

The Dean's Report





THE DEAN'S REPORT

CONTENTS

FROM THE DEAN	2
ACADEMIC PROGRAMS	6
Education Initiatives.....	6
Curriculum Reform.....	7
RESOURCES	10
Program News.....	10
Endowed Chairs.....	12
Critical Support.....	12
Federal Funding.....	14
DISCOVERIES	16
How the Brain Works.....	16
Controlling DNA.....	18
Corralling Infections.....	20
Obesity.....	22
Fighting Cancer.....	24
Building on Bones.....	26
Cost of Care.....	27
OUTREACH	30
Caring for Communities.....	30
International Impact.....	32
PEOPLE	34
Leadership.....	34
Honors.....	36
Students.....	39
Alums.....	44
In Memoriam.....	47
GIFT REPORT	50
FACTS AND FIGURES	56

FROM THE DEAN

Taking the Long View of the School's Role in Combating Disease

IN WRITING TO YOU, the friends and alumni of Harvard Medical School, I must note upfront what an incredible honor it is to serve as dean of the Harvard Faculty of Medicine, a group that is truly unsurpassed by the scholarly communities at any other medical school in the world.

Upon becoming dean of HMS, an obvious question that confronted me was, Should my focus be to stay the course in order to maintain the excellence of this amazing institution or should I consider a less conservative posture, one that would seek to identify some major new opportunities, even if these might engender some level of institutional change? The real question is, Are we as good as we can be? And if

not, should we be satisfied to simply remain the best?

Although we are delighted that HMS is deservedly held in high regard around the globe, we must remember that the goal of Harvard Medical School is not to win the tournament of rankings. Rather, we seek to combat disease and suffering caused by disease, and there is no shortage of work to be done against this implacable foe. Against this enemy, staying the course is not an option. In addition, the world around us is changing dramatically in many dimensions, and any organization as complex as HMS must, even to remain where it is, continually assess its goals and its strategies based upon the world today and the world that we see developing over



the next several years. We cannot avoid the need for an honest self-assessment, comparing our present state against our highest aspirations. We must be prepared to embrace the potential changes that might be suggested.

So, how do we assess what changes might be needed in response to these challenges?

First of all, we have to remind ourselves that at its core Harvard Medical School is, after all, a medical school. It is an institution whose central identity involves educating medical students, preparing the greatest physicians that it possibly can for leadership positions here and around the world. That fact may sometimes be hard to remember because, as a total organization, the School has a budget for research and operations that vastly exceeds the expenditure for medical education. Rest assured I will insist that medical education receive the attention and resources it requires.

Recently, HMS completed a comprehensive medical curriculum review process that took place over the past several years. The resulting plan is now being implemented (see page 7) and, as dean, I will work with the educational leadership to see that the implementation goes smoothly. If changes are needed, I will do what is necessary to accomplish them. The structure of the clinical years is also being reorganized, with the principal clinical year for each student now taking place around an experience in one of the major hospitals, thereby creating greater coherence and continuity.

I would also like to find a way to implement one of the recommendations of the education reform committees that was put on hold. That specifically was a requirement that HMS students engage in an in-depth scholarly activity. This is something I think is exceptionally important for a school with the aspirations of HMS. Of course, many of our students do engage in scholarly activities. But many more can be helped to engage in an in-depth scholarly experience, which could represent wet-lab research, clinical research, or any number of other scholarly endeavors. The result would be better positioning of our graduates for leadership roles in whatever career path they choose.

One of the primary causes of concern in medical education is the state of indebtedness that many of our students face. I am dedicated to finding ways to increase the financial aid available to them to mitigate the effect that significant debt has on their choice of professional goals. Addressing this issue will leverage the ability of our students to become the leaders that they can and should be.

The School is also one of the greatest sites in the world for graduate and postgraduate scientific training in the biomedical sciences. This kind of training and education is also a part of our core identity and must be kept vibrant and well funded. This is a major challenge in the current environment.

HARVARD MEDICAL SCHOOL, in addition to being an educational institution, is a research institute of amazing size and breadth. The preclinical units of HMS are a series of basic science departments and a smaller number of social science departments. These are outstanding by any criteria, and our faculty is of the highest quality. Keeping our Quad departments at the leading edge, and seeing to it that they are well positioned to respond to scientific opportunities is a wonderful responsibility of the dean.

Similarly, our clinical departments based at our affiliated hospitals and institutes are extraordinary in their size, diversity, and quality. Although HMS does not directly employ the faculty based at these independent institutions, they are very much a part of the faculty of Harvard Medical School, both in my view and in that of the outside community of science.

These Harvard-affiliated hospitals are extraordinary institutions; the five top hospital-based research programs in the United States are all Harvard affiliates. While our hospital-based faculty can, quite effectively, live their professional lives largely within their own hospitals, there is a tremendous desire among them to reach out across the hospitals, to the Quad, and to the University as well. Though this certainly occurs now, the extent to which it occurs can be broadened. I am dedicated to facilitating these interactions between hospital and Quad faculty, since they can only enhance our scientific impact.

WHEN CONSIDERING OUR OVERALL status as a faculty of medicine, we can therefore ask several important questions. Despite our excellence, are we optimally organized in the current environment to

- take full and maximal advantage of the most exciting aspects of modern science;
- interact most effectively as a faculty based on the Quad and at the affiliated hospitals and research institutes;
- interact robustly with the other schools of Harvard University;
- take full advantage of physical and financial resources of the Medical School; and
- effectively mentor and develop our faculty?

I believe the answer to these questions is no; we are not yet where we need to be. We need to seize more opportunities in the current whirlwind advance of basic science, collaborate more consistently across departments and institutions, and more optimally utilize our available resources. We need to aggressively augment the mentoring we provide our faculty and the leadership opportunities we afford them.

These will need to be long-term goals that we work on consistently for the foreseeable future. Yet there are some immediate issues that I face and that the School faces, which give some indication of what paths I think HMS

should embark upon soon.

The first is the Clinical Translational Science Award, a mandate from the National Institutes of Health to consolidate much of the clinical and translational research across our community. Each of the Harvard major teaching hospitals—Massachusetts General, Brigham and Women’s, Children’s, and Beth Israel Deaconess—has a General Clinical Research Center, and each hospital has maintained its center through competitive funding for the last 30 to 40 years. NIH has paid millions of dollars a year to offset the cost of beds, nursing, nutritional support, administrative support, and physical structures in which certain kinds of studies can be done that otherwise would be impossible to do.

During my early career at Harvard, I virtually lived out of the General Clinical Research Center at the then Beth Israel Hospital. I was interested in understanding why some people were insulin resistant. These patients were often referred to me because I became known as an expert in the area, and I would admit them to our General Clinical Research Center. While studying these patients, I was able to have nurses take blood specimens, assess the response to insulin infusions, remove blood cells for studies in the lab, and precisely control their nutritional intake. I would not have been able to do these studies without the GCRC, and there are hundreds of other investigators like me.

The problem is that these centers became a bit administratively ossified—in part because of the structure NIH put in place. It became difficult to innovate. In addition, there was very limited ability to collaborate between the distinct Harvard-affiliated GCRCs. NIH hinted at the need for change for many years, but nothing happened. And then a couple years ago NIH director Elias Zerhouni, through his roadmap initiative, announced that all of these centers would be ended by 2010, and institutions would either lose them or need to roll them into a new kind of grant. This is the Clinical Translational Science Award (CTSA), which aims to incorporate previous General Clinical Research Centers while adding many other required elements related to education and career development for clinical and translational

researchers, outreach to the community, and regulatory support. The goal is to transform clinical and translational research both as a practice and as a career path.

The catch is that Harvard can only have one CTSA. This is the first time that there would be a cooperative, broad-ranging clinical research initiative across Harvard with the exception of the Dana–Farber/Harvard Cancer Center. But the new organization would be on a much broader scale and would be unique in that the Medical School itself would be the recipient of the grant. The new entity would unify aspects of these clinical research centers in all the hospitals; for example, if an investigator at Massachusetts General needed equipment and capacity that only resided at Beth Israel Deaconess, the researcher would be able to use it without much difficulty—we hope. There would also be a reduction of redundancy

across the centers, and the saved resources would actually be put into more infrastructure, new technology development, support for career development, and pilot grant programs.

The Medical School would oversee the distribution of funds to all of the hospitals and other Harvard schools associated with the grant. There would be an additional \$16 million in new funds committed by each hospital, the Medical School, and the University’s new Harvard University Science and Engineering Committee (HUSEC). The changes to be engendered by this grant would be transformative and the impact on HMS profound.

THE BROAD AND RAPIDLY evolving field of bioengineering also presents Harvard with tremendous opportunity and need. This new wave, including cellular, molecular, and tissue engineering, along with nanotechnology and the more traditional devices and implants, is something that HMS cannot avoid being involved in, in a big way. The Medical School Quad and the University do not have major efforts in this area. There are many important concentrations of research in the hospitals, but they are not coordinated intellectually. In this sense, it is a very propitious time for a new level of commitment and coordination in the field.

**We need to seize
more opportunities in
the current whirlwind
advance of basic science,
collaborate more
consistently across
departments and institutions,
and more optimally utilize
our available resources.**

We are in the early phases now of having discussions among the new School of Engineering and Applied Sciences, HMS, and the Faculty of Arts and Sciences to put together a plan for a very major investment in bioengineering. I hope that one significant part of the new Harvard University Allston campus might be in this area. I am personally committed to this being the case.

ONE OTHER AREA OF opportunity relates to the importance of human genetics today. The field of human genetics has been transformed such that the human organism is now a subject for study in ways that were unimaginable a few short years ago. Many of the important breakthroughs that will lead to understanding, treatment, and prevention of disease will come from these new investigations.

Although there are pockets of excellence in this area of genetics within our Quad faculty, it is not generally a substantial emphasis. We have an extraordinary genetics faculty on the Quad, but its predominant focus is on other, though equally important, questions in biology. Harvard Medical School faculty at our affiliated hospitals, however, include many of the world's greatest human geneticists, and some of them are members of our Genetics Department.

I am now working very closely with an executive committee and Clifford Tabin, our chair of genetics, regarding the future of human genetics across the broad Harvard community. We are developing plans for launching a more coordinated and robust effort in the field, perhaps involving all of Harvard University. Whatever form it finally takes, I believe that with a significant intellectual effort on our part, and with some major investment, we can create an organization for human genetics that will be unrivaled anywhere on Earth.

IAM DEDICATED, AS WELL, to exploring what I refer to as pharmacology, therapeutics, toxicology, and chemical biology. Years ago, all medical schools had departments of pharmacology. Then there was the revolution in cellular and molecular biology, and many such departments left behind

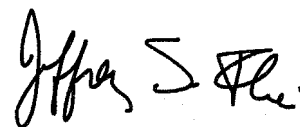
their capacity to develop therapeutics and instead took up molecular approaches to signal transduction and other aspects of cell biology. The results were often, and continue to be,

spectacular science. But there has been an unintended consequence. Just as we are positioned to take greatest advantage of modern scientific breakthroughs to accelerate discovery of new therapies, we find ourselves lacking an identified major program in which people focus on these goals. I think there is an intellectual discipline here that is exceptionally important, and we can seize the high ground with a few additions to our faculty and, perhaps, once again find new ways to involve our hospitals and other schools of Harvard. We could become a leader in the field and, more importantly, have a huge impact on human health.

What are the approaches to these challenges in the short run? We have decided that it is necessary to have a strategic-planning process to engage the community. We will consult broadly across the hospitals, the University, the departments, and the faculty. My conviction, and the reason I am so optimistic about the future, is that when we talk about these issues straightforwardly and openly, the most productive directions we can take to reach our goals will become clear.

I am energized and excited about the possibilities and believe that it will not take a decade to bring about these potential changes. Our efforts, I am sure, will enlarge our capacity to fulfill our shared mission:

To create and nurture a diverse community of the best people committed to leadership in alleviating human suffering caused by disease.



Jeffrey S. Flier, MD
Dean of the Faculty of Medicine



ACADEMIC PROGRAMS

New Harvard Department the First to Span Schools

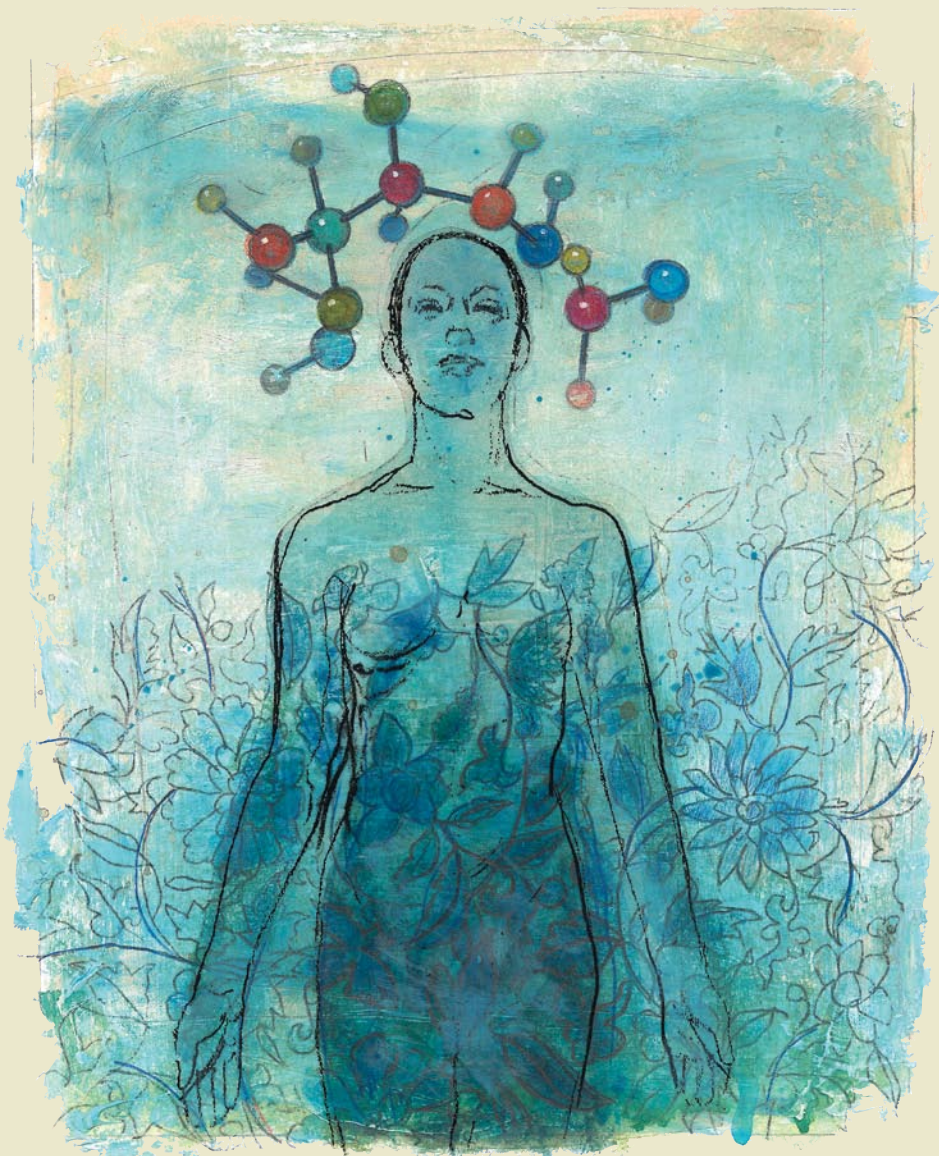
HARVARD UNIVERSITY HAS ESTABLISHED the Department of Developmental and Regenerative Biology, the first in the University's 371-year history to be based in more than one school. Faculty will come from both HMS and the Faculty of Arts and Sciences. The department eventually will be located in the new Allston science facility but is now operating with faculty dispersed at FAS and HMS-affiliated hospitals.

David Scadden, the Gerald and Darlene Jordan professor of medicine at HMS and Massachusetts General Hospital, and Douglas Melton, a Howard Hughes investigator and the Cabot professor of the natural sciences at FAS, will head the

new department. Scadden and Melton are also the founding co-directors of the Harvard Stem Cell Institute, which they say will be strengthened by the new academic organization.

"Creating this department clearly signals that Harvard is going to be bold and is going to lead in forging new connections between basic science and human health," said Scadden.

He explained that the department can "create exciting and unique educational opportunities for students at all levels by bringing these worlds together. Placing it in Allston will create an organizing hub to bring together the medical and Cambridge campuses. It is an experiment. If successful, it may transform the University." ❁



Global Health Residency Fetes First Grads

The Division of Social Medicine and Health Inequalities at Brigham and Women's Hospital honored the first graduates of the Howard Hiatt Residency in Global Health Equity and Internal Medicine, Nancy Lange and David Walton, in a ceremony in May 2007. Founded in 2004, the program is named for Hiatt, professor of medicine at HMS, former dean of the School of Public Health, and the founder and associate chief of the Health Inequalities Program at BWH. The residency gives BWH internal medicine residents an opportunity to focus on culturally competent health care and the reduction of health disparities, including field rotations, while simultaneously fulfilling the requirements for an MPH.

"Through the residency, I've gotten to really see the cutting edge of this growing field," said Lange, who noted that in a traditional residency, she would not have had time to work abroad.

Walton, who graduated

with an MD from HMS in 2003, has worked with Paul Farmer and Partners In Health in Haiti and has researched drug-resistant tuberculosis in the former Soviet Union. Lange, who received her medical degree from Cornell University in 2003, has studied waterborne illnesses in Brazil, participated in an AIDS initiative in Senegal, and worked at the Partners In Health site in Rwanda.

Pictured at the event are (from left) Hiatt; Lange; Farmer, the Maude and Lillian Presley professor of social medicine at HMS; Walton; and Jim Yong Kim, head of the HMS Department of Social Medicine, who is also the François-Xavier Bagnoud professor of health and human rights at HSPH. ✱



Medical Education Reform Enters Year II

The series of vignettes below covers changes in the second year of the new integrated curriculum at HMS.

Anatomy of Patient–Doctor II

Looking at the ongoing Medical Education Reform from an anatomical perspective, Patient–Doctor II forms the spine of the reformed second-year curriculum. PD-II gives students hands-on instruction in how to conduct a physical examination. And according to William Taylor, associate professor of medicine at Beth Israel Deaconess Medical Center and PD-II's director, the new second-year Human Systems course will graft its schedule of basic science instruction onto the teaching schedule followed in PD-II.

Robert Stanton, associate professor of medicine at Joslin Diabetes Center and co-director of Human Systems, describes the coordination: "We talked with Patient–Doctor II and asked, what is the magic order in presenting human systems? What would work best for the way that Patient–Doctor II teaches exams in the hospital?"

Past efforts at coordination achieved a measure of success, ↔

Graduate Program Announced In Translational Medicine

The HMS Division of Medical Sciences will offer a new graduate program in Human Biology and Translational Medicine (HBTM) beginning in the fall of 2008. The program will be under the Biological and Biomedical Sciences umbrella and will be headed by Thomas Michel, a professor of medicine at Brigham and Women's Hospital and a member of the BBS faculty. The program will be taught by faculty from the Quad, affiliated hospitals, and Harvard

University. This new graduate program engages a new cohort of HMS physician-scientists from Harvard's teaching hospitals who have not previously been involved in graduate student education. Joseph Loscalzo, the Hersey professor of medicine at BWH, provided the initial impetus for creating the program and engaged many other members of HMS in the design, including David Golan, professor of biological chemistry and molecular pharmacology and professor of medicine at BWH, and Connie Cepko, Howard Hughes investigator and professor of genetics.

The curriculum for the new course of study will focus on training students in the fundamental mechanisms and essential methodologies of human biology and disease-oriented research. The Harvard-affiliated hospitals are providing support for six BBS graduate students to be admitted to the program each year. HBTM will also connect undergraduate and graduate students and clinical trainees to programs across Harvard for further training in human biology and translational medicine in multiple departments and disciplines. ✱

→ but some topics were taught out of sequence with work done in the PD-II exam room. The best example of curriculum improvement is the presentation of the musculoskeletal system. Teaching students to perform that exam “is now going to be beautifully coordinated with a musculoskeletal medicine segment of Human Systems that’s going to occur early in the second year,” according to Taylor. Under the old curriculum, musculoskeletal science was taught in the spring.

Restitching Tapestry of Human Systems

Second-year pathophysiology historically has resembled a disjointed caterpillar: a series of segmented courses, each moving on its own and not necessarily in sync with the others. Instructors did not make the connections for students between their respective specialties. To reattach and realign the parts, the new curriculum has created one year-long, longitudinal course, Human Systems, that began in September 2007.

Under the old approach, for instance, “When students were taking the gastrointestinal course, they would hear about a patient with chest pain and think, ‘It can’t be a heart attack because we’re taking GI,’” said Barbara Cockrill, assistant professor of medicine at Massachusetts General Hospital, and one of three co-directors, along with Robert Stanton and David Cardozo, for the new Human Systems. Explains Cockrill, “We wanted to make sure that the students had a more real-life approach, where you don’t know why the patient has chest pains,” and it could very well be a heart attack.

To achieve these improvements, all the course instructors planned the new year together, “so the dermatologist knows what the rheumatologist is teaching and can highlight dermatological issues that come up in rheumatology,” Cockrill said. “Then we can look back, and the rheumatologist can say to the students, ‘As you learned in dermatology....’”



In right photo are William Taylor (center), director of Patient–Doctor II, and Robert Stanton (left), who co-directs the closely coordinated course Human Systems with Barbara Cockrill (right) and (in left photo) David Cardozo.

Pharmacology Leads Off Second Year, Plays Role in Human Systems

Beginning with the 2007–2008 academic year, what had been a five-week block on pharmacology in the students’ first year kicked off the second year as a two-week introductory block under course director Carl Rosow, professor of anesthesia at Massachusetts General Hospital. The shorter block, an introduction to basic principles of pharmacology, does not mean short shrift: the principles Rosow and his colleagues teach are elaborated upon in the Human Systems (pathophysiology) courses that follow throughout the second year.

“The pharmacology course isn’t just two weeks,” said Rosow. “There is more pharmacology rather than less, and it is taught in a sequence—alongside pathophysiology—that will, hopefully, be more intuitive for the students.”

Human Development: Why People Do the Things They Do

“Why is it that a 17-year-old would take you up on a dare to drink 38 shots of tequila, but a 35-year-old would not, given that their brains are essentially the same in the regions that exercise good judgment?” asked Steven Schlozman,

assistant professor of psychiatry at Massachusetts General Hospital. Such questions are the stuff of Human Development, the study of changes throughout a person’s life—biological, cognitive, emotional, and moral—that govern healthy maturation.

In past years, this material was distributed among various courses. Now HMS has joined the majority of medical schools, which offer Human Development as a stand-alone course. It takes up one afternoon session a week during a five-week block starting in August of the second year, preceding Psychopathology and paralleling courses in both Pharmacology and then neurobiology (called Human Nervous System and Behavior), taught during the same time frame.

Research suggests that practicing physicians may overlook developmental differences between patients or factors that affect normal development unless the doctors are explicitly trained to do otherwise, according to Schlozman, who co-directs the new course with Jonathan Alpert, associate professor of psychiatry, also at MGH. They will be joined by instructors from throughout the Medical School, reflecting both the

multidisciplinary nature of the field and the technological advances of the last two decades that have enabled the field of human development itself to develop.

Health Policy: The Context for Practice

HMO. PPO. Utilization review. Ask any doctor who has had an insurance company breathe down her neck and she will tell you that being a skilled physician now takes more than correctly diagnosing the patient. The alphabet soup and work-talk of health care financing and policy permeate the examination room as do symptoms and disease.

In September, the formerly elective Introduction to Health Care Policy became a required fall course for students in the new integrated curriculum (with some exceptions such as dental students).

“Health policy directly affects how our students will be practicing medicine when they’re out in the real world,” said Haiden Huskamp, associate professor of health care policy. “Understanding how the policies will affect their clinical decision-making and their patients is important.”

Being deemed educationally essential posed an instant challenge to course directors Huskamp and Barbara McNeil, chair of the Health Care Policy Department: the intimacy of a course that once had only 30 students had to make way for new teaching approaches when upwards of 150 now pack the lecture hall.

“Whereas in the past, every session was taught with the full group of students,” said Huskamp, “now we have more of a lecture format, with case discussions, and then we break up into small groups where students can dig into some of the issues with one or two faculty from around the Medical School.”

Tutorial Format Grows with Students

Tutorials are part of the DNA of Harvard medical education. But it is not unfair, according to David Cardozo, to say that they expect too much free as-

sociation from students—self-propelled learning in a system lacking structure.

“Students would take a paper case of a clinical problem, read it out loud, and investigate different aspects of it,” said Cardozo, an assistant profes-



In the new curriculum, the course on health care policy is now required, which greatly expands enrollment and has necessitated reorganizing the class formats, according to directors Haiden Huskamp (right) and Barbara McNeil.

sor of neurobiology. “The style of the tutorials was unchanged, from the very first case students saw in the first year to the last case they saw in the second year. But the students’ knowledge and skill set had evolved significantly during that time.” The static tutorials did not boost the intellectual challenge in recognition of those higher abilities.

The result? Student assessments reported boredom with tutorials. Moreover, too much was left to student taste in terms of study topics. Recognizing the problem, instructors tinkered with tutorials in recent years. Students and tutors both gave the new approaches an enthusiastic thumbs-up, leading to a group—Cardozo, Julian Seifter, Thomas Aretz, Michael Parker, and Benjamin White—that developed the more structured “developmental tutorials,” which are being

vetted with course directors in advance of a hoped-for debut in the 2008–09 academic year.

The group proposes to replace or augment paper cases with videotapes of real patients. More importantly, tutorials will be integrated under thematic canopies. The tutorials for all courses will touch on the same themes but grow more challenging as students progress through the first and second years, in acknowledgment of their advancing skills.

Toward Evidence-based Pedagogy

“In the same way we talk about evidence-based medicine, we should be making evidence-based decisions about our students and courses,” said Edward Krupat, director of the HMS Center for Evaluation and an associate professor of psychology in the Department of Psychiatry at HMS and Beth Israel Deaconess Medical Center. Like a car on a maintenance schedule, faculty take their courses and clerkships for regularly planned checkups to the center, which Krupat calls “the assessment/evaluation conscience of the Medical School.” The center warehouses voluminous data—from student and peer assessments to outside consultants’ critiques—for the faculty and administration to use. And it provides consultation to faculty seeking better methods of testing students. The center also oversees the Objective Structured Clinical Exam (OSCE) at the end of the second and third years, in which students practice their examination skills on actors posing as patients.

To ensure that curriculum reform is not a faith-based initiative, the center will take its measuring tape to that as well. Krupat has begun surveying current third- and fourth-year students—those who began their medical education under the old curriculum—to learn how well that curriculum met their needs. And he will do the same for students in the first two years of the new curriculum. All those surveyed will be followed up until their graduation and perhaps beyond. ❖

RESOURCES

Gifts Honor Former Dean, Rename Conference Areas

TWELVE MEMBERS OF THE HMS Board of Fellows raised more than \$12 million to benefit the Medical School community in honor of Joseph Martin, who stepped down as dean of the Faculty of Medicine in June 2007 after 10 years of service. Among the farewell tributes to Martin at the end of his decade-long tenure was the establishment of the Joseph B. Martin Scholarship Fund. The fund will provide financial aid to selected MD students, who will be known as “Martin Scholars.” The Board of Fellows raised both current and endowment gifts totaling over \$3.6 million, and an additional anonymous donor contributed an endowment gift of \$2 million, for a total of more than \$5.6 million for this scholarship fund.

In addition to the scholarship, the donations will fund

a professorship in Martin’s honor, the Joseph B. Martin Professorship in Basic Research, and the Technology Development Accelerator Fund, which backs the development of new technologies in the life sciences generated by Harvard investigators. In a further show of support, Board of Fellows member Maurice Pechet, together with his wife, Kitty, and sons, Tiron and Taine, sponsored the renaming of the HIM conference room the Pechet Family Conference Room.

