



The Connector

newsletter for graduates, students, faculty and friends of HST

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HST Alum in the Role of His Life



HST Alum in the Role of His Life

-Lily U. Burns-Hernandez & Lora B. Maurer

Perhaps being the sole director of the second-year show at Harvard Medical School helped prepare James Eadie for the myriad roles he would play in his life. It's clear that these roles—from student, to emergency medicine and critical care resident, to international medical education director, to Air Force combat physician, to stateside military medical director, to entrepreneur, to husband, and eventually to father—all shaped Eadie's life and make him the man he is today.

Born in upstate New York near Albany, Eadie grew up with a supportive family who encouraged his curiosity as a child. His father, who worked in public health, and his grandfather, a physician, both played a significant role in his choice of career. Following undergraduate studies at the University of Michigan, Eadie came to HST.

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HST Alumni Network

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(Eadie Cont...)

Prior to interviewing at HST, Eadie admits he knew nothing about the program. However after meeting with several members of the HST Administration, he understood what it meant to be part of the HST community.

In addition to his family, HST deeply influenced Eadie's career. He felt welcomed into a small, tightly knit HST community in 1995 where, having come from the University of Michigan as one of thousands (albeit a summa cum laude biomechanical engineering graduate), he could tell that he "mattered." HST fostered his intellectual curiosity and encouraged critical thinking.

"Whether interacting with Patty [Cunningham] or meeting Farish Jenkins, who surprised the heck out of us by having memorized our biographies, I was blown away by the tremendous dedication and family values embodied in HST. HST gave me a home and an identity...I still look at [HST] as my identity. I say 'I went to medical school...I did HST!' The curriculum was outstanding, challenging, and unrelenting. I'm so grateful to all the people who helped me there. It was a family and community I was welcomed into from day one."

As required by his ROTC scholarship at Michigan, Eadie joined the military upon completion of his residency in emergency medicine. He was first deployed to Balad, Iraq in September 2005 where he served as team chief and critical-care transport team physician and underwent flight physiology training. Due to his exceptional HST training, Eadie began asking a lot of scientific questions. Prior to his arrival on the scene, there had been no data collected, so he and a colleague designed a yearlong data-collection study of what they were seeing in the field; they procured an IRB exemption to carry out a descriptive study.

The nature of Eadie's work in Iraq demanded that he let go of any expectations or preconceived notions about what he'd see and do in the field. For example, the first patient he saw in the ICU – an older, gray-haired gentleman – turned out to be a Department of Defense contractor (as opposed to the expected soldier) who had stopped taking his Lasix and was in stage IV congestive heart failure. Luckily, Eadie and other members of the critical care transport team were able to stabilize the patient and transport him for treatment. While in the field, Eadie witnessed a considerable amount of trauma, and, to his surprise, roughly one-third of the patients turned out to be cardiac patients. Other conditions Eadie treated included septic shock for PID, viral cardiomyopathy, stroke, appendicitis, kidney stones and pediatric trauma.

Following his overseas tour, Eadie was fortunate to return home to Texas in 2008, a few days before his first son Garrett, now 5, was born. (The Eadies now have a second son, Dylan, who is one-and-a-half.) Once back in Texas, he took on administrative duties as the Medical Director of the Air Force Academic Medical Center, and found he truly enjoyed the administrative and business aspects of the practice. In this role, he focused significant energy on enhancing the research productivity of the organization through which he increased research funding from \$2000 when he arrived to \$650,000 by the time he left.

Eadie's wife, Christina Sebestyen, MD, an obstetrician affiliated with the University of Texas, is in private practice in Austin where the family moved after leaving the Air Force. Eadie took over the financial and business management roles of his wife's practice and helped build it to a successful, vibrant business while winding down his work with the military and pursuing his MBA.

Through the work with his wife's practice and his MBA, Eadie found he loved the business world. He recently joined Santé, an Austin venture capital firm <http://santeventures.com/>, focusing on the life sciences. As a full-time team member, Eadie feels this work is a natural fit for his HST training. He is delighted to be working with fellow HST alum Jim Graham, a graduate of the Biomedical Enterprise Program (BEP). Eadie feels that entering the venture capital arena is "almost [like] going back to HST." He's studying new technologies using the critical, clinical, quantitative approaches honed in at HST, and asking, "Will this make a difference clinically? Will clinicians use this? How will this tackle a problem?"

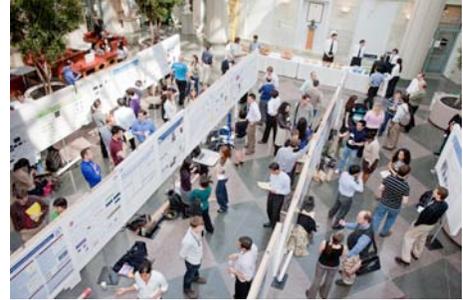
Eadie's varied career has brought him to this assessment of the current state of healthcare in the U.S.: "We as a culture, as Americans, as physicians, seem grossly unprepared to have the discussions we need to have [about current challenges]. We seem to be unprepared to talk about the things we need to talk about. This is my biggest concern: how can we reign in costs when we've never said 'no', we've always said 'yes' to everything...you can't say 'yes' to everything. We need to ask what is the cost-benefit analysis. I am troubled about how we as a nation use limited resources to provide the best care."

