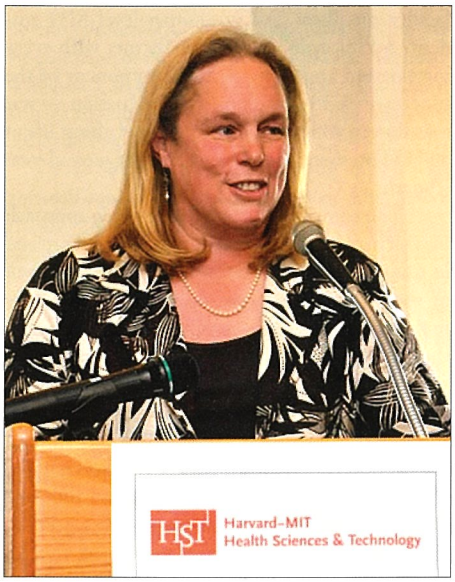
Summer 2008

The Connector

newsletter for graduates, students, faculty and friends of the Harvard-MIT Division of Health Sciences and Technology

Farewell to directorship, but not to HST



Justin Knight

Martha Gray thanks the attendees who gave testimonials during the May 6 reception honoring her years of service as Director.

Almost 12 years ago, I was honored by being asked to serve as Director of HST. I had the good fortune of taking over from others who had nurtured and built HST into something great, and I would like to think that I continued in that tradition. I am proud of what we have built together over the past decade, and I believe that in another 10 years HST will be even more vibrant and stronger than it is now.

As you all know well, HST is a pioneer in interdisciplinary educational and research programs; it draws upon the extraordinary resources of Harvard, MIT, their research centers, and HMS's teaching hospitals to provide students and faculty with a unique range of educational and research opportunities. By crossing institutional boundaries, we educate and cultivate leaders of the life sciences, create knowledge, and generate cost-effective preventive, diagnostic and therapeutic innovations. It is our goal to create free-flowing paths of dialogue and scientific pursuit so that no matter where you are working within this community, HST is there, serving as a conduit for ideas.

In the months and years to come, I am looking forward to expanding the spirit of a "university without walls" that lies at the very heart of HST's success. Working with other institutions and, in particular, with the government of India's new Translational Health Science and Technology Institute (THSTI), I plan to take the ideas and model of HST outside of this local incubator to create a "family" of HST organizations. It is a tribute to what we have done to see others, across the nation and around the world, work so vigorously to imitate some or all of HST.

It must be said that the mission and goals of HST depend on our core fundamental value; to have a big impact, one needs to work as a part of a team with people in different professions and disciplines. One of the most satisfying things about working in HST these past years has been working on a team with all of you. The changes that have been so kindly attributed to me during the celebration on May 6, and also in what has been written, should instead be attributed to you; all these changes came from a large group of people working together to build the Division. Good ideas came

(continues on page 13)

HST Forum focuses on disease and treatments

The 21st HST Forum, held at HMS' New Research Building, featured 55 research posters by students, followed by a plenary session, keynote speaker, and a reception. The total attendance of about 200 included members of the HST Advisory Council, which had met that morning, as well as 10 students newly admitted to HST.

The plenary session was opened by Martha Gray, PhD '86, the Edward Hood Taplin Professor of Medical and Electrical Engineering at MIT, who looked back to the 11 previous poster sessions she had introduced during her tenure as Director of HST as the high points of student creativity and meetings of the HST community. She then introduced Amy Farber, PhD, the Founder and Executive Director of the LAM (Lymphangioleiomyomatosis) Treatment Alliance, dedicated to fostering and funding research to find a treatment for this rare lung and multi-system disease affecting 250,000 women worldwide. Farber told the moving story of her own illness. The LAM Treatment Alliance's Board, chaired by Professor Robert Langer, has designated two two-year Judah Folkman Fellowships for HST Students.

Gray next introduced the keynote speaker, Dennis W. Choi, MD '78, PhD, Executive Director of the Neuroscience, Human Nature and Society Initiative of the Comprehensive Neuroscience Center at Emory University in Atlanta. Starting with his earliest childhood experiments in the basement — as told in his HST admissions essay — Gray reviewed his stellar career, which included professorships at Stanford, Washington, Boston and Oxford Universities, as well as the Executive Vice Presidency for neuroscience at Merck Research Laboratories. She also recognized his service on the HST Visiting Committee.

David M. Barron

HST alumnus Dennis W. Choi speaking on therapy of brain diseases at the 21st HST Forum.

Under the title "Getting to Treatments for Brain Diseases: New Partnerships," Choi proceeded with what he called a combination of scientific presentation and personal travelogue. He led the audience through several historical stages of treatment of diseases of the brain: the ancient medicinal (herbal) stage, the stage of apothecaries, the emergence of the pharmaceutical industry (19th century), the age of proven value (1970s) and, hopefully, the age of design marked by the purposeful creation of drugs.

After reviewing the laborious, very costly, financially risky and often failed paths of development of effective drugs, he proposed and explored a change of the current *modus operandi* to a model of partnership between the NIH, nonprofit organizations, academia and industry.

A brief period of discussion, moderated by HST Director David E. Cohen, was followed by the presentation of the newly established Martha Gray Prizes for Excellence in Research, in honor of her 12 years of leadership and contribution to HST (see page 3 for winners).

IN MEMORIAM

Taplin was friend as well as benefactor

John Taplin, a dedicated supporter and long-time friend of HST, died on April 11. He was 94. John's vision has been that advances in human health require both reduced barriers to translation from the academy to industry, and collaboration between engineers and physicians. He really enjoyed seeing these ideas realized through students and faculty in HST. Indeed, so much of what HST has become today has been enabled by generous gifts of time and financial resources from John and his wife, Virginia.

An MIT alumnus, John graduated with a degree in electrical engineering in 1935. He went on to become a prolific inventor and entrepreneur. He developed many products, including the Fenwal plastic blood bag (a worldwide standard for handling blood) and rolling diaphragm seals for aircraft and automobile engines.

John's first interactions with HST date back to the early 1970s. His gifts through the first decade of HST led to the creation of the Edward Hood Taplin Professorship, named in honor of his brother, who passed away at a young age because adequate medical assistance was not available. In a fitting recognition to John's vision and contributions, MIT recently designated that the holder of the Taplin chair be the director of HST. Over the last decade, John remained actively engaged in the development of HST. In 1996, he and Virginia established the Taplin Awards program through a $2 million gift. These awards supported virtually all of our new faculty hires over the last decade, as well as new program developments such as BioMatrix.

—Martha Gray

HST Admissions Update

MEMP and SHBT Programs

HST concluded a lively PhD admissions cycle at the end of April that has resulted in a stellar incoming class of MEMP and SHBT students.

Five new PhD candidates will be entering the Speech and Hearing Bioscience and Technology program, a number of whom will begin in June 2008. The Medical Engineering/Medical Physics program will welcome 18 new students (a 19th candidate will defer until 2010). While the overall number of applicants was down somewhat this year, perhaps reflecting a natural leveling of the applicant pool after a few years of sharp growth, neither program had any difficulty attracting and interviewing strong candidates.

The MEMP program, in fact, interviewed a greater number of candidates this year than in any of the past several years, due to an expanded number of telephone interviews conducted with applicants in Asia. The recent change in MEMP admissions — requiring MIT applicants to MEMP to apply directly to HST (while still admitting Harvard applicants jointly) — and putting data and applications online for committee members, meant that the entire process was streamlined.

One of the great successes of PhD admissions this year is in the number of women matriculating into the programs. Forty percent of the SHBT class and 44 percent of MEMP matriculants are women, a reflection, in part, of strenuous recruitment of admitted female candidates.

—Catherine Modica

MD Program

The work of the HST MD Admissions Committee began last September and continues as of press time. Once again, there was an extremely deep and talented pool of applicants for the 30 positions in the class. Matthew Frosch, MD, PhD, served as Chair of the Committee, with the three subcommittees lead by Drs. Tom Byrne, Stan Finkelstein and Stuart Forman.

As has been the case for several years, applicants were interviewed by a panel of two faculty members and one upper-level MD student. Additionally, Frosch briefly met with every interviewed applicant. A new component of the process — more recruiting than evaluation — was a session in which applicants learned about life as an HST student from current first- or second-year students.

The committee took a step-by-step approach in which all interviewed candidates were discussed in one of the three subcommittees. Roughly half of these applicants were then advanced to the main committee. This committee, composed of the subcommittee chairs, the chair of the admissions committee, the HMS liaison, the MD-PhD liaison, several other senior faculty and two senior students, assessed these applicants based on their application and reports from interviewers and the subcommittee. Discussion and scoring followed the model of NIH study sections, with a primary and two secondary reviewers presenting the applicant, discussing strengths and weaknesses and recommending rough scoring ranges. Following group discussion, applicants were scored by all members of the group, and these results were used to determine a rank order for admissions. This list was then presented to Robert Mayer, MD, HMS Associate Dean for Admissions, who accepted it without changes.

After several years of growth, the number of applications has stabilized near 670. From this pool, 156 applicants were interviewed, with 81 moving forward to the main committee for discussion and ranking. Offers were made to 37 applicants, using historical data as a guide.

—Matthew P. Frosch, MD, PhD

The Connector

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The Connector is a quarterly publication of the Harvard-MIT Division of Health Sciences and Technology. The staff and board of The Connector would like to thank the HST alumni, faculty, staff, and students who contributed to this issue. Please send reports of your recent activities and personal news to the above address or email. Previous issues of The Connector can be found at http://hst.mit.edu.