Together, these contributions also allowed for the renaming of the Conference Center at Harvard Medical in the new research building, the Joseph B. Martin Conference Center. The center was officially dedicated in a ceremony in October 2007, which included the burial of a time capsule that was created when the building opened in 2003. ❁



Countway Reinvents Library As Center for Informatics

The Countway Library's fourth floor has been transformed into an expansive and airy meeting place—the new home of the Center for Biomedical Informatics. “It will be a real workplace with an emphasis on openness and collaboration,” said Alexa McCray, associate professor of medicine and co-director of the center along with Isaac Kohane, the Lawrence J. Henderson associate professor of pediatrics and health sciences and technology. McCray is deputy director and Kohane is director of Countway Library.

The pair, working with colleagues, conceived of the center two years ago as a place for clinicians and researchers to come together to engage in multidisciplinary translational research. The idea was that in an age of burgeoning information, the opportunity has never been greater for finding cures to disease. Yet because the information is coming in from so many different sources and in such different forms, finding meaningful patterns in the data has been a real challenge.

During renovations the center remained available to researchers working on projects such as the Autism Consortium, whose goal is to better understand and treat autism. The Boston-wide consortium plans to enroll 1,200 families affected by autism and to collect genetic and behavioral information, as well as

History Center Expands Its Reach

The Center for the History of Medicine, on the lower level of Countway Library, is regarded as having one of the most extensive collections of rare books, personal papers, and archives in the world, available to any researcher. Director Scott Podolsky (right), who joined the center in December 2006, is helping to bring these collections to the attention of researchers worldwide.

Of particular interest are the manuscripts and personal papers of physicians and scientists that have been donated to the center. “Of these tremendous manuscript collections that we have, and we have over 900 written manuscript collections ... most of those are relatively invisible to researchers and clinicians,” said Podolsky, who is a member of the Social Medicine Department and an internist at Massachusetts General Hospital.

One way the center intends to reverse this is by going digital. A high-priority



project is to increase the number of “finding aids” online, which alert researchers to items in the center's collection when they type relevant terms into a search engine. Podolsky is also approaching current faculty on the Quad and at the affiliated hospitals about donating their personal papers to the center.

In addition, the center's staff is reaching out to HMS departments and committees and advising them on how to store papers and materials for short-term use and telling them how to take advantage of the center's archives for historical use. ❀

imaging and epidemiological data.

The center's staff, including people with backgrounds in bioinformatics, computer science, clinical medicine, and library science, is developing hands-on bioinformatic tools that the autism researchers and others can use to analyze data.

Meanwhile, McCray and her colleagues are dreaming up other ways to bring people together. “We have this cool idea of a matchmaking service whereby if I'm a researcher and I'm interested in collaborating with, say, a biostatistician, we'll have a database of people who are willing to collaborate,” she said. ❀



Joseph Martin, former HMS dean, cuts a ribbon at the ceremony renaming the new research building conference center in his honor. With him are HMS dean Jeffrey Flier (center) and HMS Board of Fellows chair Jack Connors.

Genomics Extended At the Broad

The Broad Institute of MIT and Harvard received two grants in genomics during the 2006–2007 academic year, totaling nearly \$300 million.

In November 2006, the Broad received a nearly \$200 million four-year competitive renewal grant for large-scale DNA sequencing. The funding, from the National Human Genome Research Institute (NHGRI), is supporting a ➔➔➔

Endowed Chairs

As a Quad-based endowed chair, the **Steven P. Simcox, Patrick A. Clifford and James H. Higby Professorship** will support the mission of the Medical School through patient and consumer education, said then HMS dean Joseph Martin, opening the chair celebration in November 2006. The first incumbent is Anthony Komaroff, editor in chief of Harvard Health Publications. Donor Steven Simcox described him as a master communicator, educator, clinician, and businessman. When he had stepped up to the microphone, Komaroff explained that he is by nature a generalist; fields of interest stretch as far as the eye can see. He is convinced, he said,



considering the breathtaking sweep of recent advances in communication and biomedical technologies, “This is really the most exciting time in the history of medicine.” He appears above with his wife, Lydia Villa-Komaroff.

Following Joseph Martin, then HMS dean, who opened the May 2007 speaking program for the new **Augustus Thorndike, MD, Professorship in Orthopedic Surgery**, Peter Slavin, president of Massachusetts General Hospital, described the chair’s namesake as one who “probably did more than any other physician to advance the field of sports medicine.” After graduating from HMS in 1921, Augustus Thorndike, now deceased, became an orthopedic surgeon and immersed himself in sports medicine at a time when the field did not yet exist. Slavin said that he was confident the first incumbent, →

HIV Vaccine Work Gains Millions from NIH, Gates Fund

The HIV Vaccine Trials Unit at the Medical School, a member of the National Institutes of Health–supported HIV Vaccine Trials Network, was awarded seven years of funding in spring 2007 during a recompetition from the National Institute of Allergy and Infectious Diseases. The award totals \$12 million with supplemental support expected for the larger vaccine studies. The unit, whose principal investigator is Raphael Dolin, the Maxwell Finland professor of medicine (microbiology and molecular genetics) and dean for academic and clinical programs at HMS, was funded by the NIAID for the previous seven years.

One of the interesting aspects of the grant, said Dolin, is its multi-institutional organization. Though based at HMS, the unit runs clinical studies at Brigham and Women’s Hospital under the direction of Lindsey Baden, an assistant professor of medicine, and at Fenway Community Health in Boston, under Kenneth Mayer. Michael Seaman, an assistant professor of medicine, directs the unit’s laboratory, located at Beth Israel Deaconess Medical Center.

“The unit conducts clinical trials of candidate HIV vaccines in healthy

volunteers,” Dolin said. “We do phase I, II, and larger IIb trials. The initial trials study safety and immunogenicity of candidate vaccines, and the larger trials are intended to look at efficacy.”

According to Dolin, the vaccines being studied are preventive approaches to HIV infection and disease, emphasizing stimulation of T cell immunity. The most advanced candidates are based on either DNA or adenovirus, both types resulting in the introduction of HIV proteins into the body to spark an immune response. The unit also is looking at combination vaccines that use a two-pronged “prime–boost” approach to provoke immunity. One of these candidates, which has recently completed phase I testing, utilizes the adjuvant effect of interleukin-2 fused with IgG and was developed by Norman Letvin, professor of medicine, and Dan Barouch, associate professor of medicine, both at BID.

“We look at the efforts of this unit as part of a community response to control AIDS and to develop an HIV vaccine,” Dolin said. “It’s a tough scientific problem, but it’s the best hope for control of this dreadful pandemic.”

The previous summer, HMS →→

→ variety of projects. One is The Cancer Genome Atlas Pilot Project, which is working to identify mutations associated with certain cancers. The project is jointly funded by the NHGRI award and a grant from the National Cancer Institute.

The Broad is also sequencing the genomes of mammals such as the mouse, dog, horse, and elephant. When the work is completed, scientists will be able to compare the results to the human genome and identify DNA sequences that have been conserved over time and across species, which may shed light on human biological functions.

The grant also supports genomic studies of microscopic organisms

such as bacteria and viruses and the development of more efficient large-scale DNA sequencing.

In March 2007, the Stanley Medical Research Institute pledged \$100 million to the Broad to establish a research center at the institute that will combine genomics and chemical biology to advance the understanding and treatment of severe mental illnesses such as schizophrenia and bipolar disorder. The gift will fund the center for the next 10 years and will allow the institute to expand its current psychiatric disease research. Edward Scolnick, senior lecturer on genetics, has been named director of the center. ❖

→ investigators were prominently represented among the 165 scientists from 19 countries who were part of the new Collaboration for AIDS Vaccine Discovery, funded by 16 grants from the Bill & Melinda Gates Foundation. Announced in July 2006, the \$287 million in awards created an international network of collaborative research consortia to accelerate the pace of HIV vaccine development.

In the program, Norman Letvin serves as principal investigator of a five-year, \$18 million grant for work on vac-

cines utilizing adenovirus and mycobacteria vectors. Dan Barouch and Michael Seaman, along with Raphael Dolin, also received significant Gates funding as members of this and other teams.

“It’s been only 25 years since the first cases of AIDS were identified,” said Letvin. “Yet in this brief period of time, HIV has taken an unthinkable toll on the human population.

“It’s clear that the need for cooperation and shared scientific resources among the world’s AIDS researchers has never been more urgent.” ❄

→ Bertram Zarins, would “aggressively carry Dr. Thorndike’s legacy further down the field.”

Created by a gift from the Warren Alpert Foundation in honor of Joseph B. Martin, MD, PhD, dean of the Faculty of Medicine from 1997 to 2007, the **Joseph B. Martin Professorship in Basic Research** will support a faculty member, still to be named, in any one of the basic science departments at HMS. The endowment will be augmented through the Harvard University Professorship Challenge Fund. The Alpert Foundation was established by Warren Alpert, a longtime supporter of medicine and biomedical science who passed away in 2007.

The **Roman W. DeSanctis Professorship in Medicine** was celebrated in November 2006, with William Dec, chief of the MGH Cardiology Division, as the first incumbent. A friend and former classmate of Dec’s at Johns Hopkins Medical School, Laurence Friedman, traced Dec’s educational and professional path. One underlying message was that “it is never about Bill.” During his remarks, Dec passed the compliments on to DeSanctis, saying that no MGH physician has more loyal or grateful patients. →

Harvard Grants Provide Gap Funding, Accelerate Research

The first recipients of grants from the Technology Development Accelerator Fund were announced by Harvard’s Office of Technology Development (OTD) in June 2007. Established by the Office of the Provost and OTD, the Accelerator Fund supports the development of new technologies in the life sciences generated by Harvard investigators. New technology arising from academic research is typically at an early stage and therefore often considered premature for funding from traditional sources—industry in particular. The Accelerator Fund was established to fill this gap and enable scientists to advance their inventions more quickly from the research stage to the development stage, which may allow them to get products into the marketplace faster.

Out of six projects chosen from a total of 27 applications received from the Harvard research community, five originated at HMS. These five, which received a total of \$1.2 million, include Suzanne Walker, professor of microbiology and molecular genetics, for her project “OGT Inhibitors to Treat Diabetic Complications”; Pamela Silver, professor of systems biology, for “Improving Binding Efficiency of Protein-based Therapeutics”; Arlene Sharpe, the George Fabyan professor of comparative pathology, for “Modulating

the Immune Response to Treat Disease: PD-1 Small Molecule Modulator Screening”; José Halperin, associate professor of medicine, and Gerhard Wagner, the Elkan Blout professor of biological chemistry and molecular pharmacology, for “Translation Initiation Inhibitors for Cancer Therapy”; and Stephen Harrison, Howard Hughes investigator and professor of biological chemistry and molecular pharmacology and of pediatrics at Children’s Hospital Boston, and Gary Frey, research fellow in biological chemistry and molecular pharmacology, for “Fusion Inhibitors for HIV.” ❄

At the celebration of the Alice and Rodman W. Moorhead III Professorship of Neurobiology are (from left) first incumbent John Maunsell, Alice Moorhead, then HMS dean Joseph Martin, and Rodman Moorhead. The Moorheads are longtime supporters of brain research.



→ The **Giovanni Armenise–Harvard Professorship in Basic Biomedical Sciences** will fund the work of a faculty member in the HMS Department of Biological Chemistry and Molecular Pharmacology. No incumbent has yet been announced. The professorship aims to advance investigation that transcends traditional departmental boundaries and supports collaborative initiatives with Italian scientists and biomedical research conducted in Italy. The source of the funding is the Giovanni Armenise–Harvard Foundation for Scientific Research, created in 1995 by the Italian Count Giovanni Auletta Armenise in the name of his uncle.

Established to support scientific interaction between the Giovanni Armenise–Harvard Foundation and Massachusetts General Hospital, the **Giovanni Armenise–Harvard Foundation Professorship in Neurology**, based at HMS, will promote collaborations in neurology between Italian and Harvard scientists. Though not yet named, the first incumbent will be on the faculty at MGH.

The June 2007 reception for the **Victor J. Dzau Professorship in Medicine at HMS and Brigham and Women’s Hospital** marked two milestones at the Medical School. One was the establishment of this endowed chair in cardiovascular research and, as Eugene Braunwald, the Hersey distinguished professor of medicine, pointed out, the second was the culmination of Joseph Martin’s decade as HMS dean in leading the celebration as his last official act. “Included among his many accomplishments is his strengthening of the ties between the Medical School and the hospitals,” Braunwald said. In describing Victor Dzau, who is the former head of the Department of Medicine at BWH and currently chancellor for health affairs at Duke University, BWH president Gary Gottlieb said the cardiovascular researcher was “among the Brigham’s greatest minds.” During his remarks, Dzau said the intention of the chair is to “impact cardiology for many years to come,” and he called himself privileged that Marc Pfeffer is the first incumbent.

When it was his turn to speak at the June 2007 celebration of the **Morton N. Swartz, MD, Academy Professorship**, Dennis Ausiello, the Jackson professor of clinical medicine at Massachusetts General Hospital, captured the tone of the event, saying, “We are here today celebrating a legend and a legend in the making.” Chair namesake Morton Swartz, a 1947 graduate of HMS, has been a professor of medicine at the School and MGH since 1970. Stephen Calderwood, HMS ’75, the first incumbent of the chair, is an investigator and teacher in microbial pathogenesis and infectious diseases at HMS and MGH. The professorship is the second for the Academy, both recognizing the importance of education. When Swartz took the mike, he began with a confession about his role in a flash flood at Vanderbilt Hall when he was a medical student, a story that led into a brief physics lesson and culminated in a testament to Calderwood’s creative achievements. Calderwood returned the favor, insisting that the day was an honor to Swartz. →

Center Funded for Mapping Cancer Genome

HMS, in conjunction with Brigham and Women’s Hospital, is one of seven institutions that received funding from the National Cancer Institute in October 2006 to establish a Cancer Genome Characterization Center (CGCC). The centers are part of The Cancer Genome Atlas Pilot Project, which is testing the feasibility of using large-scale genome analysis technologies to identify important genetic changes in certain cancers. The centers will work together toward accomplishing this goal.

Participating HMS scientists include George Church, professor of genetics; Jonathan Seidman, the Henrietta B. and Frederick H. Bugher Foundation professor of genetics at HMS; Raju Kucherlapati, the Paul C. Cabot professor of genetics at HMS and director of the Harvard Medical School–Partners HealthCare Center for Genetics and Genomics; Isaac Kohane, the Lawrence J. Henderson associate professor of pediatrics and health sciences and technology at HMS and Children’s Hospital Boston; Peter Park, assistant professor of pediatrics at CHB; Samuel Aronson, director of information technology at the HMS–Partners Center for Genetics and Genomics; and Lynda Chin, associate professor of dermatology at Dana–Farber Cancer Institute. The HMS center will receive \$1.7 million over three years. ✱



George Church



Raju Kucherlapati

Center of Excellence in Genomics Established at Dana–Farber

In August 2007, Dana–Farber Cancer Institute received a \$16 million grant from the National Human Genome Research Institute (NHGRI), part of the National Institutes of Health, to establish a new Center of Excellence in Genomic Science. The NHGRI program funds multi-institution, interdisciplinary teams working toward advances in genomic research.

The DFCI center, led by Marc Vidal, associate professor of genetics at DFCI, is testing the hypothesis that both human genetic variations

HMS Lends Muscle to Raising NIH Budget

Flat NIH funding is threatening the progress of biomedical research, says a new report authored by representatives from nine scientific and medical institutions, including HMS. The report discusses advances made during times of robust funding and how the current funding, nearly level since 2003, has not kept up with inflation. Researchers from around the country explain that stagnant funding has already slowed progress in developing treatments for ailments such as cancer and spinal cord injuries. “The number of drugs moving into the pipeline that are based on our new, more profound genetic and molecular understanding of cancer is extraordinary—and there’s no money to handle the testing of these compounds,” said Joan Brugge, professor of cell biology and chair of that department.



Joan Brugge speaks before a Senate committee.

Titled *Within Our Grasp—Or Slipping Away? Assuring a New Era of Scientific and Medical Progress*, the report was released on March 19, 2007, the same day a Senate Appropriations Committee hearing was called to discuss the NIH budget. Brugge was one of four scientists to testify about the hardships caused by the lack of increases at the NIH. To view the report, visit http://hms.harvard.edu/public/news/nih_funding.pdf.

In addition, a new website, Science Progress, also went live on the 19th to support efforts to increase the NIH budget. The site illustrates the benefits of committed NIH funding, telling the stories of HMS researchers in their development of new therapies. Other stories on HMS research are continually added to the site (<http://scienceprogress.hms.harvard.edu>). ❖

and pathogens, such as viruses, can influence cellular networks to cause disease.

Using viral infections as a model, Vidal and colleagues investigate how genetic and environmental disruptions in complex cellular networks interact to cause disease. Specifically, the team analyzes network-level disruption and protein–protein interactions in cells caused by particular viruses and applies what is learned to genomewide variation datasets for related human diseases. The ultimate goal is to develop better models for interpreting genomewide genetic variations involved in disease. The DFCI team will collaborate with colleagues from HMS, Brigham and Women’s Hospital, and the University of Notre Dame. ❖

→ The March 2007 celebration of the **George Jacob and Jacqueline Hazel Leder Professorship**, named after the parents of the founding head of the Genetics Department, Philip Leder, rose to a celebration of the department as a whole. The first incumbent of the new professorship, Clifford Tabin, took over from Leder as Genetics Department head in January 2007 (see page 34). After an introduction by Joseph Martin, then dean of HMS, genetics professor Connie Cepko called Leder and Tabin “great scientists” and “absolutely wonderful human beings.” She said that Leder was very supportive from the start, and as a measure of his encouraging style, the department maintains about an 80 percent tenure rate with about 25 percent of the senior faculty being women. When Tabin took the lectern, he said about Leder that “the entire Medical School is indebted to him.” Leder, the John Emory Andrus professor of genetics, closed the speaking program with some history about his parents who, he said, lived a classic Ellis Island story. “My parents would have been very proud of the Leder professorship,” he said. And turning to Tabin, he added, “It is a gift that will first be fashioned by you.”

The November 2006 program announcing the **Gerald and Darlene Jordan Professorship in Medicine at Massachusetts General Hospital and HMS** was a celebration not only of the donors and the first incumbent, David Scadden, but also of the field of investigation the chair supports, stem cell biology. In his opening remarks, Joseph Martin, then dean of the Faculty of Medicine, commented that private donations are especially important in this area. MGH president Peter Slavin said that Scadden and the Jordans have brought MGH and HMS closer together in establishing this professorship and have helped position Harvard as a leader in stem cell research.

In their remarks at the November 2006 ceremony announcing the **Stephen B. Kay Family Professorship in Medicine**, both Joseph Martin—then HMS dean—and Dana–Farber president Edward Benz called attention to the longtime support the donors had given to Harvard and its medical community. Martin cited the Kay family’s contributions to the Harvard School of Public Health, Harvard Business School, and the University in addition to the Medical School. Benz explained that backing of DFCI by the Kays has gone well beyond service on the board. Benz also introduced the first incumbent, Robert Mayer, as “the leading gastrointestinal oncologist,” who, among other leadership roles, directs the Dana–Farber/Partners hematology–oncology fellowship program. Culminating the talks, Stephen Kay concluded, “You can’t fix the world, but you can get a lot of leverage helping Dana–Farber and Harvard Medical School.” ❖

DISCOVERIES

How the Nose Knows

Unexpected Complexity Seen in Odor Signal

IN MANY SENSORY SYSTEMS, lateral connections between neurons are thought to be inhibitory, carefully fine-tuning responses to the environment. But a new study by Rachel Wilson and her colleagues suggests that the olfactory system may disobey this rule. Rather than naysaying, the majority of lateral connections appear to be excitatory.

Smell begins when odor molecules bind to olfactory receptor neurons, which are located in the nasal passages in humans and other vertebrates, and in the antennae of insects. Receptor neurons then pass the information to tangles of neurons in the brain, the glomeruli, but they do so in a specific fashion: each type of receptor neuron relays information to a particular glomerulus. Since a single odor can bind to several different kinds of receptor neuron, it can activate multiple glomeruli.

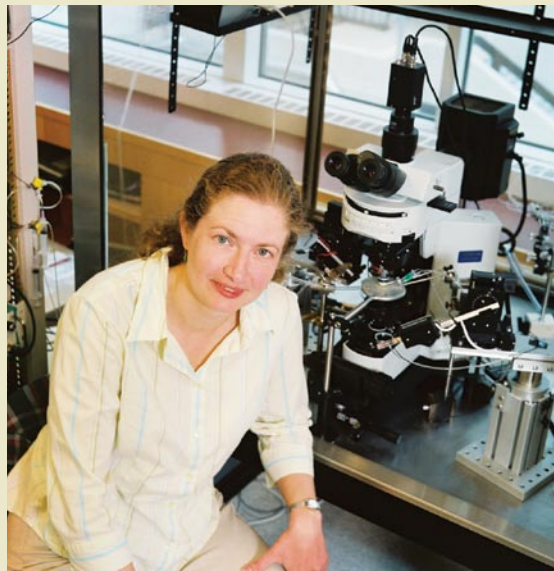
“People didn’t really understand to what degree glomeruli represent isolated information channels versus an interconnected network,” said Wilson, assistant professor of neurobiology. She and her colleagues examined the cross-talk between channels in flies and were surprised to find predominately excitatory connections. Their

findings appear in the April 5, 2007, *Neuron*.

Though the functional meaning of these excitatory connections is unclear, clues may come from watching how flies behave in response to odors when lateral excitatory connections are disrupted.

Behavior was at the center of another recent study by Wilson and her colleagues. She and research fellow Michelle Schlieff wanted to understand how the brain responds to pheromones, chemicals that trigger innate behavioral responses, such as mating. They found that pheromone-sensitive olfactory receptor neurons connect with highly specialized circuits in the brain. Neurons that were located a synapse or more away from finely tuned pheromone-selective cells were also extremely sensitive to that pheromone. On the other hand, receptor neurons specialized for a plant odor, geranyl acetate, connected with broadly tuned higher order neurons. The findings appear in the May 2007 *Nature Neuroscience*.

Pheromones are explicit signals that have evolved to trigger a stereotyped behavioral response. But the reaction to other odors can change depending on context. ❄



Rachel Wilson uses in vivo electrophysiological recordings and behavioral tests in drosophila to probe the functional architecture of the olfactory system.

Brain Size and Signal Decline With Advance of Schizophrenia

Schizophrenia was once considered to be a life sentence: once you were diagnosed, the damage was already done. But an HMS study hints at a future when therapeutic interventions might interrupt this debilitating illness.

Dean Salisbury, associate professor of psychiatry at McLean Hospital, and Robert McCarley, professor of psychiatry

at the VA Boston Healthcare System, have found both structural and functional evidence that schizophrenia is a progressive disorder, according to their study in the May 2007 *Archives of General Psychiatry*. “This changes our view of the disorder ... and could possibly lead to a therapy that could arrest the course of schizophrenia,” said McCarley.

Researchers have debated whether or not schizophrenia, which attacks both the frontal and temporal lobes

of the brain, is set at birth or develops over time. Previous magnetic resonance imaging (MRI) studies of schizophrenic patients showed no progressive changes in the brain. But a few studies near patients’ first hospitalization did show a change in brain size. Still, the results were controversial—stronger evidence was needed.

What researchers sought to uncover was a decrease in brain size corresponding to the loss of brain function. ↔

Study Links DNA Variants To Multiple Sclerosis

Ever since multiple sclerosis was first described in 1868, the cause of this persistent but unpredictable disease has been unclear. MS is partly heritable, but it seems also to require environmental triggers that spur the body to attack the insulation of its own nerve cells. Scientists have speculated that the genetic component of the disease might involve dozens of different gene variations, all contributing a small amount of risk. So far, it has been difficult to verify such low-lying culprits.

A large-scale genomic study, published in the Aug. 30, 2007, edition of *The New England Journal of Medicine*, uncovered new variations associated with the disease. The study—the most comprehensive analysis of the genetic basis of MS to date—was led by a consortium of investigators at several universities and medical centers, including HMS, the Broad Institute, and Brigham and Women’s Hospital.

Until the findings were published, the only genetic link for MS that had been verified using traditional →→



→→ Salisbury and McCarley found just that—a tight correlation between a brain wave called mismatch negativity (MMN) and the volume of the Heschl gyrus, a section of the temporal lobes.

MMN brainwaves, caused by auditory cues, are tested by playing a series of identical beeps, with an occasional “oddball” beep thrown in. The brain automatically responds to this differ-

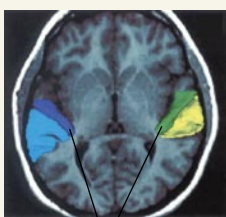
ence by producing an MMN, which originates from the Heschl gyrus.

In a series of three experiments spanning 18 months, Salisbury and McCarley found that schizophrenics’ MMN waves were initially normal but quickly diminished over time. In one test group, 14 out of 16 schizophrenia patients displayed an MMN decline over time, and in an additional test, 11 out of 11 subjects showed

a combined decrease in Heschl gyrus volume and MMN response.

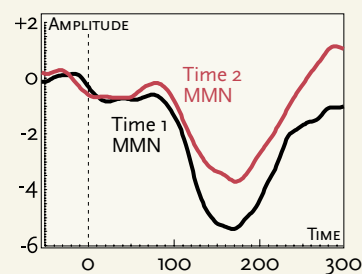
While the sample sizes were relatively small, the researchers noted that long-term studies with the psychiatrically ill can be difficult—half of their subjects never returned for further tests. Salisbury and McCarley are following up with another study of new patients as a replication sample. ✱

Normal Human Brain



Heschl gyrus

Brain Wave Amplitude in Schizophrenia



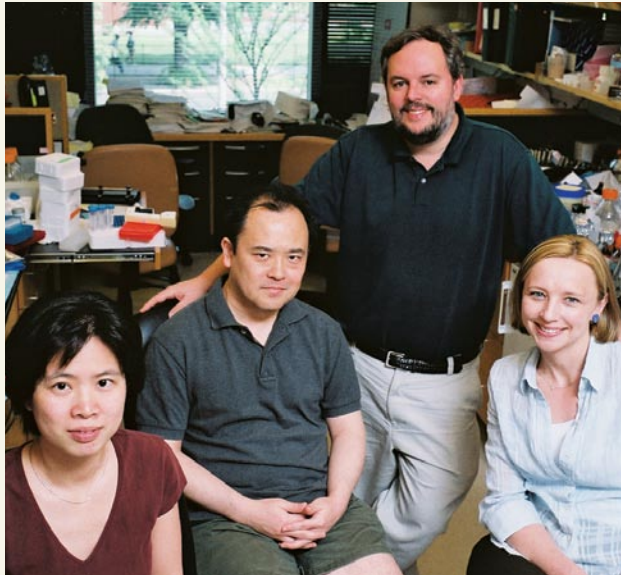
A measure of mental illness. A schizophrenic’s brain at first hospitalization looks like this normal brain (far left), showing no abnormalities in the left or right Heschl gyrus. In schizophrenics after 20 months, however, these areas decreased in size. Similarly, the schizophrenics’ MMN brain wave amplitude (near left) dampened considerably from first hospitalization (Time 1) to 20 months later (Time 2).

Hundreds More Players Spotted on DNA Repair Team

Studies Flesh Out Body's Preventive Steps Against Cancer, Other Diseases

A surprisingly vast molecular emergency team responds to the everyday nicks and dings in our DNA caused by chemicals, foods, oxygen byproducts, and radiation including sunlight, according to a study that expanded the sparse ranks of known DNA damage-response proteins from a couple dozen to a legion of more than 700.

“A cell spares no expense to modulate everything it needs to, to make sure it can optimally repair the genome,” said senior author Stephen Elledge, a Howard Hughes investigator and the Gregor Mendel professor of genetics and of medicine.



In the lab of Stephen Elledge (standing), Shuhei Matsuoka (seated, center) discovered that an unexpectedly long list of proteins respond to DNA damage. The list helped colleagues Agata Smogorzewska (right) and Bin Wang (left) uncover new molecular details on a devastating childhood condition and an inherited form of breast cancer.

“We have a much more expansive view of what cells do now when they are threatened by a broken chromosome or other insults to the DNA. It’s a much broader landscape than we anticipated.”

“The list,” as the research team refers to the new database, includes the usual suspects, such as BRCA1. When defective, this protein may confer such a high risk of breast cancer that some women with certain gene variations and

a strong family history of the disease choose prophylactic mastectomies. The database also contains surprises. For instance, an insulin-signaling pathway shared so many players that the researchers wonder if chronic DNA damage contributes to diabetes and other age-associated metabolic disorders.

