

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 the 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, the CEHS has begun to include focused efforts on problems of particular relevance to the developing world, in addition to adding more human-population based studies.

Organization

The past year has seen significant changes in CEHS's organization. The center has transitioned from a structure comprised of an administrative core, the Community Outreach and Education Core (COEC), the Pilot Project Program, three research cores, and three facilities cores to one that fulfills the new requirements of the National Institute of Environmental Health Sciences, our sponsoring agency. The new CEHS organization is comprised of an administrative core, the COEC, the Pilot Project and Career Development Program, a Global Environmental Health Sciences Program, and four facilities cores, including a mandatory Integrative Health Science Facility Core. Formal research cores are no longer required.

The center's membership currently consists of 31 faculty, scientists, and engineers, of which thirty are from MIT and one is from Harvard University (Professor David Hunter). In addition, the center has one senior research scientist and one principle research scientist, both of whom codirect the center's Bioanalytical Facilities Core. 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 assistant; and Julie Coiro, administrative assistant. The COEC is responsible for all outreach activities of CEHS, 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. The COEC is administered by Dr. Kathleen Vandiver, director; Professor Bevin Engelward, codirector; and Amy Fitzgerald, outreach coordinator.

Until the recent reorganization, research in the CEHS was organized into three research cores that built on the strengths of the center's membership. These were the Mutation and Cancer Research Core, the Bioengineering for Toxicology Research Core, and the Environmental Health Systems Research Core. The theme of each research core derived from the members' research interests, and all were linked by the center's overarching focus on defining how biological systems respond to exposure to environmental agents. The Mutation and Cancer Research Core, directed by Professor Dedon, addressed the

relationships between DNA damage, DNA repair, mutation, and cancer associated with exposure to environmental and endogenous chemical and physical agents. The Bioengineering for Toxicology Research Core, directed by Professor Linda Griffith, was created to facilitate the development of new experimental tools and analysis methods relevant to environmental influences on human health, with a range of approaches spanning the molecular-cellular systems length scales. The mission of the Environmental Health Systems Research Core, directed by Professor David Schauer, was to understand the relationships that link environmental processes and human health in terms of coexposure to chemical and biological agents. This is most aptly illustrated by the synergistic interaction of aflatoxin and hepatitis virus exposures for the induction of human liver cancer.

The CEHS continues a long tradition of providing its membership with state-of-the-art facilities cores that reflect the CEHS's research directions. The 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 doctors 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. As part of the CEHS restructuring, the former Genomics and Bioinformatics Facilities Core (which was directed by Dr. Rebecca Fry, who left MIT to become an assistant professor at the University of North Carolina) has been restructured as the Genomics and Imaging Facilities Core. The CEHS is currently seeking a staff scientist to direct this core. 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 and Pathology 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 leadership of codirectors Dr. Ravi Thadani, MIT Clinical Research Center codirector, and Professor Leona Samson, the Integrated Health Science Facilities Core was recently developed to help center members translate their research activities into the clinical and epidemiological realms. This effort involved formalizing a relationship between the MIT CEHS and the MIT Clinical Research Center to develop a facilities core that will provide services to the CEHS members involved in human health research, particularly with involvement in the studies with clinical human samples, clinical research, and statistics for human population-based studies and other activities.

A second major new program in the CEHS, the Global Environmental Health Sciences Program, led by professors David Schauer and Gerald Wogan, focuses on developing collaborative relationships between CEHS members and international researchers in environmental health, and also 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 CEHS will enhance its long-standing and successful support of pilot projects by initiating efforts to foster career development activities in the CEHS. The new Pilot Project and Career Development Program is led by professors Samson and Dedon and has the following specific goals:

- provide initial support for new investigators to establish environmental health science projects
- allow exploration of possible innovative new directions representing a significant departure for established investigators in environmental health sciences
- promote career development of junior and established investigators by stimulating investigators from other areas of endeavor to apply their expertise to environmental health research
- provide opportunities for training and mentoring of junior faculty in research relevant to environmental health sciences
- promote interactions between junior and established investigators in related disciplines
- promote cross-training of researchers in current techniques that are absent from the CEHS Core center or individual research programs

Accomplishments in 2007–2008

The CEHS has maintained a strong volume of research support, totaling over \$7.7 million in 2007–2008. These research programs are funded through a variety of sources, including the National Institute of General Medical Sciences, the National Cancer Institute, the Department of Energy, the Defense Advanced Research Projects Agency, and the National Institute of Environmental Health Sciences (NIEHS).

