

Columbia Medicine

Vagelos College of
Physicians & Surgeons

SPRING/SUMMER 2018

Scholarship Support

Making need-based
loans a thing of the past

Opioids Epidemic

Facing a problem
brought on by drugs
meant to help

JOACHIM FRANK

SCIENTIST.
INVENTOR.
WRITER.
NOBEL LAUREATE.





JÖRG MEYER

● FROM THE DEAN

Dear Readers,

When we began our yearlong celebration of the 250th anniversary of Columbia's medical school, we were known as the College of Physicians and Surgeons at Columbia University Medical Center and we had two Nobel Prize winners on our active faculty. By the time our anniversary year ended, we had become the Columbia University

Roy and Diana Vagelos College of Physicians and Surgeons at

Columbia University **Irving** Medical Center, we had **three** Nobel Prize winners on our active faculty, and we had received enough philanthropic support to become the first of our peer schools to be able to eliminate need-based student loans. Perhaps no other single year in our 250-year history has been as transformative.

Adding the Vagelos name to P&S honors the generous commitments made to our school by P. Roy Vagelos, a 1954 graduate, and his wife, Diana. They launched the 250th Anniversary Scholarship Challenge for Endowed Financial Aid in early 2017 to raise money to make VP&S a debt-free medical school for students who otherwise would need to borrow money. In December, Dr. and Mrs. Vagelos announced an additional \$250 million gift, most of it set aside for the scholarship endowment, and generous alumni, faculty, and friends contributed another \$25 million in matching gifts. These gifts should ensure that future generations of VP&S graduates can follow their dreams—into primary care, research, academic medicine, or specialization—instead of considering the impact of loan repayment on their choices.

The new name of the medical center campus we share with NewYork-Presbyterian recognizes the generosity of Herbert and Florence Irving, whose gifts over three decades to the two organizations total more than \$900 million, including a \$700 million gift announced in November to support cancer research and treatment.

The gifts from Mr. and Mrs. Irving and Dr. and Mrs. Vagelos also will benefit our research enterprise. Support from generous donors as well as our faculty's extraordinary success in being awarded peer-reviewed NIH grants (and doing so at better than changes in the NIH budget for eight consecutive years!) have enabled VP&S researchers to contribute to advances in science and medicine for 250 years. Those advances have been rewarded by external accolades, including the Nobel Prize in Chemistry that Joachim Frank shared in 2017. He now joins Richard Axel and Eric Kandel, Nobel laureates in medicine or physiology, as Nobel Prize recipients who are active members of our faculty.

We anticipated an anniversary year filled with celebration, but the events of 2017 exceeded our greatest expectations, just as the founders of our school probably could never have envisioned the 250 years of significant contributions our faculty and alumni would make to the course of medical history. Thank you to all of our friends—particularly Roy and Diana Vagelos and Herbert and Florence Irving and their families—for supporting the work we do, and congratulations, Dr. Frank, on bringing more Nobel glory to VP&S. These very special events made our anniversary year unforgettable and opened up endless possibilities for the next 250 years of our remarkable school.

With best wishes,

Lee Goldman, MD, Dean
lgoldman@columbia.edu

departments

2 **Letters**

3 **VP&S News**

12 **Clinical Advances**

- DISCOVER: A Journey Toward Help
- App Targets No. 1 Killer of Women
- Comprehensive Obesity Treatment Programs for Adults and Children

25 **Alumni News & Notes**

- Profile: Yvonne Thornton'73
- Profile: J. Nozipo Maraire'92
- Profile in Giving:
Craig Granowitz'90 MD/'93 PhD

35 **In Memoriam**

Faculty and alumni who have died

12



features



14

A Nobel Recognizes a Cool Scientific Method (Pun Intended)

By Alla Katsnelson

Structural biologists dismissed electron microscopy as “blobology,” but Columbia’s Joachim Frank spent his career developing powerful computational and statistical methods that have made cryo-electron microscopy one of the “hottest” methods of the past few years. His work earned him part of the 2017 Nobel Prize in Chemistry.

20

Opioids: How We Got Here, Where We Go From Here

By Sharon Tregaskis

Several factors may explain the hold opioids now have on Americans, but prescription opioids seem to be one of the major factors contributing to the epidemic. This article, the first of a series, sets up a discussion on what VP&S is doing to understand, treat, and prevent addiction to opioids.





Lewis "Bud" Rowland

Thank you so much for the wonderful article and spread you did on my father, Bud Rowland (Fall/Winter 2017 issue). It is really phenomenal to affirm, again and again, how well loved he was and what an impact he made. (I'm sure he would edit that sentence...)

Joy Rosenthal
Via email

Virginia Apgar

I read with pleasure in P&S News that Rita Charon will direct the Virginia Apgar Academy of Medical Educators (Fall/Winter 2017 issue). Your article includes important facts about Apgar'33, including that she was the first woman to be named a full professor at P&S [now VP&S]. She is arguably the best known VP&S graduate in the world. Every doctor and millions of patients have heard of the Apgar Score. But your Apgar bio does not mention her medical specialty: anesthesia.

Allen I. Hyman MD FCCM Sc.D.
(Hon Columbia)
Professor Emeritus of Anesthesiology

Aura Severinghaus

I can echo Dr. Alfred Scherzer's comments (Letter, Fall/Winter 2017 issue) about the willingness of Dean Aura Severinghaus to consider the applications of "outliers" for admission to VP&S. Having dropped premed as a college sophomore in order to pursue philosophy I made a late return to wanting medicine as a career. Despite my inadequate preparation, Dean Severinghaus must have regarded philosophy highly because he admitted me to the class of 1958.

Lawrence W. Norton'58
Emeritus Professor of Surgery, University
of Colorado School of Medicine

➔ send letters to: Bonita Eaton Enochs, Editor
Columbia Medicine
Vagelos College of Physicians & Surgeons
630 W. 168th St., Box 153
New York, NY 10032
Email: columbiamedicine@columbia.edu

Columbia**Medicine**

Chairman, Editorial Board

Thomas Q. Morris, MD
Alumni Professor Emeritus of Clinical Medicine

Editor

Bonita Eaton Enochs

Science Editor

Susan Conova

Contributing Writers

Avichai Assouline Rose Spaziani
Alla Katsnelson Sharon Tregaskis

Alumni News Editor

Marianne Wolff, MD

Alumni Writer

Peter Wortsman

Design and Art Direction

Eson Chan

Editorial Board

Alex Bandin, MD	Rebecca Lichtin'19
Jessica Buesing'18	Lisa Mellman, MD
Nicole Curatola'18	Stephen Nicholas, MD
Ron Drusin, MD	Stephen E. Novak
Kenneth Forde, MD	Carmen Ortiz-Neu, MD
Bruce Forester, MD	Ajay Padaki, MD
Oscar Garfein, MD	Richard Polin, MD
Sankar Ghosh, PhD	Donald Quest, MD
Lee Goldman, MD	Alan Schechter, MD
Tom Hickernell, MD	John Schullinger, MD
John Henry Ignatiev'19	Joseph Tenenbaum, MD
Jay Lefkowitz, MD	Emily Vail, MD

Columbia Medicine is published twice a year for alumni, faculty, students, and other supporters of the Columbia University Vagelos College of Physicians & Surgeons. It is published by the college and the VP&S Alumni Association through the VP&S Office of Communications. Additional content can be found in the online edition at columbiamedicinemagazine.org.

Lee Goldman, MD

Dean of the Faculties of Health Sciences and Medicine and Chief Executive of Columbia University Irving Medical Center

Christopher DiFrancesco

Chief Communications Officer

Address correspondence to:

Bonita Eaton Enochs, Editor
Columbia Medicine
630 W. 168th St., Box 153
New York, NY 10032
212-305-3900

Email: columbiamedicine@columbia.edu

 Join the medical school's Facebook page at www.facebook.com/columbiaps

Alumni should update their addresses by writing the Alumni Association at the address above or calling the alumni office at 212-305-3498.

Faculty and staff should contact their departmental administrators to update their addresses, which are obtained through the Columbia University personnel system.

All others with address changes should contact VP&S Communications at 212-305-3900.

Scholarship Program Begins This Summer To Benefit Students with Financial Need

When P. Roy Vagelos entered Columbia's medical school in 1950, the average budget for one year of medical school was estimated to be \$2,175, but if students lived frugally and spent less on room and board, bought used textbooks, and cut back on laundry and personal expenses, they might get by with \$1,776. The same bulletin that itemized those costs—the 1949-50 Faculty of Medicine Bulletin—listed 25 scholarships available for students.

Dr. Vagelos was among the recipients of those scholarships to support his medical education. A graduate of the University of Pennsylvania and son of immigrants who operated a small luncheonette in New Jersey, he benefited from scholarships at both Ivy League universities. After graduating from what is now called Vagelos College of Physicians and Surgeons (VP&S) in 1954 and completing his training at Massachusetts General Hospital, Dr. Vagelos conducted research at the NIH and later chaired the Department of Biological Chemistry at Washington University. He then joined Merck & Co. as head of Merck Research Laboratories, rising to the position of chairman and CEO of the company. He led the company during a period of growth and prominence; Fortune magazine named it the nation's most admired corporation for seven consecutive years.

Because both Dr. and Mrs. Vagelos received scholarships to support their higher education, they have been giving back to scholarship funds for more than 50 years. At VP&S, that support most recently took the form of a challenge to commemorate the 250th anniversary of the medical school.

The 250th anniversary steering committee, chaired by Dr. Vagelos, identified the challenge as a fund-raising goal for the anniversary and named it the 250th Anniversary Scholarship Challenge for Endowed Financial Aid. It was launched in early 2017 with a \$25 million gift from Dr. and Mrs. Vagelos, a gift used to match contributions of \$50,000 or more for endowed scholarships to incentivize alumni and other friends of VP&S to join this effort.

Gifts from alumni and others soon followed, and Dr. and Mrs. Vagelos announced in December an additional gift of \$225 million for a total of \$250 million—\$150 million of which was designated to endow the fund to help VP&S eliminate student loans for students with the most need. Scholarships from the endowment will support medical students who qualify for need-based financial aid, currently about half of the student body.

At Revisit Day in April—when accepted students were invited back to VP&S for a second look before committing to one medical school—



Roy and Diana Vagelos with
Columbia President Lee Bollinger
and VP&S Dean Lee Goldman

JENNY GORMAN

VP&S announced that all new students and those moving into their second, third, and fourth years for the 2018-19 year will have access to scholarships instead of loans if they qualify for need-based financial aid.

In addition, for students graduating in 2018, VP&S announced plans to convert up to \$5,000 in loans to scholarships.

The 2017 gifts bring Dr. and Mrs. Vagelos' total giving to medicine at Columbia to more than \$310 million. A portion of the gift announced in December will support VP&S priorities of Columbia's precision medicine initiative and basic science research and endow a professorship to honor the Vagelos family's longtime doctor and friend, Thomas P. Jacobs, MD, professor of medicine.

"Roy and Diana Vagelos truly understand that having a scholarship fund of this magnitude puts medical school within reach of the most talented students, regardless of their ability to pay," said VP&S Dean Lee Goldman, MD. Noting that high debt levels often drive medical students to pursue higher-paying specialties over less lucrative ones, such as internal medicine, pediatrics, or medical research, he added, "The income generated from this endowment will allow us to replace loans with scholarships for students with financial need, thereby allowing them to choose a medical specialty based on their true passion and highest calling, rather than on income potential."

"This idea of giving young people the kind of support that allowed us to pursue our own education at Penn, Barnard, and Columbia has been a driving force in our lives for some time," said Dr. Vagelos. "We want P&S graduates to be able to do what

they really love to do in their lives and in the medical profession, whether it's clinical care or biomedical research. We've been lucky enough to have the chance to make a difference and we want to be sure future graduates will have the same opportunity."

About \$140 million of Dr. and Mrs. Vagelos' total giving over

the years has been structured to encourage others to make matching gifts, making the Vageloses responsible for about \$450 million in philanthropy to the medical school.

In addition to the latest gifts, the couple gave \$53 million to support the design and construction of a state-of-the-art medical and graduate education center that now bears their name. The Roy and Diana Vagelos Education Center, an award-winning structure at 104 Haven, opened in August 2016.

Roy and Diana Vagelos have given more than \$310 million to Columbia's medical school.

New Name for 250-Year-Old School

The December 2017 announcement of the latest gift from P. Roy Vagelos⁵⁴ and Diana Vagelos accompanied an announcement from Columbia University President Lee C. Bollinger that the College of Physicians and Surgeons would be officially known as the Columbia University Roy and Diana Vagelos College of Physicians and Surgeons—VP&S for short.

"There are no more fitting names to have affiliated with our medical school than those of Roy and Diana Vagelos, who have made such tremendous contributions to medicine, education, and science," said President Bollinger. "The new name recognizes all Roy and Diana have done, and will do, to transform education, medical



COLUMBIA UNIVERSITY
Vagelos College of Physicians and Surgeons

research, and patient care at Columbia. Generations of students and patients will benefit from the generosity of their spirit and the sweep of their vision."

Dr. and Mrs. Vagelos have long had ties to Columbia. They met in New York City in 1951 while Roy Vagelos was at VP&S and Diana Touliatou, who grew up in Washington Heights, was studying economics at Barnard College. She attended the High School of Music & Art, colloquially known as "the Castle on the Hill," in Harlem (the school in 1984 merged into LaGuardia High School of Music and the Arts). The couple married in 1955 in a Greek Orthodox church in Washington Heights; both had parents who emigrated from Greece. Mrs. Vagelos currently serves as vice chair of the Board of Trustees at Barnard, where the school's multi-use Diana Center building, completed in 2010, is named in honor of her leadership and support. Dr. and Mrs. Vagelos recently gave Barnard a gift to support creation of a teaching and learning center, which will help as Barnard becomes one of the first liberal arts colleges among its peers to institute a technology requirement. Their gift will fund the learning center's computational science center, an endowed director position for this center, and an endowed chair in chemistry; they recently committed a matching gift of \$10 million for scholarships.

Their giving to the University of Pennsylvania has supported undergraduate science education programs related to energy research, molecular life sciences, and life sciences and management and has funded a new chemistry lab. "We've even supported a project at my old high school in Rahway," says Dr. Vagelos. "We are very dedicated to what we think is the most important thing: education."

New Departments: Emergency Medicine, Medical Humanities and Ethics

Columbia Trustees have approved two new departments for the medical school, bringing the total number of academic departments to 27.

The Department of Emergency Medicine was approved in 2016 and the department's inaugural chair, Angela M. Mills, MD, joined VP&S earlier this year from the University of Pennsylvania. She is the J.E. Beaumont Professor of Emergency Medicine at VP&S and chief of emergency medicine services for the Columbia campus of NewYork-Presbyterian Hospital.

At Penn, Dr. Mills was professor of emergency medicine and vice chair of clinical operations in the Department of Emergency Medicine. A national leader and expert in emergency medicine, Dr. Mills is a Muhlenberg College graduate who graduated with Alpha Omega Alpha distinction from Temple University School of Medicine. She was chief resident in emergency medicine at the University of Pennsylvania. She has focused her research on emergency diagnostic imaging, clinical operations in emergency services, and the evaluation of undifferentiated abdominal pain. She has authored more than 90 scientific publications and received research funding from federal agencies and industry.

The designation of the new clinical department recognizes the evolution of emergency medicine as an academic discipline. Emergency medicine was recognized as the 23rd medical specialty by the

American Board of Medical Specialties in 1979. VP&S now joins leading medical schools with academic emergency departments that will further contribute to the academic rigor and research in the field. Until now, adult emergency medicine had been a division within the Department of Medicine while pediatric emergency medicine had been a division within the Department of Pediatrics.

The other new department, the Department of Medical Humanities and Ethics, is chaired by Rita Charon, MD, PhD, a VP&S faculty member since 1982 and currently professor of medicine. Medical humanities and ethics is a broad term that covers several areas of study—philosophy, literary studies, history, religious studies, law, social sciences, and the arts—meant to help students and medical professionals understand and address the complex human experiences inherent in health, illness, and death.

Dr. Charon will lead the department's pursuit of three primary goals: education, research, and scholarship in the medical humanities and the arts; ethical, legal, and social research and scholarship in emerging fields of socially complex translational sciences; and research and scholarship on professionalism and social justice in health care. The department will have divisions devoted to ethics, narrative medicine, and professionalism and health care justice. Joining Dr. Charon to direct the divisions will be Sandra Soo-Jin Lee, PhD, a



Angela M. Mills

Rita Charon

Stanford University anthropologist and bioethicist with an international reputation in the ethics of precision medicine and human genomics, and David Rothman, PhD, a historian and scholar of social medicine whose Center for Medicine as a Profession will join the new department.

As founder of Columbia's Program in Narrative Medicine—and creator of the field itself—Dr. Charon has made the teaching of narrative studies at Columbia University and particularly at the medical center a national and international model for how clinicians and trainees in all health care professions can comprehend and heed their patients' complex experiences of illness. She directs the Program in Narrative Medicine, the Columbia Commons IPE interprofessional education programs, and the Virginia Apgar Teaching Academy for Medical Educators.

Dr. Charon began her medical career as a general internist after receiving her MD degree from Harvard. She became a literary scholar and completed her PhD in English at Columbia in 1999.

Her research has been supported by the NIH, the NEH, the Josiah Macy Jr. Foundation, and several other private foundations. She has published widely in leading medical and literary journals.

New Chair for Pediatrics



Jordan Orange

A physician-scientist at Baylor University has been named chair of pediatrics at VP&S and pediatrician-in-chief at Morgan Stanley Children's Hospital of NewYork-Presbyterian. Jordan Scott Orange, MD, PhD, succeeds Lawrence R. Stanberry, MD, PhD, who chaired pediatrics at Columbia since 2008.

Dr. Orange has been professor and vice chair for research in the Department of Pediatrics at Baylor College of Medicine in Houston since 2012. Before that, he spent nearly 10 years on the medical faculty of the University of Pennsylvania. At Baylor, Dr. Orange was director of the Pediatrician-Scientist Training and Development Program and chief of immunology, allergy, and rheumatology. At Texas Children's

Hospital, where he was the Louis and Marybeth Pawleek Endowed Chair, he directed the Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiency and the Center for Human Immunobiology.

An international leader in pediatric primary immunodeficiency and the immunobiology of human natural killer cells, he has been continuously funded by the NIH and published more than 250 papers.

Dr. Orange received bachelor's, PhD, and MD degrees from Brown University, trained in pediatrics at Children's Hospital of Philadelphia, and completed a clinical fellowship at Boston Children's Hospital and a research fellowship at Harvard.



PHOTOS BY AMELIA PANICO

Medical Students Celebrate Match Results

The 156 Columbia students participating in the 2018 Residency Match were among approximately 17,740 U.S. medical students who learned about their matches on March 16. The most popular residency results among VP&S students were internal medicine (34 students), psychiatry (17), pediatrics (10), emergency medicine (9), obstetrics and gynecology (9), orthopedic surgery (9), dermatology (8), and neurology (8). Thirty-five percent of VP&S students will do all or part of their residency in New York City.



Medical Students Launch Music at Bedside Program

On some days in the halls of Milstein Hospital Building, the silvery sound of a violin playing “Somewhere Over the Rainbow” floats in the air. On other days, it might be a Bach Cello Suite or holiday carols by a brass quintet. The music is live and the performances are thanks to the new Music at Bedside Program, a collaboration between VP&S students and palliative care professionals at NewYork-Presbyterian. The program’s goal is to soothe and entertain patients enduring painful conditions.