The list may speed research into the DNA damage response and related diseases, including cancer, said postdoctoral fellow Shuhei Matsuoka, first author on the paper. For the study, he started at the top of the signaling network by asking which proteins do the DNA damage sensors call into action. The comparative analysis between damaged and undamaged cells relied on new mass spectrometry techniques developed by Steven Gygi, an associate professor of cell biology and the paper’s co-senior author.

The function of many of the known proteins has an obvious connection with DNA damage—especially the ones playing some part in replication, recombination, or repair. The big surprises are the proteins in other functional categories, such as RNA transcription and processing and protein metabolism, modification, and trafficking. ❄

↔ techniques is in the region encoding human leukocyte antigens (HLAs), a large cluster of genes responsible for preventing the immune system’s T cells from attacking the body’s own tissues. This analysis confirmed that HLA is the dominant genetic link, but went further to pinpoint two others. These genes are involved in the immune system, lending another piece of evidence to the widely accepted hypothesis that MS is an autoimmune disease. One encodes the interleukin-2 (IL-2) receptor, which has also been linked to two other autoimmune diseases: type 1 diabetes and Graves disease.

“This study will likely spur further research into the connection between these seemingly separate conditions,” said David Hafler, the Jack, Sadie, and David Blackstone professor of neurology.

The other region harbors a gene for the IL-7 receptor, which helps control the activity of a class of immune cells called regulatory T cells. The same variant was also linked to MS in two papers appearing simultaneously in *Nature Genetics*.

The genes account for just a small amount of individual risk, but they point to molecular pathways underlying the disorder and potential treatment targets. The consortium is planning to dig deeper by collecting larger numbers of samples and scanning the genome more comprehensively. “We’ve begun to find genes,” Hafler said, “but there will be many more.” ❄

Small Stretches of RNA Regulate Neighboring Genes

Until recently, there was no reason to believe that genes lying in proximity along a chromosome had much to do with one another. But in the last five years, Isaac Kohane, the Lawrence J. Henderson associate professor of pediatrics and health sciences and technology, and others have discov- ↔

Protein Plays Role in Reproduction, Skin Regeneration

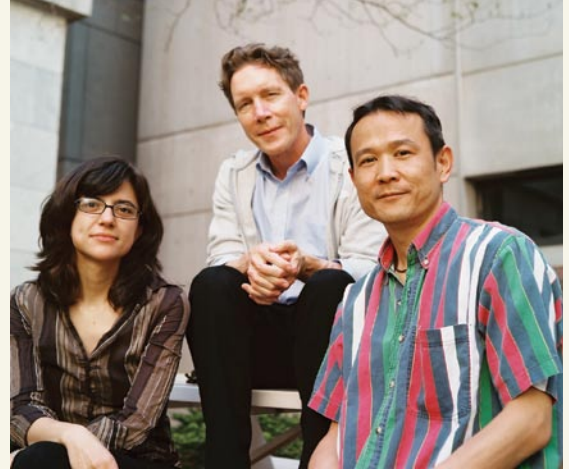
Though humans have been preoccupied with the mystery of female fertility, there is a facet that has been largely ignored. Baby girls are born with a finite supply of nascent egg cells, or oocytes. To become fully viable, an oocyte has to divide twice, the first time just after the chromosomes have doubled and carried out their characteristic crossing over and recombination. Yet oocytes essentially stop all activity soon after their chromosomes have mixed and matched. Beginning at puberty, one or a few of the cells are chosen each month to undergo the first division. They will divide for the second time only if fertilized.

“It is a remarkable suspended animation that we know very little about—it is really a major unanswered question in biology,” said Frank McKeon, professor of cell biology. Even more confounding, in 1961 a Danish researcher showed that

these arrested oocytes are easily damaged by ionizing radiation, which raises the question: how does this population of vulnerable and essential cells maintain its integrity? McKeon and his colleagues have hit upon a surprising answer.

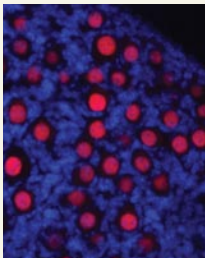
Other cells depend on the well-known protein p53 to monitor and weed out errors, and many scientists assumed p53 would play the same role in oocytes. McKeon and colleagues have discovered the job is actually carried out by a closely related protein, p63. The findings, which appear in the Nov. 30, 2006, *Nature*, could lead to a new understanding of why some women are infertile and how they might be helped.

P63 may hold the key to an equally critical, though very different process, namely the skin’s ability to replace the tissue it sloughs off. McKeon and his colleagues found that p63 plays a critical role in maintaining a steady pool of regenerative epithelial stem cells, most likely by enhancing the potential of the stem cells to divide.



From left, Filipa Pinto, Frank McKeon, and Makoto Senoo showed that stem cells with a certain mutant protein have an impaired ability to proliferate and regenerate skin tissue.

“The fact that p63 is essential for these epithelial stem cells, while other master regulators have been identified for blood stem cells and spermatocyte stem cells, suggests a fundamental requirement for tissue specificity of these regulators that we don’t understand,” said McKeon, who reported the findings in the May 4, 2007, *Cell*. “Dissecting the genetic programs controlled by these regulators will tell us much about how stem cells function and how they go awry in cancer.” ❖



Illuminating egg guardian. A stain for p63 lights up the egg cells of a 5-day-old mouse, turning them bright red at the beginning of cell division. Division then halts while the red signal stays on for about a year.

ered that neighboring genes often get turned on together. It has not been clear, though, how they are jointly controlled.

Now, Kohane and his colleagues have identified a regulator. They found that microRNAs—small snippets of single-stranded RNA derived from genes that do not code for proteins—can influence gene activation by suppressing their chromosomal neighbors. The finding, reported in the March 20, 2007, *Proceedings of the National Academy of Sciences*, was the result of a meta-analysis, a combination of data from multiple studies, each utilizing chemical-reaction arrays on microchips.

Over the past few years, microRNAs have attracted a lot of attention due largely to their ability to silence the expression of other genes. MicroRNAs have also been shown to play an important role during development, and their dysregulation is related to disease states like cancer. “We wondered whether microRNA could be the cause of a concerted

action of genes near each other,” said Kohane, who is also the director of the Countway Library of Medicine.

The researchers combed through dozens of microarray datasets from mouse tissues, focusing on patterns of gene expression near genetic regions encoding microRNA. “On average, we found a massive dip of expression around microRNA,” Kohane said. This suppression was found in a variety of tissues, which suggests that microRNAs exert their control throughout the genome.

Transcription factors were the most commonly suppressed genes, implying that the inhibitory effect of microRNA is indirect. And genes related to chromatin remodeling, a process that goes awry in diseases such as cancer, were particularly well targeted for microRNA silencing. “The control of inactivation near microRNAs may cause a predisposition to cancer if disturbed,” said Kohane. ❖

Protein Cuts Early Infection Down to Size

Researchers have found a crucial step in the early warning system that activates the body's defenses against influenza, hepatitis C, rabies, and related infections. The sensing pathway, their paper reports, depends in part on signaling by



From left, Young Shin, Michaela Gack, and Chengyu Liang in the lab of Jae Jung, along with colleagues, identified a key signaling molecule in the rapid immune response to influenza, hepatitis C, and related viruses.

an antiviral molecule that belongs to a large family with recognized but poorly understood antiviral credentials.

The molecule, TRIM25, helps transmit the alarm soon after a virus invades a cell. The resulting biological chain reaction limits virus replication by flooding the cell and surrounding tissue with antiviral and inflammatory chemicals. These signals help cells attract warriors from the adaptive immune system to the site of infection for a systemic response. (A well-known relative blocks HIV replication after infection.)

The study "provides a detailed mechanism for how the host reacts against a viral infection to generate antiviral activity," said senior author Jae Jung, professor of microbiology and molecular genetics at the New England Primate Research Center.

Ten years ago, immunologists thought they had figured out how cells defend themselves against the initial assault of unfriendly bacteria, viruses, and fungi. Molecules on cell surfaces called Toll-like receptors, a family of 10

proteins in humans, recognize the microbes and start a cascade of signaling that turns on the interferons, cytokines, and chemokines of innate immunity.

Toll-like receptors are not the only game in town anymore, a recent review proclaimed. The fast-moving field has revealed a more extensive innate immunity network that quickly kicks in as soon as microbial infection begins and long before the adaptive immune system gets going.

One key innate sensor was discovered only three years ago. Retinoic acid-inducible gene I stands guard inside cells and activates the same intracellular virus-clearing chemicals as the Toll-like receptors. Graduate student Michaela Gack hunted for its molecular partners. She identified TRIM25 and detailed its crucial role in the resulting pathway. Mouse cells without TRIM25 showed a 100-fold increase in viral replication and were unable to produce interferon-beta, which helps fight viruses.

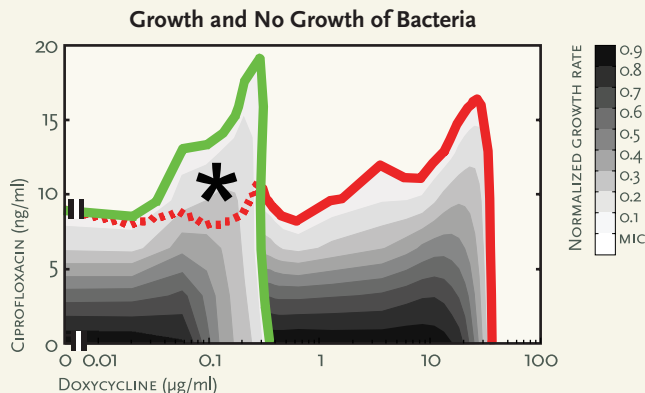
The study reveals a crucial role for TRIM25 in antiviral immunity, Jung said. Gack received the Millipore "Young Cell Signaller 2007" award for her work. ❖

Drug Combo Targets Resistant Bugs

Conventional wisdom holds that when bacteria are battling for survival against antibiotic treatment, resistance to a drug will always give a bug a competitive advantage. But a study from the lab of Roy Kishony, assistant professor of systems biology, finds that under certain conditions, a combination of drugs could actually handicap resistant strains.

Drug combinations can be characterized as synergistic, additive, or antagonistic, depending on whether the combined effect of the two drugs is larger than, equal to, or smaller than what would be predicted by their individual activities. Graduate student Remy Chait explored the effects of suppressive drug combinations on bacteria

Fate reversal. Bacteria are exposed to increasing concentrations of doxycycline paired with ciprofloxacin, a drug that is suppressed by doxycycline. The shaded regions show bacterial growth rates, and the colored lines represent the lowest drug concentrations to reduce growth to nil in doxycycline-susceptible bacteria (green) and resistant bacteria (red). With this suppressive combination, a region of drug concentration emerges in which susceptible bacteria grow and resistant ones do not (asterisk).



sensitive to the antibiotic doxycycline and bacteria resistant to it.

The researchers found that when

doxycycline is combined with a synergistic drug, erythromycin, the resistant strain outcompeted the susceptible ➔

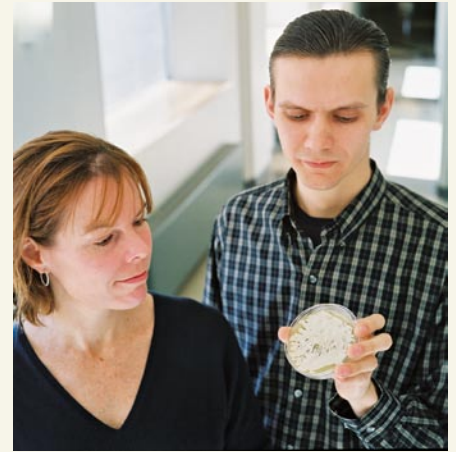
Genetic Blueprint Drawn for Natural Antibiotic

Antibiotic-resistant infections loom as one of health care's growing problems, with the potential to undo some of the stunning progress society has made in combating infectious disease. The most useful antibiotics target vital processes common to all bacteria, enabling them to fight a range of bacterial infections. One compound that has attracted attention is moenomycin, a molecular weapon produced by certain bacteria. Like penicillins, this substance destroys the cell wall of pathogenic bacteria, but it attacks a different step in cell wall formation that is not the target of resistance. In its natural form, it is not useful in humans as a drug, but scientists in several labs have been working on ways to create a similar compound that could be used clinically.

Reporting in the March 26, 2007, *Chemistry and Biology*, the lab of Suzanne Walker, professor of microbiology and molecular genetics, details

the bacterial genetic pathway used to produce moenomycin, which can serve as a blueprint for creating new drugs. The team, led by postdoctoral fellow Bohdan Ostash, worked with Bruce Birren, director of the Microbial Sequencing Center at the Broad Institute, to sequence the genome of *Streptomyces ghanaensis*, the soil-dwelling microbe that produces the compound. Enough was known about moenomycin to predict what the necessary genes might look like. The team identified a cluster of genes that produces the product, and when they transferred the gene cluster to a different organism, it produced moenomycin derivatives.

With this set of instructions, scientists can now try to tweak the pathway to formulate similar molecules that are more useful as drugs. Having microorganisms produce the compound themselves is the best way to make fragments of the drug quickly to see what the



By uncovering the genes responsible for making the natural antibiotic moenomycin, Bohdan Ostash and Suzanne Walker have a starting point for manufacturing novel spin-off drugs in bacteria.

minimal structural portion is that retains full activity. Walker's team has since been able to create several moenomycin analogs using the biosynthetic genes and has begun to investigate their properties.

Although current genomic sequencing efforts on microbes focus on pathogens, Walker believes that knowing the genomic sequences of soil microbes is important, too. "The majority of natural products that are antibiotics or antitumor agents come from soil microbes," she said, and her work demonstrates that these "little natural-product factories" can be tools for drug development. ❖

→ one at all levels of drug concentration. But when doxycycline is combined with ciprofloxacin, a drug that doxycycline suppresses, there was a region of drug concentration at which the resistant strain lost the battle.

From left, Remy Chait, Roy Kishony, and Allison Craney found a way of combining drugs that puts resistant bugs at the losing end of an evolutionary battle.



It appears that when a cell develops resistance to doxycycline, the drug no longer suppresses the effect of ciprofloxacin on the cell. "Effectively, the bacterial cell sees two poisons, one of which—the suppressor—is a partial antidote to the other," Chait said. "Taking them together is harmful for all the cells. But those cells resistant to the suppressor also no longer receive its partial benefit, and they do worse at drug concentrations in which the drug's effects as an antidote outweigh its effects as a poison."

The study offers the counterintuitive finding that an antibiotic, if paired with another in the right way, can be used to discourage resistance against itself. This reversal of fortune, detailed in the April 5, 2007, *Nature*, so far is limited to bacteria growing in vitro, but it suggests a new avenue of research for pairing drugs to counteract resistance in patients. ❖

Tail Injection Cures Brain Inflammation in Mice

Overcoming two major hurdles, scientists have delivered small interfering RNA (siRNA) into the brains of mice with a tail vein injection and protected them from deadly viral encephalitis. The researchers designed a molecular package that crossed the blood-brain barrier and then spread through the brain to treat the disease.

The results suggest that it may be possible to direct promising →

→ gene-silencing therapies to the brain. In one experiment to test the specificity of the brain-targeting system, for example, the researchers knocked down *SOD1*, the most commonly mutated gene in the inherited form of amyotrophic lateral sclerosis (ALS), a common, fatal motor neuron disorder with no effective treatment.

It is believed to be the first clear-cut case of delivering siRNA to the brain without injecting directly into the organ. The project was conducted by postdoctoral fellow Priti Kumar in the lab of Premlata Shankar and Manjunath Swamy, assistant professors of pediatrics at the Immune Disease Institute (formerly the CBR Institute for Biomedical Research).

The RNA fragment works against the fatal viral encephalitis by silencing a shared genetic sequence in the Japanese encephalitis virus and West Nile virus, two related mosquito-borne flaviviruses, the researchers showed last year. The big drawbacks were that the siRNA worked only in the localized infected cells near the injection site and could not travel through the brain like the viruses.

After some tinkering, the researchers developed a molecular package composed of a piece of rabies virus to distribute the siRNA throughout the brain's blood vessels and a cell-penetrating peptide to pass through vessel walls into the brain. Seven out of nine mice challenged with Japanese encephalitis virus survived after an intravenous injection of the peptide combination carrying the siRNA, compared with none of the untreated infected mice.

"It is proof of principle, but there is a long list of things to do before it will be ready for clinical trials in people," Swamy said.

The list includes further toxicology and bioavailability studies on the targeting peptide technology as well as devising a better packaging system to ensure more siRNA arrives in the brain, Kumar said. ❄

Another Bad Rap for Sat Fats: Messing Up Muscle Metabolism

One warning sign of impending type 2 diabetes is the accumulation of fat in muscle tissue. That flab is more than just excess baggage, according to new work from Joslin Diabetes Center researchers. Fats, and specifically saturated fats, weigh down a key gene regulator in muscle cells, report assistant professor of medicine Mary-Elizabeth Patti and colleagues in the May 25, 2007, *Journal of Biological Chemistry*. Their results show how a high-fat diet may trigger the metabolic changes seen in obesity and type 2 diabetes.

The team had previously found that levels of two gene activators in the PGC-1 family were reduced in people at risk for type 2 diabetes even before they developed the disease. These proteins regulate an array of metabolic genes responsible for proper mitochondrial function, and their levels have a major impact on energy balance. Both genes and environment affect the expression of these genes as well as the risk of diabetes.

In the environmental corner, obesity,

overeating, and a high-fat diet all diminish *PGC-1*-gene expression. In their new study, Patti and coworkers searched for the specific nutrients responsible for

reducing the level of the gene activators in muscle cells. They ruled out sugar, insulin, and excess amino acids before finding that high levels of saturated fats depressed transcription of the genes.

"The saturated fatty acids, also known as the 'bad' fats, reproduce the same pattern of gene expression in our muscle cells as we see in obesity, in people on high-fat diets, and in type 2 diabetes," Patti said.

The net result is impaired mitochondrial function and a decreased fat-burning capacity, which could exacerbate the build-up of fat in muscle cells.

The good news is that the effects of saturated fats on *PGC-1* can be reversed by giving the cells good fats, such as polyunsaturated omega-3s, by exercise, and by drugs commonly used to treat type 2 diabetes. ❄

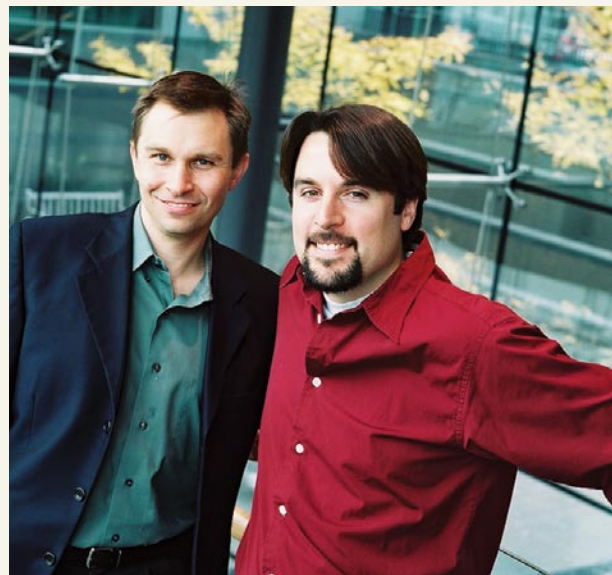


Mary-Elizabeth Patti and colleagues discovered that a high level of saturated fats produce a pattern of gene activation in muscle cells similar to that caused by obesity and type 2 diabetes.

Healthy Life Extended In Obese Mice

A compound that increases the life span of yeast, worms, and fruit flies now has been shown to improve health and survival in mice fed a high-calorie diet. Treatment with resveratrol, a plant-derived molecule found in red wine, prevented many of the health consequences of obesity, even as →

David Sinclair (left) and Joseph Baur found that resveratrol, which can extend the lives of lower organisms, also keeps overfed mice healthy.

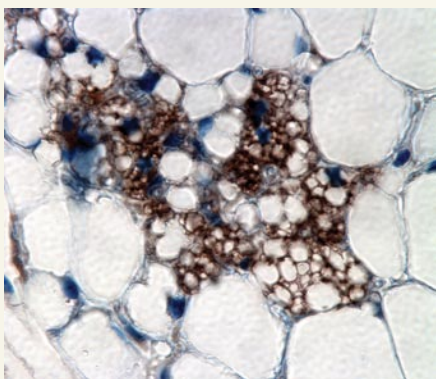


Molecular Switch Holds Promise for Controlling Obesity

Though it can cause waistlines to bulge, fat is not all bad. White fat cells store surplus calories, but there is a type of adipose tissue—brown fat—that generates heat and actually counters obesity. Bruce Spiegelman and his colleagues have now identified a molecular switch in mice for production of this good fat.

The molecular pathway appears to be controlled by a gene, *PRDM16*, that is active in brown but not white fat. Spiegelman, a professor of cell biology at Dana-Farber Cancer Institute, working with Patrick Seale, research fellow in biology, and colleagues inserted *PRDM16* into white fat-precursor cells and implanted the cells under the skin of mice. The precursors generated brown fat cells. In further

experiments, the scientists found that *PRDM16* turns on a meta-

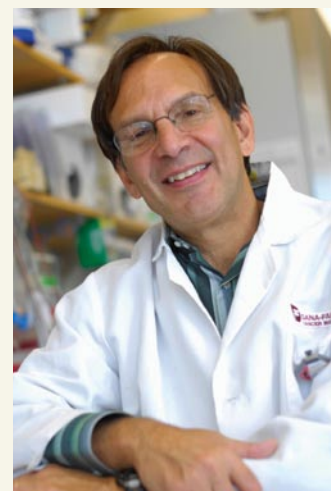


Brown fat cells, which generate heat and counter obesity, are surrounded by white fat cells that store surplus calories.

bolic pathway controlled by two genes: one that was discovered in Spiegelman's lab and one that allows cells to release large amounts of energy as heat. The findings appear in the July 2007 *Cell Metabolism*.

The researchers plan to overproduce the protein *PRDM16* in mice and overfeed them to see if they resist becoming obese. If the strategy works, turning up the equivalent switch in people could provide a new strategy for controlling obesity.

"Human adults don't have much brown fat, but there is some, and from a therapeutic perspective, the question is whether that pathway can be reactivated," said Spiegelman. "You might not have to implant a large amount of engineered precursors in people who are at risk for being obese. In theory, you would only have to reduce the accumulation of white fat by 1 percent or so to have an effect." ❄



A team of researchers including Bruce Spiegelman identified a molecular switch in mice that turns on development of beneficial brown fat from precursor cells.

↔ mice gained weight. The compound was identified by David Sinclair, associate professor of pathology, in a screen of molecules that enhance the activity of Sirt1, the mammalian version of the protein Sir2 that has been shown to affect life span in lower organisms. This study, published in *Nature* on Nov. 16, 2006, is the first in a series of studies by Sinclair's group to determine whether resveratrol has the same impact on mammals.

The study compared three groups of mice: one fed a normal diet; another that began a high-calorie, high-fat diet at middle age; and a group that began the same high-calorie diet at middle age but were simultaneously treated with resveratrol. After six months of treatment, the mice that received resveratrol had a significantly higher survival rate than the high-

calorie group that did not.

Though resveratrol did not prevent mice from gaining weight on a richer diet, it did prevent health problems that arise with obesity, such as fat deposits in the liver. Treated mice also had lower levels of glucose and insulin in their blood and higher insulin sensitivity. In a test of motor skills, the resveratrol-treated mice outperformed untreated overweight peers and even showed improvement with age. An analysis of gene expression in the liver tissue of the mice found that resveratrol reversed many of the patterns of gene expression caused by a high-fat diet.

So far, the most reliable way to extend life span of an organism is through calorie restriction. Sinclair, who is also a co-director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging, believes that resveratrol

is keeping mice healthy by triggering the same life-extending response that a strict diet does. "We've been going up the tree of life from yeast to worms to flies, showing this molecule extends their life and mimics calorie restriction," he said. However, Sinclair added, "There's a lot to figure out about how resveratrol is working, but if we provide the benefits of caloric restriction in humans, it might allow us to keep many more baby boomers healthier in their old age by treating or forestalling key diseases of aging, such as type 2 diabetes and cardiovascular disease." The daily dose of resveratrol given to mice in this study is the equivalent in humans of 100 glasses of wine, so its role at normal dietary levels is unknown. More potent activators of human SIRT1 are in development and may enter clinical trials as early as 2008. ❄

Inhibitor Could Aid Assault On Deadly Brain Tumors

Imaging Technique Tracks Tumor Shrinkage

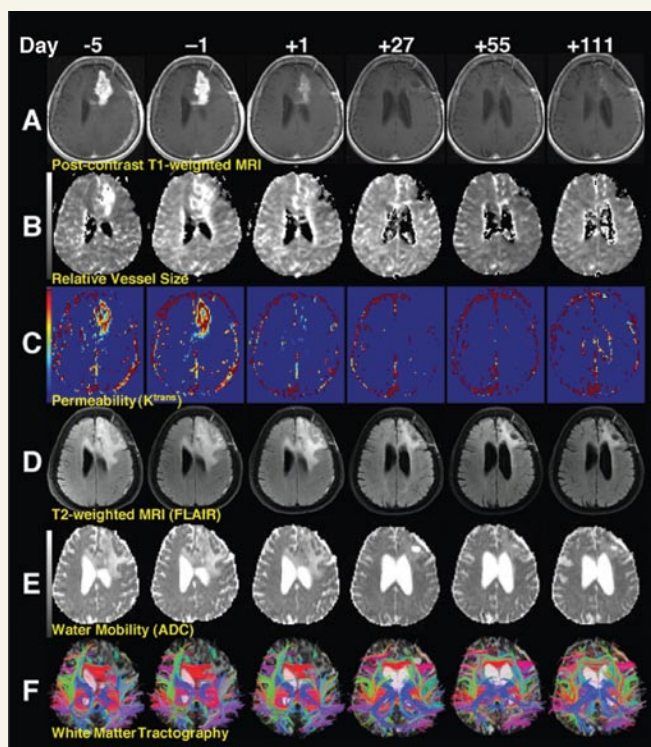
Several years ago, Rakesh Jain and his colleagues began peering through tiny glass windows implanted in the backs of tumor-carrying mice. What they saw surprised them. The blood vessels surrounding and feeding the tumors were a disorganized maze, carrying blood briskly in some places while allowing it to stagnate in others. In some areas, vessel walls were tight while in others they were filled with pores that leaked fluid.

In 2001, inspired by these observations, Jain, the A. Werk Cook professor of radiation oncology (tumor biology) at Massachusetts General Hospital, made a seemingly radical proposal: repairing

and normalizing a tumor's blood vessels could pave the way for delivering cancer drugs.

Working with Tracy Batchelor, associate professor of neurology, and

Gregory Sorensen, associate professor of radiology, both at MGH, Jain decided to try normalizing the vasculature surrounding tumors with an angiogenesis inhibitor, AZD2171. In a



A tumor's retreat. Images from the best-responding patient show the potential effects of an angiogenesis inhibitor on glioblastoma. Numbers at the top correspond to days before or after starting treatment. Row A shows the tumor, in white, shrinking over time. Row B indicates the relative size of small blood vessels in the brain, which also shrink. Row C shows the permeability of the glioblastoma blood vessels, which drops from the first dose. Rows D and E depict edema diminishing in regions around the tumor. And row F reveals tracts of white matter in the central part of the brain becoming more visible around the tumor as edema subsides.

Key to Corneal Transparency Made Clearer

The cornea of the eye appears as an oasis of clarity compared to other tissues of the body with their snarled mesh of blood vessels. Vision depends on the cornea enforcing this rigorous ban on blood vessel growth, but how it does this remains poorly understood.

"This phenomenon—avascularity of the cornea—has really been a feature of the cornea that has been puzzling for millennia," said Reza Dana, of Schepens Eye Research Institute and Massachusetts Eye and Ear Infirmary, where he is an associate professor of ophthalmology. He and colleagues have proposed an intriguing solution to the puzzle. In the July 25, 2006, *Proceedings of the National Academy of Sciences*, they argue that vascular endothelial growth factor receptor 3 (VEGFR-3) may act as a magnet for certain signals, luring them away from other receptors that, when activated, promote blood vessel growth.