Eadie is now—and has always been—directing his own show. Still amazed that HST allowed him the time and space to direct the second-year show—"HST supported that!"—Eadie acknowledges HST as the linchpin in his multi-faceted, interdisciplinary career. Reflective, he views success, not as an ending, but as a process—a journey that includes having fun and facing challenges along the way, where personal fulfillment—including children, friends and family—goes hand-in-hand with professional achievement. Characteristically modest and appreciative, Eadie credits HST for playing a key role in both arenas.

24th Annual HST Forum *by Patricia Cunningham*

The 24th HST Forum was held on Thursday, April 14, 2011 at the Tosteson Medical Education Center at Harvard Medical School. The Forum is the annual showcase for student research. Through this event, the exciting depth and breadth of HST science and accomplishment are highlighted for admitted MD and PhD candidates, current students, faculty, staff and other members of the HST, HMS and MIT communities.

This year, 42 students presented posters on their current research. The poster session was followed by a keynote address given by R. Rox Anderson, MD (HST '84) on "Magic Bullet-ology!" The speech was quintessentially "HST," and was very well-received by current as well as prospective members of the HST community.



HST Forum photos by David M. Barron



Following Dr. Anderson's talk, a number of student prizes were awarded.

Soon-to-graduate Corinna Zygourakis received the Seidman Prize for Outstanding HST Senior Medical Student Thesis.

In the context of an amazingly impressive array of articulately presented student research, the following students received the Martha Gray Prize for Excellence in Research in the categories: named:

Mark Scott (MEMP), Imaging, Acoustics and Optics
Mitra Dowlatshahi (MD), Cell and Molecular Biology
Vineeta Agarwala (MD/PhD), Bioinformatics and Integrative Genomics
Vikram Pattanayak (MD/PhD), Biomedical Devices
Sidharth Puram (MD/PhD), Cell and Molecular Biology
David Lin (MD), Physiology and Systems Biology
Alice A. Chen (MEMP), Regenerative and Rehabilitative Biomedical Engineering



A number of faculty were also recognized for their teaching and mentoring accomplishments.

The Irving M. London Teaching Award to Matthew Frosch, MD (HST '87), PhD--for his captivating ability to bring the human brain to life in the neuroanatomy portion of HST.130, Introduction to Neuroscience.



The Thomas A. McMahon Mentoring Award to Sangeeta Bhatia, MD (HST '99), PhD (MEMP '97)--for her exceptionally dedicated, caring, empowering mentoring of PhD students.



The Seidman Prize for MD Research Mentoring to Mary Bouxsein, PhD--for her tireless, enthusiastic, confidence-building mentoring.

Separately, BEP students selected **Robert Padera, MD (HST '00), PhD (MEMP '98)** to receive the **BEP Teaching Award** for his tremendous clarity in Pathology and Biomaterials and consistently "going beyond" to help BEP students achieve a solid clinical foundation.

HST Graduation, May 24, 2011



The 2011 HST Graduation was held in the spectacular meeting rooms on the sixth floor of the new MIT Media Lab E14 building on Tuesday, May 24. Master of Ceremony Richard Mitchell, MD, PhD provided his usual witty opening remarks to the nearly 200 faculty, students, staff and family members in attendance. Jeffrey Flier, MD, dean of the faculty of medicine at Harvard Medical School, Claude Canizares, PhD, associate provost, MIT, and HST director David Cohen, MD, PhD, congratulated the students and wished them success in their careers as physicians, engineers and entrepreneurs.

They spoke to the enormous success of the HST program, now in its fifth decade, and attributed the success of the program to its students, faculty, and the unwavering commitment of MIT and HMS.

They were followed by Cathal Kearney, the student speaker. Mr. Kearney, a graduate of the MEMP PhD program, gave a talk that was heartfelt, funny, charming, a wee bit irreverent, positive and inspiring – much like the speaker!



On one of his more serious notes, Kierney said “...the real thrust of HST is educating students who have a strong multidisciplinary understanding:

students who cannot only converse at the intersection of the disciplines but who are comfortable existing within each discipline.” Kierney particularly thanked Drs. Mitchell, Padera, and Gehrke for their inspirational training both within and outside the classroom. The program heads then handed out presents to the graduates of the HST Masters, PhD and MD programs, reading a personal vignette about each student as they crossed the stage.

After the presentations to the students, three members of the faculty received awards. Mary L. Boussein, PhD, co-director of the HST 020 Musculoskeletal Pathophysiology course, was presented with the Seidman Prize for MD Research Mentorship; Robert Padera, MD, PhD, co-director of the HST 030 Human Pathology course, accepted the Biomedical Enterprise Program Faculty Teaching Award; and Henry Klapholz, MD, was honored with a Special Faculty Recognition award on the occasion of his retirement after 25 years from the direction of the HST 070 Human Reproductive Biology course.