The Music at Bedside Program began to take shape in spring 2017, when VP&S Musicians’ Guild leaders wanted to create a program that combines their passion for music with patient care. The program is under the guidance of Craig Blinderman, MD, associate professor of medicine and director of adult palliative medicine at NYP/Columbia.

“Alleviating suffering is not simply achieved with finding the right medicine or plan of care but often happens with our touch, our words, our presence, and, I believe, with art,” says Dr. Blinderman. “Music is perhaps the most accessible art form, especially for those who are in pain and cannot concentrate on words or images. So the Music at Bedside Program fits in perfectly with the goal of palliative care.”

The program launched in the fall with 25 participants from the Musicians’ Guild under the leadership of violinist Stefanie Gerstberger’19 and cellist Shaheen Malick’20. This year, the guild is led by instrumental guitarist Andrew Sanchez’21.

Students play weekly in the cardiac medicine and neurosurgery units, where patients are recovering from surgery or suffer from chronic illnesses that keep them hospitalized for long stretches. In December, caroling groups visited several units, including cardiac medicine, rehabilitation, and bone marrow transplantation.

“The patients are always surprised to see someone with an instrument walk into their room,” says Mr. Sanchez.



Musicians’ Guild members frequently perform outside of formal campus venues. Here, from left, are Stefanie Gerstberger’19, Cory Chang’20, and Shaheen Malick’20 as they perform at the Tenafly Public Library in New Jersey.

Ms. Gerstberger likes to play her violin in the corridors. “I can reach more rooms, and patients come out and look for me,” says Ms. Gerstberger, who was playing the violin in another music therapy program when a patient woke up from a coma. “Music relieves stress for the entire unit: patients, families, nurses, and doctors. I really feel like I’m making someone’s day better. In the classroom, we are trained to become empathetic doctors, but nothing is as effective for feeling empathy as playing in the wards.”

The students also say taking part in the program has helped them as well. “Helping patients this way fosters a true sense of purpose,” says Mr. Malick. “Playing music in the hospital has a therapeutic aspect for us.”

— Rose Spaziani



AMELIA PANICO

Class of 2020 Transitions to Major Clinical Year

The 174 members of the Class of 2020 marked the start of their major clinical year with the Steven Z. Miller Student Clinician’s Ceremony on Jan. 5. The ceremony, which marks the transition of second-year students from the classroom to patient-centered training in hospital and ambulatory settings, has been a VP&S tradition since 1998. Three members of the class designed a pin to attach to the white coats they received when they enrolled. The ceremony is named for the late Steven Z. Miller’84, the Arnold P. Gold Associate Professor of Pediatrics at VP&S, who founded the first transition ceremony.

RhoGAM at 50: A Drug Still Saving Lives of Newborns

Rh disease has essentially been eradicated in high-income countries but until the late 1960s was one of the most severe and devastating conditions for newborns, killing approximately 10,000 infants a year and causing brain damage in many more in the United States alone.

The disease is almost completely prevented by RhoGAM, a drug developed in the 1960s by Columbia researchers John Gorman, MD, and Vincent Freda, MD, and a pharmaceutical company researcher, William Pollack, PhD. In February, Columbia researchers and physicians joined guests from around the world to celebrate RhoGAM's 50th anniversary.

"I still marvel at how a low-tech solution could have such impact," said Dr. Gorman, former director of the blood bank at what is now NewYork-Presbyterian/Columbia University Irving Medical Center, to the audience gathered for a panel discussion to celebrate the drug. "It's the most cost-effective drug ever produced. There have been no fatalities in 50 years, and it saves \$1 billion every year by preventing high-risk Rh pregnancies. Plus, there's peace of mind for Rh-negative mothers. How lucky can you be?"

Rh disease can develop when a woman with Rh-negative blood is pregnant with an Rh-positive fetus. In these cases, when fetal red blood cells cross into the mother's circulation—usually at delivery—the mother's body begins producing antibodies that can attack and kill a fetus's red blood cells. It takes some time to produce such antibodies, so the first Rh-positive child is typically spared. But each subsequent Rh-positive fetus increases the odds the mother will become "sensitized" to the fetus.

Once a woman is sensitized, her antibodies can cross the placenta to destroy the red blood cells of her fetus, which can lead to miscarriage, brain damage, or the newborn's death. Roughly 15 percent of American women have Rh-negative blood.

Dr. Gorman set out to cure Rh disease with Dr. Freda, an obstetrician, and Dr. Pollack, chief research scientist at the Ortho Pharmaceuticals lab. Two physicians based in Liverpool, England, Cyril Clarke, MD, and Ronald Finn, MD, were independently pursuing the same goal. Alvin Zipur-

sky, MD, a Toronto-based pediatrician, who was working in Winnipeg at that time, was studying the extent of the transfer of fetal red blood cells into the maternal circulation throughout pregnancy and at parturition.

By the early '60s, when the researchers started their work, much of the scientific foundation for such a treatment already existed. It was known, for instance, that Rh disease would not occur if Rh-negative mothers did not develop the antibodies. It was also understood that injecting someone with antibodies made by other people against a given antigen prevented the recipient from producing her own antibodies against that antigen.

That suggested to Drs. Gorman and Freda that administering anti-Rh antibodies to an Rh-negative mother soon after delivery would prevent sensitization to the Rh antigen and subsequent Rh disease. Technically, the breakthrough had been possible since 1941, when Philip Levine discovered the cause of Rh disease. It just did not occur to anyone to put it all together.

"Vince Freda and Bill Pollack grasped this triple conjunction immediately," Dr. Gorman said. "And they had the will and the resources to do something about it. They turned this idea into reality, doggedly overcoming difficulties, withstanding the immediate pushback, doubt, and skepticism of virtually the whole blood bank community."

Perhaps the skeptics had a point: Rh immune globulin (RhIg)—the anti-Rh antibody in RhoGAM—is paradoxically the same agent that causes Rh disease and can kill babies in the womb. And the more "dangerous" the antibody, the more effectively it prevents sensitization.

"But there it was: RhIg, a fully optimized molecule, in plentiful supply from the legions of Rh mothers already Rh-sensitized," said Dr. Gorman. "No need for clever chemists to synthesize, fine-tune, and test a novel molecule, as is the case with most new drugs."

In the mid-1960s, Drs. Gorman and Freda obtained anti-Rh antibodies from Dr. Pollack and showed that they prevented sensitization in Rh-positive subjects, paving the way for RhoGAM's official regulatory approval in the United States in 1968.

The benefits were immediate. The first person to receive the approved drug—Marianne Cummins—received the injection just hours after it became available. Ms. Cummins, her husband, and her physician, David Landers, MD, were also present in February to tell her story. In 1968, Ms. Cummins was 29 and pregnant with her third Rh-positive child but had not become sensitized. RhoGAM prevents sensitization—as long as it is administered within 72 hours after delivery. She had read in the newspaper about the new treatment, which was to be released on June 1. However, her due date was May 27. If she delivered on time, she would miss the chance to use the drug by one day.

After the Division of Biologics Standards (the forerunner of the FDA) approved the drug, the release date was moved up to May 29 and on that day, at Holy Name Hospital in Teaneck, N.J., Ms. Cummins became the first person to receive RhoGAM. She would go on to have another child, but this time with a newfound peace of mind.

Within a year of RhoGAM's debut, nearly every pregnant Rh-negative woman in the United States, Canada, and most of Europe received the



John "Jack" Gorman, left, with Vincent Freda

drug, saving the lives of millions of Rh-positive babies. For their work, Drs. Gorman, Freda, Pollack, Finn, and Clarke received the Lasker Award in 1980.

“I was very happy that Rh disease was eliminated [here], as were all my colleagues,” Dr. Zipursky said at the celebration, “but about 10 years ago, I suddenly realized that maybe Rh disease is not gone,” noting that getting it into the hands of mothers in poor countries is a remaining challenge.

Dr. Zipursky and Vinod Bhutani, MD, a neonatologist from Stanford University, founded CURhE, the Consortium for Universal Rh Disease Elimination, to increase access to and affordability of RhIg. The consortium is joined in this endeavor by other groups that sent representatives to the Feb-

ruary panel discussion: Funmi Banire, founder of Rhesus Solution Initiative, a Nigeria-based NGO, and Gerard Visser, MD, PhD, a Dutch obstetrician and member of the International Federation of Gynecology and Obstetrics.

“I thought the problem of Rh disease was over,” Dr. Visser said, “until CURhE showed it still exists in half the world. Three hundred thousand children dying or being handicapped every year is just too many. We know preventative measures are always preferable. It’s so easy. Why aren’t we capable of doing the easy thing?”

RhoGAM is now produced by Kedrion Biopharma, which co-sponsored the 50th anniversary event.

— Joe Neighbor

Bequest Sets Stage for Support for Cancer

Columbia University and NewYork-Presbyterian announced in November that Florence Irving and her late husband, Herbert Irving, have given \$700 million to the two institutions to advance cancer research and treatment.

In a joint statement issued by Columbia President Lee C. Bollinger, VP&S Dean Lee Goldman, and NYP CEO Steven J. Corwin, the leaders underscored the significance of the largest gift in the medical center’s history: “What is perhaps less well understood is that the dramatic advances now within our reach will be realized only by harnessing the learning of many different scientific disciplines and such work requires enormous institutional resources. The Irvings have given us the means to engage in that collective effort, and we are determined to reward their ambitious vision.”

The \$700 million bequest, which includes \$600 million in new funds, brings the Irvings’ total donations to Columbia University and NewYork-Presbyterian to more than \$900 million over the past three decades. The medical center campus shared by the two institutions was renamed in 2016 to honor the Irvings; the institutions are now known as Columbia University Irving Medical Center and NewYork-Presbyterian/Columbia University Irving Medical Center.

The Irvings’ historic gift will have a profound impact on research and clinical care at what is already one of the world’s preeminent academic medical centers at a time when new scientific tools and techniques are allowing researchers and clinicians to better understand how cancer begins

and grows—and how to fight its spread. The new resources will help Columbia and NewYork-Presbyterian recruit the best basic scientists, physician-scientists, and clinicians dedicated to producing a range of innovations in patient care, including improved efficacy of radiation therapy, new surgical approaches, and the development of a variety of new therapeutic options for patients. Facilities also will be expanded at the Herbert Irving Comprehensive Cancer Center, one of 47 cancer centers designated as comprehensive centers in the United States and one of the first to be designated by the National Cancer Institute for its capabilities in both cancer research and clinical care. More than 4,000 new cancer patients are treated at Columbia each year.

The Irvings’ philanthropy will be felt across a wide range of scientific disciplines, including cancer genomics, immunology, computational biology, pathology, and biomedical engineering. A key focus will be to further advance cancer research and clinical care in Columbia’s Precision Medicine Initiative, which, in partnership with NewYork-Presbyterian, explores the genetic and genomic basis of cancer and other life-altering diseases.

The Irving name has long been associated with Columbia and the Columbia campus of NewYork-Presbyterian. The medical center is home to the Herbert Irving Pavilion, the Irving Cancer Research Center, the Irving Institute for Clinical and Translational Research, the Irving Radiation Oncology Center, the Irving Bone Marrow Transplant Unit, and the Herbert Irving Comprehensive Cancer Center. The



Herbert and Florence Irving

Irvings also have long supported Columbia’s work through named professorships, faculty chairs, and clinical and research facilities. Their giving to Columbia began with their 1987 endowment of the Irving Scholars program for early-career clinical investigators.

Florence and Herbert Irving were born and raised in Brooklyn. Herbert Irving, who died in 2016 at the age of 98, was a co-founder and former vice chairman of Sysco Corporation, the nation’s largest food distributor. Florence Irving has served in leadership positions on the boards of several non-profit institutions.

“Herbert and I have always been proud to help the terrific doctors at Columbia and NewYork-Presbyterian,” said Florence Irving. “It meant everything to him to be able to support world-class research and caregiving that makes a difference in people’s lives. I am honored, as he always was, to be associated with these great institutions and the special people who make them what they are.”

Caroline Park, Latest VP&S Olympian

Columbia medical student Caroline Park recently enjoyed the journey of a lifetime to the 2018 Olympics in South Korea, where she played on the historic unified Korean women's ice hockey team.

Ms. Park's hometown is Brampton, Canada, but her parents were born in South Korea. In 2013 she received an unexpected email from the Korea Ice Hockey Association while she was working as a clinical research assistant at the Hospital for Special Surgery. The email invited her to try out for the Korean women's ice hockey team in recognition of her many years as a player. Her love of the sport started in childhood, when she played hockey with her older brother. She played for the Mississauga Junior Chiefs, Canada's junior league team, and was recruited to Princeton University to play for its team. After Princeton, she joined a mixed hockey club and kept playing while doing research at HSS.

A few weeks after Ms. Park received the email, she boarded a plane to Seoul. The pull of her parents' birth city was strong. She grew up close to her Korean grandmother, who lived with the family in Canada. Korean was spoken at home. That trip was the first of many trips to

South Korea over the next five years. She entered VP&S in 2015 and took a leave of absence to train for the Olympics but returned in 2017 to resume her major clinical year with four back-to-back rotations at NewYork-Presbyterian. Upon completing her rotations, she rejoined the team in South Korea for more training.

"The culture of hockey transcends a country's culture," says Ms. Park, whose teammates include a few other recruits from North America who have joined the native Koreans. On the ice, Ms. Park plays forward and is known by her Korean name, Park Eun-jung. She approaches athletic competition as she does everything else. "I want to be a great hockey player and become a great doctor. Whatever I'm doing in the moment, I do it 100 percent."

After competing in the Olympics in February, she shared her favorite moments, how she played through an injury, and her future plans.

"There were so many amazing moments," says Ms. Park. "Some highlights include playing our first game on Olympic ice as a unified team and being on the ice when we made history by scoring the first goal ever for Korea at the Olym-



Caroline Park at the 2018 Olympics

pics. The underlying feelings during all of these moments were pure excitement, happiness, and pride. It was an indescribable feeling to hear the roar of the crowd as we entered the stadium to walk in the opening ceremony as the host country. Being able to play on home ice in front of family, friends, and Korean fans was such an honor. The fans were incredible, including the North Korean cheerleaders. They were so supportive and cheered for us until the last buzzer in every game, regardless of the score. The roar of the crowd when we scored the first goal was so loud, I couldn't hear my teammates on the ice. Hearing the fans' chants and cheers filled me up with so much joy and pride every game."

Because of an injury suffered shortly before the Olympics began, Ms. Park did not play much during the first two games of the Olympics but she was able to play more during the final three games.

She says she was surprised by how quickly the South Korean team bonded with the North Korean players. "They were so friendly and warm. They were no different than any of us, and we became close. I think the unified team reminded everyone of how sports can transcend cultures and barriers. It was a privilege to be a part of something bigger than just a hockey game. Time will tell if it will have any lasting impact, but being a part of this team afforded me the opportunity to get to know remarkable women who very few people would ever get to meet."



Jenny Thompson, second from right, and the team that won gold in the 4x100m freestyle relays at the 2000 Olympics in Sydney, Australia

Though her Olympics career is probably over, Ms. Park says she would like to be involved with the team or the Olympics organization in a medical capacity after she finishes medical school and training. “I would love to combine my interest in hockey and sports with my medical career, and that’s why I have always had a strong interest in orthopedics. I’ve had to deal with my fair share of injuries playing sports, so it would be great to use my experiences to relate to and help others.”

She has now resumed her studies at VP&S. “I completed some rotations before taking my leave of absence, but I still have a large majority of major clinical year left to complete.”

Ms. Park is not the first Columbia medical student or graduate to compete on the world stage as an Olympian, but she is thought to be the first to compete in any Winter Olympics.

Three alumni—Benjamin Spock’29, Stephen Rerych’75, and Valeria Silva Merea’12—were already Olympians when they started medical school. Dr. Spock won a gold medal at the 1924 Olympics in Paris as a member of the crew team for Yale, his undergraduate alma mater. Dr. Rerych won two gold medals for swimming at the 1968 Summer Olympics in Mexico City. Dr. Silva Merea swam for her native Peru in the 2004 Olympics in Greece, and in 2008, just five days before arriving at VP&S, she competed in the Beijing Olympics.

Jennifer Thompson’06 was a member of the USA women’s swim team before and during her years at VP&S. One of the most decorated Olympians in history, she won 12 medals, including eight gold medals, in 1992, 1996, 2000, and 2004 Summer Olympics.

Another athlete, John Lattimer’38, was a track star at Columbia College who won eight metropolitan area Amateur Athletic Union hurdling championships and set a record as a decathlon champion. He won the 50-yard dash at the Millrose Games, an indoor track and field meet held in New York City each year since 1914. During his military service he won the 200-meter hurdles for the 7th U.S. Army at the GI Olympics in Germany. After his death, Dr. Lattimer’s daughter found a letter inviting him to the 1936 Olympics in Berlin, an invitation he apparently turned down to continue his studies at VP&S.

—Rose Spaziani



Students in a workshop discuss important issues from different perspectives

Medical Center Holds First Interprofessional Day of Action

Faculty and students throughout the medical center were excused from classes on April 5 to participate in a daylong interprofessional curriculum. The first Interprofessional Day of Action brought together more than 1,800 students from nine schools and programs to attend seminars and interactive workshops that conveyed the necessity of teamwork among health care workers.

The day opened with a welcome message from Lee Goldman, MD, dean of the Faculties of Health Sciences and Medicine and chief executive of Columbia University Irving Medical Center.

“Today is important for us, not only as a community but also for the future of health and medicine,” said Dean Goldman. “We believe in health care as a team sport. We increasingly work together with people who have different training and skills that complement the ones we have, so collectively we make a team that is far better than any one individual can possibly be. I see this event as a ‘first annual’ and as part of our process to bring all of our faculty and all of our students together more often and in meaningful ways.”

“Our approach to interprofessional education at Columbia differs from other institutions,” Dr. Charon said. “Our narrative approach results in individual-to-individual contact within the context of health care teams. We don’t gather to discuss operating room checklists or who does what at the cardiac arrest code. Instead, whether with faculty groups or student groups, we invite participants to grapple with fundamental issues of the human condition.”

Columbia Commons IPE has run programs for students, faculty, and staff but decided to reach a wider audience this year with Interprofessional Day of Action. Participants represented all health-related programs at Columbia: nursing, dentistry, nutrition, physical therapy, occupational therapy, medicine, pastoral care, social work, and public health.

Workshops were centered around a collaborative problem-solving activity on pressing topics such as the opioid epidemic, diversity and bias, and veterans’ health. Each workshop was filled with a mix of students from different programs, and they learned about each other’s perspectives by working together on a project.

Olivia Molineaux, a second-year medical student, emphasized the importance of understanding the expertise of other professionals: “We get in our bubbles very easily. It is good to remember that we’re not going to be the experts on everything and we’ll need input from other people.”

Clinical advances

By Avichai Assouline



Wendy Chung with
a young patient

JOHN ABBOTT

DISCOVER: A Journey Toward Help

Living with an undiagnosed disorder can be both frightening and exhausting.

DISCOVER—Diagnosis Initiative: Seeking Care and Opportunities with Vision for Exploration and Research—is a unique center at Columbia. The program is designed to diagnose rare and complex diseases and to develop novel and individualized treatments for patients.