VEGFR-3 was not thought to be expressed in the cornea. Yet through tissue staining techniques in mice, Dana and colleagues discovered that the protein is, in fact, expressed on

the epithelial cells making up the cornea's outer surface. The researchers tried to induce inflammation in the corneas, but found that recruitment of inflammatory cells and growth of new blood vessels was blocked. When the epithelium was removed, however, significant vessel growth occurred, and it appeared to be caused by the vessel growth proteins, VEGF-C and -D.

In a telling experiment, the researchers removed corneal epithelium and introduced VEGFR-3 alone. Angiogenesis was inhibited.

Though Dana's idea of a ménage à trois, with VEGFR-3 seducing away the vessel growth factors VEGF-C and -D, is still a hypothesis, it is clear that maintaining corneal clarity "is critically dependent on expression of VEGFR-3," he said. This leads to the intriguing possibility that the protein might be used to ameliorate the kind of rampant blood vessel growth that occurs in diseases such as corneal vascularization, the second leading cause of blindness in the world, and age-related macular degeneration.

VEGFR-3's anti-angiogenic powers might even be harnessed in the fight against cancer. "We've had a lot of positive feedback from oncologists," said Dana. *

phase II clinical trial, the researchers gave the drug, in pill form, to 30 people with recurrent glioblastomas, the most aggressive type of brain tumor. The patients had not responded to conventional treatment.

“My hope was that, in addition to benefiting patients, we could also learn something about normalization,” said Jain. To do that, the researchers needed to develop methods for imaging inside the brains of their patients.

In the January 2007 *Cancer Cell*, the scientists report on the first 16 patients. The results are promising. Almost immediately, the patients experienced a period in which small blood vessels decreased in size and became less leaky. This window of normalization lasted an average of a month. The treatment also caused tumors to shrink as much as 50 percent, though the overall benefit varied among patients. Unexpectedly, the patients’ brains became less swollen.

The researchers have been analyzing the remaining patients. “The clinical piece has held up,” said

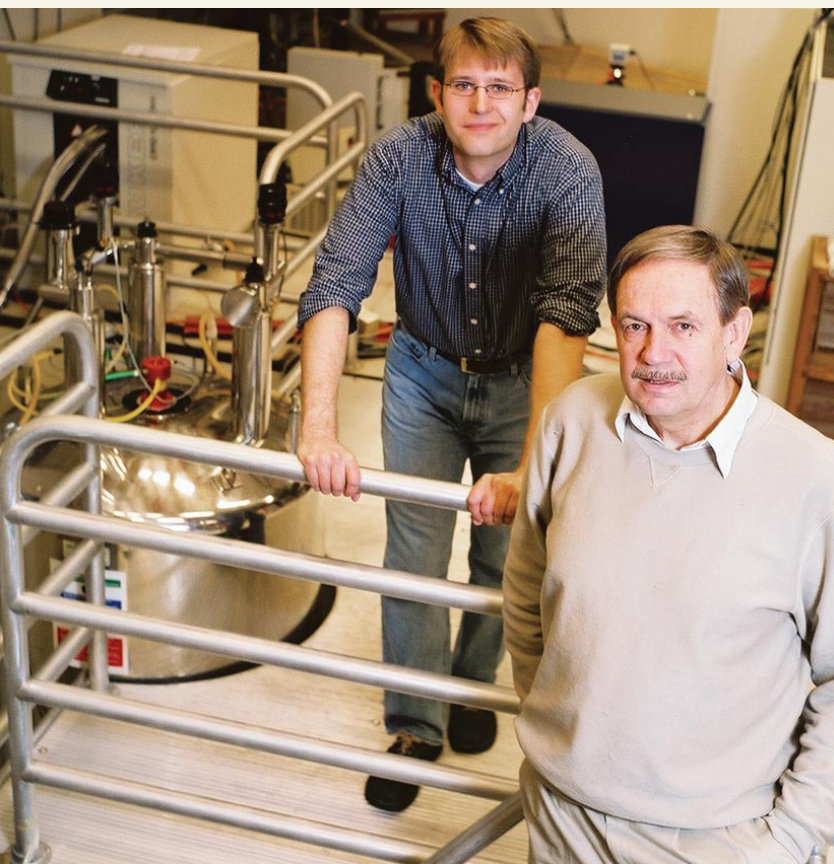


After hypothesizing that angiogenesis inhibitors could improve the vasculature of tumors, Rakesh Jain (left) sought a clinical partnership to test his theory in patients. Tracy Batchelor (center), who treated the brain tumor patients in the study, said that an-

Batchelor. The researchers are launching an international clinical trial of 300 patients with recurrent glioblastoma that will test the combination of AZD2171 and chemotherapy hoping the chemo will have a better chance of reaching the full tumor through genes normalized via the inhibitor. In

giogenesis inhibitors could have an unexpected benefit: ameliorating the debilitating swelling that some patients experience. Gregory Sorensen used a variety of MRI techniques to help Jain and Batchelor visualize the events unfolding in patients’ brains.

addition, they recently received funding from the National Institutes of Health to launch a phase II trial with 40 newly diagnosed glioblastoma patients, who may have a better chance of responding to drug delivery enhanced by AZD2171. “This is what we wanted to do from the beginning,” said Batchelor. ❖



Small Synthetic Molecule Curbs Cancer Growth

Screening Technique May Accelerate Search For New Class of Anticancer Drugs

A newly identified compound, one that is providing unique insights into regulation of genes at the stage in which RNA produced from the DNA is translated into protein, may also light the path to a new form of cancer treatment.

The findings, reported by Gerhard Wagner, the Elkan Blout professor of biological chemistry and molecular pharmacology, and his colleagues, in the January 26, 2007, *Cell* provide the latest proof of principle for an elusive but promising concept: combating disease by blocking normal protein interactions with small molecules. →→

Using a novel high-throughput screen, Gerhard Wagner (right), Nathan Moerke, and colleagues have identified a small synthetic molecule that can disrupt the progression of cancer by blocking two specific molecules from binding, which is necessary to initiate the translation of proteins vital to cell proliferation.



T. Rex Protein Sequenced in High-tech Tour de Force

Closest Living Cousin to Fearsome Predator May Be Chicken

In a venture thought to lie outside the reach of science, HMS researchers have captured and sequenced tiny pieces of collagen protein (which makes up most of the connective tissue) from a 68-million-

year-old *Tyrannosaurus rex*. The protein fragments, seven in all, appear to most closely match amino acid sequences found in collagen of the present day chicken, lending support to a still controversial theory that

“Any well-preserved fossil between one and 68 million years is now a target for doing sequences. You can break open these bones and see if they have any well-preserved tissue,” said John Asara (front). He is shown with (from left) Lisa Freimark, Lewis Cantley, and Matthew Phillips.

Role of Bone-growth Protein Described in Fracture Healing

Since their discovery 40 years ago, the bone growth proteins have been a subject of intense scrutiny—for good reason. Not only do they help bones to form and grow, they also help repair those that are broken or fractured. Yet much about the proteins remains mysterious. Bone morphogenetic protein 2, the most abundant of them all, is used clinically to promote spinal fusion, and yet the way it carries out its bone-healing activities remains unclear.

Vicki Rosen, professor of developmental biology at the School of Dental Medicine, working with Kunikazu Tsuji, a research fellow in Rosen’s lab,

and colleagues, has conducted experiments that shed light on how BMP2 functions in the early stages of healing. Their study appears in the December 2006 issue of *Nature Genetics*.

So critical is this protein in the formation of bone that mice born without the gene die before birth. To get around this problem in the lab, Rosen and her colleagues created transgenic mice with a gene for the protein that could be turned off specifically in the limbs. At birth, the limb bones of the mice looked relatively normal, but they did not mature properly. And they were unable to initiate repair when frac-

tured. Moreover, their bones appeared to fracture more easily.

Upon closer inspection, Rosen and her colleagues found that the limb bones exhibited less type II collagen, a component of the extracellular matrix needed to strengthen bone, which probably accounts for their tendency to spontaneously fracture. In addition, the researchers found that cells at the fracture site express surface receptors that when bound by the growth protein cause the cells to differentiate into those vital for repair.

Rosen and her colleagues are currently assessing the contribution of other key bone morphogenetic proteins in the process of fracture healing. ❄

→ “There is always some skepticism about whether one can actually inhibit a given protein–protein interaction using just a small molecule,” said research associate Nathan Moerke, the study’s lead author.

The researchers identified several small molecules in a screen of 16,000 compounds designed to block the binding of two translation initiation factors, an interaction necessary for the production of proteins vital to cell proliferation. The most promising of the discovered chemicals—called 4EGI-1—induces programmed cell death in some cancer cells, stops the growth of others, and inhibits cellular expression of cancer-causing proteins, the HMS researchers found. The

tiny molecule achieves these monumental feats by blocking the union of two proteins whose binding is required to initiate translation of most growth- and proliferation-related proteins but is not so crucial for production of most other proteins.

Still, the synthetic warrior did not prove potent enough to be considered a viable drug candidate. It is not only this molecule, however, but also the high-throughput analysis enabling its discovery that holds promise for a potential cancer therapy. “The next step would be to either design better analogs of this compound and test them in the same experiments or use this assay to screen more libraries for better initial compounds,” Moerke explained. ❄

birds and dinosaurs are evolutionarily related. The findings appear in the April 13, 2007, *Science*.

“Most people believe that birds evolved from dinosaurs, but that’s all based on the architecture of the bones,” said John Asara, instructor in pathology at Beth Israel Deaconess Medical Center, who, working with colleagues at HMS and other institutions, sequenced the protein fragments over the course of a year and a half using highly sensitive mass spectrometry methods. “This allows you to get the chance to say, ‘Wait, they really are related because their sequences are related.’”

The mere existence of such exceedingly ancient protein defies a longstanding assumption that fossilization, the process by which protein is replaced by mineral, is complete by one million years.

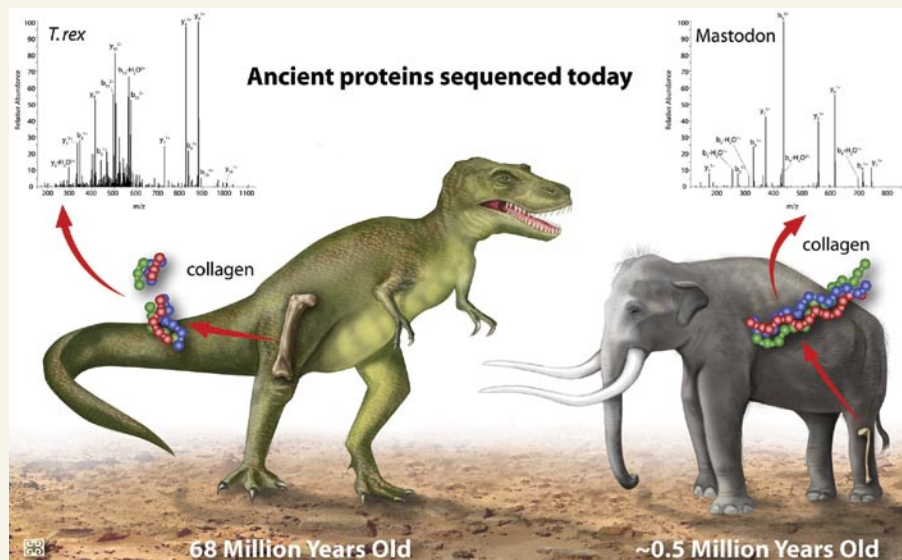
“Basically, this is the breakthrough that says it’s possible to get sequences beyond one million years. At 68 million years, it’s still possible to get

sequences,” said Lewis Cantley, a professor of systems biology and the William Bosworth Castle professor of medicine at HMS and BID. In addition to the seven dinosaur sequences, Asara, director of the mass spectrometry core facility at BID, and his colleagues isolated and sequenced more than 70 protein fragments from a 160,000- to 600,000-year-old mastodon, providing further evidence of the staying power of ancient protein.

“I think what this says,” Cantley continued, “is that when people make new discoveries now, if they want to get maximum information out, they have to immediately handle material in a way that first of all will avoid contamination and, second, ensure that whatever is there gets well preserved because it can be interrogated.”

Still, it may be the rare fossil that is as pristinely preserved by the environment as the *T. rex* and mastodon specimens analyzed in the current study. “Nature has to give you the opportunity to do this first,” Asara said. ❖

Protein content spans time, species. Collagen fragments from a 68-million-year-old *Tyrannosaurus rex* and a 160,000- to 600,000-year-old mastodon were analyzed by mass spectrometry. The peptides were measured for mass and fragmented to reveal their amino acid sequence. Then the sequences were compared to those of living animals. The majority of *T. rex* sequences were found to be identical matches to amino acid sequences found in chicken collagen alpha 1. Others matched the newt and frog.



Treatments Tested For Resistant TB

Ten years of experience with chronic multidrug-resistant (MDR) and extremely drug-resistant (XDR) tuberculosis in Peru shows that aggressive treatment can save lives even in poor countries and in outpatient settings, said Carole Mitnick, instructor in social medicine. The results support immediate large-scale implementation of comprehensive ambulatory treatment, she said, to stem the epidemic of MDR-TB and XDR-TB that infects about 1.5 million people every year.

In analyses that are under review for publication, Mitnick and colleagues at Partners In Health report good outcomes in 66 percent of 666 MDR-TB patients and in 60 percent of the 48 who have XDR-TB. The observational studies extend a 2003 report published in *The New England Journal of Medicine* on the first 75 patients treated in the first three years of a free, comprehensive, individualized program in Lima.

Mitnick’s research involves the first large-scale individualized, ambulatory therapy that demonstrates improved results, particularly compared with the widespread practice of repeated courses of noncurative therapy for MDR-TB, which can lead to XDR-TB and persistently high mortality. The refined approach also offers a respite from additional deadly hospital-acquired resistance, she said.

Further improvement requires randomized trials of MDR-TB treatments, Mitnick and colleagues argued in a policy paper in the Nov. 6, 2007, *PLoS Medicine*. The publication was timed to coincide with the annual meeting of the International Union Against TB and Lung Disease in Cape Town, South Africa.

For drug-susceptible TB, randomized clinical trials helped identify and prove the remarkable benefits of →

Savings Could Offset Cost of Expanding Medicare to Near-elderly

Savings After Age 65 Might Be Pronounced for People with Chronic Disease

While the overall cost-effectiveness of Medicare benefits has been much debated, a new study shows that adults who previously could not get health insurance needed more doctor and hospital visits once they enrolled in Medicare than people who could afford private health insurance before receiving Medicare. The study, from HMS researchers, appears in the July 12, 2007, *New England Journal of Medicine*.



John Ayanian (left), J. Michael McWilliams, and colleagues have shown that uninsured near-elderly patients with diabetes or cardiovascular disease likely would require fewer medical resources after entering the Medicare program if they had been insured prior to age 65.



Created in 1965, Medicare now covers nearly 43 million elderly and disabled Americans. In 2006, the program cost \$374 billion, and it is expected to grow to \$524 billion by 2011. According to the Kaiser Family Foundation, Medicare spending as a share of GDP is estimated to increase from 2.7 to 4.7 percent by 2020 as a larger proportion of the population survives well beyond age 65.

“Expanding coverage to uninsured near-elderly adults may not cost as much as previously thought,” said J. Michael McWilliams, research fellow at Brigham and Women’s Hospital.

“Particularly for those with heart disease, hypertension, or diabetes, earlier access to effective treatments can prevent costly complications and reduce health care needs after age 65.”

Despite the size of Medicare, some people are still falling through the cracks. John Ayanian, professor of health care policy at HMS and of medicine at Brigham and Women’s Hospital, says that Congress may expand the program to uninsured adults in their late 50s and early 60s, since private insurance available to individuals in this age group can be prohibitively expensive for people with chronic health problems like diabetes or heart disease.

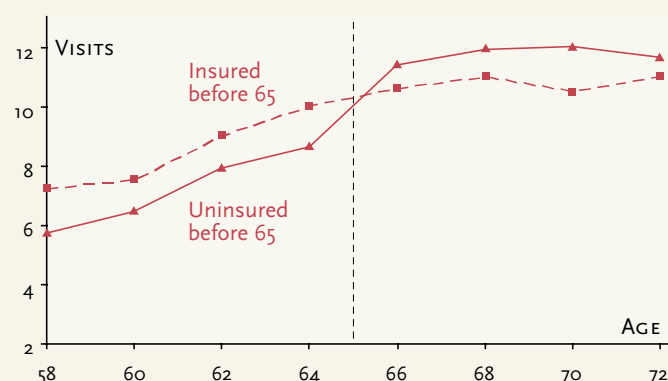
→ a short course of treatment, reduced from 24 to six months, with better outcomes. The same could be true of new MDR-TB drugs, such as fluoroquinolones, which would save money and relieve patients from the prohibitively long duration and toxicity of current MDR-TB regimens, Mitnick said.

The outlook for randomized clinical trials has changed from impossible to imperative, she asserts. A new design implemented for drug-resistant HIV infection allows for regimens tailored to the great variability in disease and drug tolerance. Trials could be conducted in the 40 programs now treating 30,000 people in poor regions. More people believe high-quality treatment is the right of every TB patient and is sound public health practice. And, for the first time in 30 years, several new classes of anti-TB drugs are in preclinical and early clinical testing. ❄

Care comparisons. In a study of Medicare usage, obtaining coverage at age 65 was associated with significantly greater increases in doctor visits for previously uninsured adults compared to previously insured adults with cardiovascular disease or diabetes (left graph), but not for adults without these conditions. Medicare coverage at age 65 was also associated with significantly greater increases in hospitalizations for previously uninsured adults compared to previously insured adults with cardiovascular disease or diabetes (right graph), but not for adults without these conditions.

McWilliams and Ayanian compared how previously uninsured and insured adults each used health services before and after entering Medicare. The →

Number of Doctor Visits per 2-Year Period by Adults with Chronic Disease



Vaccines: Who Needs Them?

The development of an effective vaccine is always a cause for celebration; as preventive measures, vaccines historically have had an enormous impact on health. But making new immunizations accessible to all who need them is an entirely different problem. New vaccines and other technologies “are very attractive, but they’re also much more costly than older vaccines,” said Tracy Lieu, professor of ambulatory care and prevention. “The pace of this development has proceeded so swiftly that our health care finance system struggles to catch up.” Lieu has been working to appraise the costs and benefits of new health care technologies, particularly vaccines, and to examine how they are distributed in the United States and around the world.

Many vaccines are used in industrialized countries for years or decades without reaching developing countries, where infectious disease rates are usually higher. Of the one million children under the age of five who die every year from pneumococcal infection (which can cause pneumonia, bacteremia, and meningitis), 90 percent live in developing countries without the vaccine. Lieu participated in a cost-effectiveness analysis of pneumococcal vaccination with researchers at the University of Medicine & Dentistry of New Jersey and the Johns Hopkins Bloomberg School of Public Health. The study, published in the Feb. 3, 2007, *Lancet*, offers evidence that vaccinating infants in developing countries against pneumococcal infection would be highly cost-effective. According to their analysis, pneumococcal vaccination could prevent 262,000 deaths per year in children aged 3 to 29 months. Lieu said that this type of study can help people imagine the potential outcomes of investing in health care; the results helped spur new

Tracy Lieu said that cost-effectiveness analyses, like her recent one for pneumococcal vaccination, can make a difference by “helping people imagine what the world would be like if health care services were used equally.”

international funding for pneumococcal vaccination in poor nations.

Though the United States has easy access to the newest vaccines, many children do not have insurance that covers them.

A study published in the Aug. 8, 2007, *Journal of the American*

Medical Association and led by Lieu and Grace Lee, assistant professor of ambulatory care and prevention, found that limited federal and state funding for vaccines leaves underinsured children increasingly at risk for not getting needed immunizations. Children who are either uninsured or publicly insured through Medicaid can obtain vaccines through a federal program. But many children have private insurance that does not cover vaccination and have limited access to federally purchased vaccines. Lieu pointed out that the full range of vaccines from birth until 18 years of age costs \$900 or more, a financial burden many families cannot afford. ❄



→ difference was clear: upon receiving Medicare at age 65, the once-uninsured adults started going to the doctor and to

the hospital more than the previously insured people.

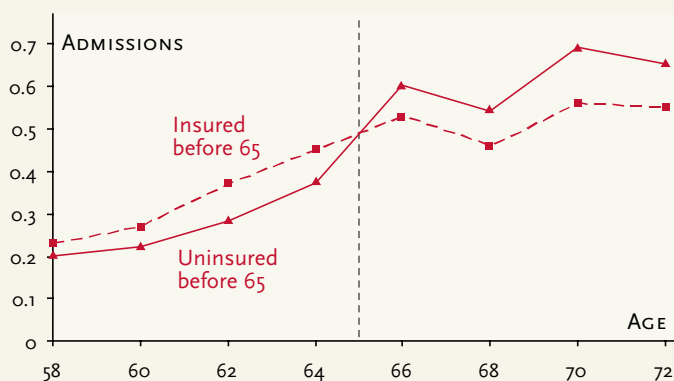
The need for health care was especially noticeable

in adults with heart disease or diabetes, illnesses that can be life-threatening when left untreated, but manageable if caught early. “This is a group for whom medical advances in recent decades have had an impressive

impact on health. If people with heart disease or diabetes are uninsured, they often have to forego very cost-effective therapies,” said McWilliams.

According to the researchers, expanding Medicare to uninsured adults may not only improve their health but also reduce the demand for costly health care in the future. “These benefits are likely to be substantial and may partially offset the costs of expanding coverage,” said McWilliams. The researchers are now extending this study of health services and costs to assess the effects on health for uninsured near-elderly adults who become eligible for Medicare coverage. ❄

Number of Hospital Admissions per 2-Year Period for Adults with Chronic Disease



OUTREACH

New Family Van Extends Services

IN JUNE 2006, THE Medical School's Family Van made two major advances, putting a new van on the road and extending its services to two other communities, Jamaica Plain and Hyde Park. Van director Jennifer Bennet said, "Hyde Park has demonstrated a real need for our services, and I am confident that with the partnerships we've made with community organizations and the van's reputation for compassionate curbside care, the site will be successful."

The van travels to seven predetermined locations in some of Boston's most vulnerable communities, offering confidential medical screenings, health education, and referrals to area services. It focuses mainly on diabetes, obesity, hypertension, nutrition, glaucoma, prevention of HIV and other sexually transmitted diseases, prenatal care, reproductive health, and oral health. The van has seen more than 87,000 at-risk individuals since it was first launched in 1992. ❁



HMS Students Promote Sexual Health in Boston Schools

Educating Boston's middle and high school students about sexual health is no easy task, but that's what an ongoing group of HMS student volunteers has been doing for the last 10 years. Prevention, Health Awareness, and Choice through Education (PHACE) is the longest-running project funded by the HMS Office of Enrichment Programs (OEP), which annually supports 10 to 15 student-initiated community projects. PHACE volunteers work in Boston Public Schools' McKinley subdivision, which caters to students with emotional and behavioral problems.

Like other OEP programs, PHACE is student-run. The 2007 coordinator, second-year Shalini Lal, has to apply for renewed funding and recruit and train HMS students. Every spring, pairs of HMS first-years talk to the public school students weekly about everything from contraception, sexually transmitted infections, and reproductive anatomy to relationships, sexuality, sexual harassment, and teen pregnancy. Said Lal, "Our goal is to provide the students with everything we possibly can, everything we know, so they can be safe."

HMS students, too, benefit from PHACE. Their interest in the program is twofold, said Lal, who joined as a first-year. By participating in PHACE, students help both the community and themselves by staying informed about the latest sexual and reproductive health information.

This year, Lal plans to assess how much information the middle and high school students have retained by quizzing them at the beginning of the term and again once all the lessons have been completed. PHACE's popularity with the McKinley district is already a marker of its success, however, and there often are not enough HMS students to teach every classroom.

To that end, Lal hopes that more people will get involved. Lack of sexual education is a rising problem. "PHACE meets a need not being met anywhere else," she explained. She hopes to recruit nonstudent members of the HMS community to lend the program extra strength, and she would like to arrange a schoolwide sexual health workshop as a quick, effective way to share the educational materials. ✨



Part of Shalini Lal's responsibility as 2007 coordinator of the PHACE program is to recruit and train fellow student volunteers.

Science from the Heart

Since 2003, Boston and Cambridge students in grades six through nine have submitted their original rap songs, dances, skits, essays, and artwork to a panel of judges at HMS. It's not that the Medical School has become an American Idol showcase for talented schoolchildren. These students are participating in Reflection in Action: Building Healthy Communities (RIA), an annual spring program for students to share their voices in whatever medium they choose, on whatever health-related topic they choose.

The HMS Office for Diversity and Community Partnership developed RIA to celebrate the civil rights movement and to interest students in science. The one-day event broadens students' awareness of potential careers in health fields and encourages creative thinking while teaching them about important health issues. In three years, the number of participants has doubled from 200 to 400, and the number of submissions has expanded from 44 to more than 200. The reason for RIA's popularity is simple: it approaches students through existing interests in art and performance or through the medical concerns of their families, friends, and communities.

Unlike many programs that emphasize the technical side of science, RIA "encourages the kind of student who's creative," said dean for diversity and community partnership Joan Reede. In past years, a young man rapped about asthma, two homeless sixth-grade girls wrote and performed a skit about low self-esteem and feeling invisible, and another girl

→→



Pictured beside the new van are key staff and physicians (from left) van founder Nancy Oriol, Jennifer Bennet, Rainelle Walker-White, Sandy Allonen, Heather Lynch, and Bikash Verma.

Symposium Spotlights Rising Scientists



At the March 2007 New England Science Symposium at HMS, graduate student Diedra Wrighting shows her poster, “STAT3 Regulates Hecpudin Expression Downstream of Inflammation.” Established in 2002, the symposium seeks to encourage postdoctoral fellows and both graduate and undergraduate students to build careers in the biomedical sciences. The event offers Silen Awards in each of two categories, oral presentations and poster sessions. This year, first prize for oral presentations went to Richard Guyer of the University of Pennsylvania. First place for posters at the graduate

level and above went to Richelle Williams of the Harvard–MIT Division of Health Sciences and Technology and, below the graduate level, to Tashara Banks of Cuyahoga Community College. The winners came from a field of 12 oral presenters, 106 poster presenters, and 380 registered participants who, said Joan Reede, dean for diversity and community partnership, “represented 80 institutions and 23 states plus Puerto Rico and Canada.” The symposium is sponsored by the HMS Office for Diversity and Community Partnership, the HMS Minority Faculty Development Program, and the Biomedical Science Careers Program. ❖

The Armenise Symposium: Epigenetic Regulation and Human Disease

Although most people view DNA as the molecule solely responsible for inheritance, a more complex and nuanced story unfolded during the 11th Annual Symposium of the Giovanni Armenise–Harvard Foundation, held in Newport, Rhode Island, on June 8 to 10. The 2007 theme was “Genetic and Epigenetic Regulatory Mechanisms in Human Disease.”

Anyone tall enough to peer through a microscope can see that fat, hemoglobin-rich blood cells do not look anything like neurons with their long, spidery arms. Yet the same DNA is packed into the nuclei of these wildly different cells. So DNA, scientists now say, is not all there is.

Today’s consensus is that structural and functional differences among cell types are determined by epigenetic programs that regulate DNA’s activity, some of them marks from environmental assaults, some a form of memory. What makes these proteins and small molecules so important is their capacity to change genetic expression without altering the DNA sequence itself.

Epigenetic changes turn an embryonic stem cell into a specialized adult cell and transform normal cells into tumors, according to Whitehead Institute investigator Rudolph Jaenisch. In his keynote address, Jaenisch said understanding how to program and reprogram different types of cells

is one of the most important topics in biology today, because such skills would hold enormous promise for treating the ills of humankind.

Epigenetic reprogramming is a key step for creating stem cell therapies for cancer and progressive disorders such as Parkinson’s disease, yet these efforts are ensnared in ethical and political complications. Two days before the symposium began, the U.S. House of Representatives voted to expand government-supported stem cell research, a piece of legislation destined for Presidential veto despite protests from patients and families. On the same day, *Nature* published important stem cell findings from Jaenisch’s

→ created a board game called HIV-opoly. Not only do students develop their voices, but they learn about important issues from researching their projects and viewing their peers’ work.

