NSB job as a science and engineering policy analyst, writing speeches and talking points, preparing background documents for meetings, and drafting policy statements and reports. Biennially, NSB releases a report on the state of science and engineering that is aimed at policy-makers, educators, and the public. The 2012 edition included information on the approximately 20 percent average decline in state funding for the top 101 public research universities (Pitt among them) between 2002 and 2010 and how it would likely affect their education and research missions.

Wilson calls education both a moral and an economic imperative. "If we as a country really want to maintain our competitive edge—if we want to figure out innovations and discoveries for today's complex problems and tomorrow's complex problems—we really need to make sure our students have every opportunity to be challenged, to excel, and to be given a high-quality education." —Amy Whipple



Wilson outside of the White House with his parents in 2011

## MAA SAYS, "CHEERS!"

**Y**ears ago, the Class of 1938 made a pact that its last living member would pass on to Pitt med's new freshman class a bottle of aged scotch—a gift from the **Medical Alumni Association (MAA)** on its 50th reunion. This winter, **Joseph Novak** (MD '38) planned to keep this promise. Sadly, he took ill the day he was to meet **Richard Zou**, president of the Class of 2016. Novak, a prominent occupational ophthalmologist, died in January (see obituary, p. 38).

At the Alumni Gala in May, Lawton Snyder, executive director of the Eye and Ear Foundation, carried out Novak's wishes. He told Zou to gather his fellow first-years for a toast to Novak's class.

"We are grateful to be part of this ongoing tradition connecting past, present, and future physicians," says Zou.

Pat Carver, MAA director, decided to keep the tradition going by presenting a bottle of scotch to the 50th reunion class each year. **Robert Pacek** (MD '63) was surprised, and visibly moved, to receive the first of these at the gala—a 17-year-old bottle of Johnny Walker.

Pitt meders "past, present, and future" have a lot of reasons to raise their glasses.

Recently, the MAA presented the Philip S. Hench Award to **Johanna Seddon** (MD '74), professor of ophthalmology at Tufts University and founding director of its ophthalmic epidemiology and genetics service, for her accomplishments as a distinguished alumnus of the School of Medicine.

And on October 18, the William S. McElroy Award—Pitt med's recognition of a distinguished residency alumnus—will be presented to **Ian Pollack** (Neurosurgery Resident '91), codirector of the Brain Tumor Program at the University of Pittsburgh Cancer Institute, chief of pediatric neurosurgery at Children's Hospital of Pittsburgh of UPMC, and Walter Dandy Professor of Neurological Surgery at Pitt.

On August 4, a new crop of Pitt meders will don their first white coats, donated by the MAA, at the White Coat Ceremony—perhaps future Novaks, Seddons, and Pollacks will be among them. —EV



LEFT: Pat Carver, Robert Pacek, and Jen Moritz with Johnny Walker. RIGHT: Richard Zou receives a 46-year-old bottle of Whyte & Mackay's; rising sophomores will toast the Class of 1938 this summer.

VISIT THE **MEDICAL ALUMNI ASSOCIATION** AT [WWW.MAA.PITT.EDU](http://WWW.MAA.PITT.EDU).

## FREDERICK BRANCATI

SEPT. 25, 1959–MAY 14, 2013

In all areas of his life, Fred Brancati (Internal Medicine Resident '88) strove for a more compassionate approach, from his most widely read article—a humorous essay, published in *JAMA* in 1989, challenging the once-common practice of cowing interns (a.k.a. “pimping”)—to his influential work in type 2 diabetes epidemiology and prevention.

Brancati died of amyotrophic lateral sclerosis in May, three years after he was first diagnosed with the disease. He was 53.

Until January, Brancati was director of general internal medicine at Johns Hopkins University. His diabetes research covered the role of moderate exercise in prevention, the effectiveness of novel risk indicators, and the prevalence across age and ethnicity, among other areas. Last year, Hopkins named Brancati a Distinguished Service Professor of Medicine. The school also created an endowed professorship in his name.

Jeremy Berg, director of the Pitt-UPMC Institute for Personalized Medicine, became a patient of Brancati's years ago and was impressed by his bedside manner. Their daughters later played basketball together, and Berg and Brancati became friends, too. As the girls' basketball coach, Brancati “had a very light touch,” says Berg. He ranked his draft picks on how often the girls smiled.

