

## Center for Environmental Health Sciences

The overriding goal of the Center for Environmental Health Sciences (CEHS) continues to be the study of the biological effects of exposure to environmental agents, so that we may better understand and predict how such exposures affect human health. Three fundamental components influence the physiological effects of environmental exposures: the nature of the exposure, the duration of that exposure, and how well the exposed organism is equipped to deal with the exposure—in other words, the organism’s genetic susceptibility. Environmental health research at MIT encompasses a wide range of disciplines, and CEHS continues to bring together faculty members who employ a diverse set of research tools to tackle problems relevant to environmental health sciences. During the last several years, CEHS has begun to include focused efforts on problems of particular relevance to the developing world, along with adding more human population-based studies.

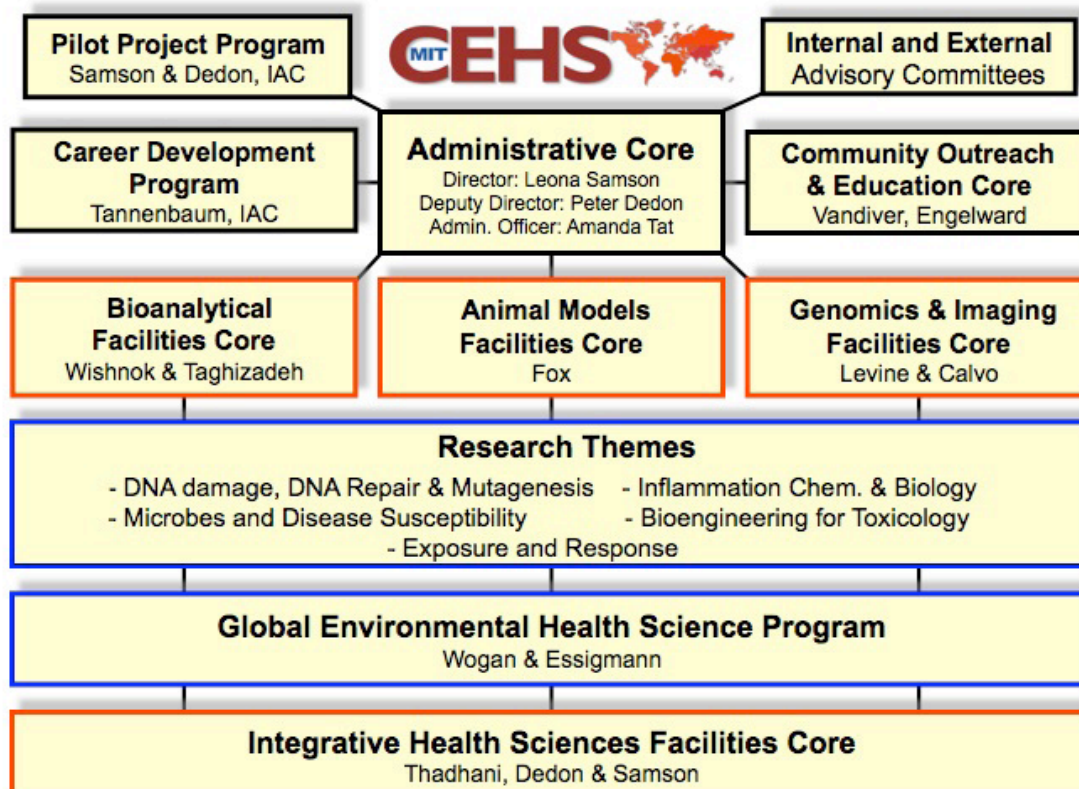
### Organization

The past year has seen significant changes in CEHS’s organization. The new organization is composed of an administrative core, the Community Outreach and Education Core (COEC), the Pilot Project and Career Development programs, the Global Environmental Health Sciences Program, and four facilities cores, including a mandatory Integrative Health Science Facilities Core. Formal research cores are no longer required. This new organization fulfills the requirements of the National Institute of Environmental Health Sciences (NIEHS), our sponsoring agency.

The center’s membership currently consists of 35 faculty, scientists, and engineers, of whom 32 are from MIT and three are from Harvard University (professors David Hunter, Jiali Han, and Ravi Thadhani). In addition, the center has one senior research scientist and three principal research scientists. The members of the administrative core, which is charged with the center’s overall operation, include professor Leona D. Samson, director; professor Peter C. Dedon, deputy director; Amanda Tat, administrative officer; Sophea Chan Diaz, financial coordinator; Julie Hammond Coiro, administrative assistant; and Peter Kemble, information technology technical specialist. COEC, which emphasizes K–12 education for teachers and students as well as adult and community outreach through the Museum of Science and the MIT Museum, is responsible for all CEHS outreach activities. COEC is administered by Dr. Kathleen Vandiver, director; professor Bevin Engelward, codirector; and Amy Fitzgerald, outreach coordinator.