What’s more, RIA shows its participants that science is accessible, not hidden behind white coats and bubbling beakers. In fact, RIA has become a way to engage students in science class, and it is being incorporated into many curricula as a class project that can raise the heads of dozing students.

The program also demonstrates the importance of community. “Reflection in Action is a community collaboration,” said Reede, and everything from professional sports teams to insurance companies have contributed to the program. Furthermore, RIA presents HMS as a part of the community, as a resource, and as an attainable goal for the creative mind. ❖



Larissa Barbosa displays her 2nd place visual entry.

CME Grows Globally, Virtually

The Department of Continuing Education again saw growth in the 2006–2007 academic year, increasing its national, international, and online presence along with the continued expansion of the conventional course catalog. This past year, 32 of the more than 250 classes were first-time offerings, and more than 60,000 clinicians, with 3,500 from outside the United States, took advantage of CME courses. Combined with the 434 CME-accredited in-hospital programs, the department awarded nearly two million credits during the academic year.

By collaborating with other institutions such as Baylor College of Medicine, Johns Hopkins University, and the University of Miami, the department has been able to conduct annual conferences around the country. A similar collaboration with colleagues

The Department of Continuing Education, headed by Sanjiv Chopra, conducts a distance-learning program with physician participants from more than 60 countries.



in Mexico has resulted in an annual conference that draws 6,000 to 7,000 attendees from Mexico and other Latin American countries. In the next academic year, the department will conduct conferences in New York City and Tokyo, and for the first time will partner with the American College of Physicians to offer a joint continuing medical education course in Health Care Quality, Efficiency, and Pay for Performance.

In its second year, the department's distance-learning initiative, CME Online, offered more than 20 courses, with an additional 70 under development. Since the online program's inception, physicians from more than 60 countries have participated. According to Sanjiv Chopra, faculty dean for continuing education, feedback on these courses has been extremely positive, with users making favorable comments on the quality and design of the courses and on the comprehensive and engaging nature of the material. ❖

↔ lab. The research made headlines: Jaenisch's group and two other teams revealed that they had transformed adult skin cells into pluripotent embryonic stem cells. These cells were incorporated into different tissue types and could be inherited by offspring. Importantly, the groups had created embryonic stem cells without running afoul of controversies about using eggs or destroying embryos.

Working in mice, the researchers found that the reprogrammed cells contributed to every tissue type after being injected into early-stage embryos, and these embryos developed into live animals. When the mice were bred, descendants of the reprogrammed cells were detected in the next generation. Additional experiments were performed as well, and the altered cells were indistinguishable from embryonic stem cells on all counts.

When it comes to cell-based therapy for human disease, however, "we are not there yet," Jaenisch cautioned. The retroviral vectors used to reprogram the cells are cancer-causing and could not be

ethically used in humans; scientists do not know whether the key transcription factors used in the research that return mouse fibroblasts to pluripotency would work for humans; and better ways are needed to separate reprogrammed cells from adult cells that remain unaffected.

These are the real-world complications of the basic science presented by Jaenisch, 18 other speakers, and numerous poster presenters at the 2007 symposium. The gathering in Newport marked the symposium's return to the United States after four consecutive meetings in Italy.

Some presenters described how epigenetic factors, such as chromatin packaging and methylation, establish a cell's identity yet leave it susceptible to change. Others focused on epigenetic functions as a way of recording what happened to one generation and passing that memory to the next.

Sixty participants accepted the invitation to this year's symposium. Scientists represented HMS and its affiliated institutions, MIT, Yale University, nine

Italian universities and research institutes, and one multinational pharmaceutical company. Foundation president Joseph Martin, then dean of the Medical School, presided, and president emeritus Daniel Tosteson, former dean of HMS, attended along with members of the foundation's board of trustees, scientific advisory board, and Italian scholarship advisory committee.

The program featured talented young scientists who have benefited from foundation programs at HMS and in Italy. Four winners of HMS junior faculty grants participated in the symposium, including two of three researchers honored in 2007. They were joined by seven recipients of career development awards, which enable Italians to return home and establish their own laboratories after completing postdoctoral training abroad.

Also on hand were two Italian science journalists, the latest recipients of annual science writer fellowships that enable Italian reporters to research stories of their choosing at HMS and participate in the symposium. ❖

PEOPLE

Tabin Appointed Genetics Chair

GENETICS PROFESSOR CLIFFORD TABIN was selected as the next chair of the Department of Genetics, taking over from Philip Leder in January 2007.

Tabin has been on the HMS faculty since 1989. Examining the genetic mechanisms that control the developing embryo, his lab has made major discoveries relating to how genes determine the organization of the early embryo and how they orchestrate the formation of various organs and structures in the body.

Robert Kingston, professor of genetics and chair of the Molecular Biology Department at Massachusetts General Hospital, became



From left, faculty members in the Department of Genetics Clifford Tabin, Constance Cepko, and Philip Leder celebrate Tabin's new leadership role in the department.

vice chair of the department. Kingston has played a leading role in the study of the way chromosomal proteins con-

trol and maintain stable patterns of gene activity.

Leder, the John Emory Andrus professor of genetics at HMS, founded the department in 1980. He has been involved in many important discoveries and advancements in genetics, including seminal work in the understanding of RNA.

Tabin acknowledged Leder's role in the success of the department, saying, "Phil Leder has established one of the greatest basic life science departments in the world. I am very proud to have the opportunity to lead the department

and hope to be able to maintain the high quality and extremely supportive environment Phil has created." ❖

Van Vactor Named Head of BBS



David Van Vactor

David Van Vactor, professor of cell biology, was named the new head of the Biological and Biomedical Sciences graduate program at HMS in March 2007. He replaced Robert Kingston, professor of genetics at Massachusetts General Hospital.

Van Vactor's research focuses on the mechanisms that guide neuronal processes to their destinations at the synapse. Using an embryonic *Drosophila* model, his lab explores which molecules control axon guidance and synaptic target recognition.

Kingston had headed the program for three years. Nancy Andrews, dean for basic sciences and graduate studies at HMS (who became dean of Duke University School of Medicine in October 2007), praised his efforts in connecting BBS to other Harvard programs.

"Bob has worked hard to ensure that off-Quad faculty and students feel like they are part of the BBS community," she said.

Speaking about Van Vactor, she added, "Davie's novel scientific investigations and his community focus make him an ideal member of the faculty to be leading BBS into the future."

Van Vactor said that he intends to carry on the bridge building that Kingston began. "I am quite confident that we can build new opportunities for synergy and interaction across our research community, while protecting the best traditions of the BBS program," he said. ❖

Affiliated Hospitals Gain New Leadership

Three HMS-affiliated hospitals named new leaders in the 2006–2007 academic year. McLean Hospital appointed Scott Rauch, professor of psychiatry, the new president and psychiatrist in chief of the hospital and chair of Partners Psychiatry and Mental Health in November 2006. Rauch ➡➡

Cohen and Blacklow Appointed to Lead Academic Programs

In July 2007, David Cohen, associate professor of medicine and health sciences and technology at Brigham and Women's Hospital, was named co-director of the Harvard–MIT Division of Health Sciences and Technology, a responsibility he shares with Martha Gray of MIT. He replaced Joseph Bonventre, the Robert H. Ebert professor of medicine and health sciences and technology at BWH, who had been co-director since 1998.

Cohen's lab studies the mechanisms that allow the liver to remove cholesterol from the blood and eliminate it from the body, which has clinical implications for cardiovascular, gastrointestinal, and obesity-related disease. He was the first to identify the role phosphatidylcholine, a lipid-binding protein, plays in directing the movement of cholesterol in liver cells. An ongoing project is defining the regulatory mechanisms of lipid metabolism from phosphatidylcholine and structure–function relationships. His group also studies



David Cohen (left) and Stephen Blacklow

the impact of obesity on hepatic cholesterol metabolism and identified the regulatory role of leptin in removing cholesterol from the body, particularly in weight loss.

Stephen Blacklow, associate professor of pathology at Brigham and Women's Hospital, became the basic sciences director of the MD–PhD program in July 2007. Blacklow had served as interim director since February, when Christopher A. Walsh, the Bullard professor of neurology, stepped down from the position.

Blacklow's research focuses on the relationship between structure and function in proteins in the low-density lipoprotein receptor family. His lab studies the mechanisms for ligand binding and release by the receptor and signal transduction by structurally related proteins. He also studies the structure and function of human Notch receptors. The long-term goal of the lab is to understand the detailed molecular basis for specificity in protein–protein and receptor–ligand interactions, emphasizing proteins implicated in human disease. ❖

New HMS Administration Dean Arrives from Main Campus

Daniel Ennis, former associate vice president for finance and financial planning for Harvard, was named HMS executive dean for administration in September 2007. He succeeded Cynthia Walker, who announced her intention to step down in the summer of 2007.

Ennis held several positions in the University's Finance Office since coming to Harvard in 2003. In his role as director of Harvard's Office of Budgets, Financial Planning and Institutional Re-

search, he was responsible for evaluating proposed operating and capital budgets for the University and tuition changes on behalf of the president, provost, and CFO. In addition, he assumed a broader set of financial leadership responsibilities including oversight of financial planning for Allston campus development.

Ennis is also a Harvard alum, graduating with a Master of Business Administration from Harvard Business School and a Master in Public Administration



Daniel Ennis

from Harvard's John F. Kennedy School of Government. He currently serves on the Alumni Advisory Board. Before joining the Finance Office he worked at McKinsey &

Company, a management consulting firm, where he led a strategic review of Harvard's central administration. ❖

→ was previously at Massachusetts General Hospital, where he served as director of the Division of Psychiatric Neuroscience Research and Neurotherapeutics. He succeeded Gary Gottlieb, president of Brigham and Women's Hospital, who had been serving as interim president of McLean.

John Fernandez was appointed president and chief executive officer of the Massachusetts Eye and Ear Infirmary and of its parent company, Foundation of the Massachusetts Eye and Ear Infirmary, Inc. He assumed the post in January

2007. Before joining MEEI, Fernandez was the vice president of clinical services at Brigham and Women's Hospital.

Ranch Kimball, who served as secretary of economic development for the Commonwealth of Massachusetts under former governor Mitt Romney, was appointed the chief executive officer and seventh president of Joslin Diabetes Center in February 2007. Kimball succeeded C. Ronald Kahn, the Mary K. Iacocca professor of medicine, who in September 2006 announced his intention to step down. ❖

Cell Biologist Honored by European Academy of Sciences

Howard Green, the George Higginson professor of cell biology, was awarded the 2007 Blaise Pascal Medal in Biology and Life Sciences by the European Academy of Sciences. The award was established in 2003 and recognizes outstanding contributions to science and technology, research, and education. Green was honored for his development of cultured skin cells for use in large-scale skin transplants for patients whose burns are too severe for conventional skin grafting. Green's lab is currently investigating differentiation of human embryonic stem cells into somatic cell types, focusing on the keratinocyte, a predominate cell in the epidermis and related tissues. He received the award in Brussels in September 2007. ❄



Howard Green

HMS Scientist Wins Lasker Award

Jack Szostak, a Howard Hughes investigator and professor of genetics at Massachusetts General Hospital, received the Lasker Award for Basic Medical Research in September 2006. Szostak, along with collaborators Elizabeth Blackburn of the University of California at San Francisco and Carol Greider of Johns Hopkins University, were honored for the prediction and discovery of telomerase in yeast, an enzyme that builds and maintains telomeres, the protective caps on the ends of chromosomes. Telomeres and telomerase were later found in human cells and identified as playing an important role in cancer and age-related illness. The Lasker Awards recognize outstanding contributions in medical research. In addition to the award for basic medical research, prizes are awarded in the categories of clinical medical research and special achievement in medical science. Nicknamed "America's Nobels," the Lasker Awards are considered one of the greatest honors for medical researchers.



Jack Szostak

Following his discovery, Szostak took his lab in a different direction and began investigating the molecular origins of life in order to understand how chemicals combined to form the first living organisms on primitive Earth. His work focuses on the ability of RNA to catalyze its own reproduction, and his studies involving a particular kind of clay that is part of this process has led to the speculation that a similar process may have led to the creation of the first cell. ❄

Scientific Grand Prize Features Heart Disease Work

Christine and Jonathan Seidman were presented with the Institut de France's 2007 Grand Prix Lefoulon-Delalande for their advancement of the understanding of inherited cardiac disorders. The Seidmans accepted the award, which included a \$682,000 prize and the Medal of the Institut de



France, in a ceremony in Paris in June 2007. Created in 2002, the Grand Prix honors scientists who have made significant contributions in the fields of cardiovascular physiology, biology, and medicine. Christine Seidman is a Howard Hughes investigator and the Thomas W. Smith professor of medicine at Brigham and Women's Hospital, and Jonathan Seidman is the Henrietta B. and Frederick H. Bugher Foundation professor of genetics. ❄

Braunwald Takes AAMC Rogers Prize

Eugene Braunwald, the Hersey distinguished professor of theory and practice of physic at Brigham and Women's Hospital, was awarded the Association of American Medical Colleges' David E. Rogers Award in October 2006. The award recognizes a medical school faculty member who has made major contributions to improving the health and health care of Americans. Braunwald is known for his discovery that myocardial infarct size can be limited by altering the balance of oxygen supply and demand, which led to the now common use of beta blockers during a heart attack. He is the author of more than 1,100 papers and the influential textbook *Braunwald's Heart Disease*. Braunwald is also chair of the Thrombolysis in Myocardial Infarction Study Group at BWH. ❄



Eugene Braunwald

Harvard Surgeon Receives MacArthur Grant

An HMS faculty member was among 25 scientists, artists, musicians, and engineers to be awarded a 2006 MacArthur Fellowship. Atul Gawande, associate professor of surgery at Brigham and Women's Hospital, was one of three Harvard University researchers selected to receive one of the grants that year. Gawande is a surgeon who has also written extensively about the culture, protocols, and technology of medical practice. He specifically looks at the reality of failure in a profession in which mistakes can cost lives. He has devised a number of solutions to improve practice, such as implementing the use of bar codes to track surgical equipment so it is not left in patients. Gawande is also an HSPH assistant professor of health policy and management, a staff writer for *The New Yorker*, a columnist for *The New England Journal of Medicine*, and author of two books, *Complications* and *Better*.

The MacArthur Fellowship consists of a \$500,000 stipulation-free grant over five years. ❄



Atul Gawande

HMS Faculty Named to NAS

Three on the HMS faculty were among the 72 members elected to the National Academy of Sciences (NAS) in 2007. These new appointees are Michael Brenner, Jonathan Seidman, and Clifford Tabin.



Michael Brenner

Brenner, the Theodore Bevier Bayles professor of medicine at Brigham and Women's Hospital, conducts immunologic studies of T cells and antigen-presenting cells in microbial and autoimmunity. Currently, his lab is examining the function of CD1-restricted T cells, including natural killer T cells, in humans and mice and the biology of cadherins in cell invasion and rheumatoid arthritis.

In the Seidman lab, Jonathan Seidman, the Henrietta B. and Frederick H. Bugher Foundation professor of genetics, works with lab co-director Christine Seidman (elected to the NAS in 2005) to integrate clinical medicine and molecular technologies to define disease-causing gene mutations and genetic variations that increase disease risk. Major research projects focus on discovery of the genetic contributions to



Jonathan Seidman

Awards Recognize Junior Faculty

Azad Bonni and David Reich are the winners of the 2006–07 Outstanding Achievement in Biomedical Research Awards, sponsored by the Genzyme Corporation. For the past six years, the award has recognized two junior HMS faculty members in preclinical departments, an assistant professor and an associate professor, who are conducting innovative research and emerging as leaders in their fields.

Bonni, an HMS associate professor of pathology, studies cell-intrinsic mechanisms that govern neuronal connectivity in the brain and how abnormalities of these mechanisms contribute to neurological disease. His lab has discovered a set of novel cell-intrinsic mechanisms that orchestrate the development of axons, dendrites, and synapses. The work is at the forefront of research on the mechanisms that control nerve cell survival.

Reich, an HMS assistant professor of genetics, focuses on mapping genetic variation in minority populations, which has led to the identification of seven risk factors for prostate cancer in a small region of the genome. These factors occur more frequently in African Americans than in European Americans and are responsible for doubling the incidence of prostate cancer in this population. He also uses genomic data in the study of evolutionary biology.

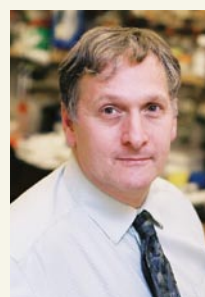
The \$45,000 awards were presented at the HMS Board of Fellows meeting in September 2007. ❄



David Reich (left) and Azad Bonni

cardiomyopathies, hearing loss, and congenital heart disease.

Tabin's lab has made major discoveries relating to how genes determine the organization of the early embryo and how they orchestrate the formation of various organs and structures in the body. Using a combination of modern and classical techniques, his lab has addressed issues such as why the heart forms on the left and not the right. Tabin is the George Jacob and Jacqueline Hazel Leder professor of genetics and head of that department (see pages 15 and 34).

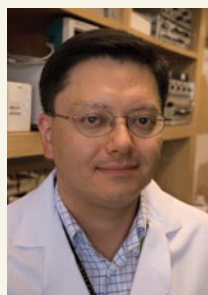


Clifford Tabin

The NAS is a private organization of scientists and engineers dedicated to the progress of science. New members are chosen in recognition of their achievements in original research. ❄

Seven in 2007 and One in 2006 Receive National Institutes of Health Director's Awards

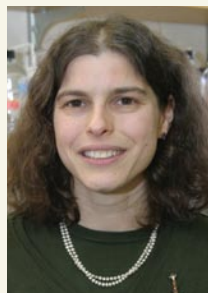
In September 2007, three HMS researchers received Pioneer Awards. Emery Brown, the Massachusetts General Hospital professor of anesthesia at MGH, will



Takao Hensch

use the award to study how drugs for general anesthesia act in the brain; Takao Hensch, professor of neurology at Children's Hospital Boston, will examine the role of noncoding RNAs in brain development and disease treatment; Frances Jensen, professor of neurology at CHB, will use her award to study how seizures in infancy affect the developing brain. The Pioneer Awards provide \$2.5 million over five years.

Four members of the Harvard Medical community received the 2007 Director's Innovator Award, a new grant that provides \$1.5 million over five years to early-career investigators. Levi Garraway, instructor in medicine at Dana-Farber Cancer Institute, seeks to apply a novel genetic and screening approach to identify changes in malignant melanoma tumor cells that could be targets for treatment; Nir Hacohen, assistant professor of medicine at MGH, will dissect immune system pathways that sense disease-causing agents; Konrad Hochedlinger, instructor in medicine at MGH, will study the reprogramming of adult mouse and human cells into embryonic cells by defined factors; Mark Johnson, assistant professor of surgery at Brigham and Women's Hospital, will examine the role of decreased synthesis of microRNA in human cancer.



Rosalind Segal

In September 2006 Rosalind Segal, professor of neurobiology at DFCI, was awarded a Pioneer Award, which supports her exploration of how proteoglycans affect stem cell growth in normal development and in brain tumors.

The awards are part of the NIH Roadmap for Medical Research, which supports scientists taking innovative approaches to biomedical research that may be too novel, too risky, or too early in development to receive traditional NIH funding. ❖



Emery Brown



Frances Jensen

IOM Names Four from HMS

Four HMS faculty members, listed below, were among the 65 new members elected to the Institute of Medicine for 2007. The IOM, part of the National Academy of Sciences, advises national policymakers on issues pertaining to health, biomedical science, and medicine.

Emery Brown

Massachusetts General Hospital Professor of Anesthesia, MGH

In his statistical research, Brown develops signal-processing algorithms and statistical methods to study how the brain and nervous system represent and transmit information. His experimental research uses combined functional magnetic resonance imaging and electroencephalogram recordings to study how anesthetic drugs induce the state of general anesthesia in the brain. (Also see story at left.)

William Kaelin

Howard Hughes Investigator, Professor of Medicine, Dana-Farber Cancer Institute

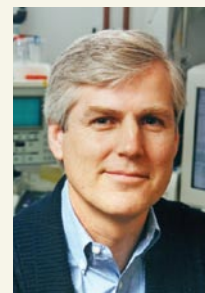
Kaelin studies tumor suppressor genes and the normal functions of the proteins they encode, with a focus on the von Hippel-Lindau tumor suppressor protein, the retinoblastoma tumor suppressor protein, and the p53-like protein p73. His group is also studying tuberous sclerosis, a hereditary cancer syndrome caused by mutations in either of two genes.



David Scadden

Gerald and Darlene Jordan Professor of Medicine, MGH

Scadden's research focuses on stem cell biology, emphasizing blood stem cells and the mechanisms by which they are governed. He has defined molecules affecting stem cell proliferation and specific components of the complex niche in which they reside. His research is linked to developing new therapies for immunocompromised patients with AIDS or cancer.



Jonathan Seidman

Henrietta B. and Frederick H. Bugher Foundation Professor of Genetics, HMS

Jonathan Seidman (also see pages 36-37) works with lab co-director Christine Seidman to integrate clinical medicine and molecular technologies to define disease-causing gene mutations and genetic variations that increase disease risk. Major research projects focus on discovery of the genetic contributions to cardiomyopathies, hearing loss, and congenital heart disease. ❖



Michelle Arnold and Tijana Ivanovic
Program in Virology, Division of Medical Sciences

Leaving her native Serbia to attend high school in Oregon and college in California allowed Tijana Ivanovic (right) to pick up at least two skills. One was salsa dancing. The other was prowess at virus research that someday may help save children's lives in the developing world.

Ivanovic is to get her PhD in virology after working with Max Nibert, professor of microbiology and molecular genetics, studying reoviruses. Reoviruses belong to the *Reoviridae* family, other members of which attack the gastrointestinal system and cause lethal diarrhea among children in poor nations. Working with a non-pathogenic virus, she discovered steps and specific virus-derived mediators creating pores in cell membranes that allow viruses to enter the cell. Ivanovic has presented her work at several conferences, including those of the American Society for Virology (ASV).

The process creating her passion for virology would have been an intellectual bait-and-switch, had it been deliberate. "Viruses seemed to be smaller and much more tractable than, say, a huge bacterium. They seemed like a simpler system by which to study similar questions. But it turns out that in virology, you're actually studying a cell" infected by a virus. "It's not as simple as I believed. Now I like that aspect. You can use viruses, a simpler system, to uncover very complicated things about how whole cells work."

Michelle Arnold, Ivanovic's erstwhile research partner and another Nibert protégé, uses genetic manipulation to study how retroviruses replicate themselves inside a cell. Arnold investigates a protein produced in the cell by the invader virus. Her research showed that the protein makes "factories" that build replica viruses. How essential this protein is in the process was uncertain. To study that question, Arnold degraded the RNA of the protein in test cells so the protein no longer was produced.

"I have been able to show that without the protein, the virus no longer replicates," she said. Down the therapeutic road, "By interfering with how that protein makes these factories, we might be able to block the virus."

Arnold also has presented her findings at ASV conferences, playing to her love of teaching. She instructed Simmons College undergraduates in lab courses, and she is the first person in her family to receive a doctorate. Her parents, a businessman and librarian, "definitely don't understand exactly what I do, but they're very supportive of me being able to do whatever I want." ❖



Kenneth Colodner
Program in Neuroscience
Division of Medical Sciences

In Kenneth Colodner's life, a longstanding intellectual passion for medicine was set aflame by the matchstick of personal loss. His grandfather died from Alzheimer's disease, his grandmother from Parkinson's.

The Long Island native, who expects to receive his PhD in neuroscience in 2008, has spent his time at HMS researching the effect of a protein, tau, on brain cells called glia. He hopes the work might someday produce therapies to inhibit neurodegenerative diseases.

In patients with Alzheimer's and similar illnesses, tau accumulates in the brain's neurons—that was well known—but also in the glia, cells that modulate the thought-transmitting neurons by strengthening or weakening synaptic responses. Working under HMS neuroscientist Mel Feany and funded by the National Institutes of Health, Colodner studied fruit flies that had been genetically induced to produce tau in their glia. No winner in the longevity contest, the fruit fly found its typically two-month life span almost halved by the brain buildup of glial tau. That was bad for the fruit fly, but good for Feany and Colodner, who discovered that the tau in the glia was toxic not only to those cells but to the neurons as well.

"Much less was known about the role of the glial tau," he said. Explaining the therapeutic promise of the work, he added, "Potentially, if you could figure out a way to prevent tau from getting into the glia, or if there are some signaling molecules that originate in the glial cells and are toxic to the neurons and you could block that pathway, then perhaps you could retard the disease."

He hopes to do both research and teaching after finishing his education. As a teaching fellow, he won a certificate of distinction from Harvard University for his work instructing undergraduates in behavioral neuroscience. The award was based on student comments. "The ability to convey science to a lay audience," he said, "is important not only for your own understanding of what you're studying but also in terms of garnering more public support." ❖



Andrew Herring Peabody Society

In the universe of people striving for public policy grants, Andrew Herring is something of a gold-medal Olympian. He beat out 2,000 competitors in a contest with a demanding judge, the World Bank.

En route to his MD in 2008, Herring got a Fulbright fellowship to study mortality differences in Costa Rica between natives and immigrants. He came across the Guaymi, migrant coffee workers from Panama, forced to work the plantations since their ancestral lands have been taken from them. “They have no national identity—they aren’t Panamanian; they aren’t Costa Rican,” Herring said. “Their infant mortality and poverty are as bad as anyone in the hemisphere. Among the hierarchy of oppression within indigenous groups, the Guaymi are the bottom.”

The World Bank gave him and his coworkers \$200,000 to provide basic medical care for the Guaymi. It is not the only time that medicine served Herring as a path toward social justice. During his Cambridge Hospital clerkship, a Brazilian man, an illegal immigrant, showed up in the ER needing a heart transplant. “For the next two weeks, I watched him die,” said Herring. He was not placed on the transplant list because undocumented aliens are at risk of being deported. “It struck me as very wrong,” he explained, since many undocumented immigrants are asked to donate organs themselves, with the assumption of equal access to donated organs among those who need them.

Mentored by Cambridge Hospital physicians David Himmelstein and Stephanie Woolhandler, Herring researched a paper suggesting that up to 20 percent of organ donors are uninsured, though the percentage of uninsured organ recipients is far smaller.

“Medicine is a way to explore these worlds of humanity in the context of a beautiful reciprocity. I feel very confident that I’m also giving back,” said Herring, who plans a career in emergency medicine.

Somehow, he juggles studies and research with being the father of a 2-year-old. Said Herring, “I’ve written a lot of things with my son sitting on my shoulder.” ❖



Sachin Jain Castle Society

Some people dream of reforming health care in America. But when your talents are not confined to American medicine, why should your ambitions be contained by one nation?

Sachin Jain received a Dean’s Award upon graduating from Harvard Business School in 2007, and he continues as a senior researcher there, writing case studies of community hospitals and academic medical centers while working toward his MD in 2008. The research has given him ideas for righting the nation’s foundering health care system. But he also finds time to serve on the board of his family’s foundation, which funnels medical services to rural villages in his parents’ native India.

A government internship during his Harvard undergraduate years showed Jain the cloistered existence of a wonk. His physician father’s career, by contrast, highlighted the human interactions of clinical practice. His determination to combine the two in his own career was clinched when he took an undergraduate course taught by Donald Berwick and Howard Hiatt, clinical professor of pediatrics and health care policy and professor of medicine, respectively (Hiatt is also a former dean of the Harvard School of Public Health). The class convinced him that medicine’s shortcomings “need to be addressed by people who are both clinically skilled and aware of the complexities of management.”

“Some people see Michael Jordan playing basketball and say, ‘I want to be like Mike.’ For me, it was, ‘I want to be like Don.’”

Barbara McNeil, chair of the Health Care Policy Department, encouraged his twin passions at HMS. His business school research could be the springboard for his medical school thesis. (He also co-edited a book, *The Soul of a Doctor*, as a student.) He hopes for a career running a hospital or hospital system while doing policy research.