Seven Receive Inaugural Martha Gray Research Awards

Seven HST students were the first recipients of the new Martha Gray Prizes for Excellence in Research. The criteria included the significance of research, the quality of design and execution, the engagement and clarity of presentation and limitations. The awards included certificates and cash prizes. The winners were announced, after the Keynote Presentation at the 2008 HST Forum, by the co-chairs of the committee of judges: Anthony Williams, Chair of the HST Advisory Board, and Robert Rubin, MD, the Gordon and Marjorie Osborne Professor of HST.

Eric Wang: "Global Patterns and Widespread Tissue-specific Regulation of Alternative nRNA Isoforms" (Bioinformatics and Integrative Genomics); *Supervisor:* Christopher Burge, PhD

Sarah Henrickson: "T Cell Sensing of Antigen Dose Governs Interactive Behavior with Dendritic Cells – an Integrative Mechanism that Sets a Threshold for T Cell Activation" (Imaging and Optics); *Supervisor:* Ulrich von Andrian, PhD

Caroline Niziolek: "The Influence of Perceptual Categories on Auditory Feedback Control" (Imaging and Optics); *Supervisors:* Frank Guenther, PhD, and Joseph Perkell, PhD

Eliseo Papa: "Affinity Profiling of Humoral Immune Responses by Microengraving" (Physiology and Systems Biology); *Supervisors:* Hidde Ploegh, PhD, and J. Christopher Love, PhD

Rameez Qudsi: "A Genetically Engineered Mouse Model of Osteosarcoma that Closely Mimics the Human Disease" (Regenerative Medicine); *Supervisor:* Stuart Orkin, MD

Benjamin Rapoport: "Neural Prosthetics for Paralysis: Algorithms and Low-Power Analog Architectures for Decoding Neural Signals" (Biomedical Devices); *Supervisor:* Rahul Sarpeshkar, PhD

Amy Xu: "Force Dependence of vWF Cleavage in von Willebrand Disease" (Cell and Molecular Biology); *Supervisor:* Timothy Springer, PhD

Khademhosseini Wins Awards for Thesis and Early Career Achievement

Ali Khademhosseini, PhD, Assistant Professor of Health Sciences and Technology and of Medicine at HMS and BWH, has won the 2007 LaMer Award of the American Chemical Society, recognizing the outstanding PhD thesis of the year. He will deliver the LaMer plenary lecture at the ACS Colloids and Surface Science Symposium at North Carolina State University. Khademhosseini is also the recipient of the 2008 IEEE-EMBS Early Career Achievement Award for significant contributions to the field of biomedical engineering as evidenced by innovative research design, product development, patents, and/or publications made by an individual who is within 10 years of completing his or her highest degree at the time of the nomination.

ERRATA

Peter Farrell's name was misspelled in the photo caption on page 1 of the Spring 2008 issue. We regret the error.

iShoe a Shoo-in

MEMP student **Erez Lieberman** (along with partner Theresa Tribble of Harvard Business School) was named Grand Champion in the Lunar Ventures 2008 Competition for the business venture, iShoe. The competition, sponsored by the Center for Space Resources at the Colorado School of Mines, encourages students in business, engineering and science to collaborate on business ventures related to space. iShoe won for its patent-pending insole that detects poor balance, rehabilitates the wearer's ability to balance, and notifies caregivers of a fall. The award comprises $50,000 in cash.

Excellence in Mentoring

Two HST faculty members received HMS's Clifford Barger Excellence in Mentoring Awards:

Elazer R. Edelman, MD '83, PhD '84, the Thomas D. and Virginia W. Cabot Professor of Health Sciences and Technology at MIT, Professor of Medicine at HMS and BWH, and Director of the Harvard-MIT Biomedical Engineering Center at HST

Kenneth D. Mandl, MD, Associate Professor of Pediatrics at HMS and CHB, and member of the HST affiliated faculty

Czeisler Receives Lifetime Award

Charles A. Czeisler, MD, PhD, the Baldino Professor of Sleep Medicine at HMS and BWH, and member of the HST affiliated faculty, is the recipient of the National Sleep Foundation's lifetime achievement award for his contributions to the sleep and health fields.

Amadio Places in Medical Poetry Contest

MD student **Jordan Amadio** won second place in the annual William Carlos Williams national poetry competition for medical students. The awards ceremony was held at the Northeastern Ohio Universities Colleges of Medicine and Pharmacy. The poem will be published in the *Journal of Medical Humanities*.

Braille Pencil Wins Innovation Prize

SHBT student **Ted Moallem** led the first-place "Braille Pencil" team in this year's MIT IDEAS Competition. Braille Pencil was awarded the $7,500 Health Innovation Award sponsored by Aleksander and Anna Anita Leyfell, which supports teams that devise creative solutions to support elderly people or those living with disabilities. Moallem and fellow team members Svetlana Sussman, Orly Lahav, Zahra Kanji, Nadia Elkordy and Harris Sussman invented a unique Braille-writing device for the blind, which enables Braille users to take notes and write for extensive periods of time. The Braille Pencil is designed to be cheap, pocket-sized and easy-to-use.

Business Plan Reaps Two Awards

Roozbeh Ghaffari, PhD '08, is a member of the business plan team Diagnostics For All, which has won two top awards for innovation. The team won first prize in the social enterprise business plan competition at the Harvard Business School. In May Ghaffari's team won the Grand Prize in the MIT 100K Entrepreneurship Competition. Diagnostics For All is a nonprofit company that will provide health care agencies and commercial organizations with a new generation of point-of-care tools to address the diagnostic and clinical management needs of the global medical community. Ghaffari is a Postdoctoral Research Associate in the Freeman Laboratory at the MIT Research Laboratory of Electronics.

Promotion

Isaac S. Kohane, MD, PhD, has been appointed Professor of Pediatrics and of Health Sciences and Technology. He is also the Director of the Countway Library of Medicine and the Co-Director of the HMS Center for Biomedical Informatics.

Leonid Mirny, PhD, has been promoted to Associate Professor with tenure in HST at MIT. He will also continue to hold a joint appointment in the physics department at MIT.

Jain is AAAS Fellow

Rakesh K. Jain, PhD, the A. Werk Cook Professor of Radiation Oncology at HMS and MGH, and member of the HST affiliated faculty, has been elected to the Class of 2008 Fellows of the American Academy of Arts and Sciences.

HST Welcomes New Communications Manager

Laurie Pass joined HST as its new Communications Manager on May 6. Previously, she was Program Manager at the MIT Workplace Center at the Sloan School, where her work has focused on directing the Center's communications strategy and publicizing their research results. She has a deep background in project management, communications and marketing, including stints as Director of Circulation Marketing at the *New England Journal of Medicine* and as Business Director at the Sloan Management Review. She holds a BA in English from Penn State.

Fran Betlyon

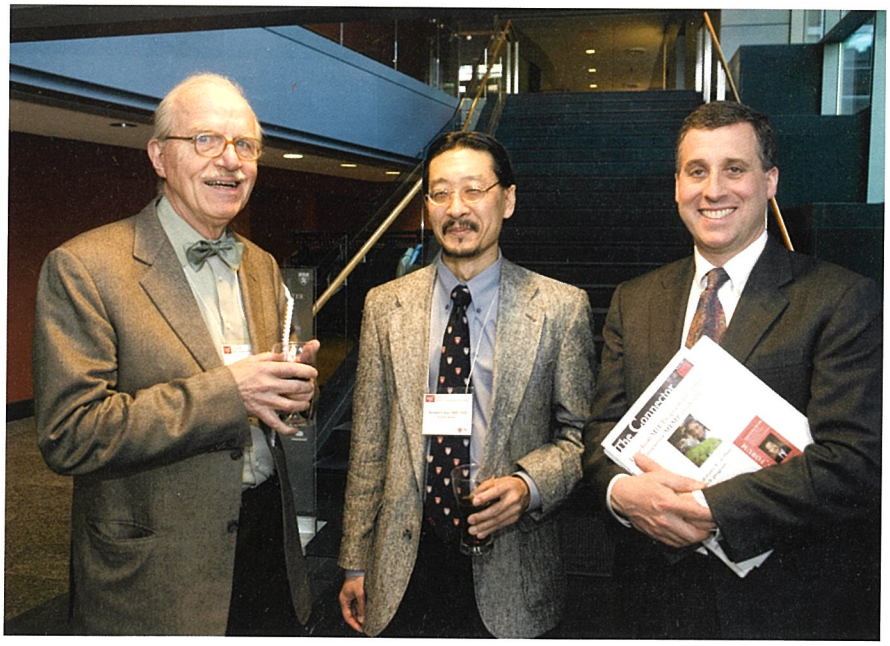
Laurie Pass

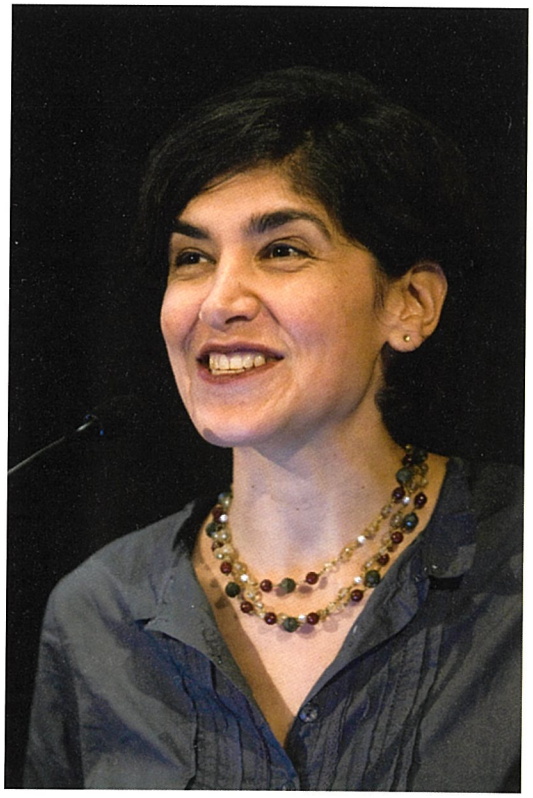
photos by David M. Barron

(right) **SHBT student Daryush Mehta explains "Ultra High-Speed Color Videoendoscopy of Human Voice Production" to David Boas and Bruce Rosen.**

(below) **Daniel C. Shannon, Dennis W. Choi and David E. Cohen.**

(lower right) **Amy Farber, Founder and Executive Director of the LAM (Lymph-angioleiomyomatosis) Treatment Alliance, tells the story of her own illness.**





(above) Five of the seven awardees of the new Martha Gray Prizes for Excellence in Research: Amy Xu (MD-PhD); Rameez Qudsi (MD '10); Caroline Niziolek, SHBT; Eric Wang, MEMP/BIG; and Benjamin Rapoport (MD-PhD).