During a visit a couple of years ago, Berg noticed Brancati using a cane and teased him about it, thinking Brancati had sprained his ankle. “ALS,” Brancati responded. “It sucks.”

Berg says, “I don't think anyone can comprehend what staring into an abyss like ALS is like, but he did it with his usual good humor and intelligence.” —Amy Whipple



Brancati

## RONALD HERBERMAN

DEC. 26, 1940–MAY 31, 2013

Ronald Herberman helped change the face of cancer treatment in Western Pennsylvania, founding the University of Pittsburgh Cancer Institute (UPCI). Under his direction, UPCI became a world-class cancer treatment and research center.

In the 1970s, Herberman, an MD, discovered natural killer cells, a type of immune cell, and determined that they could attack tumors. He became the first to use activated natural killer cells to treat advanced melanoma, as well as kidney cancer. Herberman also created a national program for improving cancer diagnosis based on immune markers, a field now known as immunodiagnosis, and developed a novel means of detecting cancer in blood, urine, and tissue.

It was this innovative work, undertaken at the National Institutes of Health, that attracted the late Thomas Detre, former senior vice chancellor for health sciences at Pitt and president of UPMC, who brought Herberman on board in 1985 to head the new institute, a position Herberman held until 2009. Within Herberman's first three years as director, he secured UPCI's designation as an NCI Comprehensive Cancer Center. He also oversaw the expansion of UPMC's oncology services into networked sites throughout Western Pennsylvania, Ohio, and West Virginia. Today, UPCI has 338 faculty members. Each year, UPCI and UPMC CancerCenter faculty treat nearly 75,000 cancer patients, bring in more than \$155 million in research grants, and conduct about 250 clinical trials.

UPCI administrator Dorothy Mann worked with Herberman for 25 years. She recalls the beginning of the institute: Five employees filled a small office in the Eye and Ear Institute in Oakland—a far cry from the \$130 million, 350,000-square-foot Hillman

Cancer Center the UPCI now calls home. Herberman refused to be discouraged by this humble start. A workhorse, he would always be the first one to the office, brainstorming, planning for the future, Mann says.

Herberman also served as Pitt's associate vice chancellor for cancer research, Hillman Professor of Oncology, professor of medicine and pathology, and chief of the Division of Hematology. In a written statement, Arthur S. Levine, senior vice chancellor for the health sciences and dean of the University of Pittsburgh School of Medicine, and Nancy Davidson, who is now director of UPCI and UPMC CancerCenter as well as Hillman Professor of Oncology, note the University owes much “to our long-standing scientific colleague and friend.” —Jeff Ihaza



Herberman

## JOSEPH F. NOVAK

JULY 26, 1915–JAN. 22, 2013

Joseph F. Novak (MD '38) left an indelible mark on workplace safety as a consultant for United States Steel, bringing a new focus to the importance of eye protection in Pittsburgh's mills.

Novak died in January. He was 97.

He began practice in ophthalmology by chance. When he was a young intern at Magee Hospital, Novak got hurt playing tennis. The injury to his calf would push him, years later, to leave his post as a surgeon at Walter Reed Hospital in D.C. Novak suffered painful varicose veins after his injury. If he wanted to continue operating, he would have to do it sitting down.

After an honorable discharge from the army in 1943, Novak shifted to ophthalmology. He noticed the lack of safety provisions for steel workers and partnered with U.S. Steel to develop and implement many of the procedures that are still in practice to this day. He designed protective eyeglasses with side shields that, in five years, reduced eye injuries at Duquesne Works by 60 percent.