Defying the stereotype of the cold-blooded businessman, Jain gave such compassionate care to a pregnant Cape Verdean during his clinical clerkship—he left home at night to attend the delivery—that she named her newborn son after him, and apparently considered him as a potential adoptive father. “She wanted to know if I had a girlfriend.” ❖



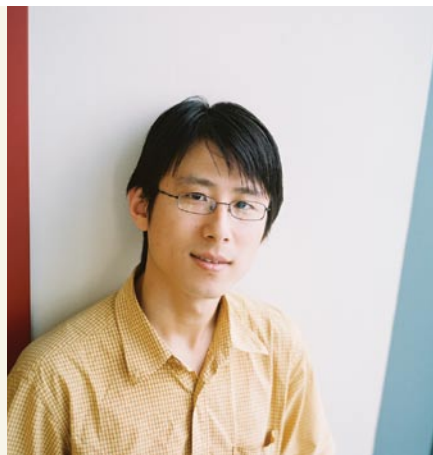
Agnieszka Janisiewicz Holmes Society

The patient with amyotrophic lateral sclerosis, a man in his 60s, showed symptoms from tiny flutterings in his muscles to a laugh that escaped at inappropriate moments. Knowing he would die, he was planning to relocate to New York from Florida so his Columbia-based doctor could oversee the end of his life.

“This was a doctor patients turned to during their time of crisis, and this is an incredibly powerful bond I’d never seen before,” said Agnieszka Janisiewicz, then a researcher at Columbia. Cementing her passion for medicine’s human side, the experience helped nudge her to HMS, after which she plans a career doing eye, nose, and throat surgery with complementary basic research.

She will deploy a formidable toolbox of experience. At HMS, she worked with some sleepy mice to study narcoleptic patients suffering from chronic daytime sleepiness. Healthy people consolidate sleep into blocks—“six hours, if we’re lucky,” the med student said knowingly. Earlier research showed that narcoleptics’ lack of a neurotransmitter called orexin, by itself, did not skew circadian patterns of non-REM and REM sleep. Janisiewicz and her colleagues investigated whether the neurons producing orexin also make other signaling molecules that aid sleep rhythms, even in the absence of orexin. Further, they looked at whether the absence of these specific neurons contributes to daytime drowsiness.

For Janisiewicz, summering as a child at her family’s rural farm in Poland, where “time stopped in the late 1800s,” forged a fascination with different cultures. This interest has led her at HMS to volunteer for programs with Navajo and Inuit peoples, studying the integration of Western and traditional medicines. From watching Navajo medicine men doing rituals outside the hospital to boating with nurses across expansive Alaska waters to reach remote Inuit outposts, Janisiewicz calls herself “blessed” to have attended HMS. She counts faculty members Anthony D’Amico, Julian Seifter and Jo Shapiro as mentors. A longtime ballet dancer, she does distance running as well, which has allowed her to stretch herself in other ways, such as



Fei Lan Biological and Biomedical Sciences Program Division of Medical Sciences

If Einstein and others who explained the physical universe owned the 20th century, the 21st may belong to explorers probing the inner space of our bodies. That realization led Fei Lan to become a genetic bounty hunter, searching for biological predators behind afflictions from cancer to mental retardation.

Lan, one of the handful of Chinese students attending HMS on Fu fellowships each year, is due to receive his PhD in 2007–08 from the Biological and Biomedical Sciences Program. Pathology professor Yang Shi calls him “the best graduate student I have worked with” because of research Lan did in his lab involving histone, the protein trellis around which DNA wraps.

Lan helped discover several enzymes (called histone lysine demethylases) that remove certain methyl groups from histones, a process that “has a very promising application in medicine.” One of the enzymes later was found to be excessive in high-risk prostate cancer patients.

Another of the discovered enzymes can mutate and lose its chemical marker-scrubbing function, a mutation that appears in patients with mental retardation. The level of inhibition of the scrubbing function correlates with the severity of the disability.

Lan was a top student at Fudan University back home, but not number one or two in his class. HMS has many of those from other Chinese universities, he said, and he is grateful that the School looked at not just his class rank but research experience as well. “Harvard gave me a very good opportunity—not only the benefit of working in a lab, but also, there are thousands of labs in Harvard Medical School. It’s a fantastic scientific environment to discover new things.”

In his (infrequent) spare time, he has taken pleasure in mentoring a teenager from Boston Latin whose parents hailed from Vietnam. “I’m a foreigner, too, and you try to show them how exciting science is,” he said. He is also a sports fan. Able to trace the most elusive genetic fugitives, Lan had a tougher time finding another quarry: fellow soccer players. “Soccer in



Sonali Mukherjee Health Sciences and Technology

The daughter of engineers and an MIT graduate who thought she would major in computer science, Sonali Mukherjee switched to biology after studying lung disease mechanics in a bioengineering course. “Computers are wonderful,” she said, “but I think the most complex engineering feat on this Earth is the human body.”

In her third-year clerkships at HMS, she cared for a 35-year-old patient with metastatic melanoma. “He was an inspiration to me. He was in a sad spot, but he wanted to go forward with his treatment.” The last she knew, he was receiving end-of-life hospice care. Her future life, meanwhile, had found a calling in researching skin cancers.

Aspiring to a career combining dermatology research with teaching, she won HMS’s Doris Duke/PASTEUR Clinical Research Fellowship, given to a half dozen students each year; hers was among 72 applications. Working with faculty members Zeina Tannous at the Boston VA Medical Center and Lyn Duncan at Massachusetts General Hospital, she studied a new, “pulsed dye” laser technique for treating basal cell carcinomas in patients whose multiple carcinomas make surgery impractical. This laser targets large blood vessels feeding the tumors. On tissue examination, more than 90 percent of smaller tumors (measuring less than 1.5 centimeters in diameter) showed complete response to the treatment. That’s “an amazing finding, because pulsed-dye laser is not considered standard of care” for basal cell carcinomas, she said. She hopes the study will help change that.

Mukherjee is to get her MD in 2008 after five years in the Medical School’s Health Sciences and Technology (HST) society. She found the program unique, when choosing among medical schools, in allowing her to marry her technology and medical interests.

Medical school has let her demonstrate her other gifts: singing, acting, and writing. A soprano, she poked gentle fun at political correctness as “Culturally Competent Carla” in the 2005 Second Year Show. She owes HST for one more thing: her new husband is himself an alumnus. ❖



Sampeter Odera School of Dental Medicine

An ordeal at the dentist is a staple of American folklore. For Sampeter Odera, a real-life dental nightmare helped set his career course. A botched anesthesia job in his native Kenya left a teenaged Odera painkiller-free during a tooth extraction. Though tough enough to play rugby, he found the tooth-taking “excruciatingly painful.”

“Given an opportunity, I will seek to change things for people who are not treated optimally,” Odera said. Scheduled to graduate from the Harvard School of Dental Medicine in 2008, he has volunteered as a student dentist with low-income Boston kids, and he hopes to return to his native country as an oral and maxillofacial surgeon. In addition to seeing patients, he wants to teach, “to plant a seed and bring forth access” to dental care.

Odera has been a research fellow at the Howard Hughes Medical Institute in Bethesda, designing a mouse model for the pathology of osteonecrosis of the jaw. That disease, in which the bone tissue dies, has been noted in cancer patients taking certain brands of a medication called bisphosphates. He found that mice injected with bisphosphates recover from a tooth extraction more slowly in the early stages of healing than those without the drug and that, in the later stages, their bone grows back more densely. The quality of the bone remains under investigation.

The start of the new millennium marked a personal beginning as well for Odera, who immigrated here after American education beckoned with opportunities he could not find at home. That hope was marred by tragedy, however. His father, who had HIV/AIDS and hoped to come here in part for treatment, died before making the trip while his family waited in their new country. Odera was just 17. His father had instilled values so the teenager could lead his family, Odera said, including a love of creativity that finds expression not only in medicine but in his hobby of architectural drafting. ❖



Jason Sanders Cannon Society

“I can think of no one in my years as society master ... whom I would regard as his equal.” Gordon Strewler based this tribute to Jason Sanders partly on the latter’s proficiency in a staggering array of fields.

He is to pick up both his MD and MBA from the Medical School and Business School in 2008. As a Rhodes Scholar, he also earned a degree in English language and literature at Oxford, where his thesis pondered “The Language of Mental Illness” in Virginia Woolf’s novel *Mrs. Dalloway*. As Sanders sees it, the humanities, social science, and science all make him a better doctor.

Medicine is his bedrock interest. Before graduating summa cum laude in his home state from the University of Oklahoma, he worked a summer as a hospital orderly. “A lot of manual labor,” he recalled. “I literally lifted patients from beds to chairs everyday, when they had breakfast, lunch, and dinner. Talking to the patients and watching doctors work sold him on medicine’s role in public well-being.

Later, he took a medicine and literature course that introduced him to patient narratives of their experience. Literature, he said, taught him “how important communication is” in healing. (He writes regularly for the Medical School’s *Focus* and *Web Weekly*.)

It was HMS’s third-year clinical clerkships that aimed him toward an MBA. “I enjoyed being part of the care delivery team—not just the physicians but the nurses and respiratory therapists” and others on the wards. “They had a lot of good ideas for how to change things, but they really didn’t have the time or wherewithal to change them.” Given the national attention being paid to improving health care systemwide, Sanders saw the window open for a manager who wanted to implement the best reforms.

“I could be, with business skills, almost a bridge” between the various professionals. “That’s what’s so exciting—you feed off the other people around you.” Hoping for a career managing a hospital system, he’s practicing by simultaneously managing studies in the joint degree program and his duties as the father of a newborn. ❖



Mark Wein Program in Immunology Division of Medical Sciences

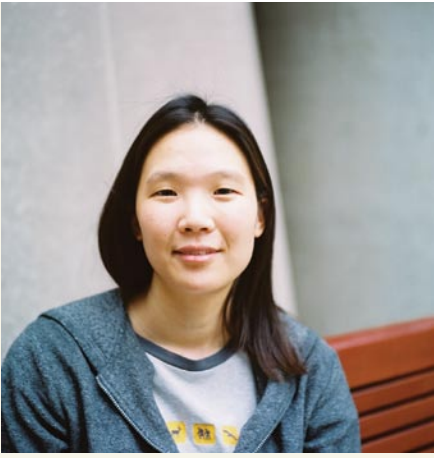
Medicine is not a surprising career pick for Marc Wein. Four family members are doctors, and watching his physician father work sold Wein on the profession. But his pathway in the MD–PhD Program detoured him down an unexpected route. He earned his doctorate in immunology in 2007 for non-immunological research that could help alleviate the suffering of people with osteoporosis.

He started out naturally enough. Immunology fascinated him because it seemed the basis of so many diseases he would be treating as a doctor. Working in the lab of his mentor, Laurie Glimcher, Wein began researching a gene, *Schnurri-3*, that the lab had discovered and that appeared to play a role in differentiating the various cells in the immune system. He studied mice that had been deprived of the gene. Surprisingly, *Schnurri-3*’s absence wrought no significant effect on the immune system. It did, however, turbocharge the production of bone mass, reversing the normal bone loss that comes with aging.

“I thought I was going to be doing my PhD in immunology. But really, this gene is much more important in the skeletal system,” he said. He found that the *Schnurri-3* protein acts as a brake on osteoblasts, the major cell type making bone.

Evolution put *Schnurri-3* in us for a reason—without it, the mice’s bones grew to the point that they filled in the space for marrow—and the effects of reducing it need to be thoroughly studied, he said. But “most of the existing treatments for osteoporosis stop the breakdown of bone. They don’t give you new bone. We’re interested in the possibility that *Schnurri-3* inhibitors might stimulate bone formation.”

Wein is to get his MD in 2009. While his research strayed from immunology, it was impressive enough to earn him an Albert J. Ryan fellowship and travel grants to several conferences, all of which allowed him to discuss his work in professional forums. Meanwhile, at least he learned one lesson of immunology: even in the lab, you are not immune to love. Wein met his fiancée when both worked in the program, and they are to be married in 2008. ❖



Ellen Yeh MD–PhD Program

Some visit Germany for its history or magnificent cities. Ellen Yeh went to study “bugs,” her word for the bacteria and fungi that are nature’s factories for producing certain life-saving drugs. It’s not that Yeh is a geek; she jogs and has hiked the White Mountains and backpacked along the Hawaiian coast with her fiancé. But she is also a passionate researcher.

To get her PhD in biophysics and her MD through the Harvard–MIT Division of Health Sciences and Technology, she has worked in laboratories in Germany as well as at the University of Michigan, Penn State, and in the lab of her HMS adviser, Christopher T. Walsh. She studied the key question of how bugs incorporate chemical elements called halogens (mainly chlorine) to endow their molecules with key drug properties. Yeh discovered an essential enzyme intermediate in that chemical process, chloramine. Her basic research might help scientists down the road chemically tweak other organisms and wring new or better drugs from them.

“I actually wanted to be a writer when I was younger, but the sciences have always grabbed me,” said Milwaukee-born Yeh, who was asked to present her findings at a symposium of select university labs working in the field. “I like the reasoning behind it. I like the challenge. I’m a skeptical person, so I always want evidence for everything. I’ve always liked the discovery aspect.” Her father is an engineer, but she was more interested in biology. She still remembers helping him build a fish pond next to their house when she was in fifth grade and having to explain to him that plants breathe in carbon dioxide and breathe out oxygen.

She credits her success partly to Walsh’s pitch-perfect balance of guidance and freedom. “He really takes care of the people in his lab. He gives you a lot of independence, but at the same time, doesn’t let you get too lost.” ❄

Judah Folkman • Class of 1957

As the oldest child, Judah Folkman, the Julia Dyckman Andrus professor of pediatric surgery at Children’s Hospital Boston, was expected to follow in his father’s footsteps. On weekends, his children in tow, Rabbi Folkman ministered to the congregants who were sick. The younger Folkman observed that the doctor, but not the rabbi, could open the oxygen tent. At the age of 10, Folkman announced that he would be a doctor.

In high school, Folkman, working in the nearby Ohio State University hospital, became interested in surgery. Noting that violinists begin learning their skills barely into grade school, a professor of surgery, Robert Zollinger, arranged for Folkman to work in his dog surgery lab, practice that Folkman continued while an undergraduate at the university.

After Folkman was accepted at HMS, Zollinger recommended him to Robert Gross, the chief of surgery at Children’s.

Gross, who performed the first cardiac septal defect repairs in babies, asked Folkman to develop a dog model to avoid the complications of heart block. He left the model’s design entirely up to Folkman. That model became Folkman’s first

James O’Connell • Class of 1982

James Joseph O’Connell, HMS 1982, was a resident in internal medicine at Massachusetts General Hospital planning a fellowship in oncology when a surprise opportunity changed his course. John Potts, O’Connell’s chief of medicine, and the late Thomas Durant, on staff at MGH and renowned in the international aid community, “corralled me” into running the nascent Boston Health Care for the Homeless Project (BHCHP). “I pictured a year of urban Peace Corps, where I could salve my late ’60s conscience,” he said. Instead, the project became his life.

Over the years, O’Connell molded BHCHP into the leading program of its kind. Originally a four-year grantee of the Robert Wood Johnson Foundation at an annual level of \$250,000, the project was taken over in 1988 by the U.S. Department of Health and Human Services, enabling greater expansion and billing to Medicaid. Today, its 350 providers, including O’Connell, provide care in three Boston-area hospital systems, 70 shelters, and on the streets.

Early innovations included establishment of respite care, partly to cope with shrinking hospital stays, and development of computerized records. Octo Barnett of MGH took the lead on the record system, which went live in 1993, enabling all the providers at all the sites to access each patient’s information in seconds. This effort won the 1993 Center of Healthcare Information Management Award for MGH’s Laboratory of Computer Science, and it has facilitated out-

professional publication and enabled development of a novel repair method for ventricular septal defects.

Gross also coached Folkman prior to presenting the paper at a national surgical meeting, preparing him for the unexpected—burned out projectors, malfunctioning mikes, etc. “He was like a pilot always looking for a place to land,” said Folkman, adding that he teaches his own students in the same way. Gross, he said, gave him “enormous responsibility without risk or penalty.”

That, in turn, gave Folkman the self-confidence he needed to face the critics of his angiogenesis theory. The concept grew out of an experiment in 1960, in which Folkman found that tumors implanted into dog thyroid glands kept alive in glass chambers would not grow beyond 1 to 2 mm, apparently because they could not recruit new blood vessels.

The idea that tumors could depend on angiogenesis was rejected for publication until 1971, when Franz Ingelfinger,



editor of *The New England Journal of Medicine*, heard Folkman speak. Since then, angiogenesis research has grown to include 39,000 published papers and 70 books. Many angiogenesis inhibitors have been identified, the first 11 in the Folkman lab. Ten anti-angiogenic drugs have received Food and Drug Administration approval for treatment of cancer and age-related macular degeneration. Other angiogenesis-dependent diseases have been identified.

His experience as a pediatric surgeon informed his work on angiogenesis, said Folkman, who is now director of the Vascular Biology Program at Children’s. One example: children with nephrotic syndrome lose proteins in the urine, including antithrombin III, which can result in death from pulmonary embolism. By analogy, he posited that cancer patients could be losing angiogenesis inhibitor proteins in their urine, and current animal experiments suggest that replacement therapy could improve cancer management. ❄

comes research. BHCHP currently is trying to move the chronic homeless, who incur by far the highest costs and mortality, into housing. O’Connell said that this should drastically reduce the loss of dollars and lives.



O’Connell, who has written the leading manual on caring for the homeless, absorbed his passion for social justice during the ’60s. After college, he struggled for 10 years to find his niche, earning a master’s in theology at Cambridge University, teaching high school, and living a hippy’s life with friends in an old barn. He also tended bar off and on and loved listening to patrons’ stories.

An experience in 1976 crystallized his ambitions. A motorcycle he was following lost control, he says. “The man broke his leg, and so I sat with him in the middle of nowhere for an hour while the others went to get help. I remember wishing I knew how to make him more comfortable, but the conversation felt as if we had known each other for 20 years. That’s when I decided to go to medical school.” ❄

Debra Yu • Class of 1992

Debra Yu, HMS 1992, still plans to practice medicine. “Every time I enter a hospital, I feel a pang, like I belong there,” she said. But Yu, once a “very nervous child” who pulled herself together into “this loud, extraverted valedictorian, the only cheerleader who was a ‘mathlete,’” has always done things differently, driven by her curiosity and her desire to improve medicine writ large.

When she matriculated at HMS, this sheltered daughter of Chinese immigrants found she “wasn’t thirsty for the knowledge of medicine.” She wanted to understand the ways of the world. Yu had spent an undergraduate summer at Genentech, and now, informed that finance would prove critical to biotechnology’s future, she became fascinated. She took a leave from HMS and was hired at Morgan Stanley by John Freund, HMS 1980, who also holds a BA and an MBA from Harvard.

Yu then “refound my passion for medical school,” where “I loved Manfred Karnovsky, who made biochemistry come alive.” Nonetheless, her sojourn at Morgan Stanley had shown her that the Food and Drug Administration and the pharmaceutical industry would determine biotechnology’s destiny. “I wanted to go crack these two nuts,” she said. “I decided not to match.”

Yu served at the FDA as a medical officer intern, followed by four years at the consulting firm McKinsey & Co., where she concluded that pharma was preoccupied with managed care, not innovation. So Yu became a venture capitalist, nurturing startups in her quest to understand how they might ➔➔

Collin Stultz • Class of 1997

For Collin Stultz, HMS 1997, growing up in Brooklyn consisted of school, twice-a-week church services, and study—his mother’s way to keep him from trouble. A Jamaican immigrant, Stultz was fascinated and bothered by what he did not understand. The incompleteness theory, that the set of mathematical truths cannot be counted, gleaned from Gödel, Escher, and Bach, set him on edge.

At Harvard College, Stultz relished big ideas like recursion theory and scientific realism—the question of what it means for a scientific theory to be true. Parental influence steered him elsewhere. “To my mother, a preacher, and a disciplinarian with no tolerance for failure, the only worthwhile professions were



medicine, law, and the clergy,” he said. Although he was not called to medicine, Stultz left it open.

The Harvard–MIT Division of Health Sciences and Technology (HST) enabled him to combine mathematics with medical service. But Stultz missed focusing on math, so after two years, he went to work with a computational biologist at MIT. He liked it so much that he got a PhD in biophysics at Harvard University before returning to HMS.

At the Medical School, Stultz loved cardiovascular pathophysiology, because the pump and plumbing aspects could be modeled in engineering terms, he said. Stultz did his internship, residency, and fellowship in cardiology at Brigham and Women’s Hospital, and he still sees patients occasionally.

Rita Fisler • Class of 2002

Her independence led Rita Fisler adventurously and circuitously to medicine. Her family could not afford Bennington College, so upon high school graduation, Fisler decamped to New York, applied to Bennington as an independent student, and got a full scholarship.

There, Fisler studied music. Following sophomore year, she took a jazz workshop in France, immersed herself in the Paris music scene, sang in the Opera of Marseille, and dropped out of Bennington. She returned to the United States five years later to attend the New England Conservatory of Music.

After graduation, she taught in Indonesia and returned home overwhelmed by the poverty there, wanting

to “work with kids who had experienced trauma,” she said. “I knocked on Bessel van der Kolk’s door at Massachusetts General Hospital,” who was conducting such research. She soon had a job and ultimately ran van der Kolk’s research projects.

There, Fisler decided to go into medicine. After van der Kolk left Harvard, she conducted a seminal study with Scott Rauch at MGH (who is now president of McLean Hospital) showing that traumatic memories are stored and recalled differently from nontraumatic memories.

At HMS, Fisler discovered she loved hands-on medicine, conducting physicals, surgery, and dermatology. She also had a baby—and two years later, another. To her dismay, after the first birth, she got a rotation 90 minutes from Harvard—more than she could handle. Nancy Oriol,

→ transform the field. After several years, she wanted to nurture the entire industry. She became a managing director at Bay City Capital, developing investment strategies, identifying areas ripe for investment, and managing investment teams.

Yu says that bringing the venture capital perspective to Pfizer, where she now serves as senior director and team leader, is “like being a missionary.”

She has convinced the company that rather than dampening drug sales—as it had feared—better diagnostics would improve the efficacy of drug treatment, and she has brought more creativity to the financial side. Additionally, with prevention in mind, she is searching for ways to mine existing data—from clinical trials, demographics, and

anything else—for portents of medical problems to come.

It is only her very high energy level that enables Yu to balance work with single motherhood. She appears at right with her 4-year-old son, Eland. ❖



Stultz's current research, on collagen, evolved from his fascination during fellowship with clotting. He read about the relevant proteins. Then he modeled their behavior according to Newton's laws. Stultz, now an HST faculty member and the W.M. Keck assistant professor of biomedical engineering at MIT, has continued using these techniques to study inflammation in arthritis and plaque formation—processes involving collagen. His work has advanced the field because, previously, collagen had been studied at relatively low temperatures with results that contradicted real-world observations. Stultz's simulations have overcome the practical barriers to studying collagen at normal body temperatures in living subjects.

Stultz also studies abnormal protein conformations in Alzheimer's and cancer metastasis. Does he miss pure math? In his medical research, he said, "you can verify things, and that can lead to bettering peoples' lives. That is much more satisfying than solving proofs." ❀



now dean for students at HMS, intervened, allowing Fisler to complete her second year of school over two years.

Several trips to the emergency room for her son's heart

disorder, Wolff-Parkinson-White syndrome, convinced Fisler to go into dermatology, rather than psychiatry, to balance her life. With Marilyn Liang, at Children's Hospital Boston, Fisler wrote an influential review of treatment protocols and outcomes for dermatomyositis, showing that early, aggressive treatment works best.

Following residency at the University of Kansas, Fisler is running the Dermatology Department at College Park Family Care Center in Kansas City, "expanding the practice tremendously to include cosmetics, lasers, and advanced surgery." Her psych background gives her a holistic perspective on her patients.

At Harvard, Fisler's list of mentors included William Taylor, her adviser. More generally, Fisler said that HMS's emphasis on analysis and communication over GPA and test scores gave her excellent preparation for "the real world of medicine." ❀

Anne Alonso

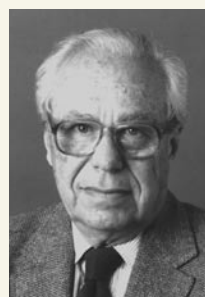


Anne Alonso, clinical professor of psychology in the Department of Psychiatry at Massachusetts General Hospital, died in August 2007 at the age of 73.

Alonso received her AB from Emmanuel College in 1956 and her MEd from the Harvard School of Education in 1969. After two internships in outpatient individual and group therapy at the Boston University Counseling Center and the MGH Department of Psychiatry, she became a fellow in outpatient individual and group therapy at MGH from 1969 to 1975, receiving her PhD in Clinical Psychology from Fielding Institute in 1980.

She served as the coordinator of Group Therapy Training in the Department of Psychiatry at MGH from 1976 to 1985. In 1982, she was appointed instructor in psychology in the Department of Psychiatry at MGH and HMS. She was promoted to assistant clinical professor in 1983, associate clinical professor in 1989, and clinical professor of psychology in 1997. She founded and led the Center for Psychoanalytic Studies at MGH, where she worked until becoming ill a few months prior to her death. ❀

Elkan Blout



Elkan Blout, the Edward S. Harkness professor emeritus of biological chemistry and the former dean of academic affairs at HSPH, died in December 2006 at the age of 86.

Blout received a doctorate in chemistry from Columbia University. After a year as a research fellow in chemistry at Harvard, he was recruited by the Polaroid Corporation, where he played an important role in the development of instant color photography. He then returned to Harvard in 1950 as an HMS research associate in pathology. In 1962, he was promoted to professor of biological chemistry at HMS. He chaired the Department of Biological Chemistry from 1965 to 1969 and retired from the University in 1991.

Blout is also known for his major contributions to the study of the synthesis and conformation of polypeptides and cyclic peptides. He received many honors throughout his career, including a National Medal of Science in 1990. Two professorships, one at HMS and one at HSPH, were established in his honor shortly before his retirement. ❀

Tucker Collins



Tucker Collins, the S. Burt Wolbach professor of pathology and chief of pathology at Children's Hospital Boston, died in June 2007 after being diagnosed

with an aggressive brain tumor six months before. He was 54.

Collins received his BA from Amherst College in 1975 and completed his MD and PhD at the University of Rochester School of Medicine in 1981. He joined the HMS community in 1981, completing his residency training in pathology at Brigham and Women's Hospital in 1986. Collins was appointed an instructor in pathology at HMS in 1985. He was promoted to assistant professor in 1986, to associate professor in 1992, and to professor in 1998. In 2001, he was named the S. Burt Wolbach professor of pathology and chief of pathology at the Medical School and Children's.

At HMS, Collins was active on a promotion review committee and had recently concluded participation on a search appointment committee. He also served as associate master of the Peabody Society for 10 years. ❖

Allan Friedlich

Allan Friedlich, professor emeritus of medicine at Massachusetts General Hospital, died in July 2006 at the age of 89.

Friedlich received his AB from Dartmouth College in 1939. After receiving his MD from HMS in 1943, he completed his residency at Massachusetts General Hospital and went on to serve as a medical officer in the Army Air Force for three years. He returned to MGH in 1947, then worked in the clinic of pediatric cardiologist Helen Taussig at Johns Hopkins Hos-

pital from 1949 to 1950. Friedlich returned to MGH for specialty training in cardiac medicine and, in 1953, was appointed an instructor in medicine. He was promoted to clinical professor of medicine in 1984 and appointed clinical professor emeritus of medicine in 1987.

Working under Paul Dudley White, founder of the American Heart Association, Friedlich performed some of the early research in cardiac catheterization. He later was one of the cardiologists to develop the first cardiac catheterization lab at MGH. ❖

Hermes Grillo

Hermes Grillo, professor of surgery at Massachusetts General Hospital, died in October 2006 in a car accident in Italy. He was 83.

Grillo received his AB from Brown University in 1943 and his MD from HMS in 1947. His training in general and thoracic surgery at Massachusetts General Hospital was interrupted by two years as a combat surgeon with the 1st Marine Division during the Korean War. He returned to Boston and MGH, completed his surgical training, and joined the staff of HMS and MGH in 1954. He was appointed professor of surgery in 1973, and in 2002, the Hermes C. Grillo professorship in thoracic surgery was established in his honor.