(left) Ann Cai (MD '10) elucidates to Jennifer Melcher, PhD, her poster on "Effective Graft-versus-Leukemia Responses are Associated with Nucleic Acid-Immunoglobulin Complexes that Stimulate TLR8 and TLR9."

The art of writing: new HST requirement trains MD students to express themselves clearly

In his latest book, *Our Underachieving Colleges* (2007), former Harvard president Derek Bok argues that college students, including those at very good colleges, no longer receive adequate training in reading and writing. Industry leaders have been complaining for years that the writing skills of many applicants — even to higher-echelon jobs — are not satisfactory.

In highly competitive medical science programs such as HST, the situation is exacerbated not only by the fact that for many students English is a second — if not third — language, but also by the reality that in order to become a successful applicant to HST, students focus very early and intensely on their science education. Such an early concentration on science usually comes at the expense of a student's humanities' education, which traditionally includes training in critical thinking (philosophy), reading (literature) and writing in various genres. In addition, technological advances in popular entertainment reduce the amount of time children and adults spend reading across all of Western culture.

Concurrently, HST course directors noted that the linguistic quality of written assignments has declined during the past decade. The papers are not as well written as one would expect, given the extraordinary brainpower that is the hallmark of HST students. Opening paragraphs, in particular, introducing the subject and setting the scene, are often poorly thought out and awkwardly phrased. Bodies of papers are usually cast in a fail-safe science-writing mold, featuring the exorbitant use of noun clusters and passive verbs, and peppered liberally with the noxious "furthermore," the loathsome "additionally," and the irritating "within."

In order to give students the opportunity to improve their writing skills and to raise their awareness, not only of their own stylistic infelicities but also of how just a few changes can transform a vexing word snake into a clear sentence, HST has begun to integrate a three-step communication component into its MD curriculum.

Its major element is a writing requirement to be fulfilled at the end of the second year. During the first two years of classroom work in HST, MD students submit seven written assignments, and one oral assignment in the form of a PowerPoint presentation, to a writing specialist. He or she reviews, edits and comments on the stylistic quality of the papers. Several courses devised new written assignments, and those course directors have adjusted final submission deadlines so that students have a few days to review the comments they received and revise their papers. The only way to get better is by understanding what was amiss and by rewriting one's sentences to aim for greater clarity.

Bodies of papers are usually cast in a fail-safe science-writing mode, featuring an exorbitant use of noun clusters and passive verbs.

The second element of the MD communication curriculum is currently built into the Patient-Doctor III course, in which all third year MD students participate. It consists of monitoring both the evolving oral and written skills as they are being tested in the stress and conflict-rich environment of the hospital wards. Students are trained in oral conflict resolution. In two written assignments, they make the transition from hard-core science writing to a more humanistic form of writing. We are asking them, for example, to describe a formative experience in the wards. To abandon the life raft of the pre-established mode of science-writing for the chaotic seas of a social form of English, without drowning in the waves of colloquialism, is often not easy for HST students.

The third and most unusual component of the communication curriculum is still under development. We envision a series of three faculty-student seminars to take place during the fourth year. For 90 minutes, students and faculty would study with a noted philosopher, religious or legal scholar. The subject of each session would be a central concept or cluster of concepts in Western or Eastern religion, law or political philosophy (such as justice, free will, duty, virtue, equality, and so on) and its subversion — or perhaps strengthening — under the impact of advanced medical technologies and their social and political consequences. The point would be not only to broaden the students' minds to consider the larger cultural and civic contexts in which they are pursuing their scientific education, but also to strengthen the HST community by having the final year culminate in cross-generational dialogue about the fundamental values that shape the daily work of physician-scientists.

We are convinced that by enriching the MD curriculum with a communication component that is, in sequence, linguistic, social and philosophical in its emphasis, we offer our students the opportunity to graduate from HST as three-dimensional professionals who know how to write and think even outside the scientific box.

—Susanne Klingenstein, PhD

MIT and Portugal collaborate on cutting-edge science

The MIT Portugal Program (MPP) was launched in October 2006 by the Portuguese Ministry of Science, Technology and Higher Education to strengthen the country's knowledge base and international competitiveness through a strategic investment in people, knowledge and ideas. Significant government funding (about $80 million) to MIT and Portuguese institutions supports this unique collaboration for five years. MPP is a high-profile effort to demonstrate that an investment in science, technology and higher education can have a positive, lasting impact on the economy by addressing key societal issues.

The initiative involves seven Portuguese universities and 14 research centers. It has targeted bioengineering systems, engineering design and advanced manufacturing, sustainable energy systems and transportation systems as key areas for economic development and societal impact. Flagship projects that integrate research across several of the focus areas are also planned. Dava Newman, PhD, Professor of Aeronautics and Astronautics and Engineering Systems at MIT, leads the bioengineering systems area and is joined by seven HST colleagues — Sangeeta Bhatia, Stan Finkelstein, Hugh Herr, Ali Khademhosseini, Robert Langer, Steve Massaquoi, and Larry Young — in the MPP education and research efforts. The collaborative research efforts with MIT faculty intersect with the new education programs in Portugal and aim to create lasting connections between academia and industry.

The mission of the Bioengineering Systems focus area of the MPP includes excellence in education, research, impact on university-industry-

(continues on page 13)

List based on information available May 16, 2008; subject to change

HST graduates

Graduate Education in Medical Sciences (certificate)

Michael Solomon Goldberg, BSc, MPhil
Toronto, Ontario, Canada
[also received PhD from MIT]
Screening, synthesis, and applications of 'lipidoids', a novel class of molecules developed for the delivery of RNAi therapeutics
Future Plans: Postdoctoral research, MIT

Sarah E. Johnstone, BA
Indianapolis, IN
[also received PhD from MIT]
Mapping the core regulatory circuitry of embryonic stem cells

Master of Engineering Biomedical Engineering

Vivian Victoria Li
Jackson, MS
[also received SB from MIT]
Design and potential clinical impact of a noninvasive skin perfusion sensor for the independent assessment of endothelial dysfunction

Dewang V. Shavdia
Reisterstown, MD
[also received SB from MIT]
Septic shock: early warning using common clinical variables

Giovanni Talei Franzesi, SB
Milano, Italy
[also received SB from MIT]
A novel polymeric microelectrode array for highly parallel, long-term neuronal culture and stimulation
Future Plans: Candidate for PhD, MIT

Master of Science Biomedical Enterprise Program

Amir Goren, BSc, MBA
Newton, MA
Assessing the economic case for stratified medicine
Future Plans: Program and alliance management, Biogen, Idec (Cambridge, MA)

Amanda Suzanne Jenkins, BS
Boston, MA
[also received MBA from MIT Sloan School of Management]
Characterizing monitoring for the diagnosis and resuscitation of shock patients
Future Plans: Associate in the Life Sciences Business Group, PRTM

Rehan Abbas Khan, BSc, MBA
Aligarh & Mussoorie, India
What future physicians want: a comparative analysis of the perception of medical students and pharmaceutical industry executives regarding future of pharmaceutical sales
Future Plans: Vice President, Oncology and Critical Care, Astra Zeneca Pharma India (Bangalore)

Daniel Spensley Rippy, BA, MBA
Sudbury, MA
Assessing decision inputs in drug development between small, early stage companies and big pharma: is there a difference?
Future Plans: President & CEO of Allegro Diagnostics (Boston)

Inder Raj Singh, BS, BSE, MPP
Pittsburgh, PA
[also received MBA from MIT Sloan School of Management]
Factors influencing the time for FDA review of medical devices
Future Plans: Position in the Malaria Program, Clinton Foundation

Lizhe Sun, MBA, MS
Beijing, China
Value creation through modernizing traditional Chinese medicine
Future Plans: Starting a pharmaceutical development company in China

Master of Science Biomedical Informatics Program

Julia Braverman, BA, PhD
Needham, MA
Factual versus narrative messaging: different modalities and personal involvement: looking for the best strategy of health communication
Future Plans: Research in behavioral medicine

David Alan Harmin, BA, MS, PhD
Cambridge, MA
Genomic studies of motif enrichment and conservation in the regulation of gene expression in the brain
Future Plans: Research staff, Children's Hospital Boston; Instructor at HMS

Ívar Sigurjón Helgason, MD
Kopavogur, Iceland
Predicting prescription patterns

Pankaj Sarin, SB, MD
Boston, MA
Development and evaluation of an electronic feedback system to improve physician compliance with evidence-based practices

