



Dimensions of Discovery

Dean's Report | 2013–2014

HARVARD MEDICAL SCHOOL

Educating Leaders. Exploring Frontiers. Expanding Discovery.

**From minute
life forms to the
infinite expanse
of space, HMS
researchers
explore frontiers
of medicine and
science, seeking
new knowledge
for the better-
ment of human
health.**

1 Message from
the Dean

4 Education

10 Discovery

16 Service

22 Facts and Figures

HMS Leadership

Preclinical
Department Chairs

Fundraising
Highlights

HMS by the
Numbers

Affiliated Hospitals
and Institutions

Collaborations
Across Harvard

Financial Report



It has been said that a single cell contains an entire universe. At Harvard Medical School, life itself—from the molecular to the astronomical—is a vast landscape of scholarship and inquiry. ■ Studying the most elemental levels of life, an HMS research team has encoded 70 billion copies of a textbook in DNA. At a higher level of magnitude, our scientists have developed a device that allows them to monitor how cancer cells change during metastasis. Among several global initiatives, many faculty members continue to partner with the government of Rwanda to transform that country's health care system. Reaching for the stars, an HMS scientist who studies the physiology of animals in some of Earth's more extreme environments was selected to join NASA's 2013 astronaut class. ■ On these and other horizons, the HMS community is defining the boundaries of medicine, and then surpassing them, as it explores each new dimension of discovery.

or the more than 12,000 faculty members on campus and at our 16 affiliated teaching and research institutions, as well as the more than 1,800 students and thousands of trainees at HMS, each day the study and practice of medicine ranges from dedicated clinical care to complex research and exhilarating discovery. Some days, however, are far more demanding than others.

The Patriots' Day bombings at the Boston Marathon in April brought unthinkable tragedy to our community. Of the 275 injured that day, many suffered trauma more common to battlefields than to city streets. It was a crisis that demanded our very best.

Following this horrific event, the exceptional work of untold members of the HMS community, many of whom were profoundly shaken by the violence, illustrated why medical care in Boston is considered the finest in the world.

In the years to come, these caregivers will continue to rehabilitate and heal those who were wounded both physically and emotionally.

Groundbreaking Research

From such tragedy, however, we also learn. In the wake of the bombings, Harvard Catalyst | The Harvard Clinical and Translational Science Center aided Massachusetts Eye and Ear physicians by speeding the review of a three-year study at eight area hospitals to analyze the blast-related ear injuries and hearing loss suffered by approximately 100 people.

In another example of the collaboration that we seek to foster across laboratories and disciplines, HMS scientists at the Harvard Stem Cell Institute identified a blood protein, GDF-11, that appears to trigger tissue rejuvenation in aging hearts. This discovery may one day lead to a treatment for diastolic heart failure.



Researchers also discovered a hormone, betatrophin, that may dramatically improve the treatment of Type 2 diabetes, which affects an estimated 26 million people in the U.S.

A cross-disciplinary team of engineers, clinicians and scientists began clinical testing of an implantable vaccine to prevent melanoma, the most lethal form of skin cancer, while others, using a new method of analyzing whole genome sequences of tuberculosis, identified 39 new genes associated with elevated drug resistance.

As the health care universe rapidly evolves, pioneering progress in research and translational medicine is more essential than ever before. Earlier this year, we announced a major trans-Harvard initiative, the Harvard Program in Therapeutic Science, or HiTS, charged with reinvigorating the science of drug discovery. It will be

supported by a new Laboratory of Systems Pharmacology, a multidisciplinary scientific incubator for the development of new therapeutic approaches.

New models of medical care are also being developed. Our Center for Primary Care has established innovative models of patient care at 19 primary care teaching practices. The center's Academic Innovations Collaborative is using telemedicine to integrate mental health into primary care practices, and its Leadership Initiative is developing new ways to train the next generation of primary care leaders.

At the Harvard NeuroDiscovery Center, an anonymous \$12 million gift is bolstering efforts to advance fundamental neuroscience and to identify new treatments for Alzheimer's disease, Parkinson's disease, multiple sclerosis and other neurologic disorders.



Educating Future Leaders

The future of medicine, of course, begins in our classrooms. In 2013, HMS welcomed students from 32 states and eight other countries. Fifty-four percent of the Class of 2017 is made up of women, and 19 percent of the entering students come from groups underrepresented in medicine.

The medical environment these future physicians will inhabit will be vastly different from today's. To prepare them, this past year the Program in Medical Education engaged in a rigorous and far-reaching reassessment of the first two years of the MD program.

The Task Force on Redesign of the Fundamentals of Medicine Preclerkship Curriculum is devising a bold new curriculum that will more effectively fuse basic and clinical science education. It is expected to launch in August 2015.

Our students also benefit from an environment conducive to learning. In the fall, we formally opened a new 7,500-square-foot multifunctional clinical skills center in the Tosteson Medical Education Center (TMEC) that provides the technology and adaptability that modern medical education demands.

A parallel study of all learning spaces in the TMEC, which analyzed the technological and pedagogical requirements of a 21st-century learning environment, was also completed, and we are also developing a 10-year master plan for the future use of HMS campus buildings and grounds.

The Health Sciences and Technology program (HST), a collaboration with the Massachusetts Institute of Technology, also launched a redesign of its preclinical curriculum. The program now exists within the newly created Institute for Medical Engineering and Science at MIT, complementing the Irving M. London academic society at HMS.

We have finalized the review of the Continuing Medical Education program, which was reaccredited earlier this year, and we are aggressively exploring new approaches to the expansion of a distance learning initiative.

The Master's Program in Clinical and Translational Investigation enrolled its first cohort, drawing the best candidates interested in translating research discoveries into clinical care. Our Master of Medical Sciences (MMSc) in Global Health Delivery program enrolled its second class of students, and we created a new MMSc in Medical Education.

We also added a new academic department to our roster, establishing a Department of Neurosurgery, a move championed by the chiefs of neurosurgery at four of our affiliated hospitals.

HMS educational initiatives span the globe. With the Rwandan Ministry of Health, 16 faculty members will train Rwanda's next generation of medical professionals, while in Portugal our clinical research training program grew to include 60 students. In July, we launched a new, one-year blended-learning program, the Global Clinical Scholars Research Training Program, with an enrollment of nearly 150 students.

Mery Daniel (left), who was injured in the Boston Marathon bombings, is learning to walk again with the help of occupational therapist Becky Buttiglieri at Spaulding Rehabilitation Hospital.

Achievement and Merit

Driving achievement at HMS are the many exceptional members of our community. It is impossible to list each accomplishment here, but our long tradition of leadership continued with the election of four HMS faculty members to the National Academy of Sciences. Four others were named Howard Hughes Medical Institute investigators and four more were elected to the Institute of Medicine. Alumnus Raul Ruiz '01 became a California congressman, and Jessica Meir, an assistant professor of anaesthesia at Massachusetts General Hospital, was chosen from among 6,000 applicants to join NASA's next class of astronaut candidates.

To help position the School for a more secure financial future, we launched HMS Next, an important initiative through which our community will work together to improve our operating environment, identify efficiencies and seek opportunities for revenue generation.

We have also suffered losses and made difficult choices. Neuroscientist and Nobel laureate David H. Hubel, the John Franklin Enders Professor of Neurobiology Emeritus, who served HMS for more than 54 years, died at age 87. One of the greatest philanthropists in HMS history, Count Giovanni (Nino) Auletta Armenise, passed away in the fall at the age of 81.

We also made the decision to wind down operations at the New England Primate Research Center over the next 12 to 24 months. This decision was based on a review of the long-term academic benefits and the financial costs of continuing to operate the center. We are working closely with key faculty and the National Institutes of Health on this transition.

Overall, however, HMS made impressive progress in 2013. Our stellar achievements did not happen without the hard work and inspiration of all the extraordinary members of the HMS family. In our classrooms, laboratories, clinics and hospitals, their dedication shines, even in the most challenging circumstances. I am proud to highlight some of their remarkable accomplishments, paying tribute, with gratitude, to the outstanding service that takes place here each day, be it preparing for a mission to Mars, or simply exploring the universe of a cell.

Educating tomorrow's leaders in medicine requires constant reassessment of pedagogical standards.



Dean for Students
Nancy Oriol (front left)
accompanies mem-
bers of the Class of
2017 to their first clini-
cal case presentation
on White Coat Day.

With medical knowledge swiftly increasing, the nation's health care delivery system undergoing rapid change, and biomedical science and technology advancing at a fast pace, Harvard Medical School continues to shape the future as it educates the next generation of leaders in medicine and science. In 2013, the School continued a rigorous reassessment of how to best prepare students for the professional world they will lead. At the center of this analysis is the HMS preclerkship curriculum—what we teach, as well as when, where and how we teach it.

In the past year, Program in Medical Education (PME) leaders analyzed how to recalibrate our model of pedagogy to design more highly interactive courses oriented around case-based and team-based learning and problem solving. Jules Dienstag, the Carl W. Walter Professor of Medicine and dean for medical education, charged the Task Force on Redesign of the Fundamentals of Medicine Preclerkship Curriculum, co-chaired by Richard Schwartzstein, the Ellen and Melvin Gordon Professor of Medical Education and director of The Academy at HMS, and Melanie Hoenig, assistant professor of medicine, with exploring the creation of a new course of study for the first phase of the four-year MD program. The resulting curriculum, which leads to the Principal Clinical Experience (PCE), will more fully integrate basic science and clinical medicine in an innovative program more developmentally appropriate for student learning. Task force members looked at four specific areas: content and organization, pedagogy, clinical skills and assessment. A parallel group also explored changes to the School's physical learning spaces to better support the new pedagogy.

Rather than separating normal and abnormal physiology into the first and second years, for example, the task force considered how structure and function, and both normal and abnormal physiology, might be taught together in the preclerkship curriculum using organ systems as the organizing principle. Normal heart anatomy and physiology would be presented along with cardiovascular pathophysiology and disease. These courses would be formulated to prepare students for the year of core clinical clerkships (the PCE) that follows.