Joseph Madsen, MD '81, president of the HST Alumni Association, welcomed the newest members of the HST alumni/ae. While the graduates might not be fully or immediately aware of the benefits associated with being HST alumni, he said, in years to come, the fruits will be clear. Dr. Madsen emphasized the importance of the HST program and the strength that members of the HST community have when they stand together.

The group then adjourned to a nearby reception featuring delicious hors d'oeuvres and a string quartet to continue their celebration. Click [here](#) to view the photo gallery.

Please join us in congratulating the HST Graduating Class of 2011 whose names are listed below:

**Certificate
Graduate Education in Medical Sciences**

Ericka Anderson, BS

also received PhD from Massachusetts Institute of Technology

Thesis Topic: The Role of Stra8 in spermatogenesis: Spermatogonial differentiation, meiotic initiation, and tumor formation

Heisoog Kim, BNG

also expects PhD from Massachusetts Institute of Technology, September 2011

Thesis Topic: Advanced MR Imaging Technique for Investigating the Oxygenative Mechanism and the Biomarker in Glioblastoma

Anita Shukla, BS

also received PhD from Massachusetts Institute of Technology

Thesis Topic: Controlled Release Films and Functional Surfaces -Targeting Infection, Inflammation, and Bleeding

Pedro Valencia, SB

Thesis Topic: Development of a microfluidic platform for the high-throughput engineering, screening, and optimization of targeted nanoparticles for cancer therapy

Christopher J. Zopf, BS

Thesis Topic: A Gene Oscilloscope to Probe the Dynamics of Transcription Regulation

**Master of Engineering
Biomedical Engineering**

Jessica Karen Wong

also received SB from Massachusetts Institute of Technology

Thesis Topic: Optimizing a Protein-RNA Aptamer Gene Regulatory System using an Engineered Peptide Library

**Master of Science
Biomedical Enterprise Program**

Rafael Diaz Trevino, BNG, MBA

Thesis Topic: An Analysis of the Differences between National and Local Coverage Determinations of Medical Procedures in the US

Joshua Gottlieb, BS

also received MBA from Massachusetts Institute of Technology

Thesis Topic: Orphan Drugs: Future Viability of Current Forecasting Models, in Light of Impending Changes to Influential Market Factors

Meera S. Gupta, BS

also received MBA from Massachusetts Institute of Technology

Thesis Topic: Effect of Patent Law Changes on the Innovation Strategy of Chinese and Indian Life Science Companies as Reflected in the US Patent Filings

Andrew J. Koert, BS

also received MBA from Massachusetts Institute of Technology

Thesis Topic: Factors Influencing FDA Clearance Time for Medical Device 510(k) Applications

Ashish S. Kothari, MBBS, MS

also received MBA from Massachusetts Institute of Technology

Thesis Topic: Impact of the CE marking on the exit opportunities and valuation of medical device companies

Zeenat J. Patrawala, SB, MBA

Thesis Topic: A Comprehensive Guide to the Three Biosimilar Markets (Europe, US, Japan) and Regulatory Pathways

Joseph P. Sterk, AB

also received MBA from Massachusetts Institute of Technology

Thesis Topic: Assessing the Impact of Tumor Evolution on Oncology Drug Development and Commercialization

Ridhi Tariyal, BS

also received MBA from Harvard Business School

Thesis Topic: Finding Utility for Genetic Diagnostics in the Developing World

**Master of Science
Biomedical Informatics**

J. Stewart Evans, MD

Thesis Topic: Comparing Long-Term Antiplatelet Strategies to Prevent Morbidity and Mortality in Patients with Drug-Eluting Coronary Stents

**Master of Science
Health Sciences and Technology**

Bennett C. Bullock, BA, MS

Thesis Topic: Auditory Pathway Responses to Parametrized Vowels in Autism Spectrum Disorders

Suh-Kyung Lee, BS

Thesis Topic: Investigation of Acquired Hearing Loss in Dopamine Beta Hydroxylase (DBH)-Mutant Mice

**Doctor of Medicine
Medical Sciences****Adewole Adamson, BA, BS**

also received MPP from Harvard University

Thesis Topic: TIMP1 is preferentially expressed in Th1 and Th17 cells in a STAT dependent manner

Xi Chen, BS, PhD

Thesis Topic: External fluid environment controls proliferation and maintenance of neural progenitor cells

Yicheng Chen, BA

Thesis Topic: Regulatory mechanisms of joint-enriched uncultured adult stem cell function

Ai-ris Yonekura Collier, BS

Thesis Topic: Immunotherapeutic potential of cultured lymph node stromal cells

Marlys S. Fassett, BA

also received PhD from Harvard University

Thesis Topic: The Nur77 family and T cell tolerance

Ruth K. Foreman, BA

also received PhD from Massachusetts Institute of Technology

Thesis Topic: Reprogramming Cellular Identity using Defined Factors

Sarah E. Henrickson, BA

also received PhD from Harvard University

Thesis Topic: Dynamics of T cell activation in vivo

Sam H. Horng, BA

also received PhD from Massachusetts Institute of Technology

Thesis Topic: Identification and functional characterization of two patterning genes, Zic4 and Ten_m3, in topographic map formation of the visual pathway