“We are doing medical detective work by using genetic and genomic tools,” says Wendy Chung, MD, PhD, director of DISCOVER and the Kennedy Family Professor of Pediatrics (in Medicine).

The program sees about three to four patients a week, most of them children. In addition to Dr. Chung, the program’s case management team includes a physician, coordinator, genetic counselor, social worker, and nurse practitioner. The team also works with about 50 specialists throughout the medical center.

The case management team searches for a diagnosis by combing through each patient’s medical records and test results, which are usually extensive. Patients then see between five and 10 specialists over one to two days and get any tests that have not been done yet. If the team diagnoses

the patient with a known disease, the patient is linked to the relevant specialists.

If the patient has a rare disease with no known standard of care, the team will enroll the patient in research to further characterize the condition. In some cases, DISCOVER uses gene-editing technology to reproduce in cell lines or mice the genetic mutations associated with the patient’s disease to test for possible treatments.

This continued study of patients who have no known disease has resulted in the discovery of more than 30 rare diseases.

“It’s a journey,” says Dr. Chung. “For some patients, we make a diagnosis in 14 days. In others, we find it a year after they’ve seen me, because we go back and look again. I’ve had some patients for 15 years, and we’re only now figuring out what’s wrong. If the reason for a disease is genetic, it’s likely we will eventually find it.”

The DISCOVER program can be reached by calling 212-342-4622 or visiting the program’s website at www.cumc.columbia.edu/discover.

App Targets No. 1 Killer of Women

Although heart disease is the No. 1 killer of women in the United States—it causes more deaths than all types of cancers combined—many women are underdiagnosed and unaware of their risk.

“Love My Heart,” a new app developed especially for women by two cardiologists who specialize in women’s cardiovascular disease, is designed to raise awareness among women and prevent heart disease. The app was developed by Sonia Tolani, MD, and Natalie A. Bello, MD, assistant professors of medicine.

“Studies show that even when they’re having a heart attack, women don’t go to hospitals as urgently as men, because they’re afraid to be viewed as hypochondriacs,” says Dr. Tolani.

“Many women even avoid going to the doctor for a checkup because they are afraid to be judged as overweight.”

The “Love My Heart” app, Dr. Tolani says, lets women understand their risk level in the privacy of their own home. Using a series of 12 questions, the risk calculator determines a woman’s personal risk of developing heart disease. “Women have different risk factors than men,” says Dr. Tolani. “Diabetes doubles risk of heart disease for men but triples the risk for women, for example. And complications during pregnancy and early menopause also impact risk.”

Based on the individual risk factors, the app helps the user devise a Heart Plan with realistic goals to support healthy weight, healthy diet, exer-

cise, and smoking cessation. Users select goals, such as skipping dessert or getting off the subway a few stops early, and are prompted throughout the day to log their progress. “Exercise doesn’t have to be at the gym,” says Dr. Tolani. “If you put a timer on your watch and do it, it counts.”

“A large number of women—about 80 percent of us—have at least one risk factor for heart disease, but only 16 percent of us have had a discussion with our health care provider about those risks,” Dr. Tolani says. “We hope the app sparks new conversations among women and with their providers.”

The app is available in the Apple app store and will soon be available for Android devices.

Comprehensive Obesity Treatment Programs for Adults and Children

Two unique multidisciplinary programs at Columbia help children and adults who suffer from obesity, a chronic disease that often leads to other health issues, such as diabetes, cancer, liver disease, and kidney disease.

For adults there is COMMiT, the Comprehensive Obesity and Metabolism Management and Treatment program. Advice to patients about obesity management used to be simple, says the leader of COMMiT, Marc Bessler, MD, director of the Center for Metabolic and Weight Loss Surgery at Columbia and professor of surgery. “We told people how to lose weight, and they were able to or not. But now, with the focus on obesity as a chronic disease, we recognize that we have to keep working at finding better ways of managing the condition and its consequences.

“There are almost as many reasons why people become overweight as there are people who are overweight,” says Dr. Bessler. “The COMMiT team understands the social, emotional, and behavioral factors in an individual’s life and environment that can affect their weight and their health.”

The COMMiT team brings together surgeons, internists, endocrinologists, gastroenterologists, nurses, and dieticians to provide a multifaceted approach to weight loss. This kind of multidisciplinary team can promote healthier lifestyle choices in various ways, from offering meal plans, delivering stress management and mindfulness therapy, and recommending the latest medications to offering nonsurgical procedures or minimally invasive surgery.

For children, the Families Improving Health Together—FIT—program provides comprehensive care for obese children ages 2 to 9.

“Treatment and prevention of obesity are most effective when started early,” says FIT director Michael Rosenbaum, MD, a pediatric endocrinologist at the Naomi Berrie Diabetes Center and professor of pediatrics

and of medicine. “Only about 15 percent of adults who lose weight keep it off, but children tend to sustain the loss of body fat better than adults.”

Obesity affects multiple organs and systems, but care for children with obesity is usually fragmented, with few centers able to address the multiple issues that can arise from pediatric obesity. In the FIT program, children receive care from a multidisciplinary team of cardiologists, gastroenterologists, endocrinologists, and other specialists. The entire team reviews each child’s needs to develop a holistic plan, including healthy diet and exercise. The plan is tailored for each family, based on a detailed assessment of what the family likes to eat and the exercise options available where the family lives. As part of the treatment, the FIT team asks the child’s entire family to adopt new dietary and exercise interventions.

“Approximately 75 percent of children seen in the FIT program have at least one adiposity-related comorbidity, such as low vitamin D or dyslipidemia,” says Dr. Rosenbaum, “but because of the diverse on-site expertise, we are able to address these problems without having to refer patients to another appointment in another clinic. The patients and their families seem to appreciate it. Over 90 percent of them have come back for their follow-up visits with their physician and nutritionist.”

Both the FIT and COMMiT programs—and their patients—benefit from bringing specialists from various disciplines onto one treatment team, allowing doctors to address obesity in a more holistic and convenient way for the patient. Through programming like this, Columbia recognizes and treats obesity as a chronic multisystem disease that persists across the entire lifespan.

COMMiT can be reached at 212-305-4000.

FIT can be reached at 212-305-9237.





A Nobel Recognizes a Cool Scientific Method

(Pun Intended)

Joachim Frank Honored with 2017 Nobel Prize in Chemistry

Until late last year, an amber-colored structure stood on a window sill in Joachim Frank's lab, where it glowed, backlit by the late morning sun. You would be forgiven for thinking that this series of oddly shaped plastic contours, serially mounted in a wooden frame, was a topographical map of some kind. But the object was a 3-dimensional reconstruction of a part of a molecular machine in the cell called a ribosome, the first reconstruction of its kind and a creation made in Dr. Frank's lab more than three decades ago.

In December, Dr. Frank packaged it up and shipped it to the Nobel Museum in Stockholm, where it now lives as an artifact representing his journey toward the 2017 Nobel Prize in Chemistry. Dr. Frank, a physicist-turned-structural biologist, was one of the trio of scientists awarded the prize. He and his co-laureates, Jacques Dubochet and Richard Henderson, were honored for their work in developing a technique called cryo-electron microscopy (cryo-EM) that today allows researchers to visualize biological molecules—proteins, RNA, and DNA—in exquisite detail.

“A cool method for imaging the molecules of life” was how Professor Göran K. Hansson, secretary general of the Royal Swedish Academy of Sciences, described the technique in announcing the prize on the morning of Oct. 4. His pun referred to a key step in cryo-EM: suspending the sample in water rapidly cooled to form a glasslike structure that acts as a freeze-frame and a contrast enhancer for biological molecules.

Dr. Frank, professor of biochemistry & molecular biophysics at VP&S and professor of biological sciences

at Morningside, was not the refrigeration guy; he was the image guy. His contribution to the technique over his 40-plus-year career has been to develop powerful computational and statistical methods that combine multiple blurry images into one sharp one. For years, structural biologists dismissed electron microscopy as “blobology,” convinced that it would never yield high-resolution structures. But Dr. Frank's approach, called single particle reconstruction, helped set the stage for a molecular imaging revolution, creating a technique that can capture every bend, twist, fold, and pocket in a protein's structure to provide an unprecedented view of how these molecules conduct their cellular business. Along the way, Dr. Frank's lab—based at VP&S for the past decade—has revealed some fundamental elements of how a cellular machine called the ribosome does its crucial job of synthesizing proteins.

“It is incredibly gratifying to see this kind of acknowledgment of the whole field,” says Dr. Frank.

Attracted to Science at an Early Age

Seated in his VP&S lab's conference room just two days after returning from the Nobel ceremony in Stockholm, Dr. Frank, dressed casually in blue trousers, shirt, sweater, and a well-worn pair of sneakers, initially seems a bit exhausted by the prospect of giving yet another interview about his life's work. But it is not long before the gleam returns to his eyes as he reaches deep into the history of structural biology and of his own research.

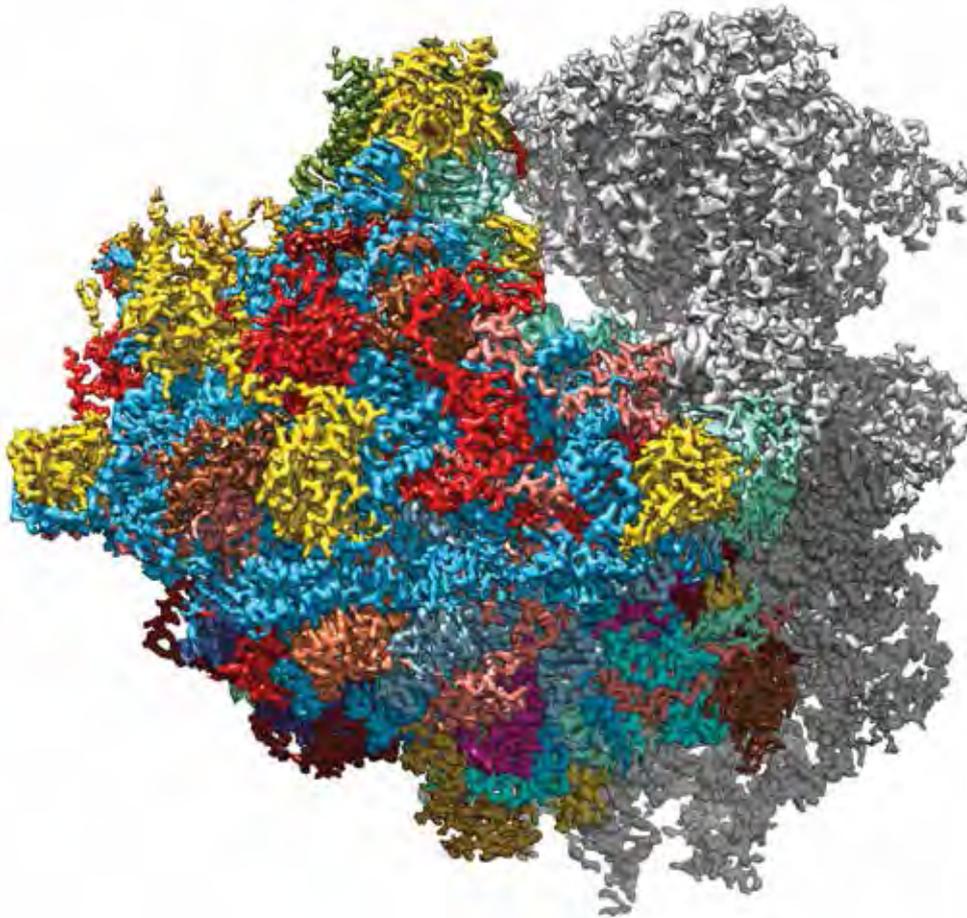
Dr. Frank was drawn to science at an early age, an interest he attributes to a search for order spurred by the tumultuousness of his wartime childhood in Siegerland,

By Alla Katsnelson

Germany. He first bumped shoulders with electron microscopy as a master's student in physics in the mid-1960s: His mentor had an old electron microscope in his office that he fiddled with, and the technique piqued Dr. Frank's interest. Poking around in physics abstracts, he found a researcher named Walter Hoppe at the Technical University of Munich who wanted to use electron microscopy to image biological molecules. Dr. Frank showed up at his door and signed on for a PhD.

Electron microscopy was invented in the 1930s, but initially no one envisioned using it for biology because it requires the sample to be placed in a vacuum—in which biological molecules collapse into a structureless heap—and because the image is achieved by bombarding the sample with electrons, which also destroys its structural integrity. Dr. Hoppe had started out using a technique called X-ray crystallography, which remains a mainstay of structural biology. However, not all molecules can be crystalized, and for those that can, the crystal structure might very well differ from the molecule's native state. “The crystal formation selects one conformation to the exclusion of others,” Dr. Frank explains. “And the conformation that's selected might not be functionally relevant.”

Reconstruction of the *Trypanosoma cruzi* ribosome at 2.5 angstrom resolution, obtained in Dr. Frank's lab. The resolution in large parts of the molecule should be sufficient for design of effective drugs against Chagas disease.



COURTESY OF THE FRANK LAB

When Dr. Frank started his doctorate, he found himself at the heady center of structural biology's early days as Dr. Hoppe and a handful of other pioneers set out to use electron microscopy to get around these problems. By the time he defended his dissertation in 1970, computer-based image processing had advanced to the point where researchers could envision enhancing images obtained with low-dose electron microscopy.

The generally accepted approach was to tilt the copper grid on which the sample lay inside the microscope, capturing the projection of the molecule serially at each angle and then mathematically combining the series of resulting micrographs into a single image. But even at low doses, wallowing a sample with electron beams multiple times destroyed it. What's more, the approach worked primarily for symmetrical or regularly ordered molecules. Generalizing the technique to tackle asymmetry was crucial because most molecules in the cell, and complexes of molecules that form to perform specific cellular functions, are not symmetrical.

Dr. Frank thought he had a better idea. After all, an electron microscopy sample consists of hundreds of thousands of copies of a biological molecule, each copy in a random orientation. Rather than repeatedly beaming the same molecule multiple times, one could take a snapshot containing multiple copies of the molecule. It should be possible to work backward to determine their viewing angles to reconstruct them. He described the idea in a concept paper in 1975, but it did not make much of a splash. “The community thought I was crazy, that it was never going to work,” recalls Dr. Frank.

That same year, Dr. Frank took up his first independent position at the Wadsworth Center, a public health research facility in Albany, N.Y. He began trying to realize his theoretical idea with various molecules, knowing that the big difficulty would be to develop a computational method for averaging traces of molecules that were captured in different conformations or from different views. Back then, researchers ran their analyses in shared computing centers, on computers as big as refrigerators that packed about a thousandth of the computational punch of an iPhone, he recalls. But on the plus side, these facilities were a venue in which scientists from different fields could interact. In 1980, a lucky glance one afternoon at data printouts belonging to a laboratory medicine researcher gave him the jolt of insight he needed to design a powerful statistical framework to solve the problem.

Meanwhile, another chance encounter introduced Dr. Frank to the ribosome, which became his lab's workhorse and muse. Ribosomes are essentially mobile protein-building machines: They translate the instructions of the DNA code, using the messenger RNA code to string together amino acids carried by transfer RNA. Yet the molecular



JÖRG MEYER

mechanics of the process were largely unknown. Because of the organelle's complexity, size, and asymmetry, Dr. Frank immediately embraced it as the perfect test specimen.

Fueled by these developments, the lab was a tremendously productive place to work, says Jose-Maria Carazo, PhD, now head of the biocomputing unit at the National Center for Biotechnology in Madrid, who arrived as a postdoc in 1986. "Joachim had everything in place so we could advance quickly," Dr. Carazo says. "His philosophy was that you should not try to acquire tools from here and there; rather, he wanted to create an enabling environment."

That year, Dr. Frank and a postdoc, Michael Radermacher, succeeded in creating the first 3-dimensional reconstruction of the larger subunit of the ribosome—the very one that Dr. Frank sent to the Nobel Museum. A few years later came a structure of the whole molecule, though its resolution, at 45 angstroms, was more than an order of magnitude larger than the atomic scale that X-ray crystallography can achieve. Still, it captured the attention of a few biologists, among them Rajendra K. Agrawal, then a PhD student in biochemistry at Banaras Hindu University in India, who happened to be studying the ribosome. Dr. Agrawal's research was based on the theory that this messenger RNA-reading machine functioned by switching between at least two conformations, and he thought Dr. Frank's method could prove it.

"To tell you the truth I was sort of naïve about the resolution limits of the technique at the time," says Dr. Agrawal,

who went to the Frank lab for a postdoc in 1994. "When I saw that paper, I got excited without paying attention to the resolution, which was very, very low." He arrived to a lab filled mostly with computers and microscopes, with just a tiny space for the kinds of biochemistry experiments he was accustomed to doing. Most of the team was developing the 3D-EM method, not studying biology. "It was kind of a gentle shock," he recalls. "For a month or so, I thought, 'I hope I didn't make a mistake!'"

It turned out to be no mistake at all. His first paper in the lab, published within a year of his arrival, brought the resolution down to 25 angstroms, a point at which the molecule began to yield some big functional mysteries. This reconstruction allowed the researchers to visualize how the ribosome interacted with mRNA and tRNA as it went about the process of translation. For Dr. Frank, that paper was a turning point. "Finally, I thought, 'Oh my God, I can really make contributions to biology,'" he says. "Before that it was not so clear."

Dr. Frank's lab continued to improve the resolution of the technique, making several important discoveries along the way at a rapid clip. The researchers were able to see where, exactly, the tRNA makes contact with the ribosome and shortly thereafter to visualize a protein called the elongation factor G binding to the ribosome to advance mRNA and tRNA forward, thereby building the amino acid chain. They also managed to accomplish what Dr. Agrawal had most hoped to achieve: clearly seeing the two conformations of the ribosome.

The ribosome became his lab's workhorse and muse. Because of its complexity, size, and asymmetry, Dr. Frank immediately embraced it as the perfect test specimen.

At the same time, another research team was homing in on an atomic-resolution structure using X-ray crystallography. “I remember we were coming back to Albany on the same flight, and I found him a little dejected because he thought it looked like it was all over for us,” says Dr. Agrawal. “But I said, ‘Joachim, I think it’s all only starting for us.’” X-ray crystallography could capture only fixed states of a molecule, but cryo-EM could capture the dynamics. By going back and forth between the two techniques, a fuller picture of the protein’s function could be built. And that’s just how it happened: In 2000, Dr. Agrawal and colleagues published a paper demonstrating the ratcheting motion that the two subunits make as the ribosome moves down the mRNA strand. “That was the first time that a real, very large conformational change was discovered,” Dr. Frank recalls. “People got excited by the fact that you could really see molecules in multiple conformations and you could really see they differed from what actually crystallography told you.”

Warm and Nurturing Environment

Despite the intensity of the work in the Frank lab, trainees who have passed through the lab remember it as a warm and nurturing environment and Dr. Frank as a mentor with a light touch, a deep sense of humor, and a few subtle surprises up his sleeve. Robert Grassucci, the lab’s senior microscopist, came on board in 1986 as a technician. He was in his freewheeling 20s at the time, and his much older boss initially seemed somewhat staid, the stereotype of a German scientist. Mr. Grassucci stopped by the lab one weekend and found Dr. Frank playing some unexpected music. “I was like, ‘Huh, that’s kind of cool, what’s this old prof doing jamming to Bob Marley?’” he recalls. “So I thought, OK, that’s something we have in common.”