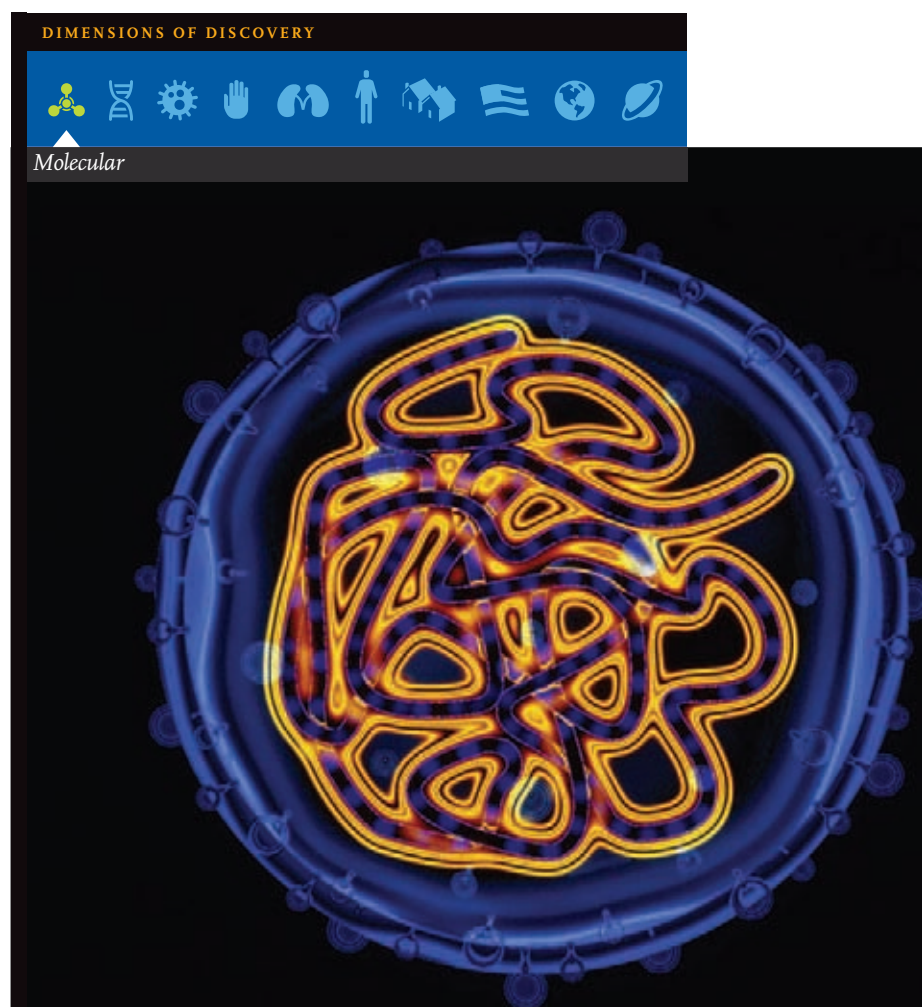
While acknowledging that core basic science is essential to the preclerkship period, this approach recognizes that the richness of more advanced science may be best presented to students who have been seasoned by the core clinical year. During the third and fourth years, students would return to, and delve more deeply into, integrated/basic, population and clinical sciences, choosing electives that better align with their individual career paths. Social science topics, such as medical ethics and health care policy, would be introduced during the preclerkship curriculum and

would be reinforced after students acquire more experience and context in clinical settings. By choosing a research area for Scholars in Medicine projects after the PCE, students will develop a better sense of the areas of health care or biomedical science in which they are interested. This far-reaching effort will be introduced in August 2015.

Clinical Skills Center

In tandem with these broad curriculum reassessment efforts, HMS embarked on major improvements to its campus facilities, to better accommodate student needs and new pedagogical approaches. In the fall of 2013, HMS opened its new \$5 million clinical skills center, a project spearheaded by Jane Neill, associate dean for medical education planning and administration. Located in the Tosteson Medical Education Center (TMEC), this 7,500-square-foot multifunctional center houses 18 examination rooms equipped with 47 video cameras for monitoring student performance. It also has advanced exam scoring technology and observation workstations for objective structured clinical exams (OSCEs), clinical assessment, and development of faculty clinical teaching skills. Retractable walls between 10 of the exam rooms allow for expansion to accommodate mannequin simulation sessions.

James Chou, professor of biological chemistry and molecular pharmacology, and colleagues unravelled the 3-D atomic structure of an ion channel protein that plays a central role in viral assembly and release in the hepatitis C virus.



Medical Education Center Programming Study

The clinical skills center construction and the curriculum redesign prompted a further evaluation of the TMEC, which was last renovated in the late 1980s. Under the leadership of Dienstag, Neill and Richard Shea, associate dean for campus planning and facilities, an eight-month architectural programming study of the building was conducted. The study evaluated teaching and student space needs in the context of overall curriculum redesign goals, including how new teaching technologies will be used, and how more flexible, multipurpose space can be incorporated into the historic building.

Campus Master Plan

HMS is also developing a campus master plan for use in establishing longer-term space planning and real estate decisions. Findings from this planning framework will improve understanding of the type of facilities required to meet the future research, educational and administrative needs of the School. Recommendations are expected in early 2014.

Laboratory of Systems Pharmacology

Another key construction project begun in 2013 is the new Laboratory of Systems Pharmacology (LSP), to be housed in the Giovanni Auletta Armenise Medical Research Building. The labo-

Using next-generation sequencing technology, George Church, the Robert Winthrop Professor of Genetics, encoded his book *Regenes* in DNA. This vial contains 70 billion copies of the book.



ratory is the cornerstone of HiTS, the Harvard Program in Therapeutic Science, led by Peter Sorger, the Otto Kraye Professor of Systems Pharmacology. The Harvard-wide initiative focuses on understanding disease processes and responses to drug interventions in cells, tissues and humans.

The LSP's mission is to advance novel pathways in drug discovery and research. The 4,800-square-foot lab, scheduled to open in the spring of 2014, will support multidisciplinary teams of scientists, engineers and physicians from HMS and its affiliated hospitals and research institutions. All will work together to integrate computational and systems approaches into each phase of drug development. This novel approach is the driving force in the LSP's quest to reinvent the science of therapeutic drug and device discovery, development and evaluation.

Redesigning Health Sciences and Technology

The Health Sciences and Technology (HST) program, a joint HMS and Massachusetts Institute of Technology program, was strengthened in 2013 by the creation of the Institute for Medical Engineering and Science at MIT. The institute complements the HMS London Society, the academic society that is home to the HST program. In addition to taking specially designed preclinical courses at both HMS and MIT, MD and PhD students in the HST program pursue intensive biomedical research to prepare them for careers as physician-scientists or medically oriented researchers.

Director of MD-PhD Program

In August, Loren Walensky, associate professor of pediatrics, was appointed director of the Harvard-MIT combined MD-PhD program. In this NIH-supported program, students pursue both advanced degrees, integrating science and medicine to propel the next generation of biomedical breakthroughs. The program has graduated more than 500 students since its establishment in 1974, many of whom hold senior leadership positions at the nation's top medical schools, research institutions and biotechnology firms.

Teaching and Education Initiatives

HMS faculty continue to build on programs made possible through five Harvard Initiative on Learning and Teaching (HILT) Hauser grants, which are designed to strengthen and broaden the scope of existing learning and teaching activities, and address current and future pedagogical needs. One group is studying the use of virtual dissection tools for dynamic anatomy instruction and evaluation, while another is implementing the use of a new teaching method centered on team-based, interactive basic science instruction.

The Academy at HMS

Professional development, educational innovation and research, and community building are core missions of The Academy at HMS. For the first time in its history, academy events drew more than 1,000 faculty during the academic year. Among the event highlights were Medical Education Day and the Symposium on the Science of Learning, each of which support the PME's mission to emphasize analytical reasoning and to integrate basic



(From left) HMS Dean Jeffrey S. Flier and Dean for Medical Education Jules Dienstag cut a ribbon, held by John Scully, engineering and construction project manager, to open the new clinical skills center. The multifunctional center incorporates new technologies for teaching and assessing clinical communication and physical exam skills.

and clinical science throughout the curriculum. Medical Education Day focused on integrative teaching, including strategies for linking basic and clinical science within the classroom and at the bedside. The Symposium on the Science of Learning examined the cognitive and neurological principles that may contribute to curiosity and motivation in learning.

Mentored Casebook in Its 10th Year

The Mentored Clinical Casebook Project, an elective course, marked its first decade. Offered in the first year of the curriculum, the course gives 30 students, mentored by HMS faculty, exposure to patient cases in a manner that provides a more integrated understanding of the biological science affecting each patient's case history. At the end of the year, students produce a 30-page scholarly manuscript that interweaves each patient's personal narrative with learned basic and clinical science principles. A group of former students is compiling the patient-based perspectives into a compendium of essays, and course directors are working on a retrospective review of the program.

Capstone Course Expanded

In 2013, enrollment doubled in a pilot capstone course designed to help students make the transition from medical student to intern. The course syllabus was expanded, with new lectures added on diagnostic error, the application of physiology to clinical practice, motivational interviewing and renal management. The highly successful cardiac auscultation series, in which students learn to identify the patient-specific differences in heart murmurs, and new modules on vascular access and respiratory management, gave students an opportunity to focus on these important clinical skills before beginning the first year of residency. The course continues to emphasize the balance between management of clinical issues

and the best methods for approaching emotionally complex tasks, such as establishing code status, pronouncement, interacting with family after a death and being emotionally present for patients who have life-threatening illnesses.

Student Scholars Propel Discovery

More than 150 HMS students are actively engaged in the Scholars in Medicine Program, now in its second year. In order to help students acquire the tools needed for a lifetime of research, they are required to choose a scholarly research project and, with a faculty mentor, develop it over the course of their time at HMS. Research areas are wide ranging, from genetics to bioinformatics, from clinical interventions to health systems improvements and policy recommendations.

