

proach—a single drug for a single cancer with a single mutation—but the cancer cells' rapid resistance, as observed in the clinical trials, also shows how much remains to be learned. "In the case of Vemurafenib, we need a much more sophisticated understanding of the drug pathways," he says. "Most of that massive resistance is due to bypasses, where one pathway turns off and the next turns on."

Sorger strongly advocates the use of more mathematical and computational methods to supplement biology's traditionally descriptive approach. When he taught at MIT, he co-founded its Computational and Systems Biology Initiative, and now his lab uses quantitative models to study the biological circuitry controlling decisions about programmed cell death, a process radically altered in cancer cells. "My interest in quantitative methods grew organically from being incredibly dissatisfied with this very anecdotal picture," he says. The new program in

therapeutics will draw on MIT's position as a leader in computational biology, and Harvard's in systems biology (driven by the creation of the department of systems biology at HMS in 2003). "We need a radical rethink in the way that we organize and interpret biological data," he says. A more integrative research approach, based upon predictive models of cellular networks, will help explain and predict drug side effects and interactions. "Many drugs provoke paradoxical responses," he says. "These are effects that, once understood, could be applied in industry. It's time to rethink some of these underlying concepts." (For an initial outline of the new approach, see "A New Prescription for Drug Development," <http://harvardmag.com/pharmacology>.)

Such an integrative approach will require more interdisciplinary collaboration. A key component of the therapeutics initiative is a new Laboratory of Systems Pharmacology (LSP), a therapeutics re-

search facility. Additionally, a therapeutics foundry will aim to develop methods and technologies for smarter drug design—for example, using known molecular parts to build proteins with desired functions. The LSP (construction is scheduled to finish in the spring) will eventually house an estimated 60 researchers from Harvard, MIT, and Tufts, and hospitals including Massachusetts General, BWH, and the Dana-Farber Cancer Institute. Researchers will have similarly varied backgrounds, ranging from experimental to computational biology, and from basic to translational to clinical research, all working in a single physical space. "Colocalization drives interdisciplinary science," says Sorger, praising the benefits of proximity among researchers. "No electronic technology we've discovered has been more than an aid." Loscalzo, whose own lab employs both experimental and computational approaches to medically relevant issues, hopes that by working alongside each other, researchers

University People

Peak Professors

Faculty of Arts and Sciences dean Michael D. Smith has named a new cohort of Harvard College Professors. The five-year professorships (five are conferred annually) recognize superb undergraduate teaching and advising. Honorands receive extra research funding and a semester of paid leave or summer salary. This year's cohort is: Joseph D. Harris, Higgins professor of mathematics; Steven R. Le-

vitsky, professor of government; Michael J. Puett, Klein professor of Chinese history and chair of the committee on the study of religion; Jennifer L. Roberts, professor of history of art and architecture and chair of the committee on degrees in the history of American civilizations (read about her presentation at the May learning and teaching conference in "Talking about Teaching," page 48); and Maryellen Ruvolo, professor of human evolutionary biology.

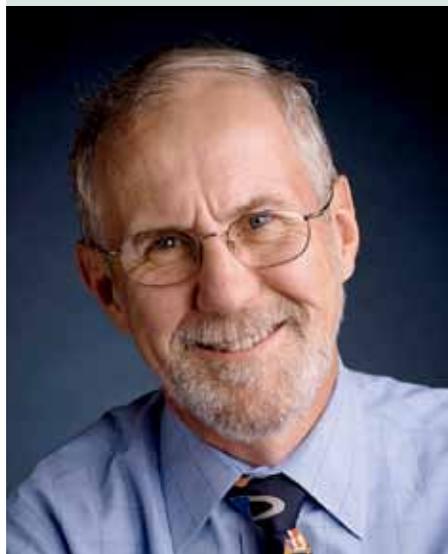
Scientists at the Summit

Eight Harvard faculty members have been elected to the National Academy of Sciences: Mitzi I. Kuroda, professor of

medicine and professor of genetics, Harvard Medical School (HMS); astronomer Ramesh Narayan, Cabot professor of the natural sciences, Faculty of Arts and Sciences (FAS); Norbert Perrimon, Stillman professor of developmental biology, HMS; Daniel L. Schacter, Kenan professor of psychology, FAS (see "The Social Life of Memory," page 10); Beth A. Simmons, Dillon professor of international affairs, FAS; Gerhard Wagner, Blout professor of biological chemistry and molecular pharmacology, HMS; Fred M. Winston, Andrus professor of genetics and tutor in biochemical sciences, HMS and FAS; and Horng-Tzer Yau, professor of mathematics, FAS.

Extraordinary Economist

The American Economic Association has conferred the 2013 John Bates Clark Medal on professor of economics Raj Chetty, who uses large data sets to examine taxation, employment, and education policy (see "Kindergarten Matters," November-December 2010, page 13). The medal recognizes the U.S. economist under the age of 40 judged to have made the most significant contribution to economic thought and theory. He was awarded a MacArthur Foundation Fellowship in 2012.