Sravisht Iyer, BS

Thesis Topic: A biomechanical model for estimating loads on thoracic and lumbar vertebrae

Shilpa M. Joshi, SB

Thesis Topic: Biomechanical Healing of Porcine ACL enhanced by Collagen-Platelet Composites

Seth J. Kleinerman, BA

Thesis Topic: Biochemical characterization of amyloid B-protein assemblies in the brains of patients with Alzheimers disease

Ryan M. Lanning, BS

also received PhD from Massachusetts Institute of Technology

Thesis Topic: Tumor Vasculature and Microenvironment during Progression and Treatment: Insights from Optical Microscopy

Natalie L. Leong, BS

Thesis Topic: Evaluation of non-viral gene transfection of BMP-7 in mesenchymal stem cell osteogenesis

Walter C. Lin, BA

Thesis Topic: Chronic in vivo two-photon imaging of synaptic plasticity in the adult mouse visual cortex in response to fluoxetine

Michael A. Mohan, BS

Thesis Topic: Dextromethorphan for mechanical allodynia in patients with traumatic spinal cord injury

Tafadzwa Muguwe, BA

Thesis: The role of human SET protein in HIV infection

Rameez Qudsi, BA

Thesis: Characterization of a novel mouse model of osteosarcoma that mimics the human disease

Christopher James Stapleton, BS

Thesis: Thrombospondin-1 modulates the angiogenic phenotype of human cerebral arteriovenous malformation endothelial cells

Srinivas R. Viswanathan, BS, MS

also received PhD from Harvard University - *Thesis:* Lin28: A MicroRNA Regulator with a Macro Role

Corinna C. Zygourakis, BS

Thesis: Downstream mediators of Sox6 control over cortical interneuron development

**Doctor of Philosophy
Medical Engineering/Medical Physics**

Alice A. Chen, BS

Thesis Topic: Engineering Humanized Mice with Implantable Hepatic Tissues for Drug Development

Rahmatullah H. Cholas, BS, SM

Thesis Topic: Collagen Scaffolds in Full- and Hemi- Resection Spinal Cord Injury Models

Benjamin Diop-Frimpong, BEng

Thesis Topic: Cancer Drug Delivery: the Role of Extracellular Matrix Structure

Paul Z. Elias, BS

Thesis Topic: Collagen Scaffolds for Treatment of Penetrating Brain Injury in a Rat Model

Joseph W. Franses, BS

Thesis Topic: Regulatory Roles of Endothelial Cells in Cancer

Evita V. Grant, BA

Thesis Topic: Polyethylenimine: A Potent DNA Adjuvant

Nathaniel D. Huebsch, BS

Thesis Topic: Integrin-Adhesion Ligand Bonds as 3D Mechanosensors that Modulate Mesenchymal Stem Cell Fate

Cathal J. Kearney, BA, BNG

Thesis Topic: Non-Invasive Shock Wave Stimulated Periosteum for Bone Tissue Engineering

Jinkuk Kim, BS

Thesis Topic: Regulatory RNAs in Mammals: Genomics, Function, and Evolution

Joshua Korn, BS

Thesis Topic: Copy Number Variation in the Human Genome: Tools, Methods, and Applications to Disease

Jack M. Milwid, BS, SM

Thesis Topic: Discovery of novel anti-inflammatory proteins inspired by bone marrow mesenchymal stem cell secretions

Antonio Molins, BS

Thesis Topic: State-Space Modeling of MEG Time Series

Suraj J. Patel, BS

Thesis Topic: Identification of a Gap Junction Communication Pathway Critical in Innate Immunity

Stephanie M. Pieciewicz, BS

Thesis Topic: Heparan Sulfate Glycosaminoglycan Regulation of Vasculogenesis

Somponnat Sampattavanich, BS

Thesis Topic: A general method for studying autocrine signaling and its impact on cancer cell growth

Kyle C. Smith, BS

Thesis Topic: A Unified Model of Electroporation and Molecular Transport

**Doctor of Philosophy
Speech and Hearing Biosciences and Technology**

Nancy F. Chen, BS, MS

Thesis Topic: Characterizing Phonetic Transformations and Fine-Grained Acoustic Differences Across Dialects

Wendy Gu, BS, MEng

Thesis Topic: Neural Abnormalities Underlying Tinnitus and Hyperacusis

Caroline A. Niziolek, BS

Thesis Topic: The Role of Linguistic Contrasts in the Auditory Feedback Control of Speech

Ryuji Suzuki, BS, MS

Thesis Topic: Responses from Electric Stimulation of Cochlear Nucleus

Tianyu T. Wang, BS

Thesis Topic: Two-dimensional Speech Signal Processing and Modeling

Rebecca R. Woodbury, BS

Thesis Topic: Behavioral and Neural Correlates of Deep and Surface Anaphora

HST Research, Honors, & Awards

RESEARCH:

Sangeeta N. Bhatia, MD '99, PhD '97, Professor of Health Sciences and Technology and Professor of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, was co-author of "Nanoparticles that communicate in vivo to amplify tumour targeting."