Graduate Education and Global Programs

PhD Programs. The School's PhD programs, led by Dean for Graduate Education David Golan, the George R. Minot Professor of Medicine, continue to thrive, ranking among the best nationally and enrolling more than 140 new students each year in a range of disciplines. Despite an increasingly constrained funding environment, the number of training grant slots awarded in 2013 for graduate education at HMS was higher than ever before, as was the number of individual fellowships awarded to students. Each award is attributable to the concerted efforts of faculty and staff who worked with students to create successful proposals. In the past year, the Division of Medical Sciences was awarded 77 training grant slots totaling \$3,200,000, and more than 100 individual fellowships totaling more than \$3,600,000. Here too, curriculum innovation and reform advanced in 2013, with both the Program in Graduate Education and the PME-awarded joint funding from HILT for a decanal priorities proposal that will assist with faculty development and curriculum assessment efforts associated with ongoing curriculum development.



DIMENSIONS OF DISCOVERY



Cellular

In January 2013, nine first-year PhD students entered the inaugural class of a new therapeutics graduate track; up to 12 more are slated to begin the program in 2014. This curriculum instructs students pursuing life-science doctoral degrees on how to translate cellular and molecular discoveries into clinical applications, accelerating new drug discovery and development. Internships are required in one of several areas, including the pharmaceutical and biotechnology industries, clinical research and regulatory science. The therapeutics graduate program complements the Leder Human Biology and Translational Medicine Program, which provides an integrated enrichment experience that supports PhD students pursuing careers in translational research.

Master of Medical Sciences Programs. Four active master's programs now include a newly merged Master's Program in Clinical and Translational Investigation, which launched this year in collaboration with Harvard Catalyst; a Master of Medical Sciences in Global Health Delivery; a Master of Medical Sciences in Biomedical Informatics; and a new Master of Medical Sciences in Medical Education.

In 2013, HMS welcomed the second class of students pursuing MMSc degrees in global health delivery, which includes a five-year joint MD-MMSc degree program as well as a two-year MMSc-only program. The program, which successfully combines mentored research and education, is training physicians who will lead and improve health care delivery systems in resource-poor settings around the world. Integrating courses offered through HMS, Harvard School of Public Health (HSPH) and Harvard Business School, the program focuses on development of the tools needed to perform social and delivery science and policy research through the completion of field-based mentored research projects.

Aaron Cypess (above) and Yu-Hua Tseng, assistant professors of medicine at Joslin Diabetes Center, led a team in identifying the genetic expression and function of human brown adipose tissue (BAT), or brown fat, which, when activated by cold, helps the body burn calories. Cypess holds a cooling vest used to activate BAT.

To further train tomorrow's medical education leaders and researchers, the two-year MMSc in Medical Education program will focus on the research that underlies innovation in medical education. The program will begin in July 2014.

Global Programs

Global Clinical Scholars Research Training Program. In July, HMS launched this one-year blended-learning program with an enrollment of nearly 150 students from throughout Africa, Asia, Canada, Europe, the Middle East and the U.S. Intended for clinicians and clinician-scientists who seek advanced training in clinical research, the program focuses on epidemiology and biostatistics, using an integrated instructional approach that combines traditional teaching methods with online lectures, webinars, in-person workshops and team-based learning. Scholars develop and present a faculty- and peer-reviewed research proposal at the conclusion of the program.

Clinical Research Training in Portugal. The Harvard Medical School–Portugal Program in Translational and Clinical Research and Health Information, now in its fourth year, is building on its success and now offers a two-year certificate program in clinical and translational research. Enrollment in the certificate program grew to 60 Portuguese physician-students in 2013. Designed to provide sophisticated clinical and translational research instruction, the program takes residents and junior faculty through a blended-learning model that includes online instruction, interactive webinars and intensive on-site workshops. Students in the certificate program come from teaching hospitals and biomedical research institutions throughout Portugal. This program provides a dynamic model for the development of other global training programs.

Global Health Delivery Education. HMS continues to develop an academic science of global health delivery for health practitioners facing challenging diseases and conditions in resource-constrained settings. Last summer the School, together with Brigham and Women's Hospital, renewed its Human Resources for Health Program with the government of Rwanda and a consortium of U.S. institutions so as to continue providing both academic and clinical instruction and training to health care leaders in the African nation. In June 2013, faculty from HMS and its affiliates toured teaching hospitals in Rwanda with members of Rwanda's Ministry of Health, and developed plans for the second year of the program while assisting with the creation of global health delivery education and research programs there.

For a fifth year, the three-week Global Health Delivery Summer Intensive Program was offered in collaboration with HSPH, enrolling 30 students in Boston. A related one-week summer course in global health delivery, which focused on issues such as malaria control, testing and treatment, was taught for the first time in Rwanda.



Mirebalais University Hospital in Haiti. To address overwhelming health care needs in Haiti, a coalition of government, corporate and academic partners opened the Mirebalais University Hospital on the outskirts of Port-au-Prince in April. The effort was led by Partners In Health, a global health care delivery nonprofit cofounded by Paul Farmer, the Kolokotronis University Professor of Global Health and Social Medicine and head of the Department of Global Health and Social Medicine. The 300-bed teaching hospital, which has six operating suites, can treat more than 500 people daily, and functions as an educational facility for Haitian health care providers who are assisted and trained by visiting HMS physicians and students.

Continuing Medical Education

A strategic review of the continuing medical education program, reaccredited this year, was finalized in 2013. Substantial improvements were made to the infrastructure of the Department of Continuing Medical Education, and the program is actively exploring new ways to expand its distance learning initiatives. The department also collaborated with the Harvard Graduate School of Design to offer a novel course in emergency room design that enhances services and optimizes patient outcomes. Under the leadership of Sanjiv Chopra, faculty dean for continuing education and professor of medicine, the department continues to educate thousands of practicing physicians, helping them to

During a group teaching session on the musculoskeleton, Lyle Micheli (far right), clinical professor of orthopedic surgery at Boston Children's Hospital, demonstrates the physical examination of the knee to second-year students.

integrate new knowledge into clinical practice. In addition to the more than 270 accredited courses offered in traditional lecture settings, 75 courses were offered online and 40 more courses are in development. In aggregate, enrollment in online courses totaled 70,000, with half of those enrolled from the U.S. and half from any of 170 other countries. Courses are offered without charge to doctors in 85 developing countries.

Increasing Scholarship Aid

To reduce financial burdens on students, HMS continues its efforts to provide assistance. In 2012-13, the average debt per graduating student was \$104,100, about 10 percent lower than five years ago. Approximately 20 percent of the graduating class benefited from loan-forgiveness programs, receiving nearly \$875,000 in debt relief. Some students were eligible for additional relief, including \$80,000 after completing residency. Need-based scholarships totaling \$15.5 million were awarded by the School, representing an increase of 4 percent over the previous year. Contributions by HMS alumni continue to be a critical source of scholarship aid, with ongoing efforts by the Office of Resource Development to increase support.

Discovery

Bone marrow on-a-chip is one of several microfabricated organs developed at the Wyss Institute for Biologically Inspired Engineering, directed by Donald Ingber, the Judah Folkman Professor of Vascular Biology at Boston Children's. The functional human organs-on-chips provide alternatives to conventional cell culture and animal models for drug discovery development applications.

Men love to wonder, and that is the seed of science.

— Ralph Waldo Emerson

Biomedical research breakthroughs and significant technological advances have made this an era of unprecedented research opportunity. Yet despite progress in understanding, preventing and treating human disease, the U.S. biomedical research community faces formidable funding pressures that threaten vital endeavors that could lead to improved treatments for some of our more intractable health threats, such as Alzheimer's disease, cancer, heart disease and HIV/AIDS.

In 2013, the research community at HMS contributed significantly to scholarship through publishing, and continued to lead the field in revolutionary discoveries and technologies, such as the detection of nearly 200 new regions of genetic code that may

Alexandra Golby, associate professor of surgery and radiology, practices clinical neurosurgery with a focus on the treatment of brain tumors and epilepsy. In the first-of-its-kind Advanced Multimodality Image Guided Operating suite at Brigham and Women's Hospital, Golby's team is involved in collaborations that advance intraoperative navigation systems and incorporate functional imaging in the operating room.

contain undiscovered cancer genes, and the development of a programmable glue made of DNA that may have applications for the regrowth of human tissue.

This year, the combined research efforts of HMS and Harvard School of Dental Medicine resulted in \$282.8 million in funding for sponsored programs, representing 34 percent of Harvard University's sponsored portfolio, including \$236.4 million in federal awards. Of those grants, \$220.2 million came from the National Institutes of Health.

While the dedication invested in the pursuit of scientific inquiry is immeasurable, the research conducted at HMS, highlighted below, provides a glimpse into the remarkable breadth of exploration at the School. Learn more at hms.harvard.edu/research.