Many of Dr. Frank’s students and postdocs were from overseas, and he and his wife, Carol Saginaw, took them in for holidays and made sure they settled in and found their footing. “I was not paying attention to those things then, but when I think back now, he was such a family-oriented person all along, always trying to make us comfortable,” Dr. Agrawal says, noting that Dr. Frank would often point him to Indian restaurants in town or drive him to see music concerts.

By that point, the group had brought the resolution of cryo-EM down to 11.5 angstroms, making it possible to see the double helix of the RNA and even some features of proteins in the ribosome. Dr. Frank and his team continued probing the mechanism of this molecule in action. In 2001, his postdoc Christian Spahn, now a professor at the Charité Institute of Medical Physics and Biophysics in Berlin, collaborated with Jennifer Doudna’s lab, then at Yale, to create a cryo-EM image of the virus hepatitis C hijacking a cell’s DNA via its ribosome with the help of an RNA element

called an internal ribosome entry site. “We could see this element grabbing and holding on to the small subunit of the ribosome, which was really spectacular,” says Dr. Frank. “There are these rare moments where you look at a structure and suddenly realize that there is really something fascinating—and that you are probably the first human being to understand this particular thing,” says Dr. Spahn, who was a postdoc in the Frank lab between 1998 and 2004.

Ultimately, it was not cryo-EM that first pinned down the structure of the ribosome at atomic scale but X-ray crystallography. That achievement was recognized with the 2009 Nobel Prize in Chemistry, and Dr. Frank’s work was fundamental to the work of one of the recipients who used a reconstruction produced in the Frank lab to check the validity of the structure. It took until the advent of a new type of electron-detecting camera in 2012 for researchers to achieve the atomic structure of the ribosome using cryo-EM. That technology, Dr. Frank explains, has democratized the method. “The technique was sort of waiting for that breakthrough,” he says. Indeed, in 2015 cryo-EM was named Nature magazine’s Method of the Year.

“Joachim didn’t just shape the field directly, with his intellectual contributions of the math and physics, but also indirectly,” says Yaser Hashem, PhD, group leader at the Institute of Cellular and Molecular Biology in Strasbourg. “By using the technology and constantly being in contact with the companies that made it, his work really guided the development of the microscopes.”

The Other Joachim Frank

In parallel to research, Dr. Frank actively pursues other creative endeavors, specifically photography and writing, both fiction and poetry. He has submitted his pictures to exhibits and was an active contributor to the storytelling website Cowbird until it shuttered in 2017. As a testament to his willingness to embrace serendipity, when the website’s founder held a farewell party for Cowbird last summer in Vermont, Dr. Frank drove up to celebrate with 30 or so people, most of whom were strangers to each other.

He is also, he jokes, a budding inventor, having designed a fine-dining implement called a “sporknik”—fork on one end, knife on the other, and spoon in the middle—which his son-in-law 3-D printed in stainless steel. (Buy yours online for \$130.) “Joachim can get so excited about something, like a kid,” says Dr. Hashem, who was a postdoc in the lab between 2010 and 2014. “Whether it’s a new theory or a scientific article he read, or something in the newspaper, or anything at all, he would just come spill it out and get us talking about it.”

Although Dr. Frank rarely brought these parallel pursuits into the lab, his group was well aware of their place in his life. And of course, they contributed to the scientific work in their

“People got excited by the fact that you could really see molecules in multiple conformations.”

own ways, most directly in the writing: “You could give him a draft of a paper and then he changed something here and there, and suddenly it was a golden text,” says Dr. Spahn. But also in scientific imaging. Soon after Dr. Agrawal, now a senior scientist at the Wadsworth Center and a professor at the University at Albany, struck out on his own, he emailed Dr. Frank a paper describing one of the first structures his lab solved. “Within half an hour he wrote me back about the figure, and said, ‘Raj I think the colors are biting each other, you have to change it,’” Dr. Agrawal says. “He was very, very particular about first impressions of the pictures.”

Indeed, color choices in paper figures have long been a standing joke between Dr. Frank and Dr. Agrawal. When the two researchers began to make serious progress on the ribosome in the mid-1990s, Dr. Frank established the colors of the two subunits: light blue for the larger subunit, pale yellow for the smaller one. One morning in 2005, while attending the same conference, they emerged from nearby guesthouses with great amusement to find each other wearing sweaters of the complementary hue: Dr. Frank in light blue and Dr. Agrawal in pale yellow. “So, here we are, the very small and large subunits, and we somehow started to dance, moving our hands like the conformational change between the two subunits that we had discovered!”

Dr. Frank is also known for putting his writing skills and his penchant for the absurd on display at an annual cryo-EM conference, which generally ends with an absurdist skit. Each year he finds himself with a central role in creating or performing the skits. One year he and his colleagues transformed the trailer of the 2009 science fiction movie “Avatar” by replacing the actors’ faces with those of key researchers in the community and changing the dialogue to frets about achieving better resolution. “Every time, it was extremely hilarious,” says Dr. Hashem. “This is really where you see his great sense of humor.”

The Early Morning Nobel Call

Dr. Frank was fast asleep when the Nobel announcement was made in the wee hours of Oct. 4. He heard the telephone ring around 5:20 a.m. but attributed the commotion to a new puppy yapping to be taken outside. About 150 miles due north, in Albany, Dr. Agrawal was up early to watch, as he has for the past few years, the Nobel Foundation’s live telecasts, sure that he would eventually hear his old mentor’s name. This year it finally happened: “Cool chemistry! He said cool chemistry!” Dr. Agrawal whooped excitedly to his wife, Dr. Manjuli Sharma. “This is Joachim—it can’t be anyone else!”

Dr. Frank invited Dr. Agrawal, Dr. Spahn, Dr. Carazo, Dr. Hashem, and Mr. Grassucci, along with their families, to join him and his family in Stockholm for the week of Nobel festivities in December. “That week I saw him the happiest



Joachim I have ever seen him,” says Dr. Spahn. Dr. Frank describes the experience as “a fairy tale.” On a night off from the formal events of the week, his colleagues—his scientific offspring, as it were—presented him with a gift: a telescope. “It represents a different direction of viewing the world from the one I was familiar with,” he wrote on his blog.

Not that the familiar direction has lost its allure: As this new era of cryo-EM unfolds, much exciting work remains to be done. “The enthusiasm from the recent breakthroughs is completely justified, but it is still not always so easy to get high-resolution structures,” says Dr. Spahn. “All of this is at the border of chemistry and biology, where randomly colliding molecules start to have ordered features. This is where biological complexity is created.”

Dr. Frank is particularly excited about the prospect of using cryo-EM to track how molecules within the cell change their shape to do their jobs. His group is working with a lab in Wisconsin to map this dynamic process, the so-called conformational continuum of molecules. Traditionally, researchers have assumed that molecules going from one conformation to another do so by taking the lowest-energy route, but that turns out not to be the case, he says. Instead, they can pass through many states that are energetically counterintuitive yet still necessary to their function. “You can really see how molecules actually behave,” he says.

As Dr. Frank forges ahead, Columbia University too has expanded its support for cryo-EM. Plans call for building an entire core facility dedicated to the technique. That means that after sharing a couple of microscopes and other equipment with multiple labs for the past few years, the group will soon have access to new state-of-the-art digs with three new high-end machines. “The sky is wide open now,” Dr. Frank says. ❖

Dr. Agrawal and Dr. Frank frequently dress in the colors of the ribosome’s subunits when they get together. This photo—with the ribosome depicted in the background—was taken when Dr. Frank recently visited Dr. Agrawal’s lab at the Wadsworth Center.



OPIOIDS:

HOW WE GOT HERE, WHERE WE GO FROM HERE

William Head “Will” Williams was the kind of person who might have entered VP&S as a medical student, says his father, Bill Williams. He was bright, vivacious, a voracious learner. Instead, Will entered VP&S in 2012 as an anatomical donation, dead at age 24 from an accidental heroin overdose.

Will had a mix of anxiety and attention deficit hyperactivity disorder that made school a rough fit. Studying from home in his senior year, he thrived—mixing tutoring in AP physics and AP calculus with two internships as a day trader. When he turned 18 that year, he plunged into active trading full time, earning enough as a day trader by age 20 to fund a trip around the world.

He also had a passion for martial arts, says his father, and at some point, his martial arts instructor, a man he considered a mentor, introduced him to heroin. He began by snorting. The instructor suggested that Will’s occasional use—“chipping”—would not lead to addiction.

“But it was a problem for William,” says his dad. “It was the beginning of the end.” Will was 22 when a friend of his called to alert Mr. Williams and his wife, Margot Head, that their son was using heroin. The friend, worried about Will’s safety, described Will as out of control. Over the next two years, Will tried everything: outpatient and inpatient treatment, 12-step programs, and inpatient and outpatient detox, punctuated

by multiple overdose-related emergency room visits. “The Greek word *agony* comes from a wrestling match, a contest,” says Mr. Williams, a retired high school theater teacher. “The agony of an addict—at least for William—was the contest between wanting to recover from his addiction and the siren call of the drugs.”

Following a final overdose, Will’s heart stopped beating. After being revived by EMS, he spent more than six weeks in the hospital. He first underwent a protocol called therapeutic hypothermia in an attempt to assist and preserve neurologic function. He was sedated to help avoid seizures and further brain damage, and his brain was scanned regularly. It became clear that his brain had been damaged beyond repair by the lack of oxygen in the crucial minutes he was in cardiac arrest. “While his heart function was restored, the damage to his brain was too great,” Mr. Williams says.

Intent that Will’s death not be in vain, his parents and his sister, Elizabeth Hope, decided to donate his body to VP&S after removing him from life support. “In another time, in a better era,” says his father, “William might have entered the College of Physicians and Surgeons not as a cadaver but as the gifted and talented young man he was.”

Images of Will’s tissues now illustrate the digital manual provided to VP&S students as their guide to anatomy training. His parents have become tireless

**FIRST IN A
SERIES ABOUT
WORK BEING
DONE AT VP&S
TO UNDERSTAND,
TREAT, AND
PREVENT OPIOID
ADDICTION**

BY SHARON TREGASKIS

**ILLUSTRATIONS BY
DAVIDE BONAZZI**

crusaders in the campaign to confront opioid addiction and prevent overdoses, which killed more than 42,000 Americans in 2016—a record number—and was the No. 1 killer of Americans under age 50.

AN EPIDEMIC IS BORN

Any brief explanation of how the opioid epidemic began would be an irresponsible simplification. The epidemic likely has many roots, some dating back to the 19th century. Street drugs—such as those used by Will Williams—have been around for decades, and aggressive tactics by pushers have contributed to their popularity. Their cheap price, the role of organized crime in importing and distributing them, and their increasing potency—sometimes from dangerous combinations of ingredients—have been factors in the upward trend of use of drugs in all socioeconomic communities.

The blame for the current epidemic, then, can be placed on any number of factors that might explain the hold drugs now have on American life, but the more recent escalation of the opioid epidemic points toward prescription opioids. The vast majority of the 11.8 million Americans who reported using opioids in 2016 consumed not heroin but prescription pain relievers, according to the federal Substance Abuse and Mental Health Services Administration. Only 13 percent of individuals who misused pain relievers—by taking them at a higher dose or at greater frequency than their physician had directed—took them to get high. More than 60 percent were attempting to

offer only to end-stage cancer patients and to people who had recently had major surgery. Suddenly opioids seemed like a viable solution to all manner of chronic aches and pains. Vicodin became the No. 1 prescription drug in America.

By the late 1990s, the stage was set. In a New York Times Magazine essay, Columbia oncologist Siddhartha Mukherjee, MD, DPhil, reflected on his own first encounter, in 2001, with a patient addicted to opioids. “Pain, we had been told as medical residents, was being poorly treated (true)—and pharmaceutical companies were trying to convince us daily that a combination of long- and short-acting opioids could cure virtually any form of it with minimal side effects (not true).”

In the early 1980s, prescription opioid formulations were limited to morphine and codeine. Vicodin was approved by the FDA in 1984; extended-release OxyContin and Percocet came along by the end of the 1990s.

Americans use 80 percent of the world’s opioids, which some blame on society’s expectation that all problems can be fixed and all pain can be managed and alleviated.

It is hard to know the kind of pain people are treating when they misuse opioids. While some have medically documented physical maladies—chronic back or knee pain from a jobsite injury or home improvement mishap, for example—a growing body of scholarship suggests that mental health problems, including anxiety and depressive disorders, post-traumatic stress disorder, and the more diffuse mental anxieties stemming from widening income inequality and other stressors of modern life, also could play a part in the skyrocketing popularity of opioids. “The problem is complex, with multiple factors likely to be interacting with each other,” says epidemiologist Deborah Hasin, PhD. “If opioids weren’t so widely available, people at risk for addiction due to, say, economic distress, might be using some other substance instead. However, the wide supply of opioids, particularly those initially obtained through prescriptions, has certainly been a major contributor to the problem.”

AMERICANS USE 80 PERCENT OF THE WORLD’S OPIOIDS, WHICH SOME BLAME ON SOCIETY’S EXPECTATION THAT ALL PROBLEMS CAN BE FIXED AND ALL PAIN CAN BE MANAGED AND ALLEVIATED.

Meanwhile, with individuals continuing to use opioids, and in the absence of a silver bullet to halt the crisis in its tracks, Dr. Hasin and other epidemiologists have their work cut out for them, answering an array of questions about the characteristics of users and prescribers to inform targeted prevention and treatment interventions as well as analyses of the efficacy of interventions such as state prescription drug monitoring programs and new pain clinic regulations. Research is also

needed on the most effective public and medical education programs to promote more informed opioid prescribing patterns and possible alternative pain treatments. “Many aspects of the needed data are there and just need to be harnessed to answer these questions,” says Dr. Hasin, who runs Columbia’s substance use epidemiology training program. “However, these efforts require time, effort, and research funding. At the same time, other potential risk factors and solutions require new data collection to provide



WILL WILLIAMS ON A VISIT TO THE NEW YORK STOCK EXCHANGE

relieve pain. Some used prescriptions that were not theirs—by using medication prescribed to others, stealing opioids from medicine cabinets, or using drugs supplied at parties. Though the CDC reported that only 40 percent of all opioid overdose deaths in 2016 involved a prescription opioid, the numbers do not indicate how many of the other 60 percent died from using illegal drugs they sought out after becoming addicted to prescription opioids.

The rise in the availability of prescription opioids began in the 1980s, when pharma started marketing what seemed at the time to be breakthroughs in manufacturing that allowed for higher-dose, time-release formulations. Before then, opioids were considered so risky they were

the information to better understand the opioid problem and its solutions, which are likely to be at multiple societal and individual levels.”

HOW OPIOIDS WORK

Like other addictive substances, opioids affect dopamine, a foundation of the biochemical communication system within the brain responsible for memory, learning, and reward. “In many diseases, there’s clearly something wrong with the body,” says neuroscientist David Sulzer, PhD. In heart disease, the cardiovascular system has a glitch. In cancer, cellular replication and division have gone amiss. “Addiction is different,” says the scientist, who investigates how dopamine signaling goes wrong in such disorders as Parkinson’s and schizophrenia.

In addiction, Dr. Sulzer says, the brain is actually doing what it is programmed to do: The biochemical reward system in the brain—the dopamine release that spurs action in anticipation of a reward—is triggered. “Opioids hijack those mechanisms to reinforce their own acquisition,” says Dr. Sulzer, whose research portfolio also includes studies of the mechanisms by which addictive drugs alter dopamine signaling. If your leg breaks, doctors can set and cast it. If your cholesterol is too high, a statin might bring your blood chemistry back to its target range. Interrupt the basic function of dopamine signaling in a bid to short-circuit addiction, however, and such fundamental human activities as learning, memory formation, and the joy of completing a task go by the wayside.

Opioids disrupt the dopamine system through two synergistic mechanisms: They make the neurons that release dopamine more responsive and increase the amount of dopamine released each time the neurons fire. While each opioid varies, in terms of its dose-response effect and the tolerance it induces, opioids as a group represent a double whammy in terms of positive reinforcement.

OPIOIDS HAVE THEIR PLACE

Despite the intense scrutiny surrounding the damage opioids inflict, clinicians agree that opioids have a place in treatment protocols. Finding the patients who need them and will tolerate them without becoming addicted is a key challenge, but clinicians in pain management also grapple with the absence of measures to quantify and independently verify pain, to assess the extent to which it impedes function or compromises quality of life.

Acknowledging that one of the causes of the current opioid epidemic is prescription medicines, the medical community, academic medicine, and government are looking for solutions that preserve the use of opioids when medically indicated. Several neurosurgery groups have come together to work with the FDA on recommendations that would create medical documentation to justify prescriptions of opioids. “Like other surgeons and clinicians, we are concerned about the impact of the opioid crisis, but we want to preserve patient access to opioids that are medically necessary,” says Columbia neurosurgeon Christopher Winfree ’96, former president of the American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Pain. “We are confident that we will be able to work with the FDA on a solution that reduces the overall availability of opioids to limit them to clinical situations that warrant their use.”

Over the past year, a working group led by James Peacock, MD, associate chief medical officer at NewYork-Presbyterian, tackled similar questions on behalf of physicians associated with the hospital, including Columbia and



Weill Cornell faculty practices, hospitalists, the NYP emergency department, and outpatient practices overseen by NYP. The group developed a dashboard to help clinicians and researchers analyze opioid prescribing patterns and determine patients at risk for addiction. “We’re not saying we should bring prescriptions to zero,” says Dr. Peacock. “There is a place for opioids in medicine, but we need to make sure medications are appropriate.”

In March, as part of Columbia’s celebration of National Patient Safety Awareness Week, ColumbiaDoctors and Columbia’s nursing school collaborated to provide training meant to combat the opioid epidemic. “Our ColumbiaDoctors personnel are standing on the front lines of this epidemic,” says chief medical officer Shunichi “Nick” Homma, MD, “and through this initiative we will better equip them with needed training to save lives that might otherwise be lost to opioid overdoses.”

In December 2017, the Irving Institute for Clinical and Translational Research hosted a brainstorming session about the opioid crisis, inviting experts from throughout Columbia, NewYork-Presbyterian Hospital, the New York State Psychiatric Institute, and Northern Manhattan community organizations. More than 60 individuals participated in discussions and presentations on ongoing research and treatment program innovations, intent on developing strategies to end the crisis. A larger symposium is planned for June 2018.

BUILDING A BETTER PAIN RELIEVER

Imagine that physicians did not need to find a way to identify which patients could tolerate opioids or develop safeguards to restrict their abuse. Research by Nigel Bunnett, PhD, focuses on finding better ways to alleviate pain.

Dr. Bunnett witnessed firsthand the shortcomings of opioids—even for people with terminal cancer—when his mother was dying. Doctors prescribed morphine to help her cope with the pain, but eventually the resulting consti-

pation became so painful she opted to forgo the opioids. “Morphine is thousands of years old,” says Dr. Bunnett. “We’ve got to do better for patients.”