Based on the recent reorganization, research in CEHS is grouped into research themes (rather than the previous research cores) that build on the strengths of the center’s membership. These research themes are as follows:

- DNA Damage, DNA Repair, and Mutagenesis
- Microbes and Disease Susceptibility
- Inflammation Chemistry and Biology
- Bioengineering for Toxicology
- Exposure and Response



CEHS continues a long tradition of providing its membership with state-of-the-art facilities cores that reflect the center's research directions. CEHS researchers use these facilities cores heavily, with each core contributing to the research of the laboratories of at least 10 center members. Under the direction of Drs. John "Pete" Wishnok and Koli Taghizadeh, the Bioanalytical Facilities Core provides center members with the latest tools, techniques, and expertise in the characterization and quantification of chemical substances and modifications of cellular molecules such as DNA and protein, as well as sophisticated proteomics and metabolomics research capabilities. This facilities core operates as a resource for the center and provides training for students and postdoctoral scholars to become proficient in mass spectrometry analysis. Under the direction of Drs. Stuart Levine and Jennifer Calvo, the Genomics and Imaging Facilities Core provides center members with both a variety of sophisticated quantitative imaging technologies and an integrated facility for microarray fabrication and analysis, database storage, database management, data mining, and modeling. These tools are critical to the goal of moving the CEHS research to higher levels of complexity in an attempt to understand the response of the organism to environmental influences at the systems level.

The Animal Models Facilities Core, directed by professor James Fox, provides center members with the latest technology for the application of animal models to environmental health research, including the generation of genetically engineered mice, embryo rederivation of imported mice, colony management, and preparation and interpretation of murine tissue by histological and image analysis.

Under the direction of professors Ravi Thadhani (MIT Clinical Research Center), Peter C. Dedon, and Leona Samson, the Integrative Health Science Facilities Core was recently

developed to help center members translate their research activities into clinical and epidemiological realms. This effort involved formalizing a relationship between CEHS and the MIT Clinical Research Center to develop a facilities core that will provide services to CEHS members involved in human health research, particularly studies with clinical human samples, clinical research, and statistics for human population-based studies and other activities.

Another major program in CEHS is the Global Environmental Health Sciences Program, led by professors Gerald Wogan (director) and John Essigmann (codirector). This program focuses on developing collaborative relationships between CEHS members and international researchers in environmental health, as well as on developing research training and education exchange programs for graduate students and postdoctoral scholars. Our global efforts thus far extend to Thailand and Singapore.

Finally, the center will enhance its long-standing and successful support of pilot projects by initiating efforts to foster career development activities in CEHS. The Career Development Program, directed by professor Steven R. Tannenbaum, focuses on promoting the career aspirations of young scientists and engineers, as well as providing new research opportunities for senior investigators who bring novel technologies and approaches to bear on CEHS research themes. The program's specific aims are as follows:

- attract and engage students, postdoctoral scientists, untenured faculty (junior investigators), and senior investigators in environmental health sciences and toxicology research and training
- provide mentorship and professional development for junior investigators
- promote research collaborations between junior and senior investigators and CEHS members
- facilitate cross training of CEHS investigators in new techniques and technologies
- provide financial support for junior investigators to establish environmental health sciences research programs
- promote career development in environmental health sciences research for young scientists in the Global Environmental Health Sciences Program

The center will continue the Pilot Project Program, overseen by the center director and the deputy director. This program has the following specific goals:

- provide initial support for junior investigators to establish new lines of research in environmental health sciences and toxicology
- allow exploration of innovative new directions representing a significant departure from ongoing funded research for established investigators in environmental health sciences and toxicology
- stimulate investigators from other areas of endeavor to apply their expertise to environmental health research
- promote the development of novel COEC activities arising directly from the research of center members

The center will establish a new Translational Pilot Project Program, which is separate from the regular Pilot Project Program just mentioned. While we plan to encourage CEHS members and others to submit translational research projects for funding through the regular Pilot Project Program, we believe that it is important as well to target translational research opportunities by providing funds to be used exclusively for translational research.

### **Accomplishments in 2008–2009**

CEHS has maintained a strong volume of research support, totaling over \$8.2 million in AY2009. These research programs are funded through a variety of sources, including the National Cancer Institute, the Department of Energy, industrial sponsors, and NIEHS.

With the continued funding from our NIEHS center grant, we were able to provide support for a number of pilot projects in 2008–2009. Pilot project funding allows for the conduct of novel research activities that use multidisciplinary approaches to the study of environmental health sciences. During the center's 2008–2009 grant cycle, we were able to fund six pilot projects and one out-of-cycle translational pilot project. Investigators and their pilot projects supported during this period include the following.