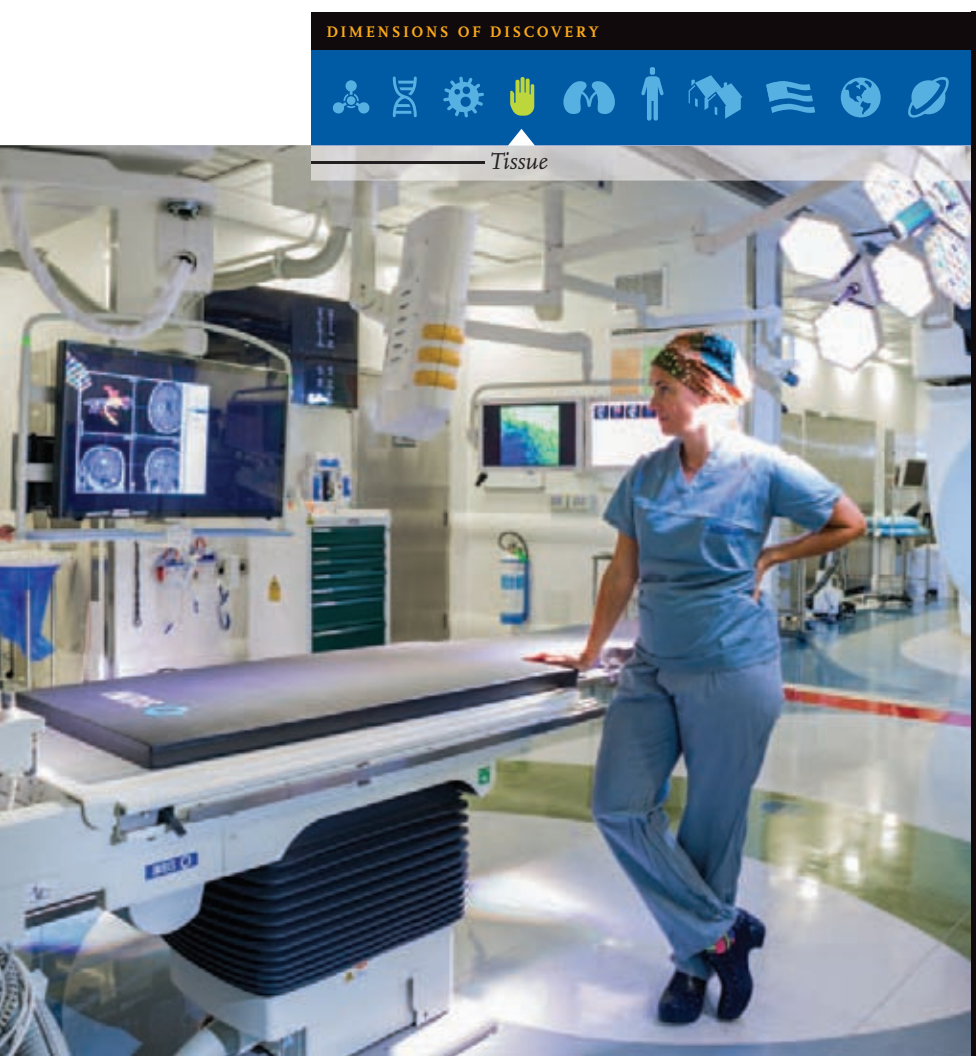
Harvard Catalyst | The Harvard Clinical and Translational Science Center

To accelerate biomedical research and speed the creation of new therapies, Harvard Catalyst | The Harvard Clinical and Translational Science Center, led by Lee Nadler, the Virginia and D.K. Ludwig Professor of Medicine and dean for clinical and translational research, leverages the combined strength of 11 Harvard schools and 16 affiliated academic and research centers to embody the "One Harvard" ideal of cooperative innovation. Harvard Catalyst fulfills three highly synchronized roles. As a *convener*, it provides educational training and forums, clinical research services, community-based research and cross-institutional regulatory support. As a *connector*, it provides advanced informatics tools, online platforms that fuel interaction, and cross-site opportunities that facilitate the exchange of ideas between clinicians and scientists. As a *catalyst*, it provides cutting-edge investigative tools and pilot funding, with its unique infrastructure providing the spark that unites a wide range of disciplines and individuals who, together, are finding new solutions to questions in medicine.

Many advances are emerging from this fertile ground. One, the Reactor program, launched in April. This program identifies opportunities and solutions in clinical and translational medicine and fosters cross-disciplinary communities. It provides pilot funding, assists in team building and resource identification, and helps researchers prepare for the launch of new ventures.

As an example of this effort, in 2012 more than 400 research teams responded to a request for proposals on how problems in clinical medicine could be resolved through the use of advanced imaging technology. Eventually 184 teams submitted formal proposals and 15 received pilot funding. In 2013, Reactor reconvened the pilot projects and awarded additional funding in January 2014 for the advancement of two projects. One is a brain imaging study led by Alexandra Golby, associate professor of surgery and radiology. Golby works in the Advanced Multimodality Image Guided Operating suite at Brigham and Women's Hospital, which houses state-of-the-art imaging equipment and interventional surgical systems.

Golby's team, working with Xiaoliang Sunney Xie, the Mallinckrodt Professor of Chemistry and Chemical Biology, Harvard Faculty of Arts and Sciences, is attempting to solve a key problem in neurosurgery—how to intraoperatively distinguish brain tumors from functional brain tissue using an imaging



Levi Garraway, associate professor of medicine at Dana-Farber Cancer Institute, finds genes and molecular pathways that lead to cancer and resistance to anticancer agents.



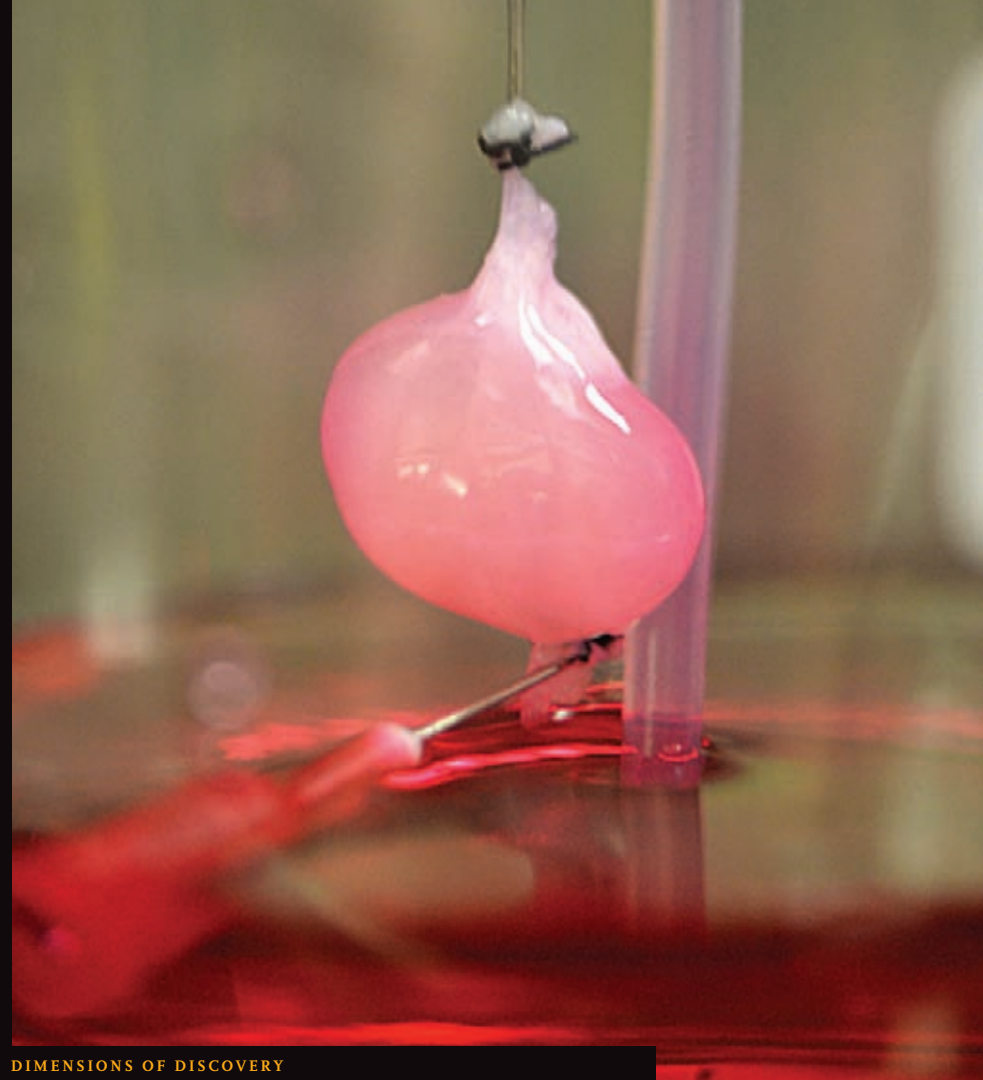
approach rather than appearance and touch, so that the tumor is removed and more healthy tissue remains. The team is developing an image-guided technique that uses scattered monochromatic light that measures shifts in energy to distinguish protein-rich tumors from lipid-rich healthy brain tissue. Based on the results of this and other Reactor pilot studies, Harvard Catalyst plans to produce innovations that will improve patient care and outcomes.

Biological Chemistry and Molecular Pharmacology

DNA-Unwinding Mechanisms Hold Clues. When DNA is copied in preparation for cell division, its two interwoven strands are separated by enzymes called helicases, which consist of six proteins arranged in a ring-shaped motor that encircles and travels along the DNA structure. A fundamental question has been whether the helicase ring encircles one or both strands of the DNA. In research published in *Cell* and *Nature*, Johannes Walter, professor of biological chemistry and molecular pharmacology, showed that the helicases from vertebrate cells and viruses encircle just one strand of DNA. Surprisingly, a helicase was found to be capable of zipping past a bulky roadblock on DNA, suggesting that the helicase can transiently open and reclose its ring, revealing a new level of plasticity in the replication mechanism. This research identifies fundamental aspects of genome maintenance and lays the foundation for understanding how replication errors might arise in diseases such as cancer.

Cell Biology

Targeting Motor Neuron Diseases. Research teams in the Department of Cell Biology are providing new insights into three neurodegenerative diseases: amyotrophic lateral sclerosis (ALS), spinal



DIMENSIONS OF DISCOVERY



A rat kidney bioengineered by Harald Ott at the Massachusetts General Hospital Center for Regenerative Medicine. Ott's team is building functional replacement kidneys on the matrix of donor organs from which cells had been stripped.

muscle atrophy (SMA) and Parkinson's disease. As published in *Cell Reports*, a team led by Robin Reed, professor of cell biology, showed that proteins that cause ALS or SMA share a biochemical pathway involved in RNA processing, providing strong support for the view that these motor neuron diseases are related. In a report in *Proceedings of the National Academy of Sciences*, Spyros Artavanis-Tsakonas, professor of cell biology, identified the genetic circuitry that regulates survival motor neuron, the gene underlying SMA. This insight may point to possible treatment strategies, as alterations in protein levels of this gene correlate with the severity of SMA. In *Nature*, Wade Harper, the Bert and Natalie Vallee Professor of Molecular Pathology, provided greater understanding of familial early-onset Parkinson's disease by comprehensively mapping how Parkin, a protein commonly mutated in Parkinson's patients, marks cellular organelles known as mitochondria for destruction. Understanding how mitochondrial survival is regulated may be key to treating this and other neurodegenerative diseases.