Abstract: Nanomedicines have enormous potential to improve the precision of cancer therapy, yet our ability to efficiently home these materials to regions of disease in vivo remains very limited. Inspired by the ability of communication to improve targeting in biological systems, such as inflammatory-cell recruitment to sites of disease, we construct systems where synthetic biological and nanotechnological components communicate to amplify disease targeting in vivo. These systems are composed of 'signalling' modules (nanoparticles or engineered proteins) that target tumours and then locally activate the coagulation cascade to broadcast tumour location to clot-targeted 'receiving' nanoparticles in circulation that carry a diagnostic or therapeutic cargo, thereby amplifying their delivery. We show that communicating nanoparticle systems can be composed of multiple types of signalling and receiving modules, can transmit information through multiple molecular pathways in coagulation, can operate autonomously and can target over 40 times higher doses of chemotherapeutics to tumours than non-communicating controls. (von Maltzahn et al. *Nat Mater.* 2011 Jun 19;10(7): 545-52)

Emery N. Brown, MD, PhD, Professor of Health Sciences and Technology and Professor of Computational Neuroscience, Massachusetts Institute of Technology, Warren M. Zapol Professor of Anesthesia, Harvard Medical School, Massachusetts General Hospital, co-authored "Methylphenidate Actively Induces Emergence from General Anesthesia."

Abstract: Although accumulating evidence suggests that arousal pathways in the brain play important roles in emergence from general anesthesia, the roles of monoaminergic arousal circuits are unclear. In this study, the authors tested the hypothesis that methylphenidate (an inhibitor of dopamine and norepinephrine transporters) induces emergence from isoflurane general anesthesia.

METHODS: Using adult rats, the authors tested the effect of intravenous methylphenidate on time to emergence from isoflurane general anesthesia. They then performed experiments to test separately for methylphenidate-induced changes in arousal and changes in minute ventilation. A dose-response study was performed to test for methylphenidate-induced restoration of righting during continuous isoflurane general anesthesia. Surface electroencephalogram recordings were performed to observe neurophysiological changes. Plethysmography

recordings and arterial blood gas analysis were performed to assess methylphenidate-induced changes in respiratory function. Intravenous droperidol was administered to test for inhibition of methylphenidate's actions.

RESULTS: Methylphenidate decreased median time to emergence from 280 to 91 s. The median difference in time to emergence without methylphenidate compared with administration of methylphenidate was 200 [155-331] s (median, [95% CI]). During continuous inhalation of isoflurane, methylphenidate induced return of righting in a dose-dependent manner, induced a shift in electroencephalogram power from delta (less than 4 Hz) to theta (4-8 Hz), and induced an increase in minute ventilation. Administration of intravenous droperidol (0.5 mg/kg) before intravenous methylphenidate (5 mg/kg) largely inhibited methylphenidate-induced emergence behavior, electroencephalogram changes, and changes in minute ventilation.

CONCLUSIONS: Methylphenidate actively induces emergence from isoflurane general anesthesia by increasing arousal and respiratory drive, possibly through activation of dopaminergic and adrenergic arousal circuits. The authors' findings suggest that methylphenidate may be useful clinically as an agent to reverse general anesthetic-induced unconsciousness and respiratory depression at the end of surgery. (Solt et al. *Anesthesiology.* 2011 Oct;115(4): 791-803.)

David E. Cohen, MD '87, PhD, Director, HST and Robert H. Ebert Professor of Medicine and Health Sciences and Technology, Harvard Medical School, Brigham & Women's Hospital, co-authored "Genetic ablation or chemical inhibition of phosphatidylcholine transfer protein attenuates diet-induced hepatic glucose production."

Abstract: Phosphatidylcholine transfer protein (PC-TP, synonym StARD2) is a highly specific intracellular lipid binding protein that is enriched in liver. Coding region polymorphisms in both humans and mice appear to confer protection against measures of insulin resistance. The current study was designed to test the hypotheses that Pctp^{-/-} mice are protected against diet-induced increases in hepatic glucose production and that small molecule inhibition of PC-TP recapitulates this phenotype. Pctp^{-/-} and wildtype mice were subjected to high-fat feeding and rates of hepatic glucose production and glucose clearance were quantified by hyperinsulinemic euglycemic clamp studies and pyruvate tolerance tests. These studies revealed that high-fat diet-induced increases in hepatic glucose production were markedly attenuated in Pctp^{-/-} mice. Small molecule inhibitors of PC-TP were synthesized and their potencies, as well as mechanism of inhibition, were characterized in vitro. An optimized inhibitor was administered to high-fat-fed mice and used to explore effects on insulin signaling in cell culture systems. Small

molecule inhibitors bound PC-TP, displaced phosphatidylcholines from the lipid binding site, and increased the thermal stability of the protein.

Administration of the optimized inhibitor to wildtype mice attenuated hepatic glucose production associated with high-fat feeding, but had no activity in Pctp^{-/-} mice. Indicative of a mechanism for reducing glucose intolerance that is distinct from commonly utilized insulin-sensitizing agents, the inhibitor promoted insulin-independent phosphorylation of key insulin signaling molecules.