And so for more than 30 years, the English-born scientist has investigated the biochemistry of G protein-coupled receptors (GPCRs), a family of more than 850 proteins that carry messages—including pain signals—from outside the cell membrane to the cell interior. In recent years, he’s homed in on the role of endosomes, the acidic, membrane-bound vesicles central to the movement of molecules into and through the cell. “Until very recently, it was thought that endosomes were just a conduit for processing of receptors,” says Dr. Bunnett. “It was also thought that receptors only signaled from the surface of the cells and drugs were developed to target these cell surface receptors.”

Over the course of the past decade, Dr. Bunnett and his collaborators have revealed that GPCRs continue to signal from within intercellular spaces, that those signals can be prolonged, and that they are central to the transmission of pain signals. Taken together, those findings begin to suggest why some pain medications have limited effectiveness: They are designed to target cell surface GPCRs, may not cross the lipid-rich cell membrane, and may be unable to interact with GPCRs in the comparatively acidic environment inside endosomes. “The development of drugs designed to target these receptors in the right subcellular location is important,” says Dr. Bunnett. “We already have medications that target receptors in particular tissues or cells, but we want to target them to particular organelles. It’s a new approach for drug delivery.”

In 2018, Dr. Bunnett and his collaborators incorporated Endosomal Therapeutics to spur drug delivery innovations and the identification of compounds that leverage those insights. Current work includes chemical engineering to convey drugs directly to the endosome by bonding them to lipids or encapsulating them within nanoparticles and structural analyses

of individual GPCRs to identify compounds that will remain bound to the receptor in an acidic environment. “I see this as a great way of actually taking a compound all the way to a drug that could help people.”

The antidepressant tianeptine already helps people—in Europe, Asia, and South America. It lacks the sexual side effects of antidepressant compounds approved for use in the United States and appears to be effective in patients who do not respond to other drugs. Despite its use in tens of millions of patients over the past several decades, scientists did not know its molecular target in the brain. Several years ago, Columbia chemists Andrew Kruegel, PhD, and Dalibor Sames, PhD, teamed with Jonathan Javitch, MD, PhD, chief of molecular therapeutics in psychiatry, to show that tianeptine is a selective and efficacious mu-opioid receptor agonist, leading them to hypothesize that this receptor is the target through which tianeptine functions. With early support from the VP&S Interdisciplinary Research Initiatives Seed Program, the group teamed with neuroscientist René Hen, PhD, an expert on animal models of depression, to explore the behavioral effects of tianeptine. In studies using mice, published in the journal *Neuropsychopharmacology*, the team confirmed that tianeptine’s antidepressant and anti-anxiety effects are mediated by the brain’s mu-opioid receptors. This was a remarkable finding, given that other agonists of this GPCR, like morphine, heroin, and fentanyl, have previously been known only in the context of their use as powerful pain relievers, where addiction, tolerance, and physical side effects such as respiratory depression present major challenges.

In contrast, the rate of abuse with prescribed tianeptine is extremely low, and in mice, the team has shown that the compound does not induce the tolerance or withdrawal symptoms associated with morphine and other opioids. “Not all mu-opioid agonists are the same,” says Dr. Javitch. He and his colleagues have been driven by this discovery to explore in detail such “atypical opioids,” which have distinct effects compared with classical opioid drugs. Critical next steps are to understand how different opioid compounds diverge at the level of their molecular signaling and to identify the precise brain circuits at which they exert their therapeutic effects or side effects. Ultimately, this will allow scientists to design new opioid drugs that provide therapeutic effects with fewer negative side effects. In 2017, Drs. Hen, Javitch, and their chemist colleagues cofounded a new startup, Kures Inc., to try to bring a novel tianeptine analog, synthesized at Columbia, to human use, with the hope that it will be effective in patients where currently available antidepressants fail. The team is also expanding its investigation of atypical opioids—including the active compounds of kratom (*Mitragyna speciosa*), an evergreen plant native to Southeast Asia—to characterize their structure and biological effect in search of signaling profiles that could be modulated to selectively reduce pain or depression without impairing respiration or gut function or triggering addiction.

BREAKING THE CYCLE

Throughout the medical center campus and beyond, efforts are underway to come to grips with the opioids problem and find solutions, whether they lie in creating better pain relievers, improving ways to measure pain, or unraveling the mystery of why some patients can tolerate opioids and others become addicted. ❖

NEXT ISSUE: TREATMENT AND EDUCATION STRATEGIES

Who's Who

- Nigel Bunnett, PhD, the Gerald and Janet Carrus Professor of Surgical Science (in Surgery and Pharmacology) and vice chair of research in surgery
- Deborah Hasin, PhD, professor of epidemiology (in psychiatry)
- René Hen, PhD, professor of neuroscience and pharmacology (in psychiatry) and chief of the Division of Systems Neuroscience at the New York State Psychiatric Institute
- Shunichi “Nick” Homma, MD, the Margaret Milliken Hatch Professor of Medicine (in Biomedical Engineering), deputy chief of the cardiology division, and chief medical officer of ColumbiaDoctors
- Jonathan Javitch, MD, PhD, the Lieber Professor of Experimental Therapeutics (in Psychiatry), professor of pharmacology (in the Center for Molecular Recognition and in physiology & cellular biophysics), and chief of the Division of Molecular Therapeutics at the New York State Psychiatric Institute
- Siddhartha Mukherjee, MD, DPhil, associate professor of medicine
- James Peacock, MD, assistant professor of medicine
- David Sulzer, PhD, professor of neurobiology (in psychiatry, neurology, and pharmacology) at CUMC
- Christopher Winfree, MD, assistant professor of neurological surgery

Alumni News & Notes

By Marianne Wolff '52, Alumni Editor,
and Bonita Eaton Enochs, Editor

1962

Nicholas Romas was honored in December by the American Hellenic Educational Progressive

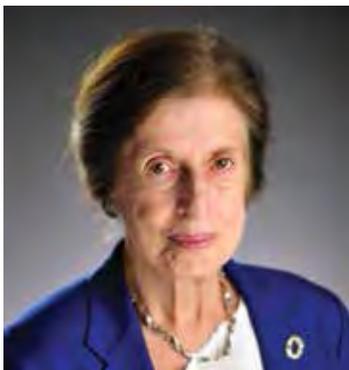


Nicholas Romas '62

Association with the Lifetime Achievement Award. Nicholas, professor of urology at Columbia, was recognized for his commitment to serving humanity through his profession and offering care and guidance for his fellow Ahhepans.

1963

Geraldine P. Schechter and **Babette B. Weksler** have co-edited a new book described in the Alumni in Print section. Geraldine is professor emeritus of medicine at George Washington University and former chief of hematology at the VA Medical Center in Washington,



Geraldine P. Schechter '63

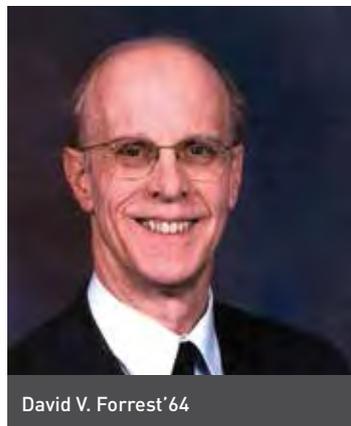


Babette B. Weksler '63

D.C. Babette is professor emeritus of medicine at Weill Cornell Medical College and former attending physician at New York-Presbyterian Hospital.

1964

David V. Forrest, clinical professor of psychiatry at VP&S, has written a book described in this issue's Alumni in Print section. David is past president of the American



David V. Forrest '64

College of Psychoanalysts and a fellow of the Explorers Club.

1965

Anthony H. Horan presented a poster titled "The History of Immuno-cryotherapy for Prostate Cancer" on Jan. 25, 2018, at the 29th International Prostate

Cancer Update in Beaver Creek, Colo. "The introduction featured the first modern reference to a 1903 case report in the Annals of Surgery about two 'cures' of two crippling sarcomas by John Rogers Jr., MD VP&S 1891," Tony writes. "He used W.B. Colley's vaccine developed at Memorial Hospital. It was composed of mixed streptococcal toxins and was the first immunotherapy for a cancer. Ten copies of the 1903 paper were snapped up by the audience." The poster went on to describe the palliation by cryosurgery to the primary of the bone pain caused by metastatic prostate cancer. "This observation was published by three VP&S faculty members in 1972. Their contribution was forgotten after the municipal hospital, Delafield, was closed by the NYC bankruptcy. Now the immunotherapy of cancer is all the rage but cryo' is forgotten."

1966



Robert J. Lefkowitz returned to VP&S in November to present the 2017 Cartwright Lecture. Several of his classmates were on hand and posed for a photo. From left are Walter Flamenbaum, David Tucker, Robert Lefkowitz, Charles Lightdale, and Bart Nisonson. Henry Spotnitz also attended the lecture but missed the photo.

1975

See the story, "Alumni Run for State, National Office," on Page 27 to read about **James Maxwell**.

1981

See Alumni in Print to read about a new book by **Bob Cutillo**, assistant clinical professor of



Bob Cutillo '81

family medicine at the University of Colorado. Bob also serves as an associate faculty member at Denver Seminary and provides patient care to underserved populations at the Colorado Coalition for the Homeless.

1983

Scott Breidbart has been named chief medical officer of Affinity Health Plan after leaving the role



Scott Breidbart '83

of chief medical officer at Solera Health in Phoenix. Scott, who also has an MBA, has more than 20 years of experience as a managed care executive. In his new position, he reports directly to Affinity's president and CEO to ensure the delivery of affordable, quality health care services to Affinity's approximately 300,000 members.

1992

Nader Moazami has joined NYU to direct a new heart transplant program launched by the Transplant Institute at NYU Langone Health. Nader, who led the heart transplant program at Cleveland Clinic, has performed more than 300 heart transplants in his career and has studied and advanced the use of mechanical devices to treat patients with end-stage heart failure. At NYU he is professor in the Department of Cardiothoracic Surgery and surgical director of heart transplantation and mechanical circulatory support at NYU Langone.

1993 MD-PhD

Roy Chuck, professor and chair of ophthalmology and visual sciences at Albert Einstein College of Medicine and Montefiore Medical Center, received the 2017 Physician Scientist Award at the annual Fight for Sight gala in December. The primary mission of Fight for Sight is to support research to cure blindness. Roy, who also has a PhD from Columbia, holds the Paul Henkind



Roy Chuck '93

Chair in Ophthalmology and is also professor of genetics at Einstein.

1993

Ellen Gallant wrote: "I always enjoy receiving *Columbia Medicine*; in particular, I enjoy hearing alumni news. I decided for the first time ever, I would send my own news. I am an



Ellen Gallant '93

interventional cardiologist near Jackson, Wyo. I love my job and the great outdoors here in Wyoming, but my big news is that I summited Mount Everest on May 23, 2017. Fifteen long, hard years went into this adventure, about the same amount of time (pre-med, med school, residency, fellowship, interventional year) that it took to become an interventional cardiologist!"

1995

See the story, "Alumni Run for State, National Office," on Page 27 to read about **Shannon Hader**.



Carl Novina '00

2000

Carl Novina has joined the scientific advisory board of Atossa Genetics, a clinical-stage pharmaceutical company developing novel therapeutics and delivery methods for breast cancer and other breast conditions. Carl, who also has a PhD from Tufts, is a leading researcher in the field of RNA therapeutics. An associate professor of medicine at Dana-Farber Cancer Institute and Harvard Medical School, he is also an associate member of the Broad Institute of Harvard and MIT.

2002

Eric Michael David has joined BridgeBio Pharma in Palo Alto, Calif., as CEO-in-residence to lead the company's gene therapy efforts. Founded in 2015, BridgeBio has built a portfolio of 15 programs that address rare genetic diseases across oncology, cardiology, dermatology, neurology, and endocrinology, developing drugs that



Eric Michael David '02

are in various phases of development, from pre-clinical to late-stage. Eric previously co-founded Organovo, a 3-D bioprinting company where he spent the past several years. He also has a law degree (Columbia Law 1996) and was inspired to combine medicine and law by people such as Columbia Law professor Harold Edgar and Phil Reilly, a 1973 Columbia Law graduate.

2003

Sara Monaco has two new books out, described in Alumni in Print. Sara is associate professor of pathology at the University of Pittsburgh Medical Center, where she is program director of the cytopathology fellowship and director of the fine needle aspiration service at Children's Hospital of Pittsburgh. She is also director of the fine needle aspiration clinic at the medical center's Shadyside Hospital.

See 2012 for news about **Joshua Willey**.

2007

Charles Haviland Mize and a team he developed, the Bhutan Emergency Aeromedical Retrieval (BEAR), received a Medical Humanitarian Award presented by Boston Biopharma. The award identifies new health care programs that have an impact on the lives of patients in underserved areas of the world. Charlie and BEAR were recognized for their volunteer efforts to help



Charlie Mize '07 with his wife, Dr. Carolyn Mize



send your news via mail, fax, or email:

Mail: Bonita Eaton Enochs, Editor
Columbia Medicine
Vagelos College of Physicians & Surgeons
630 W. 168th St., Box 153
New York, NY 10032

Fax: 212-305-4521

Email: columbiamedicine@columbia.edu

save lives in Bhutan. BEAR was created last year after the life of a patient in Bhutan with a treatable injury could not be saved because he arrived too late to the hospital. Charlie developed the program with the Royal Government of Bhutan's Ministry of Health, Royal Bhutan Helicopter Services, and Jigme Dorji Wangchuck National Referral Hospital, where he has volunteered for

the past year to help improve emergency medical services in the country. BEAR provides timely resuscitation and critical obstetric care to patients in remote parts of Bhutan, including the Himalayas. Team members are trained to respond to emergency evacuations in extreme altitudes using a high-performance helicopter equipped with an intensive care unit. The team has saved 53 patients since

its inception. Charlie—his classmates will remember him as Charles Haviland Moore—completed his emergency medicine residency at George Washington University in Washington, D.C.

2009

Jacob M. Appel has published a new novel. Read about his latest book in Alumni in Print. In addition to being a physician, an attorney, and a bio-ethicist, Jacob has published more than 13 books and 10 plays that have been performed by companies across the United States.

2012

Eliza Miller received the Robert G. Siekert New Investigator Award in Stroke from the American Stroke Association. The award encourages new investigators to undertake or

continue stroke-related research. Eliza's abstract, "Preeclampsia and Early Stroke Incidence in the California Teachers Study," was presented in January at the 2018 International Stroke Conference in Los Angeles. **Joshua Witley '03** was senior author. Both are assistant professors of neurology in the stroke and cerebrovascular disease division at VP&S.

2014

See the story, "Alumni Run for State, National Office," below to read about **Abdul El-Sayed**.

Correction

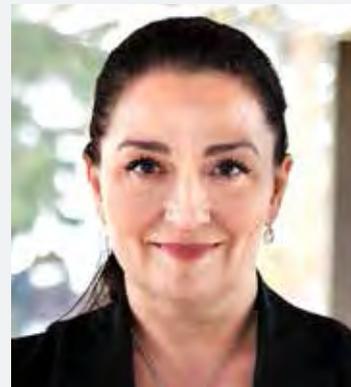
Stuart Levine was incorrectly identified as a member of the Class of 1994 in the Fall/Winter 2017 issue. He is a 1998 graduate. *Columbia Medicine* regrets the error, which has been corrected in the online edition.

Alumni Run for State, National Office

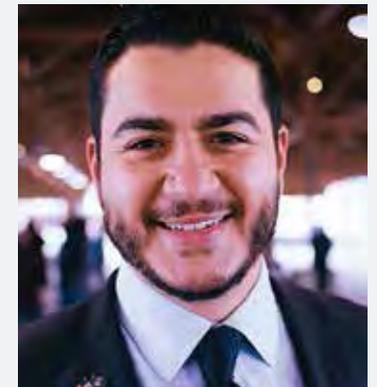
Two VP&S graduates are campaigning this year for seats in Congress, and another alumnus is running for governor of Michigan.



Jim Maxwell '75 is running for Congress in New York's 25th Congressional district. He is a native of Monroe County and a lifelong resident of East Rochester, where he has practiced neurosurgery since 1982.



Shannon Hader '95 is running for Congress in Washington state's 8th Congressional district. She is a fifth-generation native of the region, where she grew up on her great-grandfather's farmland. Most recently, Shannon was director of the Division of Global HIV & TB at the CDC in Atlanta.



Abdul El-Sayed '14 is running for governor of Michigan. He is a first-generation American, son of Egyptian immigrants who settled in Michigan. If elected, he would be the first Muslim-American ever elected a state governor and the youngest governor since 32-year-old Bill Clinton was elected governor of Arkansas in 1978. Most recently, Abdul was executive director of the Detroit Health Department.

● ALUMNI PROFILE

Yvonne Thornton'73/'96 MPH: A Pioneering African-American Perinatologist Looks Back with Pride

By Peter Wortsman



Best known for her instrumental role in refining and helping win FDA approval for the practice of chorionic villus sampling (CVS), an alternative form of prenatal diagnostic testing that can be performed safely and with minimal discomfort to the mother much earlier than amniocentesis, pioneering perinatologist Yvonne S. Thornton'73, MPH'96 broke two glass ceilings. She is the first African-American woman in the United States to be board-certified in high-risk obstetrics and the first to be accepted into the highly selective New York Obstetrical Society.

Having risen from modest means and surmounted obstacles of race and gender prejudice to reach the leading ranks of her specialty, she proudly fulfilled her father's dream that his daughters become doctors. Personally delivering more than 5,000 babies and overseeing or supervising more than 12,000 high-risk deliveries in the course of her career and pursuing landmark clinical research on weight gain prevention intervention in obese pregnant women, she managed to do it all while raising a family of her own. Her son, Shearwood III (Woody), a 2004 VP&S graduate, and daughter, Kimberly, are both MDs.

Dr. Thornton chronicled her experiences in two best-selling memoirs, "The Ditchdigger's Daughters," subsequently made into an award-winning movie and recently optioned for a Broadway musical, and "Something to Prove," the grand prize winner in the 2011 New York Book Festival.

In September 2017 she revisited her medical alma mater to talk about her life and career with *Columbia Medicine*.

"I Want to be Around When One Person Becomes Two People"

Dr. Thornton's calling in life became clear to her early on. At 8 years old, on a visit to the hospital with her aunt, a registered nurse, she witnessed a woman giving birth in an elevator and resolved, "I want to be around when one person becomes two people!"

One of six daughters (including one adopted daughter) of the late Donald and Itasker Thornton, Dr. Thornton says her parents worked tirelessly, her father holding down two and sometimes three jobs at a time and her mother cleaning other people's houses as well as her own, to put food on the table, to put clothes on their backs, and to move the family from the projects to a real home that Mr. Thornton built from scratch in Long Branch, N.J. Her mother, who had always regretted interrupting

her studies at a historically black college, Bluefield State Teacher's College (now Bluefield State College) in Bluefield, W.Va., because she didn't have the money to pay the tuition, framed and treasured every diploma her daughters earned. Given to reciting verses by Keats and Wordsworth while scrubbing floors, she convinced her husband, himself a high school dropout with a sharp mind, that education was a top priority.