Master of Medical Science Clinical Investigator Training Program

Jeremy Slade Abramson, BA, MD
Tenafly, NJ
Novel target identification in diffuse large B-cell lymphoma
Future Plans: Attending physician, MGH Cancer Center Lymphoma Program (Boston); Instructor in Medicine, HMS

Miguel Alonso Alonso, MPhil, MSc, MD
Ferrol, Spain
The role of the right prefrontal cortex in eating behavior and obesity
Future Plans: Instructor in Neurology, BIDMC

Rajendra D. Badgaiyan, MA, MBBS, MD
Somerville, MA
Dopaminergic neruotransmission and human cognition
Future Plans: Assistant Professor of Radiology and Associate Neuroscientist, MGH and HMS

Rupal Satish Bhatt, AB, MD, PhD
Framingham, MA
Mechanisms of resistance to antiangiogenic therapy
Future Plans: Instructor in Medicine, HMS; Staff Physician, Division of Oncology, BIDMC

Allison Leigh Cohen, BA, MD
Ridgefield, CT
A prospective study measuring serological markers for preeclampsia in women with preexisting diabetes at several time points during pregnancy
Future Plans: Instructor in Medicine, HMS; Research Associate and Staff Physician, Joslin Diabetes Center (Boston); Staff Physician, BIDMC

Aaron Martin Cypess, AB, MD, PhD
Brookline, MA
Human brown adipose tissue and its impact on metabolism
Future Plans: Instructor in Medicine, HMS; Research Associate and Staff Physician, Joslin Diabetes Center (Boston); Staff Physician, Division of Endocrinology, BIDMC

Ogo Ifeatu Egbuna, MD
Brooklyn, NY
Hyperparathyroidism: a plausible role for polycystin-1
Future Plans: Instructor in Medicine, HMS; Attending Transplant Nephrologist, BIDMC

Elizabeth Anne Hoge, BA, MD
Takoma Park, MD
MBSR and anxiety: therapeutic and neuroendocrine effects
Future Plans: Clinical Assistant, MGH; Instructor in Medicine at HMS

Si-Hong Huang, BA, MD
Zhang Zhou, China
Functional characteristics of HIV-specific T cell responses in infants and children
Future Plans: Motherhood, followed by a pediatric cardiology fellowship in 2009

Steven Jay Isakoff, BA, MD, PhD
Highland Park, NJ
Evaluation of p63/p73 as a biomarker to predict response to platinum in metastatic triple negative breast cancer
Future Plans: Instructor in Medicine, HMS; Attending Physician, Gillette Center for Breast Cancer, Division of Hematology and Oncology, MGH

Katherine Anne Janeway, BA, MD
New Haven, CT
Biology and treatment of pediatric gastrointestinal stromal tumor
Future Plans: Instructor in Pediatrics, HMS; Attending Physician, Dana Farber Cancer Institute and Children's Hospital Boston

Nira Ruberg Pollock, BA, MD, PhD
Brookline, MA
Development and evaluation of novel diagnostic tests for tuberculosis
Future Plans: Faculty, Infectious Diseases Division/Department of Medicine, BIDMC

HST graduates

Doctor of Medicine

Aaron Dominic Aguirre, BSE
Standish, MI
[see also Doctor of Philosophy, Medical Engineering/Medical Physics; also received SM from MIT]
Advances in optical coherence tomography and microscopy for endoscopic applications and functional neuroimaging
Future Plans: Internship and residency in internal medicine at BWH

Siraj Mahamed Ali, BA
Silver Spring, MD
[also received PhD from Harvard University]
A tale of two mTor complexes
Future Plans: Internship and residency in pathology at BIDMC

Zarine Rohinton Balsara, BA
Philadelphia, PA
[also received PhD from Harvard University]
The interaction of Chlamydia trachomatis *with mammalian host cells*
Future Plans: Internship in preliminary surgery at Duke University Medical Center (Durham, NC); Residency in urology at Duke University Medical Center

Patrick James Codd, BS
Ft. Collins, CO
Over-expression of Fezf2 *modifies the fate and differentiation of neocortical precursors from early to late development*
Future Plans: Internship in preliminary surgery at MGH; Residency in neurosurgery at HMS/MGH Combined Program

Steven Muntean Corsello, BA
Pittsford, NY
Identification of AML1-ETO inhibitors by chemical genomics
Future Plans: Internship and residency in internal medicine at MGH

Paul Brian Dieffenbach, BA
Sterling, VA
From yeast to flies: a search for the mechanisms of Tau-induced neurodegeneration
Future Plans: Internship and residency in internal medicine at Yale-New Haven Hospital

Frank Fang, BS
Albany, NY
Epithelial to mesenchymal transition and human papillomavirus-induced oncogenesis
Future Plans: Internship and residency in plastic surgery at University of Michigan Hospitals (Ann Arbor)

Hiu-fai Fong, SB
Rochester, NY
Prevalence and predictors of abnormal liver enzymes in young women with anorexia nervosa
Future Plans: Internship and residency in pediatrics / primary care at Children's Hospital Boston

Paul Matthew George, BSE, MSE, PhD
Cookeville, TN
Novel polypyrrole derivatives to enhance conductive polymer-tissue interactions
Future Plans: Internship in preliminary medicine at Stanford University; Residency in neurology at Stanford University

John Richard Greenland, BS
Boulder, CO
[also received PhD from HMS]
Vaccine antigen expression and immune responses
Future Plans: Internship and residency in internal medicine at BIDMC

Nathan C. Himes, BS
Mesa, AZ
Magnetic resonance imaging in murine models of cardiovascular disease
Future Plans: Internship in transitional medicine at New England Medical Center (Boston); Residency in radiology at BWH

Nicholas Elias Houstis, MS
West Lafayette, IN
[also received PhD from MIT]
Reactive oxygen species play a causal role in multiple forms of insulin resistance
Future Plans: Internship and residency in internal medicine at BWH

Felipe Ananda Jain, BS
San Rafael, CA
Motor neurons in the subthalamic nucleus encode reward prediction in normal primates and Parkinson patients
Future Plans: Internship and residency in psychiatry at UCLA Seml Institute for Neuroscience

Junne Kamihara, BA
Old Bethpage, NY
[also received PhD from MIT]
Studies at the hemochromatosis (HFE) locus: Gene conversions, haplotypes, and an association analysis
Future Plans: Internship and residency in pediatrics at Children's Hospital Boston

Brittany Louise Lee, BS, MS
Derby, KS
The role of host cell endoplasmic reticulum recruitment in Trypanosoma cruzi *invasion and vacuole maturation*
Future Plans: Internship and residency in internal medicine / primary care at MGH

Yao Liu, BA
Ann Arbor, MI
Expression and statin-dependent regulation of the transcription factor Kruppel-like Factor 2 (KLF2) in mouse vascular endothelium
Future Plans: Internship in preliminary medicine at BWH; Residency in ophthalmology at MEEI

Theodore Cosmo Marentis, BS, MS
Athens, Greece
Alignment and manufacturing techniques for three-dimensional tissue engineering scaffolds
Future Plans: Internship in preliminary medicine at New York Downtown Hospital; Residency in radiology at University of Michigan Hospitals (Ann Arbor)

Mark Leland Miller, BS
Prosser, WA
A novel in vitro *liver assay based on a polarized hepatic monolayer*
Future Plans: Internship and residency in orthopaedic surgery at University of Washington Affiliated Hospitals (Seattle)

Christina Elisabeth Mills, BS
Philadelphia, PA
[also received ScD from Harvard School of Public Health]
Transmission and control of pandemic influenza
Future Plans: Internship and residency in pediatrics at Children's Hospital Boston

Sonali Mukherjee Shah, SB
Yorktown, VA
Rapid analysis of the DNA binding specificities of transcription factors with DNA microarrays
Future Plans: Internship and residency in internal medicine at BIDMC

Robert Shigeo Ohgami, BA, PhD
Redwood City, CA
A proteomic screen identifies a novel player in the transferrin cycle: Flotillin-2
Future Plans: Internship and residency in pathology at Stanford University

Navid Redjal, BS
Los Angeles, CA
Combinatorial therapies for malignant gliomas: Cytotoxic synergy of CXCR4 inhibition with chemotherapy
Future Plans: Internship and residency in orthopaedic surgery at MGH

Mohammed Saeed, BS, SM
Cambridge, MA
[also received PhD from MIT]
Temporal pattern recognition in multiparameter ICU data
Future Plans: Internship and residency in internal medicine at University of Michigan Hospitals (Ann Arbor)

Jonathan Daniel Schoenfeld, BS, MPhil
Pleasantville, NY
Cancer patients treated with an autologous tumor cell vaccine develop antibodies to angiogenic cytokines
Future Plans: Internship in transitional medicine at Memorial Sloan-Kettering Cancer Center (New York); Residency in radiation oncology at BWH

Monica Sircar, SB
Bronx, NY
Investigation of the role of endothelial JAM-C in neutrophil transmigration under shear stress
Future Plans: Internship in preliminary medicine at Stanford University; Residency in radiation oncology at Memorial Sloan-Kettering Cancer Center (New York)

Anna Lea Stevens, SB
Harper, KS
[also received PhD from MIT]
Mechanical injury and inflammatory cytokines affect cartilage matrix integrity and tissue homeostasis: a mass spectrometric analysis of proteins with relevance to arthritis
Future Plans: Internship and residency in orthopaedic surgery at University of Pittsburgh Medical Center

Yee-Ping Sun, BA
Reading, MA
Identification of novel lipid mediators that regulate the resolution of acute inflammation
Future Plans: Internship and residency in internal medicine at BWH