Genetics

Sizing Up Bone Growth. Skeletal bones grow to different lengths, but until now it's been unclear how that happens. Collaborative research between teams led by Clifford Tabin, the George Jacob and Jacqueline Hazel Leder Professor of Genetics and chair of the

Department of Genetics, and Marc Kirschner, the John Franklin Enders University Professor of Systems Biology and chair of the Department of Systems Biology, built upon the knowledge that bone growth doesn't come just from cells dividing, but from cells enlarging. Using specialized imaging to measure cell mass and focusing on chondrocytes—the cartilage cells in the bone's growth plate that create a scaffold upon which calcium is deposited—the researchers identified three distinct stages of growth. Cells first grow in size while maintaining a high density of dry mass. Following this, there is a swelling stage, in which chondrocytes continue to expand in size, but also take up extra fluid. In the third stage, the swelling stops and cells once again expand to size while keeping their density constant. This final phase is variable, however, occurring to a greater extent in faster-growing bones and being the major determinant of why different bones attain different lengths. The third phase is dependent on an insulin-like growth factor linked to the regulation of proportionality differences in the skeleton. This research holds promise for treating bone growth disorders and length asymmetries.

An infant recovers at Boston Children's Hospital, wearing a special turban designed to warm babies after heart surgery.

Global Health and Social Medicine

Rwanda's Health Care Success. In less than two decades, Rwanda has turned a dismal health care system into an extraordinarily successful one that serves as a model for other African countries. An article in the *BMJ*, coauthored by Paul Farmer, head of the Department of Global Health and Social Medicine and cofounder of Partners In Health, highlights some of the country's gains. The 1994 genocide that killed or displaced millions of Rwandans left the country with only about 625 doctors in public hospitals today to serve a population of 11 million. But nurses now number 8,000, and a new corps of 45,000 health care workers, chosen in village elections, is providing access to primary care, including immunizations, family planning and prenatal care, and treatment for malaria, tuberculosis, diarrhea and pneumonia. The probability of a child dying by age 5 dropped 70 percent from 2000 to 2011. People receiving antiretroviral medications for AIDS rose from near zero to 108,000 in one decade. Nearly 98 percent of Rwandans now have health insurance, and a national computerized medical records system is in place. Farmer and his colleagues largely credit the Rwandan government for this remarkable progress. With the help of its partners, Rwanda's Ministry of Health has identified its leading causes of morbidity and mortality and is addressing them systematically.

Health Care Policy

Quality of Care and Spending for Medicare Beneficiaries. In recent years, some scholars have argued that large integrated organizations could provide Americans with better health care at lower cost. In that spirit, Medicare launched the Accountable Care Organization (ACO) program, intended to contain costs while improving health care quality by integrating care delivery, having providers share spending risk and emphasizing primary care. To determine whether organizations sharing features of the ACO model delivered better and more cost-effective care, researchers led by J. Michael McWilliams, associate professor of health care policy; Michael Chernew, the Leonard D. Schaeffer Professor of

Health Care Policy; and Bruce Landon, professor of health care policy, studied data from more than 4 million Medicare patients served by provider groups, classifying them according to size, specialty mix and type of practice—hospital-based or independent. Spending and quality measures, such as total spending, spending by type of service, 30-day readmissions and preventive services, were then assessed. As published in *JAMA Internal Medicine*, investigators' findings showed that spending was lower and the quality of care better for Medicare beneficiaries served by larger independent groups with strong primary care orientations located in areas of the country where health care providers accepted greater financial risk.

Department of Microbiology and Immunology

Species-Specificity for Gut Microbiomes. The gut microbiome, or the total array of microbes in an intestinal tract, is key to regulating immune responses outside the gut, but not just any microbial collection will do. Research published in *Cell* by Dennis Kasper, the William Ellery Channing Professor of Medicine and professor of microbiology





DIMENSIONS OF DISCOVERY



Community

and immunology, shows that animals rely on host-specific microbial partners. In the study, germ-free mice were colonized with human gut microbes, then compared with mice with species-appropriate gut microbiomes. When tested for the ability to fight infection, the immune systems of mice colonized with human microbes did not develop or function properly. The research suggests that the absence of the “right” gut microbes might make humans more vulnerable to infection. It also may shift the balance of microbes in people genetically disposed to autoimmune diseases, thus triggering onset of disease. Among factors that potentially alter gut microbiome balance are heavily processed foods, frequent use of antibiotics and antibacterial hygiene products.

Neurobiology

Processes Essential to Brain Development. Rett syndrome, a neurodevelopmental disorder associated with the X chromosome, emerges primarily in girls ages 6 to 18 months, resulting in the loss of language and motor skills, as well as seizures and respiratory problems. Research led by Michael Greenberg, the Nathan Marsh Pusey Professor of Neurobiology and chair of the Department of Neurobiology, is focusing on the gene *MeCP2*, which encodes a protein involved in synaptic development and maturation. When *MeCP2* is absent or mutated, the brain cannot properly process signals from the environment and brain development is essentially frozen in time. In a paper published in *Nature*, Greenberg’s research team revealed three sites on *MeCP2* where neuronal activity induces chemical changes key

The Center for Primary Care works to catalyze innovation in health care systems and to transform training. At Beth Israel Deaconess Medical Center, Assistant Professor of Medicine Amy Weinstein (right) works with primary care resident Bracken Babula (left) and intern Andrew Locke ’17 (center), helping to prepare a new generation of physicians in primary care.

to brain development. They found that a mutation on one of these sites, T308, prevents these chemical changes from taking place, disrupting the way *MeCP2* interacts with a crucial protein complex called NCoR, and leading to a disruption in synaptic function. How these processes work together to regulate synaptic development is key to developing possible new therapies for Rett syndrome.

Stem Cell and Regenerative Biology

Rejuvenating the Aging Heart. HMS scientists have discovered a substance called GDF-11 in the blood of young mice that, when given to aging mice, reverses cardiac hypertrophy, or thickening of the heart muscle, an important contributor to heart failure. As reported in *Cell* by Amy Wagers, the Forst Family Professor of Stem Cell and Regenerative Biology, and Richard T. Lee, professor of stem cell and regenerative biology, when GDF-11, a relatively obscure growth factor, was given to older mice, it produced a dramatic change in the heart. In just four weeks, the thickened hearts of older mice changed to more closely resemble the hearts of young mice. Other organs in the body also contain cells with surface receptors designed to interact with GDF-11. Investigations are now underway in the Wagers and Lee labs to determine whether GDF-11 has similar rejuvenating effects on other tissues affected by aging.

Systems Biology

Dynamics of Spinal Cord Patterning. In the developing embryo, the fate of cells that become the spinal cord is influenced by Shh, a protein signal. To date, scientists have theorized that Shh acts on relatively static embryonic cells, affecting their development via concentration levels and duration of exposure. This model is possible as long as cell movements are minimal and daughter cells stay close together. But HMS researchers have shown that this is not the case. In a study published in *Cell*, a team led by Sean Megason, assistant professor of systems biology, tracked the lineages of motor neuron precursor cells during neural tube development. Using a new imaging technique, they showed that these neural cells undergo intensive movements that limit the precision of positional information. Cells then migrate selectively into sharply defined domains after cell specification is determined. Studies are now underway to determine how different Shh exposure dynamics result in different cell fates, and how specified cells move to the right location.

Harvard School of Dental Medicine

Potential Pathway for Osteoporosis Therapy. Antiresorptive drugs used to treat osteoporosis work by reducing the number and activity of bone-resorbing cells called osteoclasts. But these drugs also inhibit bone-forming cells, or osteoblasts. Research led by Roland Baron, chair of the HSDM Department of Oral Medicine, Infection and Immunity and HMS professor of medicine at the Massachusetts General Hospital Endocrine Unit, aims to identify novel therapeutic pathways that can inhibit bone resorption while also maintaining bone turnover and formation at clinically acceptable levels. In a study published in the *Journal of Clinical Investigation*, Baron’s team focused on the gene *cathepsin K* (*Ctsk*). Mutations

or deletions of this gene lead to osteopetrosis, in which bones become more dense, in contrast to more prevalent conditions such as osteoporosis, in which the bones become less dense, leading to fragility and fractures. These studies of *Ctsk* revealed a coupling mechanism between bone-resorbing and bone-forming cells, demonstrating a pathway in which osteoclasts actually promote bone formation. These and other findings have helped identify inhibition of *Ctsk* as a target for new osteoporosis therapies. Advanced clinical trials, now underway, may show whether the risk of fracture is decreased in treated patients.

Office of Technology Development

Harvard's Office of Technology Development works closely with HMS researchers to identify and develop new ideas and emerging discoveries and to engage with industry partners and investors interested in fostering therapeutic breakthroughs. Its newly expanded Blavatnik Biomedical Accelerator at Harvard University provides funding and access to product development resources. New projects this year included novel cancer therapies that degrade cancer-promoting cellular proteins and novel therapies for cardiovascular disease and cancer that act by regulating lipid metabolism.

OTD also continues to expand partnerships between HMS and biopharmaceutical companies that contribute funding to the School's research programs. Among new projects, HMS researchers are working with Hoffmann La-Roche on drugs for diseases such as tuberculosis; with Takeda Pharmaceuticals on a new cancer therapy; with the pharmaceutical company IPSEN on neurologic disease therapies; and with a multi-institutional consortium led by Biogen Idec to identify new approaches to treat amyotrophic lateral sclerosis.

Information Technology

The Department of Information Technology plays a pivotal role in medical research and education. This year, under the leadership of Rainer Fuchs, chief information officer, HMS published its first IT roadmap, a multiyear strategy for providing the computational capabilities needed to support the high-caliber laboratory and clinical research undertaken by HMS scientists. In education, Internet connectivity continues to shape new paradigms for delivering content. The pedagogy at HMS is supported by web-based teaching solutions such as MyCourses, which was recently updated with new features for students and faculty, and advanced IT programs for preclinical teaching and the testing of clinical skills.