Some people are content to dream. Others do everything in their power to realize their dreams. Bucking the odds against a black, working class family in the 1950s, notwithstanding the ridicule of neighbors and co-workers, Donald Thornton decided that his daughters would become doctors. A homespun philosopher, he imbued in his children his own single-minded determination to achieve a better life for them. "If the front door isn't open," he said, "go around to the back and climb through the window. If the window is closed, try to get in through the cellar. If that's locked, go up on the roof and see if you can get in through the chimney. There is always a way to get in if you keep trying." As to the challenges ahead, he laid it on the line: "You're black and you're girls, and the world has already written you off." A realist with a dogged optimistic streak and a can-do attitude, he nevertheless insisted: "This country gives blacks a lot of grief. But it gives them a lot of opportunities too. Work hard and people will help you; doors will open."

The stethoscope, or what he liked to refer to as "that scripperscrap," was more than a mere medical device to him. A symbol of care, it also leveled the playing field. "When someone's in need of healing," Mr. Thornton reasoned, "he won't care about the color of the doctor's skin."

After earning a bachelor of science degree with distinction in 1969 from Monmouth College (now Monmouth University) in West Long Branch, N.J., middle daughter Yvonne Thornton found an open door at Columbia VP&S. Two other sisters would follow suit in the medical and dental fields.

Dr. Thornton still vividly recalls her interview with then dean of admissions, George Perera'37. Of her glowing undergraduate faculty letters of recommendation, Dr. Perera joked: "I thought I would see somebody with a halo on her head!" And when he asked her if she thought she could keep up with classmates from Yale and Stanford, she looked him in the eye and calmly replied, "I may come from a small college, but nobody can out-study me!"

True to her word, she hit the books every weekday waking hour. And come weekends she joined her siblings in the family band, “The Thornton Sisters,” another brainchild of her ever dynamic father to help fund his daughters’ studies. Winning six consecutive appearances at the legendary Apollo Theater Amateur Night, the band, in which Yvonne played alto saxophone and her mother played fretless bass and designed costumes, went on to play the Northeast college circuit and was voted Princeton’s favorite band.

She did well academically at VP&S and made time to pursue research in sickle cell disease at Rockefeller University, co-authoring her first paper, “Pharmacology of cyanate, II. Effects on the endocrine system,” in the *Journal of Pharmacology and Experimental Therapeutics*.

She had little time for socializing, but a friendship would later turn into a budding romance with an equally committed and determined fellow medical student, Shearwood J. McClelland ’74/’96 MPH, whom she married in 1974. Associate professor of clinical orthopedic surgery at VP&S, Dr. McClelland is director of the Department of Orthopedic Surgery at Harlem Hospital. (A short profile on him appeared in the Winter 2004 issue of this magazine.) Glad to become Mrs. McClelland, his wife-to-be insisted, “My parents worked too hard to help put me here at VP&S, and if I’m going to be a doctor it’s going to be Dr. Thornton!”—in honor of her father.

Donald Thornton lived to see his dream come true. Visiting his daughter one day at Roosevelt Hospital, where she trained in ob/gyn from 1973 to 1977, the sweet sound of “Paging Dr. Thornton” emanating from the P.A. system was music to his ears.

At Roosevelt Hospital, where she was named chief resident, Dr. Thornton thrived under the guidance of Dr. Thomas F. Dillon, her department chair, and Dr. Abraham Risk, head of the residency program. Given its location on 59th Street and 10th Avenue, the hospital attracted a diverse

patient population that included the working poor of Hell’s Kitchen and the upper crust of Central Park South. Often putting in 110- to 120-hour work weeks, she recalls, “I just lived and breathed ob/gyn, soaking up as much knowledge as I could. I really blossomed there.”

In 1977 Dr. Thornton returned to Columbia to pursue a postdoctoral fellowship in maternal-fetal medicine at Babies Hospital and the Sloane Hospital for Women (now the Morgan Stanley Children’s Hospital) at what was then Columbia-Presbyterian Medical Center. She would go on to receive double board certification, in obstetrics and gynecology in 1979 and special competency in maternal-fetal medicine in 1981, the first black woman certified in the field.

From 1979 to 1982, at the urging of her husband, who felt that it was time “to give back to our country,” Dr. Thornton and Dr. McClelland voluntarily served in the U.S. Navy. Commissioned as lieutenant commander of the medical corps, Dr. Thornton joined the Department of Ob/Gyn at the National Naval Medical Center in Bethesda, Md.

Of High-Risk Pregnancy and Professional Prejudice

In 1982, based on her stellar CV and a glowing professional assessment from Dr. Roy Petrie, her Columbia mentor, the chair of obstetrics and gynecology at what is now Weill Cornell Medical Center accepted her, sight unseen, as an assistant professor and full-time member of the academic

“With every high-risk delivery, I knew I had a bit of immortality in my hands.”

staff. Ob/gyn at Cornell (also known at the time as the New York Lying-in Hospital) had never had a full-time academic person of color on staff. As soon as Dr. Thornton walked through the door and the chair set eyes on her, his enthusiasm cooled. “It wasn’t verbalized, the furrow in the middle of the forehead, the quick glances, I just knew I wasn’t welcome.”

“We don’t have room for you on this floor,” she remembers him saying. “You’ll have to work in the sub-basement.”

Gritting her teeth and following a pep talk from her father—“You’re not there to be liked, you’re there to practice medicine”—she rolled up her sleeves and got to work caring for her patients as director of clinical services of Cornell’s ob/gyn clinic in the sub-basement. She remembered, “Find your opportunities in the castaway areas of life.”

The patients mattered most. As she recalled in “Something to Prove,” “I always thanked my patients for keeping me a very happy person. Because with every high-risk delivery, I knew I had a bit of immortality in my hands.” Elaborating on the special bond of obstetrician, mother, and baby, especially in maternal-fetal medicine, she explained: “This baby can have another baby, and that baby can have another, and, well, I feel like I’m promulgating life, helping the human species survive.” She has remained friendly with many patients and their children, whom she sees as an extended family. “There is nothing more satisfying than hearing from a former patient many years later that her baby, who, but for a quick intervention and a lot of luck, would have been lost, just made the fifth grade honor roll!”



Dr. Thornton at her medical school graduation with parents Itasker and Donald Thornton

Dr. Thornton earned the ultimate approval of her professional peers when she was the first African-American woman accepted into the ranks of the prestigious New York Obstetrical Society.

CVS, an Early Diagnostic Alternative to Amniocentesis

First developed in Denmark and finding its way to the United States via China, Italy, and London, chorionic villus sampling is a prenatal technique for obtaining genetic diagnostic information about the developing fetus by sampling the chorionic villus from the growing placenta. The sampling can be performed as early as the eighth postmenstrual week of pregnancy. After the method was introduced in the United States as an alternative to amniocentesis, Dr. Thornton was selected as the lead investigator in CVS trials at Cornell. The first institution to introduce the technique in New York was Mount Sinai, but faculty there proved protective of their newfound know-how, so Dr. Thornton went to Thomas Jefferson University in Philadelphia to learn it from Drs. Laird Jackson and Ronald Wapner, who were more than happy to pass on the knowledge.

“The learning curve in CVS, fine-tuning the manipulation of the thin plastic catheter to insert it in the growing placenta to get the chorionic villi out, is very difficult,” she recalls. “The tube is malleable, you have to shape it to reach where you think the growing placenta is going to be. Some doctors just couldn’t get it right, but I took to it like a duck in water.” But after other practitioners’ faulty application of the procedure and a string of infections often leading to loss of the fetus or removal of the uterus, the FDA put a hold on the technique pending further investigation of its efficacy and safety. Following extensive clinical trials, in a paper she co-authored, “Effect of chorionic villus sampling on maternal serum alpha fetoprotein levels,” published in the American Journal of Perinatology, Dr. Thornton was among those who helped convince the FDA of the viability of CVS.

The welfare and comfort of her patients and felicitous pregnancy outcomes were always her first priorities.

Then in the early ’80s, she and colleagues at Cornell faced another daunting challenge: how to care for pregnant women with AIDS. “The general mindset was that these patients came from another planet,” she recalls. With many of the women illicit drug users, “there was a social overlay and the unspoken sense of: Good riddance!” Panicked physicians and nurses resorted to triple gloving in the OR. “But after a while, a common consensus kicked in. Look, we’re health care professionals. The patient needs to be cared for. Let’s do this.”

Facing the Trauma of a Malpractice Suit and Other Challenges

“The body is a wonderful thing,” she wrote in “Something to Prove.” “If you can fend off the attacks from the hundreds of billions of microbes that conspire to undermine its every organ, if you can determine the right treatments, then the body will take it from there and heal itself.”

But sometimes a physician is faced with hard choices. In a gut-wrenching passage in her memoir, she describes the emotional toll of a malpractice suit from a patient whose life she had saved when she opted to terminate a pregnancy and remove an infected uterus to save the mother’s life. “It’s like being shot in the chest. The jagged edges may have healed but the hole is still



Dr. Thornton and First Lady Michelle Obama in 2012

there,” she says, still wincing at the memory. “That somebody whose life I’d saved would do that to me.”

Again, her father’s wisdom helped attenuate the pain and helped her move on. “You can’t hate a person,” he said. “You can hate the things they do or the ideas they have, but not the person himself.”

Soon thereafter she faced professional frustration. After being overlooked for the position of director of maternal-fetal medicine at Cornell,

“Midwives introduced me to an entirely different approach to pregnancy, encouraging me to think about obstetrics as part of the natural order, not as pathology.”

bypassed by a younger colleague who lacked her clinical training and experience who just happened to be a white male, she decided to seek opportunities elsewhere.

Following a brief stint at running a freestanding perinatal clinic in New Jersey, in 1992 Dr. Thornton accepted the invitation of her old residency program director at Roosevelt Hospital, Dr. Abraham Risk, then recently named chairman of ob/gyn at Morristown Memorial Hospital in Morristown, N.J., to join him as director of the hospital’s first center for perinatal diagnostic medicine. Local community doctors were initially reluctant to refer their patients, but they were finally swayed by the decision of insurance companies to restrict reimbursement for any perinatal diagnostic testing and care to certified perinatal centers.

At Morristown Dr. Thornton was reacquainted with the unique role of midwives. “Midwives introduced me to an entirely different approach to pregnancy,” she wrote in “Something to Prove,” “encouraging me to think about obstetrics as part of the natural order, not as pathology. [...] The midwives at Roosevelt Hospital instilled in us the understanding that [...] our empathy and humanity were every bit as important as our medical training. [...] They lived the true definition of ‘obstetrics,’ which means ‘to stand by.’ They were there not to interfere but to assist and to make sure that the mothers were as comfortable and warm as possible.”

Opting to understand the changing dynamic of American medicine from an administrative perspective, in 1996 Dr. Thornton and her husband earned

master of public health degrees in health policy and management in the executive master's program at the Mailman School of Public Health. And after returning to the Division of Maternal-Fetal Medicine at St. Luke's-Roosevelt Hospital Center, where she had trained, she decided to apply her newly acquired knowledge, accepting the position of vice chair and director of maternal-fetal medicine in the Department of Obstetrics and Gynecology at Jamaica Hospital Medical Center, a public hospital serving a predominantly minority and immigrant population in Jamaica, Queens, a position she held for three years.

But wearying of the long commute from her home in New Jersey, often being obliged to wake up in the middle of the night to rush to oversee difficult pregnancies, in 2007 she joined the faculty of New York Medical College as clinical professor of obstetrics and gynecology and the staff of Westchester Medical Center as a senior perinatologist and preceptor at the high-risk obstetrical clinic.

While at New York Medical College, she published the field's first randomized clinical trial on perinatal outcomes in nutritionally monitored obese women. She also published a suspension technique she developed for delivering morbidly obese patients that was subsequently dubbed "Thornton Suspenders."

Practicing Medicine from the Printed Page, TV Screen, and Lecture Podium

Meanwhile, another vocation beckoned. Recalling the thrill of her early stint performing and singing in the family band, and eager to reconnect with an audience, Dr. Thornton found her voice again. "When that spotlight shines on you it changes your whole molecular structure," she avows, only half tongue-in-cheek.

In addition to writing two memoirs, she is the author of a widely read medical textbook, "Primary Care for the Obstetrician and Gynecologist," and two women's health books for general readership, "Woman to Woman" and "Inside Information for Women." Also having produced three instructional videos, she is a consultant and contributor to numer-

ous lay journals and electronic media, including the Huffington Post, MSNBC, Ladies' Home Journal, and Essence magazine.

Having promoted her books and addressed women's health issues on "The Oprah Winfrey Show," "Today," "Good Morning, America," and other broadcasts, she hosted her own TV show and radio program for a time before she hit the public speaking circuit, becoming a spokesperson for the March of Dimes. She was the first woman in the 165-year history of the International Platform Association to win the Daniel Webster Oratorical Competition.

Among the highlights of her career at the lectern was the keynote address she delivered in 2003 at the commencement ceremonies at Tuskegee University, the historic African-American institution of higher learning in Tuskegee, Ala., at which she was also awarded an honorary doctor of science degree.

Other honors include a distinguished alumni award and an honorary doctor of humane letters degree from her undergraduate alma mater, Monmouth University. In 2013 she was honored as a "Living Legend" by the National Medical Association. And in 2017, VP&S saluted her achievements with the Virginia Kneeland Frantz'22 Award for Distinguished Women in Medicine. Included among "Best Doctors—New York Metropolitan Area," she also was listed in *New York* magazine as one of the top 10 maternal-fetal medical specialists in New York City.

She experienced another high point in her public speaking career in 1995 when she was asked to deliver the keynote remarks at the commencement of Bluefield State College in West Virginia, her mother's alma mater, when the school conferred on her mother, the late Itasker Frances Edmonds Thornton, a posthumous doctor of humane letters degree. "Oh, Lordy, do I remember that moment! She finally got her sheepskin!"

Setting the Record Straight and Other Philanthropic Goals

Herself the recipient of a generous scholarship from the National Medical Fellowships while in medical school, Dr. Thornton in 2014 returned the favor and sought to set straight the historical record when she established the Anarcha, Betsy, and Lucy Memorial Scholarship. The scholarship name honors three slaves who, as involuntary subjects of experimentation, helped shape advances in clinical and surgical knowledge. Dr. James Marion Sims, the 19th century doctor who was dubbed "The Father of Modern Gynecology," honed his surgical skills on these and other enslaved black women without their consent and without anesthesia. Those eligible for the scholarship are African-American female medical students who are known descendants of American slaves and are enrolled at an accredited U.S. medical school. (The statue of Dr. Sims in Central Park across the street from the New York Academy of Medicine was moved after recent protests.)

Twenty years earlier, in 1994, Dr. Thornton established the Donald E. and Itasker F. Thornton Memorial Scholarship at VP&S to honor her parents' memory and support deserving medical students.

"I remember those who helped me. It brings me full circle," she reflects. "When you give back in the form of a scholarship the recipient remembers who was there for them when they needed it. Like delivering babies, being there when one person becomes two people, it's another form of immortality, which is why I became a doctor to begin with."



Dr. Thornton with medical students and residents at Morristown Memorial Hospital

• ALUMNI PROFILE

J. Nozipo Maraire'92: Returning Home to Zimbabwe

What struck J. Nozipo Maraire'92 when she found her original VP&S application essay was that her reasons then for going into medicine had not changed. "I was idealistic. I always wanted to do something to help people. I wrote about wanting to give back to my country. More than anything, I had this incredible love of neuroscience."

A board-certified neurosurgeon, Dr. Maraire lived in the United States for 30 years before returning to her native Zimbabwe. She also is an entrepreneur who is developing a smartphone app for neurosurgeons to stay informed of advances in the field.

Dr. Maraire was born in what was known as Southern Rhodesia, a British colony. Educational opportunities were limited for blacks in Zimbabwe, and her father went abroad to college. At age 8, Dr. Maraire joined him and over the years lived in Seattle, Toronto, and Jamaica.

After Zimbabwe became independent, Dr. Maraire went home for a brief time before continuing her education in Wales, where she earned the equivalent of a high school diploma before entering Harvard to study biology. Her fascination with how the brain is wired led her to medical school.

After graduating from VP&S, Dr. Maraire did a neurosurgery residency at Yale University, where she was one of several hundred graduates vying for the single residency spot and only the second woman to complete training there. Women represent only 5 percent of practicing neurosurgeons certified by the American Board of Neurological Surgery. The numbers were even lower when she was a medical student. "I was at Columbia at a time when being a female neurosurgeon raised eyebrows," says Dr. Maraire. "I am grateful to people like Dean of Students Linda Lewis and my student adviser, Dr. Donald O. Quest, who encouraged me to pursue my dream."

After her residency, Dr. Maraire completed a fellowship in pediatric neurosurgery at Beth Israel Hospital in New York, then worked as an attending neurosurgeon in Delaware, Ohio, and Oregon before returning to Zimbabwe in 2012 with her husband (urologist Allen Chiura) and their four children.

Nothing could have prepared her for the vast discrepancy she found between the U.S. health care system and the resource-starved system in Zimbabwe. "The Zimbabwe hospital system is in tatters," says Dr. Maraire. The country's economy relies mainly on agriculture and mining, and the unemployment rate has been reported as high as 95 percent; nearly three-fourths of the population lives below the poverty line. "There are more than 14 million people in the country and only six neurosurgeons," says Dr. Maraire. "People are dying of basic conditions."

Dr. Maraire gave the example of a child with hydrocephalus, which put the child at risk of losing her eyesight, going into a coma, and even dying. "The treatment for hydrocephalus is such a straightforward procedure in America that a junior resident usually does it," says Dr. Maraire. "You put a shunt in the tummy to drain water. I never thought of the cost of shunts before, but then I realized the families here can't afford them."

A shunt costs the equivalent of a combined monthly household income of parents in Zimbabwe. Dr. Maraire contacted Econet, an international telecommunications company that serves Africa, and pitched the idea of partnering on a shunt program at Harare Hospital. If Econet agreed to buy and donate shunts to the hospital, she would insert them for free. The program started in 2014.

"Seeing this girl walk after she had the shunt procedure was amazing," says Dr. Maraire. "One of the most important things I learned from my time working in the United States was to ask: 'Who can I partner with to make a difference?' This boldness is part of the mindset in America and has made me think outside of the box."

Dr. Maraire's boldest plan yet led her and her husband to build a 10-bed hospital in Harare, the country's capital city. It will have additional specialists in orthopedics, gynecology, and general surgery. "We're doing it ourselves, brick by brick with the little we are able to scrape together month after month," says Dr. Maraire. "We'll bring together the best of Western medicine and holistic African medicine in one place."



In addition to performing surgery two days a week, Dr. Maraire runs a wellness clinic two blocks from where the hospital is being built. Then there's the smartphone app she is creating.

"We need neurosurgeon innovators," says Dr. Maraire. "If we're just technicians, we'll be pushed out by robots. We need to be at the forefront of innovations for patients." Conceiving the need for an app took shape over many years. Dr. Maraire found information about the latest medical treatments and resources easy to find in big U.S. cities, but when she worked in southern Oregon, she found herself in a place that medical device companies rarely visited. She felt isolated and began to think about ways to keep neurosurgeons informed.