Lawton Snyder, executive director of the Eye & Ear Foundation (which was once presided over by Novak), says the late doctor's work set the standard nationally for industrial eye protection. “Instances of injury to the eye in the workplace are all but nonexistent, and a lot of that is because of Joe Novak.” —JI



Novak

## IN MEMORIAM

### '40s

SOPHIE (SMRKOLJ)  
ERICKSON  
MD '45  
MAY 4, 2013

### '50s

FRANKLIN P. JOHNSON  
MD '52  
MARCH 14, 2013

### '60s

MICHAEL TALEFF  
MD '61  
OCT. 2, 2012

DAVID J. MONTAGNA  
MD '63  
APRIL 25, 2013

### FACULTY

ROGER A. BRUMBACK  
MAY 14, 2013

GIBSON P. BUCHANAN  
FEB. 2, 2013

AUTUMN M. KLEIN  
APRIL 20, 2013



## STEVE CARITIS ON WHAT'S BROKEN IN PRENATAL MEDICATION

BY KATY RANK LEV

As a child in the 1950s, Steve Caritis (Obstetrics and Gynecology Resident '73) loved taking apart appliances. When he dismantled the family toaster, his mother called him *mastro halasti*—Greek for “Mr. Fix-it,” she told him. He was told only recently that it really means “master breaker of things.”

The curious Caritis kept experimenting. Turning gears and jiggling wires fascinated him. *Why isn't this working*, he thought. *Can I fix it?*

In med school, Caritis was drawn to physiology and pharmacology. Unlike microbiology or anatomy, which required mostly memorization, pharmacology explored how organs function and tested how adding one medication affected the entire human machine. He also loved the thrill of surgery, of peering inside the body and repairing it.

Caritis chose obstetrics—a unique field wherein patients seek care for a happy event in their lives—but the science of pharmacology still pulled at him. Unfortunately, there was no field to combine the two interests.

Here, Caritis saw an urgent need. “The vast majority of medications are not FDA approved for use during pregnancy,” he says. And yet pregnant women take, on average, seven medications; chronic conditions don't disappear when sperm meets egg. This means that pregnant women, ever careful to avoid deli meat and unpasteurized cheese, are told to take everything from aspirin to insulin in doses that may not be optimal for them. For example, pregnancy increases blood-flow to the kidneys by 50 percent, so drugs like seizure medications, primarily eliminated by the kidneys, are eliminated twice as fast during pregnancy, meaning that these women aren't getting enough of the medication they need.

In pregnancy, Caritis says, “a time when we need the best pharmacologic information for the fetus and the mother, we have almost none.”

The National Institutes of Health have long encouraged the pharmaceutical industry to fund research on pregnant women. Instead, because of the inherent difficulties in studying this population and the liability risk that remains long after birth, the industry discourages clinical

trials in pregnant women.

After his residency, along with Stanley James at Columbia University, Caritis studied pregnant nonhuman primates. He performed uterine surgery to check fetal responses to interventions like labor-inhibiting medication. The work suited him, and he was good at it. In time, preventing premature labor through medication became his career specialty.

In 1975, when Caritis returned to the University of Pittsburgh as a professor in the Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, he teamed up with Raman Venkataramanan from the School of Pharmacy. The two spent the next 30 years fighting to fund clinical research one grant at a time, testing at Magee-Womens Hospital of UPMC various medications and their effects on pre-term labor. Caritis and Venkataramanan learned which medications were effective but still weren't sure of the proper dosage for the mother or the direct effects of the medications on the placenta or fetus.

Then, in 2004, the National Institutes of Health (NIH) requested proposals from researchers looking to study various medications taken by pregnant and nursing mothers. This was the opportunity Caritis had been seeking for decades. The NIH agreed that his research interests were perfect for the project. Caritis and Venkataramanan established the University of Pittsburgh as a founding

member of the Obstetric-Fetal Pharmacology Research Unit (OPRU), a multicenter network that investigates the impact of the physiological, cellular, and molecular changes of pregnancy on pharmacokinetics.

First, they studied glyburide, a medication used to lower blood sugar in women with gestational diabetes. Not surprisingly, they showed that pregnant women metabolize this drug twice as fast as nonpregnant adults; similar findings regarding labor-inhibiting medications followed. They've published multiple papers each year since the network began in *Journal of Clinical Pharmacology*, *American Journal of Obstetrics and Gynecology*, *Molecular Endocrinology*, and elsewhere.

Recently, the OPRU began studying Diclectin, a morning-sickness drug. They proved it's safe during pregnancy and also determined appropriate dosage. The medication received FDA approval in April.

As the OPRU expanded, Caritis and Venkataramanan realized they needed to recruit more scientists. In 2012, the pair earned a prestigious T-32 training grant from the NIH, bringing Pitt med what's probably the world's first postdoctoral fellowship in obstetrics and pharmacology.