CONCLUSION: These findings suggest PC-TP inhibition as a novel therapeutic strategy in the management of hepatic insulin resistance. (Shishova et al. *Hepatology*. 2011 Aug;54(2):664-74)

Utkan Demirci, PhD, Assistant Professor of Medicine and Health Sciences and Technology, Harvard Medical School, Brigham & Women's Hospital, is co-author of "Integration of cell phone imaging with microchip ELISA to detect ovarian cancer HE4 biomarker in urine at the point-of-care."

Abstract: Ovarian cancer is asymptomatic in the early stages and most patients present with advanced levels of disease. The lack of cost-effective methods that can achieve frequent, simple and non-invasive testing hinders early detection and causes high mortality in ovarian cancer patients. Here, we report a simple and inexpensive microchip ELISA-based detection module that employs a portable detection system, i.e., a cell phone/charge-coupled device (CCD) to quantify an ovarian cancer biomarker, HE4, in urine. Integration of a mobile application with a cell phone enabled immediate processing of microchip ELISA results, which eliminated the need for a bulky, expensive spectrophotometer. The HE4 level detected by a cell phone or a lensless CCD system was significantly elevated in urine samples from cancer patients (n = 19) than healthy controls (n = 20) (p < 0.001). Receiver operating characteristic (ROC) analyses showed that the microchip ELISA coupled with a cell phone running an automated analysis mobile application had a sensitivity of 89.5% at a specificity of 90%. Under the same specificity, the microchip ELISA coupled with a CCD had a sensitivity of 84.2%. In conclusion, integration of microchip ELISA with cell phone/CCD-based colorimetric measurement technology can be used to detect HE4 biomarker at the point-of-care (POC), paving the way to create bedside technologies for diagnostics and treatment monitoring. (Wang et al. *Lab Chip*. 2011 Oct 21;11(20):3411-8.)

Elazer R. Edelman, MD '83, PhD '84, Thomas D. and Virginia W. Cabot Professor of Health Sciences and Technology, Massachusetts Institute of Technology, is co-author of "In vivo and in vitro tracking of erosion in biodegradable materials using non-invasive fluorescence imaging."

Abstract: The design of erodible biomaterials relies on the ability to program the in vivo retention time, which necessitates real-time monitoring of erosion. However, in vivo performance cannot always be predicted by traditional determination of in vitro erosion, and standard methods

sacrifice samples or animals, preventing sequential measures of the same specimen. We harnessed non-invasive fluorescence imaging to sequentially follow in vivo material-mass loss to model the degradation of materials hydrolytically (PEG:dextran hydrogel) and enzymatically (collagen). Hydrogel erosion rates in vivo and in vitro correlated, enabling the prediction of in vivo erosion of new material formulations from in vitro data. Collagen in vivo erosion was used to infer physiologic in vitro conditions that mimic erosive in vivo environments. This approach enables rapid in vitro screening of materials, and can be extended to simultaneously determine drug release and material erosion from a drug-eluting scaffold, or cell viability and material fate in tissue-engineering formulations. (Artzi et al. *Nat Mater*. 2011 Aug 21;10(9):704-9.)

John Gabrieli, PhD, Grover Herman Professor of Health Sciences and Technology and Professor of Brain and Cognitive Sciences, Massachusetts Institute of Technology, co-authored "Human voice recognition depends on language ability."

Abstract: The ability to recognize people by their voice is an important social behavior. Individuals differ in how they pronounce words, and listeners may take advantage of language-specific knowledge of speech phonology to facilitate recognizing voices. Impaired phonological processing is characteristic of dyslexia and thought to be a basis for difficulty in learning to read. We tested voice-recognition abilities of dyslexic and control listeners for voices speaking listeners' native language or an unfamiliar language. Individuals with dyslexia exhibited impaired voice-recognition abilities compared with controls only for voices speaking their native language. These results demonstrate the importance of linguistic representations for voice recognition. Humans appear to identify voices by making comparisons between talkers' pronunciations of words and listeners' stored abstract representations of the sounds in those words. (Perrachione et al. *Science*. 2011 Jul 29;333(6042):595.)

Jeffrey M. Karp, PhD, Assistant Professor in Medicine and Health Sciences and Technology, Brigham & Women's Hospital, Harvard Medical School and **Robert S. Langer** Jr., ScD, David H. Koch Institute Professor, Massachusetts Institute of Technology, authored "Materials science: Dry solution to a sticky problem."

Summary: Sticking plasters revolutionized the protection of minor wounds, but they're not ideal for fragile skin. A material that mimics the adhesive properties of certain beetles' feet might provide a solution. (Karp JM, Langer R. *Nature*. 2011 Aug 31;477(7362):42-3.)

Roger G. Mark, MD, PhD, Distinguished Professor in Health Sciences and Technology and Electrical Engineering and Computer Science, Massachusetts Institute of Technology, is co-author of "A Hypotensive Episode Predictor for Intensive Care based on Heart Rate and Blood Pressure Time Series."