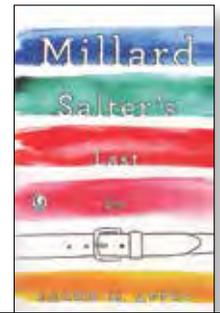
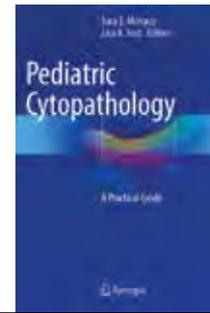
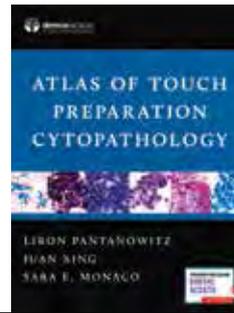
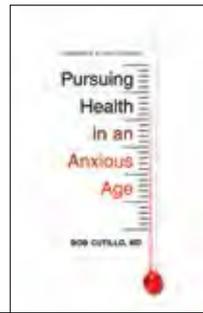
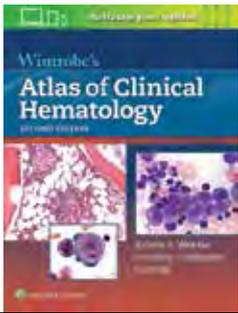
The goal of the app, called Cutting Edge Neurosurgeon, is to create a place where neurosurgeons can find information they need: clinical research breakthroughs, basic science articles, and recommendations for new surgical devices. The app also will have a resident education component and a way for neurosurgeons to track their certification renewals.

The app has been tested at Weill Cornell, the European Association of Neurological Societies, and the Latin American Federation of Neurological Societies.

Dr. Maraire thrives on her "wonderful, crazy life," as she calls it, even though striking the right balance often feels elusive. "There are days when I'm at work for 18 hours and save someone's life and feel like a goddess of neurosurgery, but then I realize I haven't seen my kids all day. Then there are days when I go to soccer games and cook dinner and I miss the call from the emergency room."

True to the younger J. Nozipo Maraire who applied to VP&S nearly 30 years ago, her career has combined the best she offered in her essay: idealism, helping people, giving back to her country, and a love of neuroscience.

— Rose Spaziani



alumni *in print*

By Bonita Eaton Enochs, Editor, and Avichai Assouline

“Wintrobe’s Atlas of Clinical Hematology”

Babette Weksler’63 and Geraldine P. Schechter’63

Wolters Kluwer, 2018

First published in 2006, “Wintrobe’s Atlas of Clinical Hematology” has been updated by a new editorial team. The new edition by classmates Drs. Weksler and Schechter in collaboration with hematopathologist Scott Ely, contains vivid visualization of every hematologic disorder and a new, highly templated format that expedites navigation, as well as a new index of figures by disorders.

“Beyond Eden: The Other Lives of Fine Art Models”

David V. Forrest’64

Outskirts Press, 2017

Dr. Forrest, a lifelong artist, conducted paid interviews with his fine arts models about their difficult but rewarding posing in the nude. What could they tell us about the emotions of being examined by an artist, a lover, or a doctor, and what are the lessons for all who examine unclothed patients? “This unique and often quite beautiful book of portraits and interviews broaches a topic surprisingly absent from most medical school curricula: intimacy,” writes Barron Lerner’86, professor of medicine at NYU.

“Pursuing Health in an Anxious Age”

Bob Cutillo’81

Crossway, 2016

Despite increasing technology and access to health care, modern society is more concerned than ever about health. Drawing from his own medical experience, Dr. Cutillo cultivates in this book a biblical understanding of the relationship between faith and health in the modern age.

“Atlas of Touch Preparation Cytopathology” and “Pediatric Cytopathology: A Practical Guide”

Sara E. Monaco’03

Springer Publishing Company, 2018

Containing more than 500 visually stunning images, “Atlas of Touch Preparation Cytopathology” is the first atlas dedicated to touch preparation cytopathology. Co-authored by Dr. Monaco with the practicing pathologist in mind, the book covers various methods of touch preparation and presents a comprehensive overview, together with visual reference guide to the diagnostic application. “Pediatric Cytopathology: A Practical Guide,” co-edited by Dr. Monaco, is a reference book designed as a practical and high-yield review of pediatric cytopathology, intended to be essential to anyone who is interested in cytomorphological findings in childhood disease.

“Millard Salter’s Last Day”

Jacob M. Appel’09

Gallery Books, 2017

In his newest book, a novel, Dr. Appel tells the heartwarming story of a man who decides to end his life before he’s too old—but then begins to reconsider when he faces complications from the world around him. “Although the theme was suicide, it was laugh-out-loud funny at times. I was crazy about Millard and will not soon forget him,” wrote one reviewer. “Jacob Appel deserves five stars for creating such a well-rounded, complex, likable character. I enjoyed his humor, his memories, and his thoughts on aging. Highly recommend for book clubs,” wrote another reviewer.

➤ *send books
(published within the
past two years) to:*

Bonita Eaton Enochs, Editor
Columbia Medicine
630 W. 168th Street
Box 153
New York, NY 10032

Send inquiries about books to
columbiamedicine@columbia.edu



Craig Granowitz

Alumnus Takes Up the 250th Anniversary Scholarship 1:1 Matching Challenge

By Peter Wortsman

“What I have accomplished is relatively small in the grand scheme of things,” says Craig Granowitz’90 MD/’93 PhD. He is a biomedical researcher who, through his career at Schering Plough, Merck, and other biomedical companies, applied his knowledge in harnessing biomedical discoveries to help people live healthier and longer lives, contributing to these companies’ success.

“It’s a privilege to bring new medicines to market and impact people’s lives—and it’s truly a team effort. I never forget how success depends on tapping the skills and ideals of others,” he says. Fulfilling what he perceives as his societal responsibility, Dr. Granowitz committed \$250,000 to establish the Jack M. and Sheila H. Granowitz Scholarship Fund at VP&S to honor his parents and support future students. His commitment was matched 1:1 by P. Roy Vagelos’54 in celebration of the 250th anniversary of the medical school. Together with his wife, Diana, Dr. Vagelos, the former Merck & Co. chairman and CEO, donated money to endow a fund to help VP&S eliminate loans for students with the most need.

“I was going to give regardless,” Dr. Granowitz acknowledges. “However, Dr. Vagelos’ challenge to alumni was an added incentive, and the anniversary is a unique milestone. I consider my gift an opportunity to support this great institution, to help future students benefit from an educational experience, and express appreciation to my alma mater for giving me the foundation to support my career interests. I’m supporting an academic vanguard that seeks to make people’s lives better.”

Dr. Granowitz looks back at his role as head of a dynamic marketing group at Schering Plough from 1999 to 2006 that advanced a therapeutic agent to treat hepatitis C. Doing a world of good also built a \$2.5 billion business. “We can now cure hep C in more than 95 percent of patients with 12 weeks of treatment. Amazing.” At Schering he also led teams that supported therapeutic agents in opiate addiction and HIV management. Later, when Merck acquired Schering, he built a global medical affairs

group at one of the world’s largest biomedical companies. He is currently chief medical officer at Amarin Pharmaceuticals, a company engaged in global clinical trials of a medicine called Vascepa. The drug could treat between 20 million and 40 million Americans with elevated baseline triglycerides, shown to be a common cause and possible high-risk marker for myocardial infarction or stroke.

A little more than a decade and a half into his career, he felt it was time to give back and connect with educational institutions and with students. In addition to supporting VP&S, Dr. Granowitz served on the American Heart Association New York City Board of Directors and the advisory boards of the American Associates of Ben Gurion University and Rabbinical College of America in Morristown, N.J.

Philanthropy fits with his philosophy of enlightened self-interest. “Thankfully, I’ve been given so many wonderful opportunities in life and have prospered. Now, gratefully, I can reinvest some of this prosperity to help others.” His attachment to future students is heartfelt. “I see my best self in them. This is a highly idealistic generation that recognizes the imperfections of the world. In giving them a boost, I’m hoping they will apply their knowledge and skills to help others. In this way, I am ‘extending myself’ to continue to do good by encouraging others to unleash their potential.”

To Dr. Granowitz, VP&S and the medical center are very much a family affair. His father, Jack Marks Granowitz, an engineer, came to Columbia in the early 1980s to help launch what was then called Columbia Technology Transfer and is today known as Columbia Technology Ventures. His brother, Eric Granowitz’85, is an infectious disease specialist. His mother, Sheila Granowitz, as a patient has benefited from the medical center’s quality of care. Dr. Granowitz remembers fondly visiting her every day after classes in his first year of medical school during one of her hospital stays. “Seeing her was like my going home from school for my snack when I was a kid. It made us both feel a little better.” His support of VP&S comes from the Granowitz Family Foundation, of which his older daughter is a board member.



Dr. Arnold P. Gold cloaks Julie Lyle '06 (now Julie Lyle Schuman) at the 2002 White Coat Ceremony.



Peter Kim, MD, PhD

FACULTY

Arnold P. Gold, MD

Arnold P. Gold, a VP&S faculty member in neurology and pediatrics for more than 50 years, died Jan. 23, 2018, leaving a legacy that extends far beyond his long career as a clinician and mentor. As a founder of the Arnold P. Gold Foundation in 1988, he became an advocate for humanism in health care and medical education. With the first Arnold P. Gold White Coat Ceremony at VP&S in 1993, Dr. Gold set the standard for introducing medical students to the human connection in patient care. Dr. Gold, most recently chairman emeritus of the foundation's board, joined with his wife, Sandra O. Gold, EdD, and VP&S colleagues to create a foundation intent on preserving the doctor-patient relationship by advancing humanism through physician education. The White Coat Ceremony model—at which new medical students recite the Hippocratic Oath to pledge their commitment to the compassionate practice of medicine—spread to nearly every medical school in the country through the foundation's

support. More than 170 medical schools and physician assistant programs throughout the world and more than 260 nursing schools have adopted White Coat Ceremonies. VP&S students, faculty, residents, and fellows also have participated in the foundation's other programs, including the Gold Humanism Honor Society.

OTHER FACULTY DEATHS

J. Thomas Bigger, MD, retired professor of medicine and former chief of cardiology, died Oct. 8, 2017.

Robert E. Burke, MD, the Alfred and Minnie Bressler Professor of Neurology (in Pathology & Cell Biology), died Jan. 1, 2018.

Paul Cannon, MD, professor emeritus of medicine and former chief of cardiology, died Jan. 2, 2018.

Ronald Fieve, MD, professor of clinical psychiatry, died Jan. 2, 2018. See more in Alumni In Memoriam, Class of 1965 PSY.

Raymond Goetz, PhD, assistant professor of clinical psychology (in psychiatry), died Jan. 8, 2018, shortly after retiring.

John E. Hutchinson III, MD, former associate clinical professor of surgery, died Jan. 18, 2018.

Virginia Kanick, MD, retired clinical professor of radiology at St. Luke's-Roosevelt, died Nov. 15, 2017. See more in Alumni In Memoriam, Class of 1951.

Peter Kim, MD, PhD, associate professor of neurology, died Dec. 5, 2017.

Simme Cynkin Klebanow, former faculty member in occupational therapy, died Oct. 20, 2017.

John Francis Nicholson, MD, retired associate professor of pediatrics and of pathology, died Aug. 30, 2017.

Emil F. Pascarelli, MD, professor emeritus of clinical medicine, died Jan. 22, 2018.

Craig Tenke, PhD, adjunct associate research scientist in psychiatry, died Dec. 21, 2017.

ALUMNI 1945

Word has been received of the Jan. 25, 2015, death of **Thomas C. Wickendon**. After practicing anesthesiology for 25 years, Dr.

Wickendon switched specialties to student health and worked with the Student Health Services at the University of Florida in Gainesville. He is survived by a daughter and two sons.

1947

James C. Monteith, a radiologist, died Dec. 9, 2017, at age 95. He served in the U.S. Navy during World War II, earning the American Campaign Medal and the World War II Victory Medal Honorable Service Button. He subsequently served in the U.S. Air Force before returning to civilian life to practice radiology at Westchester County Medical Center. Dr. Monteith relocated to Coral Gables, Fla., to become chief of radiation oncology at the Radiation Oncology Mercy Hospital in Miami. Preceded in death by a son, he is survived by his wife, Anita, a daughter, and a grandson.

Alexander C. Smith, a retired general medicine practitioner and obstetrician/gynecologist, died Dec. 3, 2017. He served in the U.S. Navy during World War II, commissioned as a lieutenant junior grade, based at the Chelsea Naval Hospital in Boston.

Dr. Smith maintained an affiliation with the Frisbie Memorial Hospital in Rochester, N.H., for 45 years, proud of providing cradle-to-grave care for families in the greater Rochester area. With obstetrics a big part of his practice, he delivered more than 5,000 babies. Upon his retirement in 1997, he volunteered for a decade at the Avis Goodwin Clinic. He also played a central role in various public health efforts, including a drive to immunize local children against polio. A leading advocate for community-based mental health services, he was instrumental in the establishment of the Stratford Child Guidance Clinic. His honors included three Rochester Jaycee Citizen of the Year Awards, the State of New Hampshire Jaycee Outstanding Service Award, and the University of New Hampshire Granite State Award for Outstanding Public Service. Preceded in death by his wife, Edna, he is survived by six children and eight grandchildren.

1950

John E. Sarno, a distinguished academic psychiatrist in the Department of Rehabilitation at New York University, died June 22, 2017,



John E. Sarno '50

of cardiac failure, a day before his 94th birthday. Best known for a unique approach he developed to treat chronic pain, which he called “tension myositis syndrome,” he was the subject of a segment on the TV news magazine “20/20” and a recent documentary, “All the Rage (Saved by Sarno).” Dr. Sarno served in the U.S. Army, stationed in field hospitals in Europe during World War II. Upon receipt of his MD from Columbia he pursued a family practice in Fishkill, N.Y., founding the Mid-Hudson Medical Group. After returning to New York City to complete residencies in pediatrics at Columbia-Presbyterian and in rehabilitation medicine at the Institute for Physical Medicine and Rehabilitation at NYU, he joined the faculty of the Rusk Institute for Rehabilitation Medicine in 1965, where he spent the next four decades honing his skills and developing his controversial theory of the psychological origins of chronic pain. While discounted by many of his medical peers, his book, “Healing Back Pain: The Mind-Body Connection,” sold more than a million copies and found a large following. He was also the author of three other

books, “The Mindbody Prescription: Healing the Body, Healing the Pain,” “The Divided Mind: The Epidemic of Mindbody Disorders,” and “Mind Over Back Pain.” Outside of medicine, his first love was music. As a student at VP&S he sang in the student glee club, The Bards, participating in an encore reunion performance in 1998. He is survived by his wife, Dr. Martha Lamarque Sarno, four children, four grandchildren, and a great-grandson.

1951

Virginia Kanick, retired clinical professor of radiology at VP&S, died Nov. 15, 2017. Longtime deputy director of radiology and senior attending at St. Luke’s-Roosevelt Hospital in New York, where she served a tenure as president of the hospital medical board, Dr. Kanick also officiated as president of the Physicians Relief Fund. She was particularly proud of her role in the development of angiography in the late ’50s and early ’60s. She served for a time on the Advisory Committee for Medical Devices at the Food and Drug Administration and as director of the New York State

Radiology Society and the New York County Medical Society. Among her extramedical passions was the study of archeology, history, and foreign cultures. She is survived by four nieces and nephews and their extended families.

Morris Freeman died Oct. 5, 2017. Born in Chotin, Romania, he emigrated with his family to the United States and served in the U.S. Navy during World War II. A 1945 graduate of the Columbia dental school, Dr. Freeman practiced dentistry for several years before opting for a career in medicine. A revered medical oncologist and longtime member of the clinical faculty in the Department of Medicine at Albert Einstein College of Medicine and an attending at Montefiore Medical Center, he practiced for more than 45 years, mentoring many medical students along the way. Upon his retirement in 2000, he wrote that his greatest regret was “the need to retire from what I enjoyed the most.” Cognizant of the many astounding advances in medicine since he entered the field, he also remained committed to equal access. Dr. Freeman once wrote on



Morris Freeman '51

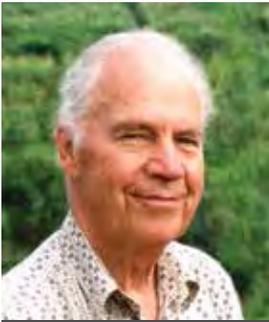
an alumni questionnaire: “The miracles of high tech medicine, unknown in 1951, are unaffordable to most of our population. With the profit potential great, the insurance and investment moguls have moved in and taken over the ‘management’ of health care delivery. For-profit business management is incompatible with good health care delivery for all our people. Physicians have been disempowered and are mere pawns in this cold and impersonal big-business machine. Medical science is doing very well. Whatever happened to compassion, the ethics, the *art* of medicine?” Dr. Freeman’s wife, Violet, died in November 2017. He is survived by a daughter, a son, Neil J. Freeman ’85, a daughter-in-law, Linda R. Aboody ’85, and three grandchildren.

1952

Murray A. Greene, a retired cardiologist and member of the clinical faculty at Albert Einstein College of Medicine, died Oct. 1, 2017. Dr. Greene served as chief cardiologist at the Bronx-Lebanon Hospital Center, where he played a key role in establishing an intensive care unit. He is survived by his wife, Eileen.

1953

John Bryant, a past director of the Columbia University School of Public Health (now the Mailman School of Public Health) and key figure in international public health, died July 5, 2017. Dr. Bryant served as a U.S. Navy pilot during World War II. The author of “Health & the Developing World” (1969), a landmark assessment of the prodigious problems and vast inequities in health care delivery in the world’s less economically favored nations, Dr. Bryant characterized his approach to international health as “going around with a big empty basket...[with] no biases to get in the way and the will to learn.” He taught on the faculties of medicine at the University of Vermont and Ramathibodi Hospital Faculty of Medicine in Bangkok, Thailand, before returning to Columbia as the Joseph DeLamar Professor of Public Health, director of the School of Public Health, and associate dean of the Faculty of Medicine (Public Health). In 1978 he moved to Washington to serve as director of the Office of International Health and deputy assistant secretary for international health in



John Bryant '53

the Department of Health and Human Services under President Jimmy Carter. In that capacity, he represented the U.S. government on the executive board of the World Health Organization and participated in a number of joint U.S.-WHO activities, including the development of the WHO Code on Infant Formulas. He also negotiated a treaty for collaborative research with the Chinese government and coordinated treaty interactions relating to health care with 22 other countries. Dr. Bryant served as a member of the U.S. delegation to the International Conference on Primary Health Care in Alma Ata, Kazakstan, then a part of the USSR. Alma Ata became a catchword for “health for all.” He subsequently served as the Noordin M. Thobani Professor and founding chair of the Department of Community Health Sciences at the Aga Khan University in Karachi, Pakistan, before returning to Vermont. He later lived in a retirement community in Charlottesville, Va. He held an honorary doctorate of science from the University of Arizona, his undergraduate alma mater. Survivors include his wife, Nancy, two daughters, a

son, five grandchildren, and nine great-grandchildren.

Sylvia Davies Diehl, a physician committed to community, maternal, and child health, died Feb. 28, 2018, a month before her 90th birthday. Over the course of her career she worked as a physician with the Madison, N.J., schools, Morristown Medical Center, and Planned Parenthood of Northern New Jersey, which she served as medical director. Upon her retirement from practice, she volunteered for Meals on Wheels, Dress for Success, and other community-oriented programs. Preceded in death by her husband, Kenneth R. Diehl, Dr. Diehl is survived by two daughters, a son, and five grandchildren.