With the continued support of our NIEHS Center Grant, we were able to provide support for a number of pilot projects for 2007–2008. 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 2007–2008 grant cycle, we were able to fund five projects for May 2007–April 2008, one out-of-cycle pilot project, and seven pilot projects for April 2008–March 2009. Investigators and the pilot projects supported during this period include the following:

May 2007–April 2008

- Sangeeta Bhatia (associate professor, Health Sciences and Technology [HST] and Electrical Engineering and Computer Science [EECS]), Microscale Engineered Liver Tissues for Evaluating Chronic Toxicity of Environmental Toxicants
- Bevin Engelward (associate professor, Biological Engineering [BE]), Development of a High-Throughput DNA Damage Sensor for Environmental Health Studies
- Jongyoon Han (associate professor, EECS and BE), Monitoring Low-Abundance Enzyme Activity by Preconcentration and Reaction in Micro/Nanofluidic Device
- Douglas A. Lauffenburger (professor, BE), Systems Biology Analysis of Nuclear and Membrane-Initiated Signaling by Endocrine Disrupting Chemicals
- Lisiane Meira (research scientist, CEHS), A Clinical Study of a Base Excision-Repair Activity, Genetic Polymorphisms, and Chronic Inflammation

January 2008–March 2009

- David Schauer (professor, BE), Mechanisms of Resistance Against Oxidative Stress by Enterohepatic *Helicobacter* Species

April 2008–March 2009

- Peter C. Dedon (professor, BE), Changes in the Spectrum of tRNA Secondary Modifications as Biomarkers of Exposure
- Catherine Drennan (associate 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, 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

Through our Center Grant funding, we continue to support the COEC, which promotes community-level scientific literacy through a variety of programs targeted at students and their teachers from grade four through the undergraduate curriculum, as well as to continue to provide faculty with outreach resources for both the research and facilities cores. One of the goals of the COEC is to create opportunities for MIT academics to participate in public health education.

The COEC continues to run three highly successful activities: the after-school sessions in October on environmental health science for Summerbridge Cambridge, an excellent academic program for local middle school students; 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 students and families from the local community, and COEC contributes a program called “A Closer Look at Exposures” to the Cambridge Science Festival.

A major highlight of the center’s activities in 2007–2008 was the fifth annual CEHS Poster Session. This event attracted over 100 participants comprised of CEHS members, students, postdoctoral scholars, scientists, and staff, as well as other MIT faculty members, presenting 42 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:

- First prize of \$500 was awarded to Aarthi Chandrasekaran, a graduate student in the Sasisekharan lab, who presented her work on “Human Adaptation of Avian Influenza A Viruses.”
- Second prize (a two-way tie) of \$100 was awarded to Tsz Yan Clement Chan, a graduate student in the Dedon lab, and to Ericka Noonan, a graduate student in the Samson lab. Mr. Chan presented his work on “Metabolomic Approaches to Characterizing Changes in RNA Secondary Modifications in Cellular Responses to Toxins” and Ms. Noonan presented her work on “Modeling the Cell Decision Process in Responses to the DNA Lesion O⁶Methylguanine.”
- Third prize of a CEHS t-shirt, mug, and lanyard was awarded to Jared Toettcher, a graduate student in the Tidor lab, who presented his work on “p53-Dependent and -Independent Mechanisms Act Synergistically to Mediate Sustained Cell Cycle Arrest.”

Postdoctoral scholar winners:

- First prize of \$500 was awarded to Scott Knudsen, a postdoctoral associate in the Manalis lab, who presented his work on “Determination of Bacterial Antibiotic Resistance using a Suspended Microchannel Resonator.”
- Second prize of \$100 went to Peter Slade, a postdoctoral associate in the Tannenbaum lab. Slade presented his work on “Enhanced Identification of Biotin-derivatized Peptides.”
- Third prize (a two-way tie) of a CEHS t-shirt, mug, and lanyard was awarded to Dragony Fu, a postdoctoral associate, and to Johan Peter Svensson, a postdoctoral fellow, both in the Samson lab. Dr. Fu presented his work on “Exploration of Molecular Repair Pathways Mediated by Human AlkB Dioxygenases” and Dr. Svensson presented his work on “Identifying Novel Human Damage Response Proteins based on Yeast Orthology.”

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 the CEHS to the broader MIT community. An abstract book was published and is available on the CEHS website for viewing.

The 2007–2008 year included several enhancements to the CEHS facilities cores. The Bioanalytical Facilities Core acquired a major new Applied BioSystems QSTAR Elite mass spectrometry system that will greatly benefit the growing center research activities in proteomics and biomarker development. The Genomics and Imaging Facilities Core acquired a new three-laser iCys Research Scanning System with full autofocus to be used by center members for high throughput cell and tissue imaging analysis. Finally, the Animal Models and Pathology Facilities Core acquired the G:BOX Chemi HR16 fluorescence and chemiluminescence range of imaging system. The transgenic facility, a service through the Animal Models and Pathology Facilities Core, continues to offer state-of-the-art services at an affordable price. Over the past year services were expanded to include a full complement of cryogenic services including laser-assisted *in vitro* fertilization. The facility continues to expand and is currently perfecting a technique of vitrification freezing that will allow us to freeze all