Leo Lee Tsai, BA, MSc
Forest Hills, NY
[also received PhD from Harvard University]
Development of an open-access low-field ^{3}He MRI system to study posture-dependence of human pulmonary function
Future Plans: Internship in surgery at BWH; Residency in radiology at BIDMC

Yifan Yang, BS
San Diego, CA
Investigation into the heterotypic cell fusion between muscle and hematopoietic cells
Future Plans: Internship and residency in general surgery at University of California, Davis Medical Center (Sacramento, CA)

HST graduates

Ellen Yeh, BA
Easton, CT
[also received PhD from Harvard University]
Enzymatic halogenation during natural product biosynthesis
Future Plans: Internship and residency in pathology at Stanford University

Glenn Chung-Wing Yiu, BA
Brooklyn, NY
[also received PhD from Harvard University]
Activin/TGFb signaling suppresses axonal growth ability in sensory neurons
Future Plans: Internship in preliminary medicine at BWH; Residency in ophthalmology at MEEI

Martin Zalesak, BSc, MSc, PhD
Zlin, Czech Republic
Transitive inference in healthy humans and implications for schizophrenia
Future Plans: Life Science Specialist, LEK Consulting (Boston)

Suzana Maria Zorca, BS
Glastonbury, CT
The role of N-linked carbohydrates in von Willebrand factor receptor function
Future Plans: Research Fellow, NIH Clinical Center, Bethesda, MD

Doctor of Philosophy Medical Engineering/ Medical Physics

Aaron Dominic Aguirre, BSE
Standish, MI
[see also Doctor of Medicine; also received SM from MIT]
Advances in optical coherence tomography and microscopy for endoscopic applications and functional neuroimaging
Future Plans: Internship and residency in internal medicine at BWH

José Orlando Aleman, BS
Carolina, PR
Gluconeogenesis as a system: development of in vivo *flux analysis of hepatic glucose production in Type 2 Diabetes*
Future Plans: Candidate for the MD at HMS

Pakwai Patrick Au, BS
Hong Kong, China
Engineered functional blood vessels in vivo
Future Plans: Postdoctoral research, MGH

Ming-Chieh Ding, BS, MSE
Pullman, WA
The electrophysiology of mechanical brain injury in rats
Future Plans: Candidate for the MD at Tufts University School of Medicine (Boston)

Georg Kurt Gerber, BA, MPH
Los Angeles, CA
Computational discovery of gene modules, regulatory networks and expression programs
Future Plans: Candidate for the MD at HMS

Carlos Alberto Gómez Uribe, SB, MEng
Mexico City, Mexico
Modeling systems of chemical reactions in biology: dynamics, stochasticity, spatial effects and model reduction

Michael Scott Christopher Hemond, AB
Lexington, MA
NMR solution structure of the C-terminal domain of the Fas apoptosis inhibitory molecule (FAIM)
Future Plans: Postdoctoral research, HMS

Grace Young Kim, BS
Irvine, CA
Detection and monitoring of cancer with superparamagnetic nanoparticles

Lily Yvonne Kim, SB, MEng
Bettendorf, IA
Microfluidic perfusion culture for controlling the stem cell microenvironment
Future Plans: Life sciences strategy consultant, Decision Resources (Waltham, MA)

Kevin R. King, BS, MS
Western Springs, IL
[also received SM from MIT]
High-throughput microfluidic living cell arrays for spatiotemporal gene expression profiling
Future Plans: Candidate for the MD at HMS

Timothy Kuan-Ta Lu, SB, MEng
Taipei, Taiwan
Combating biofilms and antibiotic resistance using synthetic biology
Future Plans: Candidate for the MD at HMS

Sasha Alanda McGee, BS
Silver Spring, MD
Non-invasive detection of oral cancer using reflectance and fluorescence spectroscopy

David-Huy Nhu Nguyen, SB
Atlanta, GA
Combinatorial lipid-like materials for intracellular delivery of small RNAs that activate innate antiviral immune responses and adjuvant vaccines
Future Plans: Postdoctoral research, MIT and Harvard University

Biju Parekkadan, BS
Manalapan, NJ
Cellular and molecular immunotherapeutics derived from the bone marrow stroma
Future Plans: Postdoctoral research

Erika Brown Wagner, BE, SM
Marietta, GA
Musculoskeletal adaptation to partial weight suspension: studies of lunar and Mars loading
Future Plans: Executive Director of the Mars Gravity Biosatellite Program and the X PRIZE Lab, MIT

Shannon Christine Wieland, BA, BS
Perrsyburg, OH
[also received MD from HMS]
Computational, statistical and graph-theoretical methods for disease mapping and cluster detection

Doctor of Philosophy Radiological Sciences Joint Program

Megan Leticia Hepler Blackwell, SB
Clarksville, TN
Cell-specific contrast agents for magnetic resonance microscopy
Future Plans: Technology specialist for Fish & Richardson

Christopher Scott Melhus, BA
Duluth, MN
[also received SM from MIT]
Advanced brachytherapy dosimetric considerations
Future Plans: Therapeutic Medical Physicist, Department of Radiation Oncology , Tufts Medical Center (Boston)

Peng Yu, BS, MA
Xi'an, China
Statistical shape analysis of neuroanatomical structures based on spherical wavelet transformation

Doctor of Philosophy Speech and Hearing Bioscience and Technology

Roozbeh Ghaffari, SB, MEng
Los Angeles, CA
The functional role of the mammalian tectorial membrane in cochlear mechanics
Future Plans: Postdoctoral research, MIT

Nicolas Malyska, BS
Coral Springs, FL
[also received SM from MIT]
Analysis of nonmodal glottal event patterns with application to automatic speaker recognition
Future Plans: Researcher, MIT Lincoln Laboratory (Lexington, MA)

Emmanuel John Simons, AB
Ludlow, MA
Chemical penetration enhancers for increased tympanic membrane permeability and improved treatment of otitis media

Fabio Albuquerque Thiers, MD
Recife, Brazil
[also received SM from MIT]
The outer spiral network and its innervation by the olivocochlear system
Future Plans: Postdoctoral research, MIT Sloan School of Management

Sherry Y. Zhao, SB, MEng
Muncie, IN
The stop-like modification of the voiced dental fricative /ð/: a case study in the analysis and handling of speech variation
Future Plans: Postdoctoral research, International Computer Science Institute at the University of California Berkeley

Doctor of Science Speech and Hearing Bioscience and Technology

Adrian Kuo Ching Lee, BE
Sydney, Australia
Influence of spatial cues on the identification and the localization of objects in the auditory foreground
Future Plans: Postdoctoral research, Department of Psychiatry, HMS and Harvard-MIT Martinos Center for Biomedical Imaging

Mapping Metazoan DNA Regulatory Motifs

Martha L. Bulyk, PhD, is senior author and **Anthony A. Philippakis** is co-author of "Systematic identification of mammalian regulatory motifs' target genes and functions."

Authors' Abstract: "We developed an algorithm, Lever, that systematically maps metazoan DNA regulatory motifs or motif combinations to sets of genes. Lever assesses whether the motifs are enriched in cis-regulatory modules (CRMs), predicted by our PhylCRM algorithm, in the noncoding sequences surrounding the genes. Lever analysis allows unbiased inference of functional annotations to regulatory motifs and candidate CRMs. We used human myogenic differentiation as a model system to statistically assess greater than 25,000 pairings of gene sets and motifs or motif combinations. We assigned functional annotations to candidate regulatory motifs predicted previously and identified gene sets that are likely to be co-regulated via shared regulatory motifs. Lever allows moving beyond the identification of putative regulatory motifs in mammalian genomes, toward understanding their biological roles. This approach is general and can be applied readily to any cell type, gene expression pattern or organism of interest" (JB Warner et al., *Nat Methods* 2008; 4: 347-53).

Bulyk is Assistant Professor of Health Sciences and Technology, and of Medicine and Pathology at HMS and BWH. Anthony Philippakis is an HST MD-PhD student.

Improved Method for Needle Biopsy of Breast Tissue

MEMP student **Brian D. Goldberg** is first author of "Automated algorithm for differentiation of human breast tissue using low coherence interferometry for fine needle aspiration guidance." The traditional method of fine needle aspiration biopsy (FNAB) of masses of the breast has low sensitivity and specificity; many specimens are non-diagnostic. The HST-affiliated Wellman Center for Photomedicine has developed a portable, low coherence interferometry (LCI) instrument for FNAB, which contains an optical fibre probe inserted into the fine gauge needle. This technique is capable of measuring depth-resolved tissue structure, birefringence, flow and spectra at a micrometer-level resolution. This system is capable of classifying adipose and fibroglandular breast tissue based on the slope and S.D. of the axial depth profile, using an automated algorithm. From 58 patients, 260 breast tissue samples were collected. The overall accuracy of the model was 91.9%, with a sensitivity of 98.1% and a specificity of 82.4%" (*J Biomed Opt* 2008; 13: 014014-29).

Guillermo J. Tearney, MD, PhD, Associate Professor of Pathology at HMS and MGH and HST associated faculty, is senior author; **Brett Bouma, PhD**, Associate Professor of HST and of Dermatology at HMS and MGH, is co-author.