April 2008–March 2009

- Peter C. Dedon (professor, Biological Engineering [BE]), Changes in the Spectrum of tRNA Secondary Modifications as Biomarkers of Exposure
- Catherine Drennan (professor, Chemistry), Structural Studies of DNA Repair Protein Human Alkyladenine Glycosylase
- Susan Erdman (principal research scientist, Division of Comparative Medicine), Inflammation-Associated Prostate Cancer: Development of Mouse Models for Assay for Environmental Contaminants
- Jongyoon Han (associate professor, Electrical Engineering and Computer Science [EECS] and BE), Direct Coupling of Nanofluidic Preconcentration Systems and Conventional Mass Spectrometry
- Michael Strano (associate professor, Chemical Engineering), Steven Tannenbaum (professor, BE), and Gerald Wogan (professor, BE), Detection of Toxic Events in the Liver in vivo Using Single Wall Carbon Nanotubes
- Bruce Tidor (professor, EECS/BE), Exploring DNA Damage Response Networks with High-Dimensional Information Theoretic Statistics

January 2009–March 2010 (out-of-cycle translational pilot project)

- Leona Samson (professor, BE and Biology), A Clinical Study of Base Excision Repair Activity, Genetic Polymorphisms and Chronic Inflammation

Through our center grant funding, we continue to support COEC, which promotes community-level scientific literacy through a variety of programs targeted toward students and their teachers from the fourth grade through the undergraduate curriculum. We also continue to provide faculty with outreach resources for the

facilities cores. One of the goals of the COEC program is to create opportunities for MIT academics to participate in public health education.

COEC continues to run highly successful activities on campus: the two-day summer workshop on environmental health science research for teachers in July and the classroom instruction sessions at the Edgerton Center for students on environmental health topics such as cell division and groundwater. In addition, the creation of a new exhibit at the MIT Museum called *The Cell* has reached classrooms as well as families from the local community. COEC also contributes a program called “A Closer Look at Exposures” to general audiences at the annual Cambridge Science Festival in collaboration with the Harvard School of Public Health.

A major highlight of the center’s activities in 2008–2009 was the sixth annual CEHS Poster Session. This event attracted over 100 participants comprising CEHS members, students, postdoctoral scholars, scientists, and staff, as well as other MIT faculty members, presenting more than 50 scientific posters in an afternoon session at MIT. This year the Myriam Marcelle Znaty Research Fund sponsored cash prizes to poster participants for first- and second-place winners in both categories.

Graduate student winners:

- The first prize (a two-way tie) of \$300 was awarded to Shao-shan Carol Huang, a graduate student in the Fraenkel lab, who presented “A Steiner Tree Algorithm Reveals Hidden Components of Signaling and Regulatory Networks,” and Mary Ellen Wiltrout, a graduate student in the Walker lab, who presented her work on “The Lesion Specificity of Rev1’s Catalytic Activity in vivo.”
- The third prize of a CEHS T-shirt, mug, and lanyard was awarded to Chandni Valiathan, a graduate student in the Samson lab, who presented her work on “Gene Expression Signatures Characteristic of Cell Sensitivity to DNA Damaging Agents.”

Postdoctoral scholar winners:

- The first prize of \$500 was awarded to Dragon Fu, a postdoctoral fellow in the Samson lab, who presented his work on “Discovery of Novel Repair Substrates and Functions for the Human AlkB Bioxygenases.”
- The second prize of \$100 was awarded to Wan Simon Chan, a postdoctoral associate in the Dedon lab, who presented “Quantification of 2-deoxyribose Oxidation Products in Oxidized DNA by Gas Chromatography-mass Spectrometry.”
- The third prize of a CEHS T-shirt, mug, and lanyard was awarded to Charles Knutson, a postdoctoral associate in the Tannenbaum lab, who presented his work on “Transnitrosation of Thioredoxin by S-nitrosoglutathione in vitro.”

The CEHS Poster Session has become an annual event that receives overwhelmingly positive feedback in terms of promoting scientific exchange and collaborations, as well as introducing CEHS to the broader MIT community. An abstract book was published and is available on the CEHS website for viewing.

The 2008–2009 year included several enhancements to the CEHS facilities cores. The Genomics and Imaging Facilities Core acquired a Te-VacS system for pipetting platforms designed to fully automate cartridge-based filtration and/or solid phase extraction processes as well as a Thinkmate XA16-2300 high-capacity storage server. In addition, CEHS partially supported the purchase of a high-throughput Illumina Genome Analyzer sequencing system, which is an integrated platform that uses massively parallel sequencing-by-synthesis technology to generate billions of bases of high-quality DNA sequences per run for genetic analysis and functional genomics. Furthermore, we upgraded the lens on the CompuCyte microscope to high lens resolution to allow scanning images of  $\pm 0.50$  microns per lines. The Animal Models Facilities Core acquired an Olympus BX41 Dual Headed Microscope as well as a Leica EG1150 modular tissue embedding system.