Sixty years after his first dissection in his parents' kitchen, Caritis is building a previously nonexistent subspecialty in maternal-fetal medicine. Not bad for a master breaker of things. ■

MARTHA RIAL



In pregnancy, Caritis says, “a time when we need the best pharmacologic information for the fetus and the mother, we have almost none.”



SCHOOL OF MEDICINE  
DEAN CHEEVER F S MD  
KRUTZCH P H PHD  
CROSS R J MD

M 2 4 0

ANESTHESIOLOGY  
SAFAR P MD  
GALLA S J MD

HARRIS L C MD  
MONHEIM L M DDS

9 5 4

8 2 2

ANATOMY  
LANSING A I PHD  
DONALDSON J C MD  
HUMPHREY T MD  
PRIMAN J MD  
LAMY F PHD  
ROSENTHAL T B PHD  
NAPOLITANO L PHD

MASTERS E M PHD  
HESS M PHD  
KRUTZSCH P H PHD  
FINCK H PHD  
CAUNA N MD  
VINCENT W S PHD

8 1 4

BIOCHEMISTRY  
HOFMANN K PHD  
AXELROD A E PHD  
KATSOYANNIS P G PHD  
KORITZ S B PHD  
BASFORD R E PHD  
MC NARY J E PHD

WELLS W W PHD

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BRAUDE A I MD  
DANOWSKI T S MD  
JENSEN W N MD  
ROBIN E D MD  
FARR R S MD  
LATHAM W MD

MATEER F M MD  
RODNAN G P MD  
MACLACHLAN M J MD  
KIBLER R F MD  
WESTERMAN M MD  
SHAPIRO A P MD

9TH FL

1183

## PREVENTIVE MEDICINE

ROGERS K D MD  
THOMPSON D S MD

DREW F L MD  
SHINDELL S MD  
WOOD C L MD

M 2 0 0

7 2 0

## MICROBIOLOGY

JERNE N K MD  
YOUNGNER J S PHD  
ABRAHAM A S MD  
BRINTON C C PHD  
FUJIOKA M MD  
HALLUM J V PHD  
HEBERLING R L PHD  
LIEBERMAN I PHD

NOLL H PHD  
RAPOZA N PHD  
STAEHELIN T MD  
STINEBRING W R PHD  
STOCK A H MD  
WETTSTEIN F O PHD

## PATHOLOGY

FARBER E MD  
LEIGHTON J MD  
SIDRANSKY H MD  
SHULL K PHD  
LOMBARDI B MD  
MARROQUIN F MD

VILLA TREVINO S MD  
OLER A MD  
MERKOW L MD  
STEWART G MD  
SCHLUNK F MD  
ITO N MD  
KEES F R

7 7 6

## PHARMACOLOGY

MC LAIN P L MD  
AUSTIN R PHD  
ARNETT E MS  
BOGNER P H PHD

KALSER S C PHD  
REDICK T F PHD  
RUSS G PHD

6 2 2

## PHYSIOLOGY

KNOBIL E PHD  
BRIGGS N F PHD  
REDGATE E S PHD  
HALL P F MD  
TONG W PHD

PECKHAM W D PHD  
SANDLER R B PHD  
HOTCHKISS J PHD  
FRIZ G PHD  
KATORSKI B PHD

6 1 6

## SURGERY

HARBISON S P MD  
FISHER B MD  
LEE S H MD  
MAGOVERN G J MD  
ROSOMOFF H L MD

KAPLAN A MD  
YATES A MD

9 1 4

ADDISON H GIBSON  
MOSES C MD  
JABLONSKI J R PHD  
NECHAJ J  
SUNDER J MS

LABORATORY

1188

## 1963 WRIT LARGE

Size isn't everything. A visitor entering Scaife Hall in 1963 saw this faculty directory upon entering the building (there are nearly 2,300 regular faculty at Pitt med today and even more "volunteer" faculty). **Safar, Jerne, Knobil, Fisher, Myers, Youngner.** This roster includes, respectively, the popularizer of CPR, a Nobel Prize winner for his parsing of immunology, a man whose work formed the basis of reproductive endocrinology, the surgeon who proved breast-sparing lumpectomy was often just as effective as radical mastectomy, one of the world's best-regarded internists who was also an early developer of computer-aided diagnosis, and the virologist behind the killed-virus polio vaccine.