In biomedical research, investigators use and generate large, complex and diverse datasets. At HMS, the demand for data storage doubles every year, driven by technologies such as next-generation sequencing, image-based analytics and high-content screening. To address this big data challenge, IT launched a new multiyear infrastructure upgrade designed to achieve greater performance and sustainability. To enhance research collaborations, the Harvard Catalyst website has been equipped with interactive search tools and the research profiles of more than 23,000 faculty

at HMS, HSDM and HSPH. The underlying software is used at more than 30 institutions nationwide, including the U.S. Food and Drug Administration. This year, IT launched HMS Research Computing, a consulting service that makes sophisticated data analytics more readily available to faculty. In the area of compliance, the first of a series of IT platforms was created to address regulatory requirements for reporting financial conflicts of interest, approval and monitoring of research involving humans, and management of other compliance factors.

A cross-disciplinary team of Harvard scientists, engineers and clinicians created an implantable melanoma vaccine. The disk-like sponge, developed at the Wyss Institute, is implanted under the skin, and recruits and reprograms immune cells "on site," instructing them to travel through the body, and to home in on and kill cancer cells.



Thelisma Heber (left) directs the Cholera Treatment Center near Mirebalais, Haiti. Partners In Health cofounder Paul Farmer, head of the Department of Global Health and Social Medicine, led a coalition of non-governmental, governmental, corporate, foundation and academic partners in opening a new hospital there.

Wherever the art
of medicine is loved,
there is also a love
of humanity.

– Hippocrates

Harvard Medical School leaders have traditionally maintained a vision for excellence in medicine that has made the School an incubator of bold ideas. Today, HMS continues to recruit innovative faculty members who drive discovery and inspire new generations of physician-scientists to improve health care around the world.

More than 12,000 faculty members work collaboratively on the HMS campus and at School-affiliated teaching hospitals and research institutes. Overseeing this prolific faculty community is Nancy Tarbell, the C.C. Wang Professor of Radiation Oncology and dean for academic and clinical affairs. Tarbell, like many among the multitalented faculty, pivots from an administrative role to one that provides lifesaving therapies for cancer patients. The deep reservoir of faculty talent at HMS has earned the School respect globally and opened doors of opportunity for the School's community as it strives to serve humanity, at home and around the world.

Supporting Faculty Aspirations

With a diverse and widespread faculty of physician-scientists, it is essential that HMS maintain an effective system of support and development. To help faculty members reach their full potential, HMS has streamlined its promotion process, administered by Dean for Faculty Affairs and Assistant Professor of Population Medicine Maureen Connelly. Now, 84 percent of promotions to the rank of professor are completed in less than one year, compared to 29 percent previously.

Many faculty appointments are initiated by our teaching affiliates and the School has strengthened efforts to provide clear guidelines to clinical department chairs who recommend faculty for appointments or promotions. Those recommendations are vetted by HMS review panels. This year, HMS held more than 70 faculty workshops at affiliate hospitals to delineate the rigorous steps necessary for candidates to advance in professorial ranking. The Office for Faculty Affairs is also completing a new handbook outlining criteria for advancement. In this academic year, 73 faculty members were promoted to professor, 146 to associate professor and 333 to assistant professor.

The recommendations of the Task Force on Faculty Development and Diversity continue to create new pathways for HMS faculty members to advance their careers. Women and minorities underrepresented in medicine now make up more than 16 percent of faculty at the rank of professor. In 2013, task force achievements included increases in the number of faculty orientations and online tracking of faculty promotions. Under the leadership of Joan Reede, dean for diversity and community partnership and associate professor of medicine, HMS has continued to collaborate

with its hospital partners in enhancing faculty mentorship skills and supporting a pipeline for the medical sciences through local and national programs for students from middle school through postdoctoral training. To support HMS diversity goals, a search task force was established, charged with considering best practices for recruiting the outstanding faculty who will train the next generation of clinicians, educators and scientists.

Diversity and Community Partnership

The Office for Diversity Inclusion and Community Partnership's pacesetter approach to the advancement of women and underrepresented minorities in academic medicine involves a number of outreach programs targeted at youngsters, teens and college students, providing opportunities in medicine and research.

Project Success. Each year, Project Success gives 20 students from Boston and Cambridge high schools the chance to work in paid summer research positions for eight weeks, mentored by HMS faculty. They also attend seminars, visit hospitals and biotechnology firms, and hone their writing and computer skills. This year, using funds received from the Boston Red Sox, the program will support 10 students over the next three summers. Among the program's many success stories is Clifton Masdea, who completed two Project Success internships. In the first, he studied the relationship between air quality and asthma in Boston schoolchildren;

Richard Frank, the Margaret T. Morris Professor of Health Care Policy, was nominated to the post of assistant secretary for planning and evaluation, U.S. Department of Health and Human Services. Frank develops policies for the elderly, the economically disadvantaged and those with disabilities.

DIMENSIONS OF DISCOVERY



Nation



in the second, he used technology to gauge the point of failure for dental implants. Now a student at Brandeis University, Masdea's interests center on astronomy and astrophysics.

New England Science Symposium. Each spring, hundreds of students from around the world descend on the HMS campus to proudly showcase their research. Launched in 2002, the New England Science Symposium this year attracted 580 participants from 200 schools and institutions in 29 U.S. states, Brazil, Kenya, Mexico, Puerto Rico and Scotland. The students are at various levels of their education and represent a wide range of ethnic groups. More than half are African American or Hispanic/Latino. Judges for their oral and poster presentations include faculty and scientists from HMS and its affiliates, Harvard University, many regional universities and area biotechnology firms.

Four Directions Summer Research Program. Three HMS alumni launched this program as medical students in 1994 and returned to campus to speak at its 20th anniversary celebration. Directed by Thomas Sequist, associate professor of medicine and health care policy and a member of the Taos Pueblo tribe in New Mexico, the program's goal is to increase the number of Native American and Alaska Natives in medicine, public health and biomedical science. These populations experience some of the greatest health disparities in the nation, in part because of the lack of physician-leaders in their communities. Cosponsored by HMS and Brigham and Women's Hospital, the program consists of an eight-week research project overseen by an HMS faculty mentor. Of more than 160 participants to date, 100 percent have graduated or are completing undergraduate degrees. Two-thirds have gone on to either medical school or graduate school.



Thanh-Nga Tran (front right), clinical instructor in dermatology at Mass General, was awarded a Dean's Community Service Award for cofounding Vietnam VAC, an organization that ensures that children in Vietnam with vascular anomalies receive high-quality specialty care.



Center for Primary Care

Under the direction of Russell Phillips, the William Applebaum Professor of Medicine, and co-director Andrew Ellner, instructor in medicine, the Center for Primary Care is addressing a critical health care need by creating models for innovation and improvement in the delivery of primary care.

Academic Innovations Collaborative. In this initiative, medical students and residents are working with local practitioners to transform the delivery of primary care in a variety of disciplines, including internal medicine, pediatrics, medicine-pediatrics and family medicine. Nineteen affiliated practices accepted the challenge to create new primary care models by incorporating four strategies into their practices: team-based care, population management and prevention, management of high-risk patients with multiple illnesses, and patient empowerment and behavior change. Many of the 260,000 patients receiving care are from Boston's underserved communities.

Behavioral Health Integration Program. More than 70 percent of primary care visits stem from psychosocial issues such as anxiety and depression, and primary care clinicians are often in the best position to detect and treat these disorders. This year, six of the center's collaborative sites were selected to integrate behavioral services into patient care; next year the program will expand. Telemedicine is being used to improve patients' access to mental health care, offering access to real-time consultations between mental health specialists, primary care practices and patients.



DIMENSIONS OF DISCOVERY



Global

Leadership Academy. To help collaborative sites manage complex change processes, including the transition to team-based care, the center's Leadership Academy provides transformation team members with a wide range of leadership, management and project implementation skills. The Leadership Academy also serves as a forum to share challenges, best practices and solutions. Faculty shape the curriculum in response to each group's needs.

Physicians as Leaders. As health care delivery rapidly evolves, physicians increasingly need to function effectively within complex organizations. The center, in partnership with the MD-MBA program, created a month-long HMS elective that exposes students to concepts and skills key to their development as managers and leaders. Interrelated themes of leadership, quality and safety improvement, innovation and operations, and systems redesign are illustrated in different contexts, including primary care, clinical specialty practice, product development and global health.

Agents of Change. In 2013, the center awarded challenge grants to four interdisciplinary teams made up of students from HMS, Harvard Business School, HSPH and MIT, with a goal of promoting health care delivery innovation in Boston's community health centers. Among projects selected was an interactive smartphone app that helps patients better manage nutrition by tracking their locations with GPS and suggesting healthy food choices when they enter restaurants. Another team is developing an educational game that can help children with asthma better adhere to their treatment plans.

Drummers celebrate the opening of the Butaro Ambulatory Cancer Care Center on the campus of Butaro Hospital, which is managed by Partners In Health and the government of Rwanda. Oncologists from Brigham and Women's, Dana-Farber and HMS mentor and train staff members there to administer chemotherapy and care for patients, providing a sustainable system of education for the next generation of health care leaders in Rwanda.

Innovations Initiative. This program catalyzes ideas that empower patients, transform the delivery of care and improve community health. The Innovations Initiative supports interdisciplinary teams in early idea generation and exploration, providing resources to develop and test prototypes and, through strategic partnerships, help implement the most promising ideas. The focus is on new care-delivery models, health care technology and systems redesign.

Service Abroad

Initiatives in the Department of Global Health and Social Medicine continue to elevate health care delivery systems around the world, with special emphasis on populations in resource-poor regions.

Improving Health Care in Rwanda. As part of a U.S. academic consortium, this year HMS again partnered with the Rwandan Human Resources for Health program. In a joint HMS and Brigham and Women's program, 16 HMS faculty will travel to Rwanda to train its medical professionals, and together work to develop a world-class, sustainable national health care system. Using case-based studies, solutions are being collaboratively developed to take corrective action to reduce malaria. Another effort focuses on implementing a perioperative antibiotic protocol to reduce the postsurgical risk of infection.