Grillo's research focused on the mechanisms of wound healing and the restoration of the trachea following surgery for stenosis and malignant obstructions, and he is widely recognized as the father of modern tracheal surgery. His 2004 textbook, *Surgery of the Trachea and Bronchi*, was immediately accepted as the authoritative text in the field. ❖



Elizabeth Dexter Hay



Elizabeth Dexter Hay, embryologist and educator, died in August 2007. She was 80 years old.

Hay attended Smith College and received her MD from Johns

Hopkins University in 1952, one of only four women in the class.

Beginning first at Johns Hopkins, then at Cornell Medical School, and finally at HMS, Hay concentrated on cell proliferation and migration. This work led to her greatest scientific contribution: understanding the extracellular matrix (ECM), a complex structure that surrounds and supports the cell and is often referred to as connective tissue. Hay was the first to show that the ECM plays a vital role in determining cell behaviors, including cell shape, cell-to-cell signaling, wound repair, cell adhesion, and tissue function. Most recently, she elucidated many of the mechanisms involved in the development of cells from more primitive to advanced forms, dubbed the epithelial-to-mesenchymal transformation.

Hay was named the Louise Foote Pfeiffer professor of embryology at HMS in 1969. As chair of the Department of Anatomy and Cell Biology, she was the first woman to head a preclinical department at HMS. ❖

Janet McArthur

Janet McArthur, HMS professor emerita of obstetrics and gynecology at Massachusetts General Hospital, died in October 2006. She was 92.

McArthur received her AB degree magna cum laude in 1935 and MS degree in 1937, both from the University of Washington. She went on to obtain her MD from Northwestern University

Medical School in 1942. She joined the HMS community in 1943 as a research fellow in medicine at MGH, where she remained for the next four decades.

McArthur was appointed an instructor in pediatrics in 1950. She was promoted to assistant clinical professor in 1960, associate clinical professor in 1967, and professor of obstetrics and gynecology in 1972. She was the first MGH woman physician to become a full professor at HMS. McArthur retired as professor emerita of obstetrics and gynecology in 1984.

McArthur made an important contribution to endocrine research with a landmark study completed in the 1970s with Rose Frisch, professor emerita at HSPH, which found that a critical level of body weight loss could disrupt a woman's menstrual cycle. ❀

Jack Mendelson

Jack Mendelson, director of McLean Hospital's Clinical Research Program on Substance Abuse, co-director of its Alcohol and Drug Abuse Research Center (ADARC), and professor of psychiatry (neuroscience), passed away in August 2007 after a brief illness. He was 77.

Mendelson earned his bachelor's degree from Johns Hopkins University in 1951 and his medical degree from the University of Maryland School of Medicine in 1955. Following medical school, he completed his internship at Boston City Hospital and his psychiatry residency training at Massachusetts General Hospital. In 1966, he became the first chief of the National Center for the Prevention and Control of Alcoholism, a division of the National Institutes of Health. In 1970, he was named chief of the Boston City Hospital Psychiatry Department. Three years later, McLean



Hospital recruited him to head its alcohol and drug abuse research program where, with his wife Nancy Mello, professor of psychology in the Department of Psychiatry (neuroscience) at McLean, he founded the ADARC. ❀

Alexander Nussbaum

Alexander Nussbaum, retired associate professor of biological chemistry and molecular pharmacology, passed away in June 2007. He was 81.

After receiving his BS at City College of New York in 1948 and MS at Purdue University in 1950, Nussbaum conducted his doctoral work in chemistry at Wayne State University, where he was the first graduate student of Carl Djerassi. He later joined Djerassi and George Rosenkranz in Mexico, where work was being carried out to develop a progestin analog that eventually led to the oral contraceptive.

While on sabbatical in 1975, Nussbaum joined HMS as a visiting professor of biological chemistry. During this time he constructed and propagated a recombinant SV40 virus that harbored foreign DNA. In 1977, he returned to HMS as associate professor of biological chemistry, then joined the Boston Biomedical Research Institute in 1982, where he established a research program on the synthesis of oligonucleotides. That same year he moved to the Quad, where he served as director of laboratories of the Department of Biological Chemistry until 1987. He retired from HMS in 2006. ❀

John Remensnyder

John Remensnyder, associate professor of surgery at Massachusetts General Hospital, died in October 2006 at the age of 75.

Remensnyder received his AB from Wesleyan University in 1953 and his MD from HMS in 1957. He completed his general surgical training at Massachusetts General Hospital

from 1957 to 1964 and then trained in plastic surgery at Johns Hopkins from 1964 to 1967. He returned to MGH to join the Plastic Surgical Division in 1967 as an instructor in surgery at HMS. In 1968, he was appointed clinical associate in surgery; in 1970, assistant clinical professor of surgery; and in 1976, associate professor of surgery. He retired in 2001.

Remensnyder was highly regarded for his skills as a plastic surgeon, administrator, and teacher. He was also nationally known for his contributions in plastic surgery and burn care. As chief of plastic and reconstructive surgery, he focused attention on the care of disfigured children, in particular those with injuries resulting from severe burns. ❀

Peter Yurchak



Peter Yurchak, associate clinical professor of medicine and a cardiologist at Massachusetts General Hospital, died in July 2007. He was 74.

Yurchak received his AB from the University of Pennsylvania in 1953 and his MD from HMS in 1957. After serving in the U.S. Air Force in England from 1959 to 1961, he returned to the HMS community and completed his training in cardiac medicine at MGH. He served as an instructor in medicine until 1969, when he was promoted to assistant professor. In 1974 he became an associate clinical professor.

Yurchak was the recipient of three HMS prizes for teaching excellence. He served as the MGH training program director for cardiology from 1994 to 2006 and was the supervisor of the Cardiac Fellows Clinic from 1970 to 2007. He was also the author of numerous journal articles on cardiology, as well as a widely used guide for medical students, *Essentials of Patient Care*. ❀

GIFT REPORT

2006–2007 Honor Roll of Donors

HARVARD MEDICAL SCHOOL'S ONGOING SUCCESS is a direct result of the generosity of donors who support its students, faculty, and programs. We extend our deepest thanks to the many people who, over the past academic year, have sustained our efforts in realizing the School's mission to alleviate human suffering caused by disease. Your philanthropy helps us secure a healthier tomorrow by continuing to foster the collaboration and education of some of the world's brightest minds.

The 2006–2007 Honor Roll of Donors gratefully

acknowledges gifts and pledges of \$1,000 or more made by individuals, corporations, and foundations to Harvard Medical School between July 1, 2006, and June 30, 2007. This publication recognizes pledges in their entirety only in the year they were endowed. And subsequent installments of those pledges are acknowledged at the gift level relevant to payments made that year.

We sincerely thank you for your continued support in building a community that promises to improve the future of medicine for all.

Dean's Council

John Warren Fellows \$10,000 or more

Anonymous (3)
S. D. Abraham
Barbara Alpert
Joel J. Alpert, MD '56
Estate of Gloria J. Anderson
Joshua Arnow
Harold L. Atkins, MD '52
Patricia Austen
W. Gerald Austen, MD '55
Neal A. Baer, MD '96
Peter M. Banks, MD '71
Majda Barazzutti
Kim A. Bendheim
Beverly Bims, PhD
Mildred F. Birchard
George A. Bray Jr., MD '57
Elyse A. Brill
Helen A. Carlos
Dr. Alfred D. Chandler Jr.
Sophia H. Y. Chang, MD
Ricardo J. Cigarroa, MD '84
William P. Collatos
Albert B. Crum, MD '57
Mayer B. Davidson, MD '61
Faith A. Davis, MD '63
Paul J. Davis, MD '63
Dan A. Ditmore, MD '57
Yolanda Ditmore
Garth R. Drewry, MD '52
Arthur S. Earle, MD '53
Gunes N. Ege, MD '58
Estate of Milton Elkin
Ralph P. Engle Jr., MD '57
Indro Fendriago
Jayne P. Finkowski-Rivera, MD '83
M. J. Folkman, MD '57
Paula P. Folkman
R. Brandon Fradd, MD '87
Howard L. Freedman, MD '73
Daniel N. Freudenberger
Robert P. Fuller
Behna Gardner

Laurence B. Gardner
Claude P. Ghez De Castelnuovo,
MD '64
Frank T. Giannetta
Michael A. Gimbrone Jr., MD '69
Paul F. Glenn
Estate of Marlene J. Godley
Estate of Isabelle W. Goldenson
Philip L. Goldsmith, MD '67
Ellen R. Gordon
Donald B. Green
Howard Green
Shirley A. Green
William B. Greenough III, MD '57
Paul C. Haake, PhD
Griffith R. Harsh IV, MD '80
Estate of Arthur R. Hartwig
George Hauser, PhD '55
Barry J. Hershey
George J. Hill II, MD '57
Helene Z. Hill, PhD
Shelly M. Hoon
Margo Howard
Ann M. Howley
Peter M. Howley, MD '72
Mark S. Hughes, MD '86
Priscilla S. Hunt
Richard M. Hunt, PhD
Neil H. Joseph, MD '67
John A. Kaneb
Herbert M. Kaplan
Robert S. Kaplan
Amalie M. Kass
John W. Keith
George H. Kidder, Esq.
Robert E. Kleiger, MD '60
Elizabeth G. Knight
J. V. Knight, MD '43
David Korn, MD '59
Arthur R. Kravitz, MD '54
Barbara N. Kravitz
Nathaniel B. Kurnick, MD '40
Sally Kurnick
James A. La Ve

Risa J. Lavizzo-Mourey, MD '79
Aya B. Leder
Philip Leder, MD '60
Morelle I. Levine
Norman D. Levine, MD '56
Seymour B. London, MD '40
Caleb Loring Jr.
Frederick H. Lovejoy Jr., MD
Jill Lovejoy
Carolyn A. Lynch
Joseph P. Lynch III, MD '73
Peter S. Lynch
Hildegard E. Mahoney
Edwin E. McAmis, Esq.
Robert W. McCarley, MD '64
Arthur S. McFee, MD '57
J. Michael McKenzie
Mark S. McMahan, MD '85
Anne J. Micheli
Lyle J. Micheli, MD '66
Alice K. Moorhead
Rodman W. Moorhead III
Herbert R. Morgan, MD '42
Daniel J. O'Connor Jr., MD '57
Richard S. O'Hara, MD '56
Laurence E. Paul, MD '90
M. Lee Pearce, MD
Donald S. Pierce, MD '57
Janet T. Pierce
W. R. Pitts Jr., MD '67
Robert C. Pozen
Paul M. Prusky, MD '55
Lynne M. Reid, MD
Carlos J. Rivera, MD '83
Estate of Bertrand E. Roberts
Estate of Fred S. Rosen
Estate of Millard S. Rosenblatt
Estate of Thomas Morgan Rotch
Daniel Rothenberg
Dr. Susan S. Rothenberg
Eunice F. Rutledge
Robb H. Rutledge, MD '49
William J. Rutter, PhD
Charles A. Sanders, MD

Elizabeth A. Sanders
Delia Nai-Yueh Sang, MD
The Honorable Patti B. Saris
Estate of Frances Saunders
Leonard D. Schaeffer
Paul R. Schloerb, MD
Sally R. Schroeder
Steven A. Schroeder, MD '64
William A. Schreyer
Arthur I. Segel
David J. Seidenwurm, MD '82
Robert N. Shapiro, Esq.
Eleanor G. Shore, MD '55
Miles F. Shore, MD '54
Richard S. Shulman, MD '67
Jesse L. Sigelman, MD '71
Richard J. Simmons, MD '57
Pamela M. Smith
Eleanor Stickney
Herman D. Suit, MD
Joan C. Suit, PhD
Lynn A. Surprenant
Donald W. Sutherland, MD '57
Roslyn E. Sutherland, PhD
William M. Taylor
Marilyn L. Thomas
Geneva S. Thorndike
William N. Thorndike Jr.
Arthur Ullian
Estate of Malcolm S. Watts
Paul L. Weiden, MD '67
Ronald M. Weintraub, MD '61
Frank M. Weiser, MD '57
Estate of Frank Widenski
Sankey V. Williams, MD '70
Dr. Richard E. Wolfe
Lee L. Zhang
Rhonda S. Zinner
Mortimer B. Zuckerman
Kathryn Zufall
Robert B. Zufall, MD '47
Morris E. Zukerman

Benjamin Waterhouse Fellows
\$5,000 – \$9,999

Marion T. Adams
Thomas W. Adams, MD '57
Joseph D. Allen
Harry J. Bigham Jr., MD '82
Ewing T. Boles Jr., MD '45
Edmund B. Cabot, MD '72
Jerome A. Chazen
Simona Chazen
Doreen P. Cheng
Dr. Hau-Kwong Chung
Mark W. Clark, MD '74
Alexander W. Clowes, MD '72
John M. Crowe, MD '57
John D. de Cuevas
Peter M. Dibattiste, MD '82
George V. DiGiacinto, MD '70
Erica L. Drazen
Jeffrey M. Drazen, MD '72
Lawrence M. Fishman, MD '60
Mrs. Lawrence M. Fishman
William J. Flynn
Robert F. Fox Jr.
Charlotte German
Laurie H. Glimcher, MD '76
Robert J. Glaser, MD '43
Victoria T. Graboys
Arthur I. Grayzel, MD '57
Kenneth L. Greif
Katherine L. Griem, MD '82
Thomas L. Hall, MD '57
Frederik C. Hansen Jr., MD '53
Stephen C. Harrison, PhD
William A. Haseltine, PhD
Arthur L. Herbst, MD '59
John B. Herrmann, MD '57
David G. Johnson
John S. Johnson
Suzanne M. Johnson
Laura Kappel
Marion Kartchner
Mark M. Kartchner, MD '57
Jean-Pierre Kinet
Talmadge E. King Jr., MD '74
Marlene Krauss, MD '79
Louis G. Lange III, MD '74, PhD '76
Rosemary L. Lee
Ting D. Lee Jr., MD '57
S. Bert Litwin, MD '59
Dan L. Longo, MD
Nancy Longo, PhD
Joseph V. Messer, MD '56
Abbott R. Miller, MD '57
Ginat W. Mirowski, MD '85
Henry Morgenthau III
Edith L. Nathanson
Alan S. Nies, MD '63
Yoko Ono Lennon
Louis Perlmutter
Martin R. Prince, MD '84
Rhonda E. Rand, MD '79
Elizabeth C. Reiling
Richard B. Reiling, MD '67

William S. Ring, MD '71
Page Robbins
Richard G. Rockefeller, MD '79
Thomas J. Schnitzer, MD '71
Jennifer J. Small
Karen L. Sobol
Abbe S. Steinglass
Peter J. Steinglass, MD '64
Morton N. Swartz, MD '47
John M. Templeton Jr., MD '68
Margaret M. Tse
Judith Verhave
Menno Verhave, MD '82
Lorraine H. Vickery
Luis Villa Jr., MD '70
Margaret G. Ward, PhD '65
Samuel P. Ward, MD '68
Estate of William E. Whitney
Stephen F. Wintermeyer, MD '85
Cynthia Yock
Paul G. Yock, MD '79
William S. Zielinski III

Alice Hamilton Fellows
\$2,000 – \$4,999

Anonymous (40)
Walter H. Abelmann, MD
Estate of Elliott Adams
Raymond Alexanian, MD '55
Claudia M. Alleyne, MD '81
Linda M. Ameri, MD '82
Mary J. Andrews
Andrew Arkin
Hugh Auchincloss Jr., MD '76
Karl F. Austen, MD '54
Robert L. Barbieri, MD '77
Craig B. Barger
Patrick A. Barnett, MD '82
Blanche S. Bast
Robert C. Bast Jr., MD '69
Joan M. Bedinghaus, MD '82
J. Claude Bennett, MD '58
Edward J. Benz Jr., MD '72
Barbara E. Bierer, MD '80
Paul S. Birnbaum, MD '82
Marcia Blacher
Stanley P. Blacher
Cecily Bradshaw
Robert Bradshaw
Estate of Edward A. Bragaline
Harold A. Braun, MD '47
Harold J. Bursztajn, MD '76
Donald E. Butterfield, MD '58
Eve Caligor, MD '82
William N. Campbell Jr., MD '38
David R. Challoner, MD '61
Mrs. David R. Challoner
Teresa W. Chan, MD '85
Ching-Yen J. Chang, MD '89
David C. Chin, MD '75
E. R. Clark, MD '82
Bertram M. Cohen
Rosalie Cohen
Sandra K. Cohen, MD '78



At a gala dinner in May 2007, Joseph Martin acknowledges the many colleagues, friends, and family members honoring him for his service as dean of the Faculty of Medicine from 1997 to 2007.

Frank V. Colombo, MD '53
Rita J. Colombo
Darrell W. Crate
Nancy B. Crate
John T. Cumutte III, MD '77, PhD '80
William H. Danforth, MD '51
Martha A. Darling
Gary Davis
S. Edward Davis III, MD '60
Estate of Ralph E. Davis
Thomas F. Delaney, MD '82
Deborah A. Devinsky
Orrin Devinsky, MD '82
Daniel Deykin, MD '57
Donald E. Dickerson, MD '57
Estate of Bernice Vaughn Dodge
Jonathan D. Dubin, MD '82
Barbara B. Ebert
Richard H. Eg Dahl, MD '50
Lucile S. El-Hage
Nabil N. El-Hage
Ruth P. Fields
Richard I. Fisher, MD '70
James W. Fordyce
Alan J. Friedman, MD '59
Michael K. Frith
Nicholas Galakatos, PhD
John R. Galvin
Paulette D. Galvin
Raif S. Geha, MD
Benjamin J. Gilson, MD '57
Michael C. Glafkides, MD '82
Robert H. Glassman, MD '87
Jill Glist
Harold L. Godwin, MD '47
Daniel L. Gornel, MD '57
Jane Grayson, MD '73
Barbara A. Greco, MD '82
Robert P. Green, MD '77
William L. Green, MD '54
Steven Greystone
Gwen W. Halaas, MD '82

Edward D. Harris Jr., MD '62
David B. Harrod, MD '57
Charles C. Hartness III, MD '82
James M. Hartsuck, MD '62
Harry E. Hartzell Jr., MD '57
Harley A. Haynes, MD '63
Emanuel S. Hellman, MD '57
Doris B. Hiatt
Howard H. Hiatt, MD '48
Donald Hillman
Patricia Hillman
David S. Hirschfeld, MD '67
Mark S. Hochberg, MD '73
Edward S. Horton, MD '57
Mark W. Howard, MD '85
John P. Howe III, MD
Edward M. Hundert, MD '84
Joseph K. Hurd Jr., MD '64
Neena Husid
B. Thomas Hutchinson, MD '58
Steven E. Hyman, MD '80
Ljubomir M. Ilic, MD '99
Gordon T. Johnson
Gary J. Jones, MD '79
Charles R. Jorgensen, MD '62
Leonard B. Kaban, MD '69
Lawrence J. Kadish, MD '67
James B. Kahn, MD '67
S. Jason Kapnick, MD '81
Katherine A. Keeley, MD '94
Cynthia N. Kettyle, MD '71
William M. Kettyle, MD '71
Benjamin N. Kightlinger, MD '55
Harvey Klein, MD '63
Phyllis A. Klein
Tamsin A. Knox, MD '82
Michael J. Koren, MD '85
Philip J. Landrigan, MD '67
Meryl S. LeBoff
Sidlee W. Leeper, MD '55
Herbert Lessow, MD '59
Patricia G. Lessow



Outgoing dean Joseph Martin (left) expresses his appreciation to Alvin Poussaint, who presented him with an East African Makonde sculpture in recognition of Martin's efforts to promote diversity at the Medical School.

Peter S. Liebert, MD '61
 Matt J. Likavec, MD '74
 Stephen J. Lipson, MD '72
 Irving M. London, MD '43
 Douglas G. Lowell, MD '82
 Oluwatope A. Mabogunje, MD '67
 Roger M. Macklis, MD '82
 Jan W. Mares, Esq.
 Michael E. Mendelsohn, MD '82
 Suzanne Merrill
 C. Noel Bairey Merz, MD '81
 Robert H. Merz, MD '81
 Katayoun F. Meyer, MD '88
 Anita Michaels
 Sam Michaels
 Hillary G. Miller, MD '82
 Anne J. Miller-Breslow, MD '82
 Michael B. Millis, MD '70
 Robert C. Moellering Jr., MD '62
 Michael G. Morley
 Eugenia S. Morse
 Arthur J. Moss, MD '57
 Robert S. Munford III, MD '70
 Robert P. Murray, MD '86
 James A. Nelson, MD '65
 Anthony B. Nesburn, MD '60
 Vinh-Khiem C. Nguyen-Phuc, MD '81
 David D. Oakes, MD '68
 Francis J. O'Brien, MD '82
 M. Patrick O'Meara, MD '50
 Gilbert S. Omenn, MD '65
 Lynn C. Osborn
 William C. Osborn
 Mark D. Oshida
 Bernard P. Ottenberg, MD '52
 Gilbert R. Panzer, MD '55
 Jane R. Parnes, MD '76
 Robert L. Parsons, MD '55
 Geoffrey R. Paul, MD '56
 Alan S. Pearlman, MD '70
 Taine T. Pechet, MD '92
 Tiron C. Pechet, MD '90

Tuyet-Mai Phan, MD '81
 Barbara Apple Pittman
 Joseph G. Pittman, MD '59
 Donald O. Pollock, MD '55
 Alfred Pope, MD '41
 Robert L. Post, MD '45
 Dorothea Poulos, MD '82
 DeWayne M. Pursley, MD '82
 Mitchell T. Rabkin, MD '55
 Lois Narwitz Resnick
 Robert H. Resnick, MD '55
 Cynthia Reyes-Ferral, MD '82
 David W. Richardson, MD '51
 Elizabeth W. Richter
 Tor Richter, MD '51
 Jose G. Rigau-Perez, MD '75
 Carol W. Robey, MD '82
 Benson B. Roe, MD '43
 John L. Roglieri, MD '66
 Fred R. Rosenberg
 Alvin A. Rosenfeld, MD '70
 Dorothy Rosenfeld
 William B. Saxbe Jr., MD '67
 David Schnell, MD '87
 Beth R. Schwartz, MD '82
 Robert E. Scully, MD '44
 Estate of Marshall J. Seidman
 James H. Shelton, MD '70
 Nancy B. Shelton
 Daniel J. Siegel, MD '82
 Warden B. Sisson, MD '63
 Marvin H. Sleisenger, MD '47
 Charles T. Smith
 David H. Solomon, MD '46
 Ronda L. Solomon
 Alfred Sommer, MD '67
 Eleanor A. Sorrentino, MD '62
 Robert M. Stark, MD '74
 Roger F. Steinert, MD '77
 David M. Steinhaus, MD '77
 Meredith D. Steinhaus
 Leo I. Stemp, MD '82

John D. Stoeckle, MD '47
 James W. Stone, MD '82
 Joan Stone
 Swee L. Tan, MD '88
 Simeon Taylor, MD '73, PhD
 Barbara C. Thibault
 George E. Thibault, MD '69
 Daniel C. Tosteson, MD '48
 Sanford Ullman, MD '71
 William F. Urmey, MD '82
 Henry W. Vaillant, MD '62
 Lucy R. Waletzky, MD
 Neill K. Weaver, MD '44
 Jonathan L. Weil
 Gordon C. Weir, MD '67
 Herbert G. Weiss
 Ruth S. Weiss, MD '51
 Melissa Welch, MD '85
 Dorothy I. Whitmer, MD '78
 Isaac Wiener, MD '74
 Russell Wigh, MD '39
 Mark E. Williams, MD
 Christopher Wilson
 Stanley H. Wishner, MD '65
 Allen R. Woolf, MD '81
 Alan C. Yeung, MD '84
 Edgar K. Yucel, MD '82

**Harold Amos Fellows
 \$1,000 – \$1,999**

Anonymous (19)
 Howard R. Abel, MD '62
 William T. Abraham, MD '86
 John R. Adler Jr., MD '80
 Marilyn B. Adler
 N. S. Adzick, MD '79
 James Aisenberg, MD '87
 Cary W. Akins, MD '70
 Bolanile Akinwale, MD '81
 Carolyn K. Aldredge, MD '64
 Sidney Alexander, MD '57
 Susan M. Allan, MD '81
 Marshall B. Allen Jr., MD '53
 Laura Alpern
 Louis M. Alpern, MD '74
 Alan Antokal
 Eugene L. Appel, MD '66
 Aaron P. Appiah, MD '82
 David Arnow
 Elissa B. Arons, MD '70
 Dr. Caroline Augustyn
 Damian H. Augustyn, MD '78
 Robert L. Bahr, MD '71
 George P. Baker Jr., MD '57
 Katharine E. Baker
 Charles F. Barbarisi, MD '56
 Claire Barger
 Elaine Barger
 Walter L. Barker, MD '53
 John S. Barlow, MD '53
 Joseph S. Barr Jr., MD '60
 Carolyn B. Becker, MD '82
 Robert A. Beckman, MD '82
 Beryl R. Benacerraf, MD '76
 Lynn J. Bennion, MD '70
 David C. Benson, MD '85
 Herbert Benson, MD '61
 Cheston M. Berlin Jr., MD '62
 Ellin Berman, MD '77
 William Bernet, MD '67
 Alexander Blum Jr., MD '47
 William P. Boger III, MD '71
 Joseph V. Bonventre, MD '76
 Helen M. Bouscaren, MD '85
 Terence Boylan
 Jerald J. Bratberg, MD '69
 Bruce J. Brener, MD '66
 Ellen Brener
 Donald K. Brief, MD '57
 Arnold M. Brier, MD '68
 Irene F. Briggan, MD '63
 Rufus K. Broadaway, MD '50
 Martin I. Broder
 Eric S. Brondfield, MD '70
 Benjamin R. Brooks, MD '69
 Susan W. Brooks
 Carl N. Brownsberger, MD '55
 Becky Bruce
 Louis P. Bucky, MD '86
 Ann B. Bull
 Thomas E. Bump, MD '76
 Boyd R. Burkhardt, MD '59
 Jean B. Burnett, PhD
 Joseph W. Burnett, MD '58
 Sheldon M. Buzney, MD '72
 Doris Cadoux
 Crawford C. Campbell, MD '87
 Herbert L. Cantrill III, MD '72
 John M. Carey, MD '45
 William B. Carey, MD '54
 Alan F. Carpenter, MD '55
 Hugh P. Chandler, MD '58
 David F. Chang, MD '80
 Laura R. Chasin, PhD
 Diana P. Cherot
 Nai-Kong V. Cheung, MD '76, PhD '78
 Edward Tobey Choate
 William R. Christensen, MD '42
 Dr. George J. Cianciolo
 Joaquin G. Cigarroa Jr., MD '47
 Mary D. Clark
 Peter F. Clark, MD '63
 Martin J. Cline, MD '58
 William D. Cochran, MD '52
 Benjamin E. Cohen, MD '69
 Helen B. Cohen
 Norman R. Cohen, MD '61
 Beverly S. Coleman
 John J. Coleman III, MD '73
 M. Donald Coleman, MD '52
 Richard L. Conn, MD '62
 John E. Connolly, MD '48
 Richard E. Conway, MD '59
 Peter G. Cordeiro, MD '83
 Howard A. Corwin, MD '58
 Jeannette Corwin, MD '58
 Frank A. Costanzo, MD '52
 Nathan P. Couch, MD '54