**Bert O'Malley** (MD '63), who went on to become the progenitor of molecular endocrinology, called the faculty "one of the most talented and intelligent groups of teachers I have seen anywhere."

"Jack Myers was the epitome of all U.S. teachers of medicine, and someone who set the highest standards for all other faculty." —*Joe Miksch*

1963 HIPPOCRATEAN



# CALENDAR

FOR ALUMNI & FRIENDS

## WHITE COAT CEREMONY AUGUST 4

3 p.m.  
Scaife Hall, Auditoriums 5 and 6  
Reception to follow  
Petersen Events Center lobby  
For information:  
Jen Moritz, 412-648-9059  
Jlm337@pitt.edu

## HEALTH SCIENCES ALUMNI RECEPTION SEPTEMBER 7

6 p.m.  
Los Angeles, Calif.

## WILLIAM S. MCELLROY AWARD PRESENTATION OCTOBER 18

4 p.m.  
John G. Rangos Sr. Research Center  
Children's Hospital of Pittsburgh of UPMC  
Recipient—Ian Pollack, MD  
Pitt chief of pediatric neurosurgery

## EVENING WITH THE DEAN NOVEMBER 3

Philadelphia, Pa.

## HEALTH SCIENCES ALUMNI RECEPTION FEBRUARY 19, 2014

Palm Beach, Fla.

## WINTER ACADEMY FEBRUARY 21, 2014

Naples, Fla.

Unless otherwise noted, for more information:  
Pat Carver, 412-648-9059, cpat@pitt.edu.  
To find out what else is happening at the  
medical school, go to [health.pitt.edu](http://health.pitt.edu) and  
[maa.pitt.edu](http://maa.pitt.edu).

No matter how much this  
little fella eats, he won't  
lose his lunch.