Innovative Tuberculosis Treatment. This year a randomized controlled clinical trial that aims to improve tuberculosis (TB) treatment was launched in collaboration with Partners In Health, its Peruvian sister organization Socios En Salud, Peru's Ministry of Health, HMS and Brigham and Women's. The study expands a research platform built during a collaboration of nearly 20 years that to date has exclusively supported observational or retrospective research. This phase 2 trial, led by Carole Mitnick, associate professor of global health and social medicine, is examining whether higher daily doses of a standard anti-TB drug, rifampin, can safely shorten the duration of TB therapy. An open question since the introduction of rifampin in the 1960s, this hypothesis has never been systematically tested because of perceived cost constraints. The findings of this trial are critical to the nearly 9 million people in the world who develop TB each year, of whom more than 1 million die.

Pipeline of Global Health Researchers. Investigating cardiovascular disease in patients with HIV in Uganda, studying surgical outcomes in Rwanda, and analyzing causes of diarrhea in Haiti—these are some of the projects undertaken by HMS fellows. HMS is among several institutions working with the Doris Duke Charitable Foundation to administer its International Clinical Research Fellowship program. The majority of fellows pursue careers in global health and apply their work to vulnerable populations around the world.



Honors and Awards

NATIONAL ACADEMY OF SCIENCES

Stuart Orkin, the David G. Nathan Professor of Pediatrics, Howard Hughes Medical Institute investigator, and chair of the Department of Pediatric Oncology at Dana-Farber Cancer Institute, received the Jessie Stevenson Kovalenko Medal from the National Academy of Sciences. Orkin was honored for his pioneering achievements in defining the molecular basis of blood disorders and the mechanisms governing the development of blood stem cells and individual blood lineages. His work has significantly advanced the understanding of human hematologic diseases and has revealed new strategies to prevent and manage these disorders.

HMS faculty members elected to the NAS in recognition of their distinguished research achievements this year include **Mitzi Kuroda**, professor of genetics, whose research focuses on chromatin organization, noncoding RNAs and epigenetic gene regulation; **Norbert Perrimon**, the James Stillman Professor of Developmental Biology, who is elucidating mechanisms by which cells and tissues communicate to form specific structures during development and to maintain homeostasis; **Gerhard Wagner**, the Elkan Rogers Blout Professor of Biological Chemistry and Molecular Pharmacology, who studies structures of proteins and protein complexes, inhibitors of protein-protein interactions, biomarker identification, metabolite levels for characterizing and monitoring human disease and ways of using nuclear magnetic resonance and other biophysical methods; and **Fred Winston**, the John Emory Andrus Professor of Genetics, whose research in yeast is illuminating eukaryotic gene expression and chromatin structure.

HOWARD HUGHES MEDICAL INSTITUTE

Four HMS faculty members were among 27 new HHMI investigators honored with appointments to the institute in 2013.

High school students from the Community Academy of Science and Health in Dorchester, Mass., work in teams to problem solve during a simulated medical emergency as part of the HMS MEDscience curriculum. The program inspires critical thinking and science literacy through an immersive premedical experience.

Vamsi Mootha, professor of systems biology at Massachusetts General Hospital, studies mitochondria, ancient cellular organelles that are the cell's power generators. His lab discovered a key ion channel that mediates communication between organelle and the cells they inhabit. It has also identified more than 12 Mendelian disease genes and has linked mitochondrial dysfunction to Type 2 diabetes and cancer.

David Reich, professor of genetics, is a world expert in showing how the mingling of genes is a profound part of human evolutionary history. His team jointly led the analysis of the genome of Neanderthals, demonstrating that it contributes 2 percent of the DNA in the genomes of present-day non-Africans. His team also uncovered seven DNA alterations that may explain why prostate cancer is about twice as common in African American men as it is in men of European ancestry.

Johannes Walter, professor of biological chemistry and molecular pharmacology, studies how our genetic information, composed of DNA, is copied before cell division, and how damaged DNA is repaired so as to prevent errors in the genetic blueprint. He has also shown how cells avoid making more than one copy of their DNA. His lab is investigating how DNA repair is promoted by the proteins produced by *BRCA1* and *BRCA2*, genes which, when mutated, greatly increase an individual's risk of developing breast cancer.

Rachel Wilson, professor of neurobiology, focuses on how the brain translates sensory information into impulses it can interpret and act on. Using fruit flies as a model organism, her lab devised a delicate technique for recording the electrical activity of individual neurons in a fruit fly's brain. She is now probing the function of the fly's antennal lobe, an olfactory relay station analogous to the olfactory bulb in mammal brains, and is investigating how information is processed in hearing.

GAIRDNER AWARD

Stephen Elledge, the Gregor Mendel Professor of Genetics and Medicine and an HHMI investigator, was one of five recipients of the 2013 Canada Gairdner International Award, which recognizes the world's most creative and accomplished biomedical scientists. Elledge's work led to the identification and characterization of a signal transduction pathway known as the DNA damage response. When DNA is impaired, this pathway sends a signal to the cell to begin repairing itself, which keeps the genome stable and suppresses tumor development. The discovery is leading to a better understanding of how cancer occurs and has inspired drug therapies now in clinical trials.

INSTITUTE OF MEDICINE

In recognition of exceptional scientific achievement and commitment to service, five HMS faculty members were among more than 70 new members elected in 2013 to the Institute of Medicine, the health arm of the National Academy of Sciences. The five HMS faculty were:

Katrina Alison Armstrong, the Jackson Professor of Clinical Medicine and physician-in-chief, Mass General

Judy Garber, professor of medicine at Dana-Farber and director, Dana-Farber Center for Cancer Genetics and Prevention

Ashish Jha, associate professor of medicine at Brigham and Women's and HSPH professor of health policy and management

Mark Schuster, the William Berenberg Professor of Pediatrics and chief of general pediatrics, Boston Children's

Christopher A. Walsh, the Bullard Professor of Pediatrics and Neurology, HHMI investigator and chief, Division of Genetics and Genomics, Boston Children's

NIH DIRECTOR'S AWARDS

Five HMS faculty received 2013 NIH Director's Awards, which support visionary science that has the potential to transform scientific fields and speed the use of research to improve health. **Vadim Gladyshev**, professor of medicine, received a Pioneer Award, which challenges investigators at all career levels to develop innovative ideas with high-impact potential. **Jeffrey Dvorin**, assistant professor of pediatrics, received a New Innovator Award, which supports emerging investigators who have not yet received an NIH Research Project Grant, so that they may undertake exceptionally innovative research. **George Church**, the Robert Winthrop Professor of Genetics, and **Peng Yin**, assistant professor of systems biology, each received a Transformative Research Award, which promotes interdisciplinary approaches and research with the potential to create or overturn fundamental paradigms. Each is a core faculty member at the Wyss

Jessica Meir, assistant professor of anaesthesia at Mass General, studies the physiology of animals living in extreme, low-oxygen environments, such as Antarctica. She is a member of the 2013 NASA astronaut candidate class.

Institute for Biologically Inspired Engineering. **Anupam Bapu Jena**, assistant professor of health care policy and medicine, received the Early Independence Award, which helps exceptional early-career scientists move rapidly into independent research positions.

INSPIRING MENTORS

Two HMS deans were among 22 distinguished professors nationwide honored this past year with the Elizabeth Hurlock Beckman Trust Award, which recognizes educators who have inspired students to make significant contributions to society.

Nancy Oriol, dean for students and HMS associate professor of anaesthesia, was nominated by Dean Jeffrey S. Flier and Cheryl Dorsey, a former student. Under Oriol's mentorship in the early 1990s, Dorsey received a fellowship from the global nonprofit Echoing Green and, with Oriol, launched the Family Van, a community-based mobile health unit aiding Boston's underserved neighborhoods for more than 20 years.

Joan Reede, dean for diversity and community partnership and associate professor of medicine, was nominated by Nawal Nour, associate professor of obstetrics, gynecology and reproductive biology, who was a fellow in the Commonwealth Fund/Harvard University Minority Health Policy program in 1998, under Reede's directorship. The experience inspired Nour to found the African Women's Health Center at Brigham and Women's, which provides culturally competent care to women who have undergone genital cutting.

Ronald Arky, the Daniel D. Federman Professor of Medicine and Medical Education and master of the Peabody Society, was honored by the Massachusetts Medical Society with its 2013 Lifetime Achievement Award, which is given each year to a member of the society who has made a lasting contribution to the practice of medicine over a lifetime and who has made significant contributions to the goals of the society.

HIPPOCRATES PRIZE FOR POETRY IN MEDICINE

Rafael Campo, associate professor of medicine at Beth Israel Deaconess Medical Center, received the Hippocrates Prize, one of the most highly regarded international poetry prizes. Campo won first prize for his poem "Morbidity and Mortality Rounds."

ENDOWED PROFESSORSHIPS

The following newly established professorships at HMS were celebrated this past academic year, recognizing the generosity of their respective benefactors and the accomplishments of their inaugural incumbents.

Rami Burstein, the John Hedley-Whyte Professor of Anaesthesia

Richard Paul Cambria, the Robert R. Linton Professor of Surgery in the Field of Vascular and Endovascular Surgery

Talal A. Chatila, the Denise and David Bunning Professor of Pediatrics in the Field of Allergy and Immunology

E. Antonio Chiocca, the Harvey W. Cushing Professor of Neurosurgery

Richard Gliklich, the Leffefeld Clinical Professor of Otolaryngology

Eric A. Pierce, the Solman and Libe Friedman Associate Professor of Ophthalmology

James Rathmell, the Henry Knowles Beecher Professor of Anesthesia

Paul Richardson, the R.J. Corman Professor of Medicine

Hao Wu, the Asa and Patricia Springer Professor of Structural Biology

For more HMS awards, please visit: hms.harvard.edu/news/all-news?tid=16.