New Regulation of Revascularization

Zoltan P. Arany, MD '98, Instructor in Medicine at HMS and BIDMC, is first author of "HIF-independent regulation of VEGF and angiogenesis by the transcriptional coactivator PGC-1alpha." This investigation explored the possible role of PGC-1alpha (peroxisome-proliferator-activated receptor-gamma coactivator -1alpha), a potent metabolic sensor and regulator, in the regulation of VEGF (vascular endothelial growth factor) and angiogenesis. After an ischemic insult, PGC-1alpha -/- mice exhibited failure to re-establish blood flow, whereas transgenic expression of PGC-1alpha in skeletal muscle was protective. This induction of VEGF did not involve the hypoxia inducible factor (HIF), but co-activation of the oestrogen-related receptor-alpha. The authors conclude that "PGC-1alpha may provide a novel therapeutic target for treating ischemic diseases" (*Nature* 2008; 451: 1008-12).

Novel Approach to Delivering Drugs to the Peritoneum

Daniel S. Kohane, MD, PhD, Assistant Professor of Pediatrics at HMS and MGH, and member of the HST affiliated faculty, is senior author of "Spray-dried lipid-hyaluronan-polymethacrylate microparticles for drug delivery in the peritoneum." Delivery of drugs to the peritoneal cavity may be useful for local chemotherapy or for prevention of peritoneal adhesions. To these ends, gradual release of drugs from the matrix is desirable. Previous approaches were limited by rapid clearance of the drug and/or by creating adhesions. The authors produced particles based on sphyngomyelin, a phospholipid which occurs naturally in the peritoneum, along with hyaluronic acid and a polymethacrylate, which accomplished slow release. When injected into the peritoneum of mice, the particles induced a mild inflammatory response, but did not form adhesions (YA Domnina et al., *J Biomed Mater Res A* 2008; Feb 6 [E pub ahead of print]).

Role of Mitochondrial Dysfunction in Pathogenesis of Disease and in Effects of Drugs

Vamsi K. Mootha, MD '98, Assistant Professor of Systems Biology at HMS and MGH, and Associate Member of the Broad Institute at MIT, is senior author of "Large-scale chemical dissection of mitochondrial function."

Author's Abstract: "Mitochondrial oxidative phosphorylation (OXPHOS) is under the control of both mitochondrial (mtDNA) and nuclear genomes and is central to energy homeostasis. To investigate how its function and regulation are integrated within cells, we systematically combined four cell-based assays of OXPHOS physiology with multiplexed measurements of nuclear and mtDNA gene expression across 2,490 small-molecule perturbations in culture muscle. Mining the resulting compendium revealed, first, that protein synthesis inhibitors can decouple coordination of nuclear and mtDNA transcription; second, that a subset of HMG-CoA reductase inhibitors, combined with propranolol, can cause mitochondrial toxicity, yielding potential clues about the etiology of statin myopathy; and, third, that structurally diverse microtubule inhibitors stimulate OXPHOS transcription while suppressing reactive oxygen species, via a transcriptional mechanism involving PGC-1alpha and ERRalpha, and thus may be useful in treating age-associated degenerative disorders. Our screening compendium can be used as a discovery tool both for understanding mitochondrial biology and toxicity and for identifying novel therapeutics" (BK Wagner et al., *Nat Biotechnol* 2008; 26: 343-51).

Activated Vitamin D May Protect the Heart of Dialysis Patients

Ravi Thadhani, MD, Associate Professor of Medicine at HMS and MGH, and member of the HST affiliated faculty, is co-author of "Activated vitamin D attenuates left ventricular abnormalities induced by dietary sodium in Dahl salt-sensitive animals."

Author's Abstract: "Observations in hemodialysis patients suggest a survival advantage associated with activated vitamin D therapy. Left ventricular (LV) structural and functional abnormalities are strongly linked with hemodialysis mortality. Here, we investigated whether paricalcitol (PC, 19-nor-1, 25(OH)(2)D(2)), an activated vitamin D compound, attenuates the development of LV abnormalities in the Dahl salt-sensitive (DSS) rat and whether humans demonstrate comparable findings. Compared with DSS rats fed a highsalt (HS) diet (6% NaCl for 6 weeks), HS+PC was associated with lower heart and lung weights, reduced LV mass, posterior wall thickness and end diastolic pressures, and increased fractional shortening. Blood pressures did not significantly differ between the HS groups. Plasma brain natriuretic peptide levels, and cardiac mRNA expression of brain natriuretic peptide, atrial natriuretic factor, and renin were significantly reduced in the HS+PC animals. Microarray analyses revealed 45 specific HS genes modified by PC. In a retrospective pilot study of hemodialysis patients, PC-treated subjects demonstrated improved diastolic function and a reduction in LV septal and posterior wall thickness by echocardiography compared with untreated patients. In summary, PC attenuates the development of LV alterations in DSS rats, and these effects should be examined in human clinical trials" (N Bodyak et al., *Proc Natl Acad Sci USA* 2007; 104: 16810-5).

Solving the Riddle of Contaminated Heparin

Ram Sasisekharan, PhD, is senior author, and **Robert S. Langer, ScD**, is co-author of "Contaminated Heparin Associated with Adverse

Clinical Events and Activation of the Contact System." The pharmaceutical company Baxter recalled its heparin in February after more than 80 deaths had been reported in the U.S. An earlier paper, also with Sasisekharan as senior author, had identified the contaminant as an oversulfated form of chondroitin sulfate (OSCS).

The present study screened suspect lots of heparin for the presence of OSCS and for other contaminants, and tested the ability of OSCS to reproduce the clinical manifestations *in vivo* in swine. It was found that OSCS activated the kinin-kallikrein pathway in human plasma, which led to the generation of bradykinin, a potent vasoactive mediator. OSCS also induced the generation of C3a and C5a, potent anaphylatoxins derived from complement proteins. Unexpectedly, activation of those two pathways was linked and dependent upon fluid-phase activation of factor XII. Swine and humans were sensitive to the effects of OSCS in a similar manner: intravenous OSCS-containing heparin induced hypotension associated with kallikrein activation in swine (TK Kishimoto et al., *N Engl J Med* 2008 April 24 [E pub ahead of print]).

Sasisekharan is Professor of Health Sciences and Technology and of Biological Engineering at MIT; Langer is Professor of Health Sciences and Technology and Institute Professor at MIT.

New Approach to Peripheral Nerve Repair

Irene E. Kochevar, PhD, Professor of Dermatology at HMS and MGH, member of the HST affiliated faculty, and Associate Director of the Wellman Laboratories of Photomedicine, at MGH, is coauthor of "Photochemical tissue bonding: a promising technique for peripheral nerve repair." Authors' abstract:

"BACKGROUND: Photochemical tissue bonding (PTB) is a novel tissue repair technique that uses visible light and a photosensitizing dye to crosslink proteins on tissue surfaces. This technique has been successfully demonstrated in a number of tissue repair models. An ideal nerve repair technique would be atraumatic and avoid placement of foreign bodies at the repair site. The epineurium is suited to photochemical repair as it is thin, translucent and has a relatively high collagen content. This study was designed to determine if PTB could be successfully applied in a peripheral nerve repair model.

"MATERIAL AND METHODS: Forty Sprague Dawley rats underwent transection of the sciatic nerve. Animals were then randomized to four treatment groups; epineurial suture repair, epineurial cuff with PTB, epineurial cuff alone, and no repair. Functional recovery was assessed at 10 day intervals using walking track analysis and sciatic function index calculations. At 90 days postoperatively, animals were sacrificed and sciatic nerves harvested for histology and histomorphometry.

"RESULTS: Functional recovery in the suture repair and epineural cuff with PTB groups were not significantly different (-70.6 +/- 17.8 versus -76.9 +/- 10.3, P= 0.64) at 90 days postrepair. Histology showed good axonal regeneration with all repair techniques. Histomorphometric analysis found no significant difference between the repair groups.

CONCLUSIONS: This study illustrates that peripheral nerves can be successfully repaired using a photochemical tissue bonding technique with results similar to those achieved with the current gold standard. With further development and refinement PTB may prove a useful tool in peripheral nerve repair" (TS Johnson et al., *J Surg Res* 2007; 143: 224-9).

Novel Colposcopic Technique for Screening for Cervical Cancer

Rebecca Richards-Kortum, PhD '90, is senior author of "Automated image analysis of digital colposcopy for the detection of cervical neoplasia." Most cases of cervical cancer can be prevented by screening for precancerous lesions. Traditional methods of screening rely upon extensive formal training and experience not generally available in the developing world. This report describes a diagnostic tool for the detection of cervical intra-epithelial neoplasia that can automatically identify neoplastic tissue from digital images. A multispectral digital colposcope (MDC) is used to acquire reflectance images of the cervix with white light before and after the application of acetic acid. The analysis of digital images is performed in two steps. First, similar optical patterns are clustered. Second, classification algorithms are used to determine the probability that these regions contain neoplastic tissue. Acetic acid induces changes in the intensity as well as in the ratio of green to red of reflected light. Twenty-nine patients were studied by means of digital colposcopy and automated image analysis and compared to histopathology. MDC had a sensitivity of 79% and a specificity of 88%. Thus, diagnostically useful digital images of the cervix can be obtained by means of a simple and inexpensive device, and automated image analysis algorithms show a potential to identify histologically neoplastic tissue (SY Park et al., *J Biomed Opt* 2008; 13: 014029).

Richards-Kortum is the Stanley C. Moore Professor and Chair of the Department of Bioengineering at Rice University in Houston.