Abstract: In the intensive care unit (ICU), prompt therapeutic intervention to hypotensive episodes (HEs) is a critical task. Advance alerts that can prospectively identify patients at risk of developing an HE in the next few hours would be of considerable clinical value. In this study, we developed an automated, artificial neural network HE predictor based on heart rate and blood pressure time series from the MIMIC II database. The gap between prediction time and the onset of the 30-minute target window was varied from 1 to 4 hours. A 30-minute observation window preceding the prediction time provided input information to the predictor. While individual gap sizes were evaluated independently, weighted posterior probabilities based on different gap sizes were also investigated. The results showed that prediction performance degraded as gap size increased and the weighting scheme induced negligible performance improvement. Despite low positive predictive values, the best mean area under ROC curve was 0.934. (Lee J, Mark R. *Comput Cardiol* (2010). 2011 Mar 22;2010(26-29 Sept. 2010):81-84.)

Ram Sasisekharan, PhD, Director, HST and Edward Hood Taplin Professor of Health Sciences & Technology and Biological Engineering, Massachusetts Institute of Technology, co-authored “Glycomics-based analysis of chicken red blood cells provides insight into the selectivity of the viral agglutination assay.”

Abstract: Agglutination of red blood cells (RBCs), including chicken RBCs (cRBCs), has been used extensively to estimate viral titer, to screen glycan-receptor binding preference, and to assess the protective response of vaccines. Although this assay enjoys widespread use, some virus strains do not agglutinate RBCs. To address these underlying issues and to increase the usefulness of cRBCs as tools for studying viruses, such as influenza, we analyzed the cell surface N-glycans of cRBCs. On the basis of the results obtained from complementary analytical strategies, including MS, 1D and 2D-NMR spectroscopy, exoglycosidase digestions, and HPLC profiling, we report the major glycan structures present on cRBCs. By comparing the glycan structures of cRBCs with those of representative human upper respiratory cells, we offer a possible explanation for the fact that certain influenza strains do not agglutinate cRBCs, using specific human-adapted influenza hemagglutinins as examples. Finally, recent understanding of the role of various glycan structures in high affinity binding to influenza hemagglutinins provides context to our findings. These results illustrate that the field of glycomics can provide important information with respect to the experimental systems used to characterize, detect and study viruses. (Aich et al. *FEBS J*. 2011 May;278(10):1699-712.)

Collin M. Stultz, MD '97, PhD, Associate Professor of Health Sciences and Technology, Associate Professor of Electrical Engineering and Computer Science, and W. M. Keck Associate Professor of Biomedical Engineering, Massachusetts Institute of Technology, was co-author of “Protein structure along the order-disorder continuum.”

Abstract: Thermal fluctuations cause proteins to adopt an ensemble of conformations wherein the relative stability of the different ensemble members is determined by the topography of the underlying energy landscape. “Folded” proteins have relatively homogeneous ensembles, while “unfolded” proteins have heterogeneous ensembles. Hence, the labels “folded” and “unfolded” represent attempts to provide a qualitative characterization of the extent of structural heterogeneity within the underlying ensemble. In this work, we introduce an information-theoretic order parameter to quantify this conformational heterogeneity. We demonstrate that this order parameter can be estimated in a straightforward manner from an ensemble and is applicable to both unfolded and folded proteins. In addition, a simple formula for approximating the order parameter directly from crystallographic B factors is presented. By applying these metrics to a large sample of proteins, we show that proteins span the full range of the order-disorder axis. (Fisher CK, Stultz CM. *J Am Chem Soc*. 2011 Jul 6;133(26):10022-5)

HONORS & AWARDS:

HST's HMS director, **David E. Cohen**, MD (HST '87), PhD, has been promoted to Robert H. Ebert Professor of Medicine and Health Sciences and Technology. A celebration was hosted jointly by HST and the GI Division of the Brigham and Women's Hospital on October 12th at Harvard Medical School.



HST Alum **Dr. Siddhartha Mukherjee** received the Pulitzer Prize for non-fiction for his book "The Emperor of All Maladies: A Biography of Cancer".



Lee C. Bollinger, President of Columbia University (left), presents the 2011 General Nonfiction prize to Siddhartha Mukherjee.



Robert Langer, the David H. Koch Institute Professor at MIT, has been named one of the winners of this year's Warren Alpert Foundation Prize, which annually recognizes researchers for laboratory discoveries with strong promise to improve human health.

Elfar Adalsteinsson and **Collin Stultz** were promoted to the rank of Associate Professor with tenure at MIT.



Jeffrey Karp was named one of The Boston Business Journals 2011 Champions in Health Care. These nurses, doctors and administrators and scientists are pioneers in the medical technology and in the way care is delivered. Winners were chosen from among hundreds of professionals nominated by their peers.



The National Institute of Statistical Sciences (NISS) has presented the 2011 Jerome Sacks Award for Cross-Disciplinary Research to **Emery N. Brown**, professor of health sciences and technology and computational neuroscience at MIT.

HST Finance Team Members **Irene Huang** and **Holly-Ann Paiva** win the 2011 Infinite Mile Award for their professionalism, commitment to getting the job done, and personal integrity.