DIMENSIONS OF DISCOVERY



Space



**Exceptional dedication
and a commitment to
leadership embody
the HMS spirit, in
which the drive to
improve human health
knows no bounds.**

HMS LEADERSHIP

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

ACADEMIC DEANS

William W. Chin, MD
Executive Dean for
Research
(May 2010 – July 2013)

Sanjiv Chopra, MB, BS
Faculty Dean for
Continuing Education

**Maureen Connelly,
MD, MPH**
Dean for Faculty Affairs

Jules Dienstag, MD
Dean for Medical
Education

**David E. Golan,
MD, PhD**
Dean for Graduate
Education

Lee Nadler, MD
Dean for Clinical and
Translational Research

Nancy Oriol, MD
Dean for Students

**Joan Reede, MD, MS,
MPH, MBA**
Dean for Diversity and
Community Partnership

Nancy J. Tarbell, MD
Dean for Academic and
Clinical Affairs

**HARVARD SCHOOL
OF DENTAL
MEDICINE**

**R. Bruce Donoff,
DMD, MD**
Dean

**ADMINISTRATIVE
DEANS**

Wesley Benbow
Interim Executive Dean
for Administration and
Chief Financial Officer
(August 2013)

Gretchen Brodnicki
Dean for Faculty and
Research Integrity

Pamela S. Caudill
Chief Research
Operations Officer

Rainer Fuchs
Chief Information Officer

Judith Glaven
Associate Dean for Basic
and Interdisciplinary
Research

Richard G. Mills
Executive Dean for
Administration
(July 2011 – July 2013)

Lisa Muto
Associate Dean for
Institutional Planning
and Policy

Susan Rapple
Dean for Resource
Development

Richard Shea
Associate Dean for
Campus Planning and
Facilities

Julie Stanley
Chief Human
Resources Officer

Gina Vild
Associate Dean for
Communications and
External Relations
and Chief
Communications Officer

PRECLINICAL DEPARTMENT CHAIRS

Stephen Blacklow, MD, PhD
Gustavus Adolphus Pfeiffer Professor of Biological
Chemistry and Molecular Pharmacology
Chair, Biological Chemistry and Molecular Pharmacology

Joan Brugge, PhD
Louise Foote Pfeiffer Professor of Cell Biology
Chair, Cell Biology

Paul Farmer, MD, PhD
Kolokotronis University Professor of Global Health
and Social Medicine
Chair, Global Health and Social Medicine

Michael Greenberg, PhD
Nathan Marsh Pusey Professor of Neurobiology
Chair, Neurobiology

Marc Kirschner, PhD
John Franklin Enders University Professor of
Systems Biology
Chair, Systems Biology

Barbara McNeil, MD, PhD
Ridley Watts Professor of Health Care Policy
Chair, Health Care Policy

John Mekalanos, PhD
Adele Lehman Professor of Microbiology and
Molecular Genetics
Chair, Microbiology and Immunobiology

Douglas Melton, PhD
Xander University Professor of Stem Cell and
Regenerative Biology
Co-chair, Stem Cell and Regenerative Biology

David Scadden, MD
Gerald and Darlene Jordan Professor of Medicine
Co-chair, Stem Cell and Regenerative Biology

Clifford Tabin, PhD
George Jacob and Jacqueline Hazel Leder Professor
of Genetics
Chair, Genetics

FUNDRAISING HIGHLIGHTS

Harvard Medical School depends upon a vast network of generous men and women who believe deeply in its mission to alleviate human suffering caused by disease. We are fortunate that our circle of supporters from the community at large continued to expand during fiscal year 2013 as we welcomed new friends to our family of alumni, volunteers, faculty, staff, foundations and corporations. In fact, more than 4,500 supporters gave more than \$86 million, making a tangible impact on our ability to help people live longer, healthier lives.

In education, these gifts are supporting student scholarships and reducing the debt burden for future graduates, ensuring that the best and brightest medical students continue to choose HMS, regardless of their ability to pay. In the area of discovery, these gifts propel the largest biomedical research engine in the world, supporting research in virtually every domain, from reinventing the science of drug discovery to establishing a better understanding of the nervous system. And finally, in the area of service, these gifts are bolstering our commitment to transform health care systems in the U.S. and abroad, including the shaping of policies that are both comprehensive and financially viable.

Learn more about the impact of philanthropy through the School's Honor Roll of Donors at <http://hms.harvard.edu/honor-roll>.

HMS BY THE NUMBERS

Total faculty **12,251** | Tenured and tenure-track faculty on the HMS campus, in nine preclinical departments **183** | Voting faculty, campus and affiliates **5,364** | Full-time faculty, campus and affiliates **9,349**

Nobel Prizes (Physiology or Medicine; Peace) **9** prizes; **15** recipients | Howard Hughes Medical Institute investigators **36** | Members, Institute of Medicine **129** | Members, National Academy of Sciences **67**

Total MD students **708** | Total PhD students **815** | MD-PhD students **180**: basic sciences **162**, social sciences **18** (total included in MD and PhD counts) | Total DMD students **146** | Total MMSc students **63** | Trainees (residents and postdoctoral fellows) **9,037**

Students entering in 2013: MD (includes 13 MD-PhD) **167** | Applicants **5,779**, Admitted **219** (3.8%) | Matriculated (includes 13 MD-PhD) **167** | Men **76** (46%) | Women **91** (54%) | Underrepresented in medicine (African American, Native American, Hispanic, Mexican American) **31** (19%) | Asian **46** (28%)

Entering PhD, DMD and MMSc students, 2013: PhD **155** | DMD **35** | MMSc **30**

Additional joint-degree programs: MD-MBA; MD-MPH; MD-MPP

Medical school alumni **9,702** (MD and MMSc degrees)

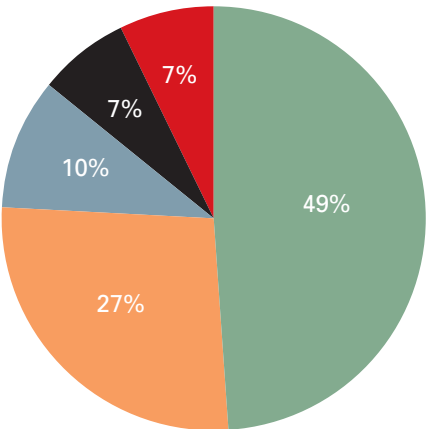
AFFILIATED HOSPITALS AND INSTITUTIONS

Beth Israel Deaconess Medical Center
Boston Children's Hospital
Brigham and Women's Hospital
Cambridge Health Alliance
Dana-Farber Cancer Institute
Forsyth Institute (HSDM affiliate)
Harvard Pilgrim Health Care Institute
Hebrew SeniorLife

Joslin Diabetes Center
Judge Baker Children's Center
Massachusetts Eye and Ear
Massachusetts General Hospital
McLean Hospital
Mount Auburn Hospital
Schepens Eye Research Institute
Spaulding Rehabilitation Hospital
Veterans Affairs Boston Healthcare System

FY13 GIFTS AND PLEDGES BY PURPOSE

- Research 49%
- Professorships & Faculty Support 27%
- Financial Aid 7%
- Unrestricted 7%
- Other 10%



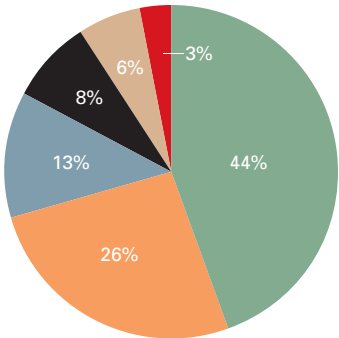
COLLABORATIONS ACROSS HARVARD

Broad Institute of MIT and Harvard
Harvard Catalyst
Harvard Stem Cell Institute
Wyss Institute for Biologically Inspired Engineering

FY 2013 OPERATING REVENUE

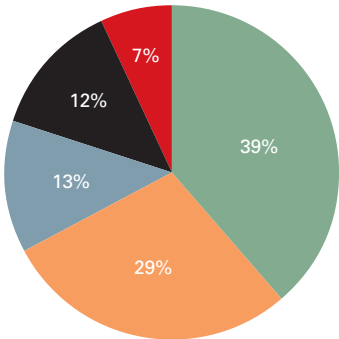
■ Research grants and contracts	\$268,841,564	44%
■ Endowment distribution for operations	\$156,714,272	26%
■ Other revenues*	\$75,468,018	13%
■ Rental income	\$47,868,645	8%
■ Gifts for current use	\$36,424,520	6%
■ Tuition (net)	\$19,712,267	3%
Total	\$605,029,287	

* Includes continuing medical education, publications, service income and royalties



FY 2013 OPERATING EXPENSES

■ Personnel costs	\$252,875,874	39%
■ Supplies and other expenses	\$185,810,539	29%
■ Plant operations and interest	\$82,591,097	13%
■ Research subcontracts and affiliates	\$81,520,899	12%
■ Depreciation	\$46,907,626	7%
Total	\$649,706,034	



FINANCIAL REPORT

Harvard Medical School—along with universities and research centers throughout the country—is operating in an environment that is undergoing dramatic change as a result of increased competition for extramural funding and significantly decreased federal resources. Despite these challenges, the School has continued to advance its mission to alleviate disease and educate the next generation of health care leaders.

HMS ended the 2013 fiscal year (FY13) with a \$44.7 million deficit, compared to a \$28.8 million deficit in 2012. To address a growing operating

deficit and to safeguard its preeminence, the School has engaged its community in launching an initiative, HMS Next, that is focused on finding and implementing operating efficiencies across the School and identifying new revenue opportunities aligned with its academic mission.

In FY13 operating revenues totaled \$605 million, an increase of \$1.3 million, or 0.2 percent. While the School benefited from greater distribution of the endowment, current-use gifts and tuition revenue, it was adversely affected by the cessation of federal stimulus funding for research from the

American Recovery and Reinvestment Act. The School’s ability to sustain revenue growth was further challenged by the impact of recent federal sequestration measures that resulted in overall decreased support for university research and delays in the review of new grant applications.

Total operating expenses in FY13 increased by \$17.1 million, or 2.7 percent, for a total of \$649.7 million, in part because of increased regulatory compliance imperatives and a continued effort to address deferred campus maintenance. Alongside these efforts, the School was able to expand

in focused priority areas through the use of both endowment funds and gifts and through prudent management of its research funding.

Looking ahead, HMS will not waver in its determination to adapt to this changing environment. The Harvard Campaign, to be launched in FY14, is just one response. Beyond that, we are committed to harnessing the intellect and resourcefulness of our entire community in working together to transform and prepare the School to compete in this new, and constantly changing, economic environment.

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