Pathogenesis of Alcohol-induced Heart Failure

Marc J. Semigran, MD '83, and **Roger J. Hajjar, MD '90**, are co-authors of "Fingerprint

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Gecko feet inspire tissue adhesive

Jeffrey M Karp, PhD, is senior author, and **Robert S. Langer, ScD**, is co-author of "A biodegradable and biocompatible gecko-inspired tissue adhesive." Gecko feet are able to adhere to vertical and inverted surfaces thanks to their adhesive foot pads and dense arrays of fibrils, each of which has numerous terminal projections. This study reports the development of a tissue adhesive that is elastomeric, biocompatible and biodegradable. It is based on poly (glycerol sebacate acrylate), a tough elastoner, combined with a thin tissue-reactive biocompatible surface coating promising covalent crosslinking to wet tissue. Tissue adhesion and biocompatibility were demonstrated in pockets on the back of rats and in porcine intestine tissue. It is expected that this work may lead to the ability to deliver drugs to tissue surfaces and have potential applications for sealing wounds and for replacement or augmentation of sutures or staples (A Mahdavi et al. Proc Natl Acad Sci USA. 2008; 105: 2307-12).

Karp is Instructor in Health Sciences and Technology, and in Medicine at HMS and BWH. Langer is Professor of Health Sciences and Technology and Institute Professor at MIT.

David Clements, via Wikimedia

This foot of a Tokay gecko shows its adhesive pads. The gecko, whose feet enable it to cling tightly while upside down or on vertical surfaces, helped inspire a new medical bandage created by an MIT-led research team.

Riding the Light

by Elizabeth Dougherty

Although photomedicine sounds novel, it has been in practice for millennia. In fact, as early as 3,500 years ago, ancient Egyptian and Indian doctors treated people with certain skin disorders by feeding them the seeds of the Bavachee plant, then sending them into the sunlight to activate the chemicals in the seeds.

It was a mid-1970s study of this earliest form of light-activated drugs that inspired R. Rox Anderson, MD '84, to forgo his plans for graduate study at Stanford and pursue medicine instead. As an HST MD student, his talent shone through. First he characterized the behavior of light in skin for the first time by applying theories from atmospheric science and using spectra of his own skin as data points. For his thesis project, he invented a laser designed to remove vascular birth marks without leaving scars.

Anderson, who is now the director of the Wellman Center for Photomedicine, has been passionate about applying light to dermatological problems ever since. "I like light," he said. "I've always liked light."

Anderson's path, however, wasn't always well lit. After graduating from MIT with a degree in biology in 1972, he spent his twenties bouncing between jobs. He taught camp in the summers and did technical lab work in the winters. Rather than starting at Stanford in the late '70s, he took a job at MGH working as a tech in a dreary photobiology lab run by John Parrish, MD, the future founder of the Wellman Center. The lab aimed to understand the molecular mechanisms behind psoralen UVA therapy — the ancient remedy for skin ailments — and apply it to psoriasis. For Anderson, the job proved illuminating.

"I fell in love with the idea of being able to work on human problems," he said. Until then, he had always felt split in two, working with people in the summer and doing research in the winter. "Medicine puts together everything I love to do." This "aha" moment changed the course of Anderson's life. He declined Stanford, signed up to take the MCATs and, the age of 30, enrolled at HMS as an HST student.

The environment HST created for Anderson allowed him to apply the physics of light to medical problems. His HST thesis, which he published in *Science*, was inspired by a lecture he attended at Beth Israel Hospital. The lecturers reported that the surgical removal of birthmarks called port wine stains often caused scarring. Riding the T on his way home from the lecture, Anderson realized some missing elements and scribbled down all of the equations he needed to solve this problem. The laser treatment he devised is still the gold standard treatment today.

Anderson thrived in the HST environment because, he said, "HST unabashedly loves science." This is important, he said, because medicine is "science for the people." That's why, though the decision to pursue an MD over a PhD was a landmark one for him personally, Anderson does not believe in the segregation of MDs and PhDs in medical science. "Science for the people includes anyone who takes both science and people seriously," he said.

For this reason, the Wellman Center employs both MD and PhD researchers with diverse skills, allowing the center to apply a variety of techniques to solve medical problems. "MDs have an unfair advantage of really understanding the problems worth solving. PhDs have an unfair advantage of understanding how to solve them," he said. "If there is separation between the two, we're in trouble."

So far, this collaborative approach has paid off. He and his colleagues have pioneered non-scarring laser treatments, permanent laser hair removal, laser skin resurfacing, erasable tattoos, laser microbeam treatments, and an infrared confocal microscope that is the highest resolution medical imaging device in clinical use today. He currently has some promising acne remedies in clinical trials. One technology, called photodynamic therapy, uses a light-activated drug that targets sebaceous glands. Another uses laser light absorbed by fats in the oil-producing sebaceous gland in the skin. The light heats the fats and disables the gland's ability to secrete the oils that cause acne. This technology may eventually replace acne drugs which, while effective, can cause birth defects.

Anderson loves to find good problems to solve, but his particular talent is mixing and matching technologies to problems. That talent has led him to apply the technology behind his acne treatment to treatments for other ailments that involve fats. His lab is currently investigating the use of the fat-seeking laser for body sculpting and for destroying the lipid-based plaques that cause atherosclerosis.

"If you're going to be a problem solver, you need to get married to a good problem," said Anderson.

Another problem that stands out to Anderson is one for which dermatology already has an effective, though cumbersome, solution.

"Dermatologists see more cancer than anyone," and they are very good at removing it, said Anderson. Dermatologists surgically remove skin cancers, even those that aren't life threatening, using a precision method where the surgeon is also the pathologist. Using this method, called Mohs surgery, the surgeon cuts away slivers of cancer and

inspects them under the microscope, aiming to get as much of the cancer as possible without removing healthy skin and causing undue scarring.

The technique is tedious, but the results are so good, said Anderson, that all cancer surgeons should probably use this same method. Only they can't. The only reason dermatologists can do it, he said, is "our patients are awake." The process simply takes too long. It is too costly and risky for surgeries requiring general anesthesia.

To make it possible to use a Mohs-like approach for all cancer operations, Anderson wants to devise a way to give the surgeon "microscopic vision" that will guide the surgery in real time. "I want to turn cancer operations into a video game," he said, fearlessly ignoring the bounds of dermatology and eagerly continuing to harness the power of light.

To Anderson, this is a problem worth getting married to.

R. Rox Anderson, shown testing the effects of laser light on fats in the lab, also teaches Biomedical Enterprise Program students about translational medicine. "If you are going to make an impact, you need to make something — a drug a device, software — and you need to interface with industry," said Anderson, who holds nearly 60 patents.

Martha Gray

(continued from page 2)

from all quarters, and there is practically nothing that I could have accomplished by myself.

In academia, when we are at our best, we are not just concerned with our own success, but rather are driven to ensure the success of all those around us. It has been intensely satisfying over the past 12 years to watch so many of you succeed in so many ways. I owe thanks to so many of you — students, faculty, alumni, staff, advisors, and friends have volunteered enormous time and energy for the benefit of HST and for me personally. It has been an honor to work with all of you — something I hope will continue, albeit in a different capacity.

To our graduates, both past and present, I encourage you to strengthen the roots you have established here at HST and remember that the remarkable people you've worked with, during your time here, represent connections that last a lifetime. With these connections, great ideas can grow.

The centuries-old wisdom from Goethe, which I've previously quoted, is as apt as ever:

Whatever you can do, or think you can, begin it
Boldness has genius, power and magic in it.

—Martha Gray

MITPortugal

(continued from page 9)

government relations, and benefit to humanity.

Cutting-edge research plays an important role in providing world-class graduate education. The Bioengineering Systems research programs involve both MIT and Portuguese faculty. In addition, several companies are expected to provide internships and research opportunities. Five main collaborative research efforts are underway, including 12 MIT and 30 Portuguese faculty from Universidade Nova de Lisboa, Instituto Superior Técnico of the Universidade Técnica de Lisboa, Universidade do Minho and University of Coimbra/CNC (Centre for Neuroscience and Cell Biology). Collaborative research projects include:

- Bioprocess and Biomolecular Engineering
- Cell and Tissue Engineering
- Computational Biosystems, Genomics and Synthetic Biology
- Biosystems Innovation, Management and Policy
- Biomedical Devices and Technologies: Hybrid Human-Machine Systems.

For more information, please visit the MPP website at www.MITPortugal.org.

—Dava Newman, PhD

Research News

(continued from page 11)

profile of alcohol-associated heart failure in human hearts." Excessive consumption of alcohol is a common cause of dilated cardiomyopathy, characterized by cardiomegaly and decreased systolic as well a diastolic function. RNA samples from a small number of hearts from organ donors and recipients with alcoholic idiopathic cardiomyopathy were studied by means of a human heart failure cDNA array, which contained 1,143 heart-specific oligonucleotide probes. Alcohol-induced heart failure was found to have a "specific fingerprint" profile of de-regulated genes. The pattern of gene de-regulation suggested a pivotal role for change in matrix, cytoskeletal and structural proteins in the development of clinical heart failure associated with alcoholism (GE Haddad et al., *Alcohol Clin Exp Res* 2008; 32: 814-21).

Semigran is Assistant Professor of Medicine at HMS and MGH. Hajjar is Professor of Medicine/Cardiology and Gene and Cell Medicine at Mount Sinai School of Medicine, New York.

Building Bridges

Anita Goel brings together physics and medicine with nanobiotechnology

by Kaitlyn Chantry

photo courtesy Anita Goel

Anita Goel testifying recently before John Kerry's Senate Subcommittee on the National Nanotechnology Initiative.

Ask Anita Goel, MD '06, PhD, what brought her to science, and her mind leaps immediately to her childhood. The daughter of Indian immigrants, growing up in rural Mississippi, she began asking broad philosophical questions inspired by her Eastern heritage, while the natural world around her inspired her to pursue a fundamental understanding of math and physics. At the same time, as a child spectator in her father's operating room, she was introduced to the world of medicine and the miracles of surgery.