Herman L. Grossman, a retired pediatric radiologist, died Feb. 11, 2018. Dr. Grossman served as a lieutenant in the U.S. Navy during World War II. After the war he opened a private pediatric practice and made house calls before pursuing advanced study in pediatric radiology at Columbia. He was a founding member of the pediatrics radiology program at Duke University, where he

held dual appointments as professor of pediatrics and professor of radiology, teaching until his retirement in 1997. Duke established a lectureship in his name. He is survived by his wife, Eunice, three daughters, and four grandchildren.

Horton A. Johnson, a distinguished academic pathologist, died of cardiac failure Dec. 24, 2017. He served in the U.S. Navy aboard the USS Atlanta during World War II. Following a time as a research scientist at Brookhaven National Laboratories, he taught on the faculty at Indiana University’s medical school and as professor and chair of pathology at Tulane University, rounding out his career as chief of pathology at St. Luke’s-Roosevelt Hospital in New York. Also knowledgeable in and passionate about art history, he volunteered upon his retirement as a tour guide at the Metropolitan Museum of Art. Preceded in death by a daughter, Dr. Johnson is survived by his wife, Caryl, four daughters, a son, two stepsons, 14 grandchildren, and two great-grandchildren.

1954

Sherwin V. Kevy, former associate professor of pedi-

atrics at Harvard Medical School and medical director of transfusion services and blood bank at Children’s Hospital Boston, died Dec. 3, 2017. He was 89. He authored more than 50 scientific papers. His research focused on the development of the current blood and red cell preservation method, the introduction of machines for platelet apheresis, and the use of in vitro gamma globulin for treating patients with multiple recurring infections. He also played a key role in the field of regenerative medicine, employing growth factors in autologous platelet concentrates. Dr. Kevy is survived by his wife, Sandra, two sons, and two grandchildren.

1955

William Lovekin, a retired cardiologist, died Feb. 25, 2018, at age 87. Dr. Lovekin began his career as one of three general physicians at the Ganado Mission Hospital, serving the medical needs of the Navajo reservation in Ganado, Ariz. Later pursuing training in cardiology, Dr. Lovekin moved with his family to New Mexico, where he served as one of three faculty members in the new medical school at the

University of New Mexico in Albuquerque. He subsequently opened his own private practice, Cardiology Associates, and later teamed up with others in a group practice that grew into the New Mexico Heart Institute. Preceded in death by his wife, Anne, he is survived by two daughters, two sons, six grandchildren, and six great-grandchildren.

Julian P. Smith, a retired obstetrician/gynecologist, died Nov. 1, 2017, at age 87. Dr. Smith served as a reserve commissioned officer in the U.S. Army, stationed in Germany. Upon being honorably discharged at the rank of captain, he completed a fellowship in ob/gyn at the University of Texas MD Anderson Medical Center, where he designed and conducted clinical trials demonstrating the effectiveness of applying multidisciplinary therapy to the treatment of ovarian cancer. As one of the founding members of the Department of Gynecological Oncology at Anderson, he became widely known for his contributions to the treatment of ovarian cancer and for his surgical techniques and teaching talents. Co-author of a textbook, “Gynecologic Oncology:



Robert H. Buker '56



Leon O. Andersen '57



Alan M. Aron '58

Management of Complications,” he trained generations of postdoc fellows in the field. Over the course of his career he taught on the faculties of Wayne State University and Loyola University and served as chief of the Department of Gynecological Oncology at the University of Maryland. He was a founding member and past president of the Society of Gynecological Oncologists, president of the Society of Pelvic Surgeons, first president of the Felix Rutledge Society, and past president of the Mid-Atlantic Gynecological Oncology Society. Preceded in death by his wife, Eleanor, he is survived by two daughters, two sons, and eight grandchildren.

John B. Zabriskie, professor emeritus at Rockefeller University and a renowned researcher in infectious diseases, died Aug. 17, 2017. He was 88. A native of Montreux, Switzerland, Dr. Zabriskie served in the U.S. Air Force after graduating from VP&S. He joined the Rockefeller faculty in 1960, rising to tenured professor and head of the Laboratory of Clinical Microbiology and Immunology. He found that the antibodies produced by the immune system in

response to streptococcal infection also reacted with cell membranes in the heart. His later medical research focused on heart cross-reactive antibodies resulting from strep throat and their migration to the brain, often resulting in serious medical consequences, including Sydenham chorea, obsessive-compulsive disorder, and Tourette’s syndrome. He is best known for his investigation of streptococcal infections and related secondary autoimmune disorders and his findings on the link between bacterial infections and obsessive-compulsive disorders in children. Also passionate about music, he studied cello for many years with Hiao-Tsien Ma, father of Yo-Yo Ma, and assisted the father in founding the Children’s Orchestra Society. He is survived by his wife, Paulette, a daughter, two sons, and six grandchildren.

1956

Raymond C. Bartlett, professor of laboratory medicine emeritus at the University of Connecticut and a former staff physician at Hartford Hospital, where he directed the residency program in pathology, died Jan. 23, 2018. Dr. Bartlett descended from a long line of VP&S alumni,

including his great-grandfather, Philo Clark (1867 graduate), his grandfather, Raymond Clark (1895), a cousin, Raymond Barrett (1921), and an uncle, Robert Robinson (1938). The author of a book, “Medical Microbiology, Quality, Cost and Clinical Relevance,” that revolutionized the field, Dr. Bartlett was proud of his impact on the cost-effective practice of medical microbiology nationwide and his pioneering role in assuring quality control in medical microbiology. In his free time, he sang tenor in a church choir. He is survived by his wife, Esther, a daughter, two sons, and nine grandchildren.

Robert H. Buker, a retired military cardiothoracic surgeon and former professor of surgery at the Uniformed Services University of Health Sciences in Bethesda, Md., died Sept. 25, 2017. The son of medical missionaries, Dr. Buker served his entire career in the U.S. Army, rising to the rank of two-star major general. He was honored with numerous medals and ribbons, notably the Distinguished Service Medal, Legion of Merit, Army Commendation Medal, and National Defense Service Medal. In retirement he

volunteered at a free senior citizens clinic in Naples, Fla., and was an avid hunter and fisherman. Survivors include his wife, Ethel, a certified nurse midwife, two daughters, and a son.

1957

Leon O. Andersen, a retired internist/cardiologist formerly affiliated with Good Samaritan Hospital in Suffern, N.Y., died Feb. 14, 2018. Dr. Andersen served as a medical doctor and captain in the U.S. Air Force, stationed in Chateauroux, France, from 1959 to 1962. In an alumni questionnaire he bemoaned in the current practice of medicine “too much reliance on laboratory testing, often needlessly expensive,” insisting, true to his VP&S training, that “meticulous history taking and physical examination are still the cornerstones of good medicine.” After he moved to Lancaster, Pa., in retirement, he created the first countywide police automated external defibrillator program in the United States. The program placed these life-saving devices in every Lancaster county police car. Survivors include his wife, Edith, and two sons, Rolf Andersen ’83 and William Andersen ’87.

1958

Alan M. Aron, a pediatric neurologist, died Dec. 26, 2017. Dr. Aron was director and professor emeritus of pediatric neurology at Mount Sinai School of Medicine in New York City. Co-author of some 40 peer-reviewed papers and as many abstracts, Dr. Aron pursued research in rational therapies for neurological disorders based on molecular biologic systems, among other areas of interest. He also particularly enjoyed interviewing applicants to medical school as a member of the Mount Sinai medical school’s admissions committee. He was listed since 1995 among New York magazine’s Best Doctors of New York and Best Doctors in America—North-east Region. Survivors include his wife, Sarah, two daughters, a son, and eight grandchildren.

Benjamin T. Santoro died Sept. 9, 2017, at age 88. Dr. Santoro served for many years as a general practitioner in Dover, Mass., where he was one of the last of an old school of doctors who made house calls. He also served as chief of emergency medicine at Leonard Morse Hospital in Natick,



Edward Kaplan '59

Mass., retiring to South Chatham in 1988. Preceded in death by his wife, Janine, and by a daughter, he is survived by three sons, three stepdaughters, and 11 grandchildren.

1959

Edward S. Kaplan, a neurosurgeon and longtime member of the clinical faculty in the Department of Neurosurgery at the University of Tennessee in Memphis, died July 18, 2017. Dr. Kaplan trained at the Mayo Clinic in Rochester, Minn., and received a master of science degree from the University of Minnesota. In retirement he served as a volunteer neurosurgeon at Church Health in Memphis and pursued a longstanding passion for history. Baptist Hospital in Memphis, with which he was long affiliated, honored him with the Pillar Award of Distinction for excellence in patient care and service in the community. He is survived by his wife, Linda, two sons, Andrew Stone Kaplan '87 and Jeffrey Stone Kaplan '89, and four grandchildren.

1962

Robinette Bell, a former associate professor in the



Robinette Bell '62

Department of Psychiatry at VP&S, died Aug. 17, 2017. She was 87. Following a five-year stint as a journalist with Look magazine, she shifted gears to study medicine. Dr. Bell specialized for many years in consultation psychiatry, working with breast cancer patients, and long pursued a private practice in Manhattan. She moved with her second husband, Dr. Neil Redford, who survives her, to Denver, where she established a private practice and joined the clinical faculty in the Department of Psychiatry at the University of Colorado. In addition to her husband, she is survived by three children and seven grandchildren.

1963

David N. Reif-Snyder, a retired internist specializing in infectious diseases and travel medicine, died Dec. 27, 2017. He was 82. A native of Mexico, he grew up in Venezuela and Colombia before moving with his family to the United States. After serving in the U.S. Peace Corps, based in Bolivia, he was one of the founding faculty members of the University of South Florida medical school. He had a private practice in internal medicine for many years and

served as chief of medicine at Bay Pines VA Hospital in Tampa. Survivors include his wife, Nelda, two daughters, two sons, 14 grandchildren, and many great-grandchildren.

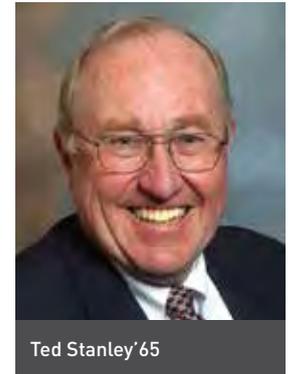
Robert A. Schaefer, a distinguished gastroenterologist and associate professor of clinical medicine at Weill Cornell Medical Center, died Feb. 12, 2018. Dr. Schaefer served as lieutenant commander in the U.S. Navy from 1965 to 1967, earning a bronze star for service in Chu Lai, Vietnam, as a medical officer in the 9th Engineer Battalion of the First Marine Division. Also avid about music, he served as director of the Yale Broadcasting Company in college and remained a lifelong patron of classical music. He is survived by his wife, Mary Jeanne Kreek '62, a daughter, a son, and two grandchildren.

1965

Thomas S. Cottrell, a research pathologist, died Sept. 17, 2017. Dr. Cottrell served in the U.S. Navy aboard the USS Scanner, rising to the rank of lieutenant. He taught at the New York Medical College in Valhalla, N.Y., and later at SUNY Stony Brook, where

he served as executive associate dean and a member of the pathology faculty in its medical school, which he helped found. He was best known for his research on diseases of the lung. Survivors include his wife, Jane, two daughters, a son, and two grandchildren.

Theodore "Ted" Stanley, who spent 50 years at the University of Utah and earned acclaim as a medical entrepreneur, died July 13, 2017, in Salt Lake City. A remembrance posted by the University of Utah recalled that Dr. Stanley, a surgeon and anesthesiologist, first hoped for a career in baseball. After unsuccessfully trying out for the Brooklyn Dodgers and deciding he couldn't make a living as a musician (he could play nine instruments by the time he finished high school), he settled on a career in medicine. He graduated from Columbia College with majors in zoology, chemistry, and music. After medical school and a few years of training at Michigan, he arranged to train at the Cleveland Clinic with Willem Kolff, one of the pioneers in artificial organs. When Dr. Kolff unexpectedly resigned



Ted Stanley '65

from the Cleveland Clinic, Dr. Stanley followed Dr. Kolff to the University of Utah. Initially planning to become a heart surgeon, he decided in Utah to add a specialty in anesthesiology. That brought him back to Columbia for two years of residency, followed by two years of service in the Air Force at Lackland Air Force Base in San Antonio. Back in Utah, his faculty appointments in surgery and anesthesiology put him on the team that performed the first total artificial heart transplant on Barney Clark in 1982. Dr. Stanley's acclaim as an entrepreneur includes his role in bringing the "fentanyl" family of opioids into medical practice. He may be best known for Actiq, a lollipop that provides a fast-acting, convenient, non-invasive opioid delivery system for pain management. Dr. Stanley and a colleague invented the lollipop, which was approved by federal regulators to treat cancer pain. The lollipop also has been used to relieve migraine and cluster headaches, severe back and bone pain, and chronic conditions. Actiq's commercial success provided a royalty stream to the University of

Utah and the Department of Anesthesiology that resulted in an endowment to support research and education and the creation of several endowed chairs. He founded several biotech companies and mentored engineers and doctors pursuing interests in research and medical devices. In 2008, Dr. Stanley was one of two recipients of the Hall of Fame awards given by the Utah Technology Council, which dubbed Dr. Stanley a “serial entrepreneur” for founding or co-founding eight life science companies and three research and educational foundations. He also was an avid train lover and enjoyed photographing wildlife at his mountain ranch, the annual gathering place for an elk hunt he hosted for 41 years. He is survived by his wife, Susan, three sons, a daughter, a brother, and three grandchildren.

1965 PSY

Ronald R. Fieve, a psychiatrist who pioneered the use of lithium to treat mood disorders, died Jan. 2, 2018, of congestive heart failure. Professor of clinical psychiatry at VP&S, he was a founder of the Foundation for Mood

Disorders in New York. According to a tribute in the New York Times, Dr. Fieve, along with colleague Ralph N. Wharton ’57, “identified lithium as the first naturally occurring medication to prevent and control a specific psychiatric disorder.” He was the author of several highly regarded books, including “Moodswing: The Third Revolution in Psychiatry,” “Prozac: Questions and Answers for Patients, Family and Physicians,” and “Bipolar Breakdowns.” In the latter text, his pioneering work, he wrote: “While many psychiatrists and psychoanalysts held on to Freud’s psychoanalytic explanation of the major mood swings, there was compelling evidence to the contrary. The medical model, with an emphasis on heredity and brain chemistry, began to replace Freud, and the age of psychopharmacology was born.” Dr. Fieve is survived by his wife, Katia von Saxe, two daughters, and four grandchildren.

1967

Daniel Garnett, a retired general surgeon, died Nov. 1, 2017. Dr. Garnett was proud of his service in the U.S. Navy, attached to a

Marine battalion during the Vietnam War. In addition to his longstanding private practice, he served as chief of staff of Swedish Hospital Medical Center in Seattle. He is survived by his wife, Stephanie, two sons, and five grandchildren.

1970

Psychiatrist **Diane Lipson Stone** died in October 2017. A member of the clinical psychiatry faculty at New York University, Dr. Stone pursued a private psychiatric practice in New York. She is survived by a daughter.

1972

David L. Curtis, a rheumatologist in private practice in San Francisco, died July 28, 2017, of acute leukemia. Dr. Curtis was a member of the clinical faculty at the University of California at San Francisco. In his free time he enjoyed skiing, tennis, biking, and hiking. He is survived by his wife, Nora, a daughter, two sons, and four grandchildren.

1975

Jules N. Manger, an internist in private practice and one of the founding members of Concord Emergency Medical Associates in Concord, N.H., died

July 25, 2017. He served in the U.S. Army in Vietnam, where he was wounded in combat and honorably discharged, winning a Purple Heart. An adjunct faculty member at Dartmouth Medical School, he served for three decades as an emergency room specialist at Concord Hospital. Dr. Manger was a supporter of Disabled American Veterans. Preceded in death by his wife, Janis, he is survived by a daughter, a son, and six grandchildren.

1977

Jonathan Greenberg, a neurosurgeon who also earned a law degree from Columbia, died Jan. 1, 2018. Professor and chair of neurosurgery at the University of Miami medical school, Dr. Greenberg served as chief of the neurotrauma service at Jackson Memorial Hospital. He was the author of a textbook, “The Handbook of Head and Spine Trauma.” Dr. Greenberg is survived by his wife, Dr. Myriam P. Garzon, four daughters, and a son.

1984

Hematologist **Kevin T. McDonagh** died of cancer Dec. 23, 2017. He served as chief of hematology,

oncology, and bone marrow at the Markey Cancer Center of the University of Kentucky before moving to Vanderbilt University to head programs in benign hematology and multiple myeloma. He is survived by his wife, Dr. Leslie Crofford.

1989

Tragedy struck **Mark Montgomery**, who was among those killed Jan. 9, 2018, in California’s mudslides. Dr. Montgomery, a specialist in hand and upper extremity surgery in group practice, was affiliated with the Santa Barbara Cottage Hospital. His daughter, Caroline, was also among the victims of the mudslides. An online tribute at the Orthopedics This Week website said he played rugby at VP&S after wrestling as an undergrad at Princeton. He completed an orthopedic residency at New York-Presbyterian/Columbia and a fellowship in hand and upper extremity surgery at Brigham and Women’s Hospital. He is survived by his wife, Catherine, a daughter, and a son.

OTHER ALUMNI DEATHS

T. Berry Brazelton ’43
John Gerster ’44
Richard Rudders ’63



The medical staff of Base Hospital No. 2 pictured in Étretat, 1917

100 YEARS AGO: Base Hospital No. 2 in World War I

Shortly after the United States declared war on Germany in 1917 in hopes of making World War I “a war to end all wars,” Presbyterian Hospital responded to the national call for doctors and nurses to serve in the war by organizing U.S. Army Base Hospital No. 2.

Base Hospital No. 2 was one of the first U.S. medical units to reach France in 1917 and was assigned to take over a previously established British army hospital in Étretat, a fishing village and summer resort in Normandy about 20 miles northeast of the port city of Le Havre.

The unit had 25 physicians and surgeons and 65 nurses, almost all affiliated with

Presbyterian Hospital and Columbia’s medical school, who cared for the war’s military casualties.

By Fall 1917, 23 more nurses joined Base Hospital No. 2. Unlike the physicians, who were members of the U.S. Army Medical Corps and received officer commissions, nurses were considered part of the American Red Cross.

On two occasions, small groups of doctors and nurses were detached from the base hospital to form casualty clearing stations near the front lines to treat wounded soldiers or stabilize them for transport to a field or military hospital. The men and

women at these stations faced additional hardships and danger, including a bombing raid on their quarters.

When the war ended on Nov. 11, 1918, Base Hospital No. 2 prepared to depart Étretat, which in days of peace was often visited by Monet and impressionist painters who came to capture the picturesque beauty of its extensive beaches and stunning cliffs. Before leaving to sail back home, the unit’s members gathered in the local cemetery to remember those left behind, including one member of the unit, Amabel Roberts, a 1916 Presbyterian Hospital School of Nursing graduate, who died from sepsis.



COLUMBIA UNIVERSITY
Vagelos College of Physicians and Surgeons

630 WEST 168TH STREET
NEW YORK, NY 10032

Non-Profit Org.
U.S. Postage
Paid
New York, NY
PERMIT NO. 3593



join us to advance cancer research at Columbia
ride 62.5, 45, 25 or 10 miles
velocityride.org

VELOCITY
COLUMBIA'S RIDE TO END CANCER

10 / 7 / 18



COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

Herbert Irving Comprehensive Cancer Center