The Bioanalytical Facilities Core has made several important additions or upgrades that provide enhanced performance and increased sample throughput. These include replacement of one of our Agilent 6410 tandem quadrupole mass spectrometers with the newer and more sensitive 6130 model and upgrades of the Agilent MassHunter workstations and software to the most recent versions. A refurbished Applied Biosystems QSTAR Elite quadrupole time-of-flight mass spectrometer was purchased to replace the QSTAR XL in 56-747, which was then moved to the Bioanalytical Core laboratory in NE47-290. The QSTAR Elite has been equipped with a nanoflow pump/autosampler/desalter system that now allows automated sample runs for increased throughput at low femtomole levels for protein digests. We also purchased an Agilent nano LC pump for the Agilent QTOF system in NE47-290 to provide increased sensitivity for proteomics experiments. The ABS Protein Pilot software for proteomics data mining and quantitation has been upgraded to the latest version. We have also acquired an additional chemical-ionization GC-MS instrument that extends our capabilities for analysis of small polar molecules, including DNA- and protein-damage products. We have submitted a proposal to the National Institutes of Health Share Instrumentation Grant Program to obtain an Agilent Ion Trap mass spectrometer for analysis of proteins, peptides, and oligomers and especially for  $MS^n$  experiments focusing on structural elucidation of unknown compounds.

### **Plans for 2009–2010**

The reorganization of CEHS is now complete, and the plans for 2009–2010 are to fully implement the changes in terms of center member participation in the Global Environmental Health Sciences Program, the Career Development Program, the Integrative Health Science Facilities Core, and the newly organized Genomics and Imaging Facilities Core, in addition to the continued successful operation of COEC and the other facilities cores. Activities in the Global Environmental Health Sciences Program will increase with the initiation of a program to host Thai graduate students in CEHS member laboratories for periods of three months to one year as part of ongoing collaborations with the Chulabhorn Research Institute in Bangkok. The Integrative Health Science Facilities Core will begin considering applications for translational pilot projects in the coming year and will continue to provide center members with guidance on moving their research activities toward biological and clinical applications. The Career Development Program will initiate formal mentoring activities for junior

members of the center that will complement departmental mentoring activities and enhance the participation of junior members in center activities. As always, the CEHS leadership will continue efforts to engage the broader MIT community in research activities related to environmental health science.

### **Pilot Project Program**

We anticipate disseminating a call for proposals in September 2009 for funding beginning October 2009, as this would allow us a better understanding of the center's renewal grant funding. It is anticipated that CEHS will provide \$25,000 in direct-cost funding for five novel and innovative research projects related to environmental health issues. Priority will be given to projects that involve collaboration and have a likelihood of subsequent independent funding. We plan to fund one or two translational pilot projects as well.

### **Career Development Program**

The new Career Development Program will initiate several activities, including a program in which junior CEHS faculty members will be mentored by more senior members. Furthermore, we will expand the Friday Forum series to include an annual session on grant-writing skills and a session providing a practical perspective on life in academic research and teaching for young scientists aspiring to careers in academia.

### **Community Outreach and Education Core Activities**

COEC will continue the activities described earlier in conjunction with the staff of the Edgerton Center. These activities include MIT Museum events and teacher workshops. In January 2009, COEC successfully began a new workshop series for health care professionals in collaboration with the MIT Clinical Research Center. As modern medical practice is becoming more molecularly based, nurses need to update their knowledge in basic cell biology and genetics. The two-day program provides continuing education credits for nurses and broadens COEC's target audience.

### **Friday Forum Lecture Series**

CEHS will continue the highly successful Friday Forum lecture series in which center members and CEHS pilot project recipients share their research programs in monthly presentations at an event intended to promote interaction among members and attract new members to the center in an informal social setting.

### **External Advisory Committee**

We will initiate plans for a meeting of the External Advisory Committee depending upon the outcome of the center's competing renewal application, which will be known sometime in the early part of the fall term.

### **Poster Session**

We will continue this successful activity again in 2009–2010.

## **Newsletter**

Our goal is to continue publishing a newsletter twice each year. The spring 2008 and fall 2008 newsletters can be viewed online, while publication of the spring 2009 newsletter is on hold to allow the CEHS leadership to prepare a memorial issue for professor David Schauer; Schauer, a long-standing center member and codirector of the Global Environmental Health Sciences Program, passed away in June of this year. All editions of the newsletter are distributed throughout the MIT community and can also be read online at <http://cehs.mit.edu/News.html>.

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*More information about the Center for Environmental Health Sciences can be found at <http://cehs.mit.edu/>.*