Dale H. Cowan, MD '63
 Deborah W. Cowan
 Jean I. Cox
 John F. Cramer III, MD '74
 Cynthia Crisp
 Richard V. Cronk, MD '65
 Perry J. Culver Jr., MD '81
 Wesley A. Curry Jr., MD '76
 Victor T. Curtin, MD '51
 David W. Dain, MD '62
 Chester C. D'Autremont, MD '44
 Barbara O. David
 Florence A. DeGeorge
 Lawrence J. DeGeorge
 Roman W. DeSanctis, MD '55
 Andrew K. Diehl, MD '72
 Judy I. Dienstag
 Jules L. Dienstag, MD
 Anthony M. DiGioia III, MD '86
 Richard B. Dobrow, MD '62
 James F. Donovan, MD '52
 Cheryl L. Dorsey, MD '91
 Douglas B. Dorner, MD '67
 Chrysoula Dosiou, MD '97
 Lois W. Dow, MD '68
 Susan C. Weil Dreyfuss, MD '74
 Michael J. Droller, MD '68
 Harold F. Dvorak, MD '62
 Donald H. Eldredge Jr., MD '46
 Leonard L. Ellman, MD '67
 John B. Emans II, MD '70
 S. Jean H. Emans, MD '70
 Karl Engelman, MD '59
 Charles J. Epstein, MD '59
 Lois B. Epstein, MD '59
 Lloyd K. Everson Jr., MD '69
 William R. Eycler, MD '43
 Ann Falchuk
 Zalman M. Falchuk, MD '67
 Daniel D. Federman, MD '53
 Elizabeth Federman
 Carolyn F. Fine
 Josef E. Fischer, MD '61
 Fred N. Fishman, Esq.
 Robert H. Fletcher, MD '66
 Suzanne W. Fletcher, MD '66
 Katherine A. Forrest, MD '67
 Robert R. Foster, MD '63
 Stanley S. Franklin, MD '56
 Albert R. Frederick Jr., MD '61
 Curt R. Freed, MD '69
 Leonard E. Freedberg, MD '71
 Robert Freedman, MD '72
 Paul Friedmann, MD '59
 Richard M. Fulks, MD '72
 Anne Galli
 Stephen J. Galli, MD '72
 G. Gregory Gallico III, MD '72
 Shirley M. Gallup, MD '49
 Homero R. Garza, MD '75
 Alan B. Gazzaniga, MD '61
 Thomas D. Gelehrter, MD '63
 Renee L. Gelman, MD '50
 David M. Gibson, MD '48

Edward B. Gilmore, MD '65
 Mark J. Girard, MD '86
 Melvin J. Glimcher, MD '50
 Ira J. Goldberg, MD '75
 Samuel Z. Goldhaber, MD '76
 Kathryn R. Goldman, MD '82
 Robert M. Goldwyn, MD '56
 William H. Goodson III, MD '71
 Cheryl Opacinch Gorelick
 Kenneth P. Gorelick, MD '67
 Winslow W. Green, MD '62
 James A. Greene Jr., MD '55
 Martin L. Greene, MD '65
 Richard W. Greene, MD '42
 Judith Grier
 Judson S. Griffin, MD '45
 Marilyn P. Griffin, MD '77
 Peter J. Grillo, MD '69
 Roy R. Grinker Jr., MD '52
 Gabriel G. Gruber, MD '72
 Thomas G. Gutheil, MD '67
 Linda D. Guydon, MD '80
 Chul S. Ha, MD '86
 Stephen V. Hall, MD '69
 William K. Hall, MD '42
 Audrey M. Hamilton, MD '83
 William D. Harley, MD '72
 Alvin H. Harris, MD '55
 Edmund J. Harris, MD '45
 Marilyn Cook Harris
 Harold B. Hawkins, MD '66
 Evelyn Z. H'Doubler
 Peter B. H'Doubler Sr., MD '55
 Nancy Heising
 Ralph A. Heising, MD '55
 W. Hardy Hendren III, MD '52
 Chester E. Herrod, MD '49
 Clement A. Hiebert, MD '51
 James T. Higgins, MD '74
 Sue P. Hitselberger
 William E. Hitselberger, MD '56
 Irene E. Hoge
 Cyrus C. Hopkins, MD '63
 Richard G. Hosford, MD '57
 Robert B. Howe, MD '62
 Daniel B. Hrды, MD '76
 Dr. Sarah B. Hrды
 Richard C. Hubbard, MD '77
 Edward F. Hughes, MD '66
 Richard E. Hughes, MD '53
 Joanne M. Huhn
 Wolfgang A. Huhn, MD
 Franklin E. Hull, MD '60
 Robert N. Hyland, MD '65
 Harris Hyman III, MD '55
 Nancy S. Inui
 Thomas S. Inui, MD
 Kenneth K. Ishizue, MD '83
 Morgan N. Jackson, MD '73
 Scott E. Jacobs
 Paul C. Janicki, MD '71
 Alfred Jaretzki III, MD '44
 Dr. William R. Jarvis
 Janine M. Jason, MD '75

Anula K. Jayasuriya, MD '84, PhD '91
 Randall D. Johnson, MD '76
 Anna S. Kadish, MD '67
 Jesse L. Kahn, MD '67
 Jill A. Kamen
 Dr. Mazen O. Kamen
 Andrew H. Kang, MD '62
 Steven R. Kanner, MD '69
 A. W. Karchmer, MD '64
 Beth Y. Karlan, MD '82
 Scott R. Karlan, MD '82
 Richard A. Kaslow, MD '69
 Samuel L. Katz, MD '52
 Arielle B. Kauvar, MD '89
 Lucien C. Kavan, MD '42
 William M. Keane, MD '70
 Richard R. Kelley, MD '60
 Douglas G. Kelling Jr., MD '72
 John T. Kelly, MD '79
 Jenny E. Kemps
 John H. Kemps
 Edward N. Kesselman, MD '74
 Jennifer P. Kingston
 Timothy M. Kingston
 Richard J. Kitz, MD
 William S. Kiyasu, MD '48
 Jan Koch-Weser, MD '54
 Anthony L. Komaroff, MD
 William Kornfeld, MD '54
 Frederic W. Lafferty, MD '56
 Charles Landau, MD '84
 Rick Larkin
 Evelyn H. Lauder
 Leonard A. Lauder
 Robert S. Lawrence, MD '64
 Steve Lawrence
 Mrs. Steve Lawrence
 Mark G. Leibold, MD '78
 Edwin D. Leonard, Esq.
 Judith S. Leonard
 Amy K. Letteney
 Stanley M. Levenson, MD '41
 Sheldon M. Levin, MD '50
 David C. Lewis, MD '61
 Eleanor L. Lewis
 John L. Lewis Jr., MD '57

Randall J. Lewis, MD '69
 R. P. Liccini Jr., MD '89
 John A. Linfoot, MD '57
 Alexander Ling Jr., MD '81
 Eugene Y. Liu, MD '84
 Margaret A. Liu, MD '81
 Francis R. Lonergan, MD '77
 Mortimer Lorber, MD '52
 Gary A. Lucido
 Sidney B. Luria, MD '43
 Elbert H. Magoon, MD '73
 Peter L. Malkin, Esq.
 Jacqueline Mansfield
 Peter B. Mansfield, MD '62
 Alfred S. Margulies, MD '74
 Alexander R. Margulis, MD '50
 R. Ralph Margulis, MD '48
 John J. Martin Jr., MD '82
 Robert J. Mayer, MD '69
 Rosemary McAllister
 David P. McCallie Jr., MD '81
 Marion D. McClure, MD '54
 Kilmer S. McCully, MD '59
 Robert L. McDowell Jr., MD '74
 Suzanne R. McDowell
 O. R. McIntyre, MD '57
 Barbara J. McNeil, MD '66, PhD '72
 David M. Mego, MD '86
 Keith Merrill Jr., MD '44
 Roger E. Meyer, MD '62
 Max Michael III, MD '72
 George Miller, MD '62
 Edison K. Miyawaki Jr., MD
 Karen Miyawaki
 Anthony P. Monaco Sr., MD '56
 Roberta A. Monson, MD '67
 Burness E. Moore, MD '38
 Doris E. Moore
 Walter H. Moran Jr., MD '55
 Lee M. Nadler, MD '73
 Thomas Najarian, MD '74
 Gerald Nash, MD '63
 Robert N. Nishimura, MD
 Joanne C. Norton
 Richard A. Norton, MD '57
 William D. O'Brien

Joseph Martin and Harvard University president Drew Gilpin Faust at the gala dinner honoring Martin's 10 years as HMS dean



James J. O'Connell III, MD '82
Jan A. Okimoto, MD '82
Dr. Emilia Oleszak
Roslyn W. Orkin, PhD '73
Stuart H. Orkin, MD '71
William C. Osborn
Henry A. Oster, MD '71
Ingrid L. Ott, MD '90
Alejandro M. Paiuk
Oglesby Paul, MD '42
Mary H. Pavan, MD '72
Douglas D. Payne, MD '66
William M. Payne Jr.
Alice Pendergast
Bill Pendergast
Clarence Pendergast
Mark G. Perloth, MD '60
Jane S. Perrin, MD '57
Mary Ann Pesce
John A. Peters, MD '54
Lawrence S. Phillips, MD '67
Ernest H. Picard, MD '55
Flora Picciotti
Romulus A. Picciotti
David F. Pincus, MD '81
Stephanie H. Pincus, MD '68
Constance S. Pittman, MD '55
Dr. Chris D. Platsoucas
Carol E. Podolsky, MD '78
Daniel K. Podolsky, MD '78
Richard O. Poe, MD '61
Suzanne T. Poppema, MD '74
Eunice S. Porvaznik
John T. Porvaznik Jr., MD '58
Malcolm R. Powell, MD '56
Patricia A. Quigley
Kenneth R. Ratzan, MD '65
Vincent F. Reale, MD '68
May J. Reed, MD '86
Philip J. Rettig, MD '72
John M. Richardson, MD '70
Ernestine Ritter
Charlotte M. Robinson
David Rockefeller Jr.
David Rockefeller Sr., Esq
Barbara P. Rockett
Francis X. Rockett, MD '57
Gerald D. Rogell, MD '67
Jonathan Rose
Lewis J. Rose, MD '78
Howard S. Rubenstein, MD '57
Anthony H. Russell, MD '74
Beverly B. Rutstein
Marc S. Sabatine, MD '94
Lynn R. Sackett
Karen L. Sadler, MD '88
Stacy P. Salob Goldman, MD '88
Richard J. Sampson, MD '63
Bruce J. Sams Jr., MD '55
Jack S. Sanders, MD '55
Dana Sankary
Richard M. Sankary, MD '82
Alan J. Sarokhan, MD '77
Andrew Satlin, MD '79
Beth K. Scharfman, MD '86
Stefan C. Schatzki, MD '56
Gerold L. Schiebler, MD '54
Leslie D. Schlessinger, MD '72
Henry E. Schniewind Jr., MD '65
Harry L. Senger Jr., MD '57
Janet B. Serle, MD '80
Uri R. Shabto, MD '86
Robert C. Shamberger, MD '75
Sandor S. Shapiro, MD '57
Cyril E. Shea Jr., MD '50
Victoria A. Shea, MD '82
Albert L. Sheffer, MD
Douglas J. Sheft, MD '61
Klaudia S. Shepard Jr.
Stephen A. Sherwin, MD '74
Mark C. Shields, MD '75
Kenneth I. Shine, MD '61
Neil S. Shore, MD '63
Dr. Cynthia K. Silbert
Jeremiah E. Silbert, MD '57
David J. Silver, MD '67
John W. Singleton, MD '57
Spyros S. Skouras Jr.
Lloyd H. Smith Jr., MD '47
N. T. Smith, MD '57
P. Frederick Sparling, MD '62
Harold C. Spear, MD '47
John B. Stanbury, MD '39
John R. Stanley, MD '74
Sean Stanton
James J. Stark, MD '71
John D. Steichen, MD '85
John M. Stein, MD '61
Bruce W. Steinhauer, MD '59
Claire M. Stiles, MD '56
Quentin R. Stiles, MD '55
Ralph W. Stoll, MD '65
Jeffrey D. Stone, MD '73
Jennifer P. Stone, MD '86
Andrea Stryer
Lubert Stryer, MD '61
William H. Sullivan, MD '58
Richard S. Swanson, MD '80
Ralph C. Sweetland, MD '66
Sandra M. Sweetnam, MD '82
Candee Swenson
Larry G. Swenson
Chester P. Swett Jr., MD '66
Dr. Ahmad Taghavy
Terry Tang, PhD
Nancy J. Tarbell, MD
Lloyd B. Tepper, MD '57
Robert L. Timmons, MD '53
Beverly J. Tucker
George L. Tucker, MD '56
John F. Tulenko, MD '58
David J. Tweardy, MD '78
Yong Uahwatanasakul, MD '63
C. Robert Valeri, MD '58
Illiana Van Meeteren
Armand D. Versaci, MD '47
Coolidge S. Wakai, MD
Mrs. Coolidge S. Wakai
Linda A. Waldman, MD '81
James W. Wallace, MD '65
Paul D. Walter, MD '71
Donald M. Watkin, MD '46
Rita M. Watson, MD '76
George S. Weber, MD '57
Joyce A. Di Bona Weiss
Robert H. Weiss
Melissa B. Welch, MD '85
John R. Wesley, MD '67
Karin E. Wetmore, PhD
George M. Wheatley, MD '33
Tracy A. White
Walter A. Wichern Jr., MD '45
Catherine M. Wilfert, MD '62
Earle W. Wilkins Jr., MD '44
Frank M. Williams, MD '64
Gordon H. Williams, MD '63
Alphonso Willis, MD '77
Katharine C. Wolf, MD '63
Marshall Wolf, MD '63
Anna K. Wolff, MD '57
Francis C. Wood Jr., MD '54
William C. Wood, MD '66
Jean Wort
Howard E. Wulsin, MD '48
Robert A. Yancey, MD '82
Chin B. Yeoh, MD '57
Lowell S. Young, MD '64
Robert R. Young, MD '61
Lawrence S. Zivin, MD '62

Corporations, Foundations, and Charitable Organizations

Distinguished Benefactors

\$1,000,000 or more

Anonymous (1)
Beth Israel Deaconess Medical Center
Brigham and Women's Hospital
Children's Hospital
Commonwealth Fund
Dana-Farber Cancer Institute
Ellison Medical Foundation
G. Harold & Leila Y. Mathers
Charitable Foundation
Jeffrey Modell Foundation Inc.
Leukemia Society of America Inc.
Marcus Foundation
Massachusetts Eye and Ear
Infirmary Foundation
Massachusetts General Hospital
McLean Hospital
MediMedia USA Inc.
The National Hemophilia Foundation

Partners Healthcare Systems
ResMed Corp.
Virginia and D.K. Ludwig Fund
for Cancer Research
Warren Alpert Foundation

Benefactors
\$100,000 – \$999,999
Anonymous (1)
A. W. Baldwin Charitable
Foundation Inc.
Alexander & Margaret Stewart Trust
American Cancer Society Inc.
American Heart Association Inc.
American Specialty Health Plans
The Annie E. Casey Foundation
The Atlantic Philanthropies
Autism Consortium LLC
Beckman Laser Institute
Biomedical Science Career Program

Breast Cancer Research Foundation
Bristol-Myers Squibb Company
Broad Institute
Burroughs Wellcome Fund
C.O.U.Q. Foundation Inc.
Cancer Research Institute Inc.
Charles A. Dana Foundation Inc.
Charles A. King Trust
Chestnut Hill Charitable Foundation
Clinton Foundation HIV/AIDS
Initiative
Commonwealth Fund
Cystic Fibrosis Foundation
Damon Runyon-Walter Winchell
Foundation
Edward and Anne Lefler Trust
Elan Pharmaceuticals Inc.
Eli Lilly and Company Foundation
Elizabeth Glaser Pediatric AIDS
Foundation

Energy Foundation
Exelixis Inc.
Foundation Fighting Blindness Inc.
Foundation for Retinal Research
Genzyme Corporation
Glaxo SmithKline Inc.
Goldman Philanthropic Partnerships
The Helen Hay Whitney Foundation
Hellman Family Foundation
The Henry Luce Foundation Inc.
Herb Gordon Foundation for
Gastrointestinal Cancers Inc.
High Q Foundation Inc.
Howard Hughes Medical Institute
International Research
Management LLC
Jane Coffin Childs Memorial
Foundation
John Merck Fund
Kendeda Fund



Donald Butterfield, MD '58 (left), and Nile Albright, MD, enjoy the company of student Devarati Mitra, HMS '10, at the annual Ezekiel Hersey Council dinner. The council recognizes donors who have made life income gifts and bequest intentions to the School.

Life Sciences Research Foundation
 Louis E. Wolfson Foundation
 Louise Littlehale Mansfield Charitable Remainder Unitrust
 Machiah Foundation
 Malcom S. M. Watts 1989 Trust
 March of Dimes National Foundation
 Mary Elizabeth Pearce Foundation Trust
 McKnight Endowment Fund for Neuroscience
 Medical Foundation Inc.
 Muscular Dystrophy Association Inc.
 National Multiple Sclerosis Society
 NFL Charities
 Nikon Inc.
 Novartis IBRI
 Oak Foundation USA
 Respironics Sleep & Respiratory Research
 Robert Wood Johnson Foundation
 Russell Sage Foundation
 Sanofi-Aventis
 The Schepens Eye Research Institute Inc.
 Sепracor Inc.
 Stuppy Family Trust
 Susan G. Komen Foundation
 V. Kann Rasmussen Foundation
 W. K. Kellogg Foundation
 Whitehall Foundation Inc.
 William T. Grant Foundation

Patrons

• **\$50,000 – \$99,999**
 Albert J. Ryan Foundation
 Alfred P. Sloan Foundation
 AstraZeneca LP
 Best Doctor
 Beth Israel Anaesthesia Foundation
 Blue Cross Blue Shield of Massachusetts Inc.

Cambridge Health Alliance
 Charles E. W. Grinnell Trust
 Charles H. Hood Foundation
 Children's Tumor Foundation
 The Francis Families Foundation
 Gustavus and Louise Pfeiffer Research Foundation
 Hereditary Disease Foundation
 J. W. Kieckhefer Foundation
 Karin Grunebaum Cancer Research Foundation
 Kiehl's Since 1851 Inc.
 Ludcke Foundation
 Macula Vision Research Foundation
 Marisla Foundation
 Max Kade Foundation Inc.
 Merck & Company Inc.
 Pfizer Inc.
 Project A.L.S. Inc.
 Rita Allen Foundation Inc.
 Royal Caribbean Cruises Ltd.
 Searle Scholars Program
 Tempur-Pedic International
 Tuberos Sclerosis Alliance

• **\$25,000 – \$49,999**

Anonymous (1)
 3M Environmental Technology & Safety
 American Epilepsy Society
 Arthritis Foundation
 Beth Isreal Hospital Pathology Foundation Inc.
 BP Corporation North America Inc.
 Cephalon Inc.
 Charles and Lucerne Beal 1979 Trust
 Christopher Reeve Paralysis Foundation
 Claneil Foundation Inc.
 Critelli Family Foundation
 Deafness Research Foundation

Doris Duke Charitable Foundation
 The Dubois Foundation
 Epilepsy Foundation
 European Molecular Biology Organization
 Harvard Pilgrim Health Care Foundation
 Infinity Pharmaceuticals Inc
 Institute of Medicine
 J. Robert Gladden Society
 Jarislowsky Foundation
 Jessie Gwendolen Morse Trust
 Johnson & Johnson
 Joslin Diabetes Center Inc.
 JP Morgan Chase Bank
 Miriam E. Lubow Trust
 New York Community Trust
 Newman's Own Foundation Inc.
 The Paul and Phyllis Fireman Charitable Foundation
 Ronald McDonald House Charities
 Spaulding Rehabilitation Hospital
 Takeda Pharmaceuticals North America
 Winslow Foundation

• **\$5,000 – \$24,999**

Anonymous (1)
 Affymetrix Inc.
 AIG Insurance
 Alex's Team Foundation Inc.
 Allan S. Gordon Foundation
 Arnold P. Gold Foundation
 Blossom Fund
 Blum-Kovler Foundation
 The Boston Foundation Inc.
 Columbia Pictures Industries Inc.
 Columbia University
 D. & M. Spurgeon Charitable Trust
 The David and Lucile Packard Foundation
 The Easter Foundation
 George Beckerman Charitable Remainder Unitrust
 The Goldman Sachs Group
 HBS Section A Class of 2007
 HBS Section I Class of 2007
 The Henry P. Kendall Foundation
 Human Frontier Science Program
 Intel Corporation
 Interface Inc.
 J.T. Tai and Company Foundation Inc.
 John H. & H. Naomi Tomfohrde Foundation
 John S. and James L. Knight Foundation
 The Klarman Family Foundation
 The Kohlberg Foundation Inc.
 LEF Foundation
 Leon Levy Foundation
 Lloyd's America Inc.
 Mabel A. Horne Fund
 The Medtronic Foundation
 National Alliance for Research on Schizophrenia and Depression

National Pharmaceutical Council
 National Philanthropic Trust
 Nurture Nature Foundation
 Penates Foundation
 Scottish Rite Schizophrenia Program
 Seth Sprague Educational and Charitable Foundation
 Silver Mountain Foundation
 SmartPower
 Stewart Brown Inc.
 Vaughan Foundation

• **\$2,000 – \$4,999**

Abbott Laboratories Fund
 Aid for Cancer Research
 AJS Ventures LLC
 Amgen Foundation Inc.
 Anna G. Lamson Irrevocable Trust
 Boehringer Ingelheim Ltd
 Community Health Systems Foundation
 Edward Budnitz Family Trust
 ExxonMobil Foundation
 Harvard Department of Dermatology House
 HBS Section B Class of 2007
 Irving & Edyth S. Usen Family Charitable Foundation
 Jazz Pharmaceuticals Inc.
 Jordan's Furniture Inc.
 Leon Lowenstein Foundation Inc.
 Mutual of America Life Insurance Company
 Sleep Health Centers LLC
 Swiss Re America
 T Rowe Price Associates Foundation Inc.
 Woodstock Lions Club
 Yvonne Cappeller Trust

• **\$1,000 – \$1,999**

Aetna Foundation Inc.
 Bambu LLC
 Charles and Sara Goldberg Charitable Lead Trust
 CIGNA Foundation
 Dr. Kenneth and Mrs. Cheryl Opacinch Gorelick Family Fund
 Friends of the Congressional Glaucoma Caucus Foundation Inc.
 Harvard Medical Faculty Physicians
 HMS Class of 1966
 Janie and Jack Atrium Mall
 Lenora & Alfred Glancy Foundation Inc.
 MetLife Foundation
 Merrill Lynch & Company Foundation Inc.
 NHP Foundation
 Philips Electronics North America Company
 Randolph Archival Fund
 Shelter Insurance Foundation

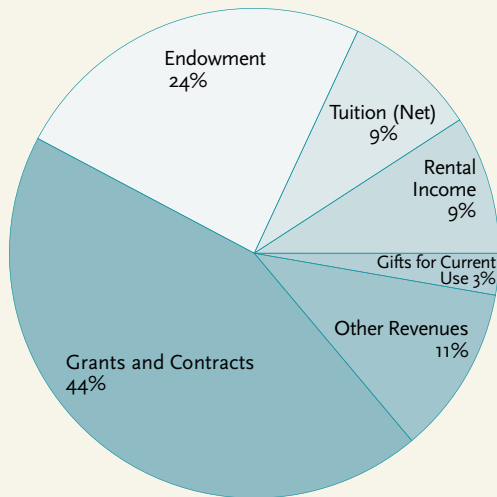
FACTS AND FIGURES

Financial Summary: Reserves and Endowment Help Balance the Budget

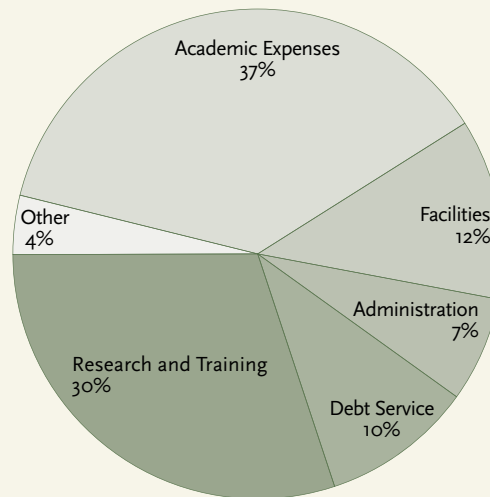
Fiscal Year 2007 proved to be a difficult year for the Medical School, which experienced an \$11 million base operating loss, representing a \$5.2 million drop over last year's results. Total federal sponsored spending has been declining at an average rate of about 2 percent a year, from \$203 million in FY05 to \$194 million in FY07. More than 80 percent of the School's sponsored program spending origi-

nates in the Quad-based departments, where there was a decline of 1 percent in direct federal spending in FY07. The year was also a challenge from the cost perspective. Capital investments for both deferred maintenance and new lab renovations increased cost by \$9.1 million. The School used the dean's reserve funds, primarily prior-year surpluses, to help balance the FY07 budget. ❁

Fiscal Year 2007 Financial Results



Operating Revenues: \$497,681,000



Operating Expenses: \$518,560,000

HMS Profile

MD Students	758
DMD Students	141
PhD Students	577
Interns, Residents, Postdoctoral Fellows	7,566
Voting Faculty	4,241
Full-time Faculty	7,933
Medical School Alumni	9,099
Dental School Alumni	2,340

As of September 2007

Affiliated Hospitals and Institutes

Beth Israel Deaconess Medical Center	Joslin Diabetes Center
Brigham and Women's Hospital	Judge Baker Children's Center
Cambridge Health Alliance	Massachusetts Eye and Ear Infirmary
Children's Hospital Boston	Massachusetts General Hospital
Dana-Farber Cancer Institute	McLean Hospital
Forsyth Institute	Mount Auburn Hospital
Harvard Pilgrim Health Care	Schepens Eye Research Institute
Immune Disease Institute (formerly known as the CBR Institute for Biomedical Research)	Spaulding Rehabilitation Hospital
	VA Boston Healthcare System



THE 2007–2008 DEAN'S REPORT was produced by the Harvard Medical School Office of Public Affairs.

EDITOR
Robert Neal

DESIGNER/PRODUCTION MANAGER
Rachel Eastwood

EDITORIAL ASSISTANT
Emily Lieberman

SCIENCE WRITERS
Misia Landau, Courtney Humphries, and Carol Cruzan Morton
With contributions by Lauren Cahoon, Lydia Flier, Jeneen Interlandi, Amita Joshi, Pat McCaffrey, Molly McElroy, and Patricia Thomas

OTHER CONTRIBUTORS

WRITING
Rich Barlow (New Curriculum and Students sections)
David Holzman (Alumni section)

ILLUSTRATION

Joseph Fiedler: cover, chapter introductions pages 2, 6, 10, 17, and 30, and above

Zina Deretsky, National Science Foundation: page 27

Other images courtesy of the following:
Dean Salisbury, page 17; Frank McKeon, page 19; Remy Chait, page 20; Bruce Spiegelman, page 23; Gregory Sorensen, page 24; John Ayanian, pages 28–29

PHOTOGRAPHY

Suzanne Camarata: page 34 (Tabin/Cepko/Leder)

Jeff Cleary: page 48 (Hay)

Steve Gilbert: pages 14 (Kucherlapati), 22 (Patti), 38 (Segal), 47 (Fisler), and 48 (Collins)

Liza Green, HMS Media Services: inside front cover and pages 11 (Martin/Flier/Connors), 12, 13, 31 (Lal), 35 (Ennis), 37 (Reich/Bonni), 51–53, and 55

John Harrington: page 15

Sam Ogden, page 23 (Spiegelman)

Graham Ramsay: pages 5, 8, 9, 11 (Podolsky), 14 (Church), 16, 18–21, 22 (Sinclair/Baur), 25, 26, 28, 29, 33, 34 (Van Vactor), 35 (Cohen/Blacklow), 36 (Green), 37 (Brenner/Seidman/Tabin), 38 (Scadden), 39–44 (Students), and 45–46 (Folkman, O'Connell, and Stultz)

Jeff Thiebauth: pages 7 and 32

Other photos courtesy of the following:

Jennifer Bennett, page 31 (Family Van); Brigham and Women's Hospital, page 36 (Braunwald); Children's Hospital Boston, page 38 (Hensch and Jensen); Dana–Farber Cancer Institute, page 38 (Kaelin); Harvard School of Public Health, page 47 (Blout); The MacArthur Foundation, page 37 (Gawande); Massachusetts General Hospital, pages 36 (Szostak), 38 (Brown), 47 (Alonso), 48 (Grillo), and 49 (Yurchak); McLean Hospital, page 49 (Mendelson); Christine Seidman, page 36 (Seidmans); Debra Yu, page 46 (Yu)



Harvard Medical School
25 Shattuck Street
Boston, Massachusetts 02115
Website: hms.harvard.edu



Recycled
Supporting responsible
use of forest resources

Cert no.
www.fsc.org
© 1996 Forest Stewardship Council

HARVARD
MEDICAL
SCHOOL