So, it was at an unusually early age that Anita Goel saw the divide between physics and medicine and began searching for an underlying unity in nature. Here, in the "wilds" of Mississippi, an interdisciplinary scientist was made.

Two decades later, Goel is the successful Founder, Chairman and CEO of Nanobiosym, Inc., an innovation engine at the nexus of physics, medicine and nanotechnology. In 2005 she was named one of the world's top 35 young scientific innovators by MIT's *Technology Review* magazine, and in 2006 she received the Global Indus Technovator Award, an honor recognizing the contributions of the top 10 leaders working at the forefront of science, technology and entrepreneurship. And these are just two of the many honors recognizing Goel's pioneering contributions since she began dedicating herself to bridging the gap between physics, medicine and nanotechnology.

The road there, however, wasn't easy. Even as a high school student in Mississippi, Goel began to notice a deeper divide between the sciences. She continued to wonder how physical processes play a role in biological processes. But these weren't the questions most scientists were considering, and the clear schism fascinated Goel. More and more, she believed that there must be a unified framework under which these two could be better understood.

As an undergraduate at Stanford, she found a unifying framework; physics and medicine came together for her at the nano level. She became fascinated with the problem of molecular machines and how they read and write information into DNA. And so began Anita Goel's sojourn into nanotechnology. After completing her BS in Physics at Stanford, Goel turned towards HST, enrolling in the MD-PhD program to continue her work in Physics at Harvard, but simultaneously branch into a more rigorous academic study of medicine.

"HST," Goel said, "was the only institution that connected the dots for me as a person. What appeals to me most about HST is the enterprising spirit, the ability to innovate, to bring together different threads from different disciplines and unite them into one fabric." HST not only understood, but encouraged Goel's desire to connect two traditionally disparate fields. Goel found in HST kindred spirits, a virtual network of people who shared her passion and vision to look across boundaries.

And while she was traveling back and forth across the Charles River, between the worlds of physics at Harvard and medicine at the medical school, HST became her intellectual "center." While everyone else was asking what physics has to do with medicine and what medicine has to do with physics, Goel reflected that "HST was the one place with the foresight and the vision to understand what I was trying to do."

This support for Goel's cross-disciplinary approach led to the epiphany that would become Nanobiosym. "One day I was meditating on the bank of the Charles, and I thought, wouldn't it be great if we could have one place where physics, medicine, and nanotechnology could come together?"

This meditation soon became a reality. Goel received a call from the military looking for an advisor who understood the clinical perspective of pathogens, was trained in the physical sciences, and had experience in nanotechnology. It was a remarkable confluence of skills that Goel just happened to possess.

Still completing her clinical training, Goel flew to Washington, D.C. and was presented with a surprising opportunity. After about two hours of answering questions, she was offered funding to help solve the problem of pathogen detection for national security. Along with this funding came speculation: given the proposed budget, too few resources in the way of time and facilities, and

(continues on page 15)

1980s

Judy Lieberman, PhD, MD '81, has been elected to membership in the American Academy of Arts and Sciences. She is Professor of Pediatrics at HMS and CH.

Jay J. Schnitzer, MD '83, PhD, Associate Professor of Surgery at HMS and MGH, and member of the HST affiliated faculty, has accepted the position of Vice President and Associate Chief Medical Officer at Boston Scientific.

Kevin Powell, PhD '89, MD, formerly of Urbana, Ill., is now a pediatric hospitalist at Children's Hospital in St. Louis.

1990s

Ralph de la Torre, MD '92, Chief of Cardiac Surgery at BIDMC (where he has built up the Cardiovascular Institute), has accepted the position of Chief Executive of Caritas Christi Health Care, the hospital chain owned by the Archdiocese of Boston. Caritas includes St. Elizabeth Hospital Medical Center and the Carney Hospital.

X. Edward Guo, PhD '94, is the editor of the new journal *Cellular and Molecular Bioengineering*, launched in March 2008 by the Biomedical Engineering Society and Springer Publishing. Guo is Professor of Biomedical Engineering at Columbia University. His research interests include *in vivo* bone adaptation, age-related fractures, and micromechanics of bone.

Kang Zhang, MD '95, PhD, received the 2008 Burroughs Wellcome Fund Clinical Scientist Award in Translational Research. The $750,000 award will support his research to identify new genes and treatments for diabetic microvascular complications. Zhang was also elected recently to the American Society of Clinical Investigation. He is Associate Professor of Ophthalmology and Visual Sciences and the Investigator Program in Human Molecular Biology and Genetics, Eccles Institute of Human Genetics, at the University of Utah.

Cassandra H. Walcott, MD '97, a practitioner at Pediatric Healthcare in Brockton, Mass., was named one of Boston's best pediatricians by *Boston Magazine*.

2000s

Allen Jeremias, MD, MSc '05 (CITP), is Assistant Professor of Medicine and Director, Vascular Medicine and Peripheral Intervention, in the Division of Cardiovascular Medicine at SUNY-Stony Brook Health Sciences Center, Stony Brook, N.Y.

Musical tribute in memory of alumnus Michael Ty

On a sunny, cold morning in April, the Ether Dome of MGH was packed to overflowing with clinicians, PhD and MD students from HST, the surviving 15 members of the MGH neurology class of 2008 — and the first piano, a Steinway upright, ever to make an appearance in the Dome. The occasion was the second annual Michael Tsan Ty Memorial Lecture, created to honor the memory of Michael Ty, MD '04, who was a neurology resident when he died in an accident on April 3, 2006.

Philip Pearl, MD, Associate Professor of Pediatrics and Neurology at George Washington University, chose to commemorate Ty, a dedicated musician as well as a neurologist, with a series of case studies of five famous musicians, interspersed with performance of an excerpt from the work of each. From Robert Schumann, who likely suffered from bipolar disorder, to George Gershwin, who died of a brain tumor, Pearl, an active jazz musician, presented fascinating tales of the neurological issues experienced by several composers of the 19th and 20th centuries.

Pearl's lecture was preceded by a remembrance of Ty written by the members of his MGH neurology class and read by Michael F. Rosenbloom, who stood on the floor of the Ether Dome, surrounded by his 14 classmates.

Michael Ty's death was called "a nonerasable tattoo" shared by his classmates, who described him as "a multidimensional man, fierce friend, dedicated husband, supportive brother and beloved son." It was a fitting tribute to a man who loved music, medicine, and his family and friends, and who is dearly missed.

—Catherine Modica

Anita Goel

(continued from page 14)

the understanding that her work would represent a paradigm shift, some skeptics in the room felt that Goel would certainly fail. And she had just five minutes to decide whether she would accept their offer anyway.

Reflecting on this crossroads in her life, Goel thinks about the inherent culture of HST. "Part of the success in innovation is the ability to risk failure," Goel said. At HST, taking chances is rewarded, even if the ultimate achievement falls short of the anticipated success. "Many times in life, we are inhibited to act on dreams. We fail to take the risk at key times when opportunity knocks on our door." HST, she said, "is an incubator for risk takers."

In Goel's case, Nanobiosym was certainly a risk worth taking. Now at the forefront of nanobiotechnology, Goel's company is a child of risk. She accepted the defense funding and did not fail, despite the nay-sayers. Goel, in fact, met all seven original milestones — and even made two extra ones. Since then, Nanobiosym has been awarded with multiple rounds of funding from the US Defense Advanced Research Projects Agency, the US Air Force Office of Scientific Research, the Department of Energy and, this past fall, a $2 million contract from the United States Defense Threat Reduction Agency, a branch of the US Department of Defense.

And that's just the beginning. Nanobiosym is expanding into India, building a nanobiotechnology park in an innovative public/private partnership with the government of India. And Goel has her sights set on bringing emerging technologies to emerging markets to solve global problems. One such vision is to adapt Nanobiosym's GeneRADAR for use in the developing world, where quick and accurate pathogen detection has an enormous humanitarian potential to cut the cost and infrastructure of diagnosing disease. In essence, Goel is envisioning the creation of what she refers to as "an ecosystem," an environment where the fruits of emerging technology can be brought into the global community to meet the greatest unmet needs.

And where will you find Anita Goel when she's not thinking about emerging technologies or improving the human condition? She's probably delving into nature — walking, meditating, or spending time with family and friends. And is she hopeful about the future of cross-disciplinary work? "Definitely," she said. She sees more and more programs building virtual platforms for individuals, despite the huge gulf still in place at the institutional level. "More could be done at medical schools across the country to bring physics into medicine. But, in general, a lot of progress has been made. I am definitely optimistic about these bridges being built."

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HST does it again: It's a Three-peat!

To borrow a phrase from Boston Red Sox announcer Joe Castiglione, "Can you believe it?!" HST has won the coveted pink flamingo in the HMS Societies Olympics for the third year in a row. Rain on May 9 did not dampen the spirits of the fierce competitors, as the games were brought inside. Under the leadership of captain Lizzy Rossin, the HST MD Class of 2011 crushed the opposition with a score of 120 — 30 points ahead of the second place finisher! It looked like a rout was in the making when HST won the first six events, but colleagues from the Cannon, Castle, Holmes and Peabody Societies provided stiff competition in events like Basketball, Tug of War and Ironman Chef. Even with a commanding lead going into the final event, it was still satisfying to see HST win the last round, the Relay Race.

Thank you, Class of 2011, for bringing home the pink again! Your sportsman-like conduct, team spirit and joy of participation are what really make you champions in our eyes!

—Patricia A. Cunningham

Michael Xiang (first-year HST MD-PhD student)

positions in the class. Matthew Frosch, MD, PhD,

—Matthew P. Frosch, MD, PhD

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