Holly-Ann Paiva and Irene Huang (pictured here with Provost, L. Rafael Reif and Vice President for Research & Associate Provost, Claude Canizares)



SGBT student **Nancy F. Chen** wins IEEE Travel Grant "Informative dialect recognition using context-dependent pronunciation modeling"

HST Alumni News:**1980s**

David Moskowitz, MD '80 on May 3, 2011, had the tremendous honor of meeting HRH Prince Charles, the Prince of Wales, along with other Marshall Scholars to discuss the future of the Programme. Prince Charles has been Royal Patron of the Programme for 22 years. Dr. Moskowitz was a Marshall Scholar at Merton College, Oxford reading Honours School Biochemistry from 1974 to 1976. Last year, there were huge student protests in London and other cities for the first time in 50 years. Students were protesting the 25% rise of tuition fees in England and Wales without a corresponding increase in Local Education Authority grants. Students argued this could force many to drop out of college. Despite this, the UK government still managed to preserve the funding for the Marshall Scholarships.

In May, **Ed Bessman, MD '81** graduated from the Johns Hopkins University Carey Business School with an MBA in Medical services Management.

1990s

Eric Mortensen, MD, PhD '90 was appointed Vice President, Medicine Development Lead for the Tasocitinib Janus Kinase Inhibitor Program, Specialty Care Business Unit, Pfizer Inc. In addition, Eric was recently married to Tenjiwe (TJ) Mortensen on January 22 in East London, South Africa & February 26, 2011 in Princeton, New Jersey.

Howard M. Loree '92, since graduation has done a 3-year postdoc in cardiovascular biomechanics at the BWH and is now working in the Boston area medical device industry. The majority of his career has been in the development of implantable blood pumps for cardiac assist devices and artificial hearts (Thoratec and Abiomed). He has also worked in tissue engineering applications for non-surgical treatment of spinal disc generation (Orthopeutics) and corneal reshaping for refractive correction (Avedro). Dr. Loree currently serves as the VP of R&D for Flow Forward Medical, an early

stage startup company at the UMass Lowell M2D2 center that is developing various cardiovascular devices. Dr. Loree lives in Littleton, MA along with his wife Ann and (9 year old) daughter Sophie. He would love to network with HST alums and can be reached at www.linkedin.com/in/howardlore or howard.lore@alum.mit.edu.

Bob Vonderheide, MD '93, developed a new clinical strategy for pancreatic cancer treatment published in Science in March 2011, based on translational research (lab and clinic). Read the full story in Nature magazine: <http://www.nature.com/news/2011/110324/full/news.2011.186.html>

Ann Celi (MD 95) and Heidi Wald (MS 92, MD 95) had an HST reunion at the National Zoo in Washington this spring. Ann is HMS faculty at BWH and she was down to visit Heidi in DC as Heidi wraps up a Health and Aging Policy Fellowship and heads back her faculty job at University of Colorado School of Medicine.



Pictured (l to r) Francesca Celi Kitch, Ann Celi, James Celi Kitch, Aviva Weiser, Heidi Wald, Samuel Weiser, and Madeline Celi Kitch.

Mark Fleming, MD '93 is the new Chair of Pathology at Children's Hospital and S. Burt Wolbach Professor of Pathology at Harvard Medical School.

Priscilla Jennings Slanetz, MD '91 is now the Program Director for the residency in diagnostic radiology at Beth Israel Deaconess Medical Center, Boston, MA. In addition, she was recently was awarded the Association of University Radiologists Research and Education Foundation 2011 Ethics and Professionalism Grant to undertake a project entitled, "Integrating reflective practice into radiology residency: a tool to teach professionalism"

Congratulations to **Rebecca R. Richards-Kortum, MEMP '90**, and her family who recently adopted a beautiful baby girl named Margaret.



The Kortum Family

2000s

Arnold Seto, MD, MPA '01, recently joined the faculty at the University of California, Irvine and Long Beach VA Medical Centers as Assistant Clinical Professor, and Director of Interventional Cardiology Research.

Jorge Conde, BEP '06, co-founded a company with **Dr. George Church** to sequence genomes. The company, called Knome, was recently mentioned in an article in the Boston Globe. Read more [here...](#)

Atul Butte, MD, PhD '04, MS '02 is recognized by the National Human Genome Research Institute for having the Genomic Advance of the Month for two papers published in September. The closely related studies, simultaneously published online Aug. 17 in Science Translational Medicine, describe the Butte team's mining of public gene-expression databases using an "opposites attract" algorithm that "pairs old drugs with new indications." Dr. Butte received tenure at Stanford University and was also made a new division chief of Systems Medicine at Stanford.

Aaron Cypess, CITP '08 was recently promoted to Assistant Professor of Medicine at Harvard Medical School. He is also now an Assistant Investigator at Joslin Diabetes Center, where he studies human brown and white adipose tissue physiology at Joslin Diabetes Center.

The Connector

newsletter for graduates, students, faculty and friends of HST



Save the Date:

HST Forum:

Date: April 19, 2012

Time: 2:00 - 7:00pm

Location: TMEC Atrium & Amphitheater,
Harvard Medical School

HST Graduation:

Date: May 25, 2012

Time: 3:00 - 6:00 pm

Location: MIT Media Lab (E14)

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 address or email below.

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