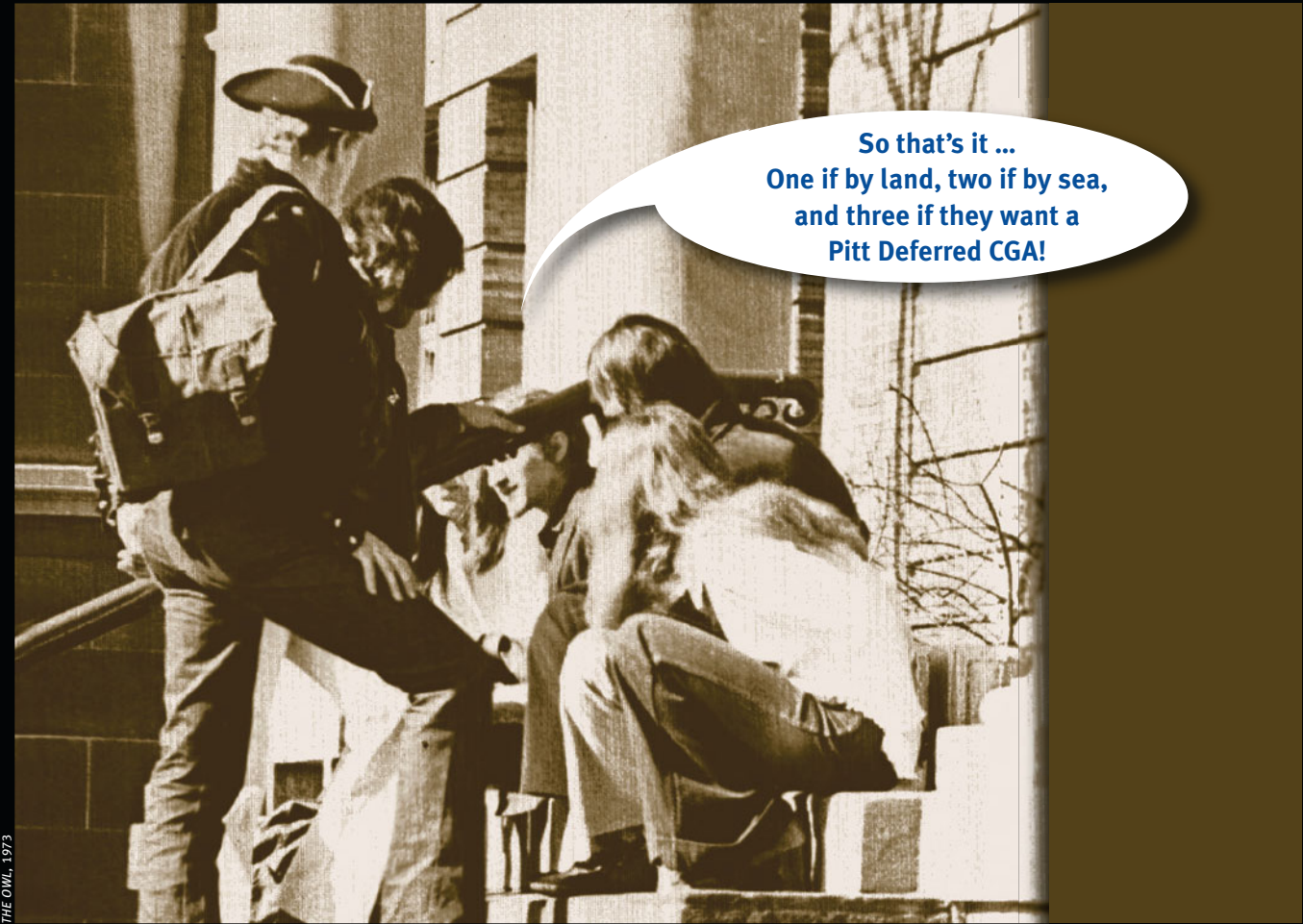
CORBIS

## FOR REAL! TWEEN SCIENCE.



**You probably try not to think about barfing too often**, but some researchers at the University of Pittsburgh think about it all the time. They are interested in the action of vomiting, which is a pretty complicated maneuver that requires a lot of muscles and nerves working together in a coordinated process. As it turns out, evidence suggests that rodents don't throw up. Ever. Not if they eat something poisonous; not if you give them medicine that causes vomiting; not even if you stimulate the nerves that cause emesis (a fancy medical term for puking) in humans and other animals. They simply cannot toss their cookies—no matter how many they eat. If we knew more about why some animals throw up and some don't, we might be able to help people who suffer from nausea because of dizziness, motion sickness, drugs that put people to "sleep" for surgery, cancer-fighting medicines known as chemotherapy, or pregnancy. Vomiting is controlled by a group of nerve cells at the bottom of the brain (in its "stem") that mice and other rodents don't have. Now researchers are looking for a way to stop those nerve cells from revving up the puke process in the first place; they are imagining a barf-free future. —*Jenifer Lienau Thompson*

Many thanks to Pitt School of Medicine prof Charles Horn, a PhD, for telling us more than we ever wanted to know about losing our lunch. For more kid-friendly science, visit How Science Works at [www.howscienceworks.pitt.edu](http://www.howscienceworks.pitt.edu)



So that's it ...  
One if by land, two if by sea,  
and three if they want a  
Pitt Deferred CGA!

THE OWL, 1973

# THE GIFT THAT GIVES BACK

When you establish a **charitable gift annuity (CGA)** with the University of Pittsburgh School of Medicine, you receive an income tax deduction and an annual payment for life. Deferred CGAs give you the option to defer the income payments so that you receive a greater fixed income later. At the time of your death, the funds you contributed when you established the CGA will benefit the school or a specific program you have designated. The examples below are based on a gift of \$10,000.

If you would like to learn more about the ways in which you can arrange for your legacy to the School of Medicine, contact:

Lisa J. Sciuillo  
Forbes Tower, Suite 8084  
3600 Forbes Ave.  
Pittsburgh, PA 15213  
412-647-0515  
slisa@PMHSF.org  
www.pitt.planyourlegacy.org

*Because of varying restrictions, Pitt is not able to offer gift annuities in some states.*

AGE	RATE	YEARLY INCOME	ESTIMATED DEDUCTION
55	4.0	\$400	\$1,851
60	4.4	\$440	\$2,231
65	4.7	\$470	\$2,956
70	5.1	\$510	\$3,691
75	5.8	\$580	\$4,268
80	6.8	\$680	\$4,791
85	7.8	\$780	\$5,502
90	9.0	\$900	\$6,190