INTERIM ED DEAN. Thompson professor of education and society Richard J. Murnane has been appointed Harvard Graduate School of Education's acting dean, effective July 1. He is the interim successor to Kathleen McCartney, who departs to become president of Smith College, as previously announced. Murnane, an economist, has examined changing demands for workers' skills in the evolving U.S. economy, and the effectiveness of education policies in responding to those changes. He also studies the effect of income inequality on educational opportunity. The search for a permanent dean continues.

will gain a deep appreciation for the power of different research methods.

The new lab will explicitly tackle complex problems like neurodegenerative or inflammatory diseases, where traditional drug-discovery methods have made little progress. “I don’t think these are intractable problems,” says Loscalzo. “We have the data sets. We have the cellular and animal models, and we know the biochemical, molecular, and cellular underpinnings pretty well.” Here, collaboration is crucial. He suggests that a better understanding of basic biology will enable clinicians to characterize disease profiles in terms of their underlying biology, rather than their large-scale, end-stage physiological effects. In many cases, Loscalzo says, “the therapies that have been used so far have been largely focused on the *end result* of a disease, not the *causes*.” Exploring those causes could lead to novel therapeutic targets, as well as more effective diagnosis and treatment in a clinical setting.

The initiative also aims to foster a more

collaborative relationship between academia and industry. The high cost of drug failures places a limit on how much companies are willing to risk. “You get stuck in a rut,” says Sorger. “Research is too expensive, so you have to go with today’s ideas, even if today’s ideas aren’t good enough.” In contrast, he says, academia is better equipped to handle long-term, open-ended questions and to investigate principles that could lead to more rational drug design and usage. To that end, a graduate program in therapeutics will train students in the science behind drug discovery and regulation, while requiring internships at pharmaceutical companies to get a taste of industry. “Exposure to real-world problems will help students think about their own research projects,” he says, by showing them what topics are best suited to each context. Nine students from existing HMS medical and doctoral programs are expected to enroll this fall in the new therapeutics certificate program.

Sorger also sees a role for academia in mediating the adversarial relationship between pharmaceutical companies and federal regulatory agencies. Regulatory science, he says, could be restructured to enable companies to alter and improve their treatment regimes during the trial process, and to continue monitoring after a drug reaches the market. “The FDA is complicit in the reductionist view of drug development, in that the approval process requires the pharmaceutical industry to identify a specific target for the drug candidate,” adds Loscalzo. Yet infrequent toxicities and nontoxic side effects are also important components of how clinicians prescribe drugs. Furthermore, combination therapies may be the way forward for drugs like Vemurafenib (new drugs are already in development to combat the observed resistance), but the current lengthy approval process discourages collaboration between industry competitors on potentially powerful drug cocktails. Plans

PFOHO’S FIRST FAMILY. Anne Harrington, professor of the history of science—and acting chair and director of undergraduate studies for the department—and her husband, John Durant, have been appointed master and co-master of Pforzheimer House. Harrington’s scholarship focuses on the mind-body connection and neuroscience; she has been a member of the faculty since 1988. Durant is director of the MIT Museum and an adjunct professor in that institution’s science, technology, and society program. The couple have an eight-year-old son, Jamie. They succeed Nicholas Christakis and Erika Christakis, master and co-master since 2009, who are relocating to Yale.



Academy Academicians

Eleven faculty affiliates were elected members of the American Academy of Arts and Sciences: David M. Altshuler, professor of genetics; Xandra O. Breakfield, professor of neurology; Paul A. Buttenwieser, clinical instructor in psychiatry; David W. Latham, lecturer on astronomy; Sara Lawrence-Lightfoot, Fisher professor of education; Joseph Loscalzo, Hersey professor of the theory and practice of physic (see “Systematic Drug Discovery,” page 54); John F. Manning, Bromley professor of law; Richard J. Murnane, Thompson professor of education and society (opposite); Charles A. Nelson III, professor of pediatrics; William J. Poorvu, M.B.A. Class of 1961 adjunct professor in entrepreneurship emeritus; and Xiaowei Zhuang, professor of chemistry and chemical biology

and professor of physics (see “Shedding Light on Life,” May-June 2008, page 40).

Science Funding Lows—and Highs

The Boston Globe’s Robert Weisman reported in April that the city had for the eighteenth consecutive year led the nation in grants received from the National Institutes of Health (\$1.78 billion in 2012), with Massachusetts General and Brigham and Women’s hospitals (Harvard affiliates) and the Medical School (HMS) in the forefront. That such funding is being reined in is a source of worry and vulnerability for the school’s research enterprise. So it was heartening that six of 27 investigator awards announced in May by the Howard Hughes Medical Institute went to Harvard scientists, four of whom

are in medicine. The winners, whose salaries, benefits, and research are underwritten for five years, are: Adam E. Cohen, professor of chemistry and chemical biology and of physics, and Hopi Hoekstra, professor of organismic and evolutionary biology and of molecular and cellular biology, from the Faculty of Arts and Sciences; and professor of systems biology Vamsi K. Mootha, professor of genetics David E. Reich, professor of biological chemistry and molecular pharmacology Johannes Walter, and professor of neurobiology Rachel I. Wilson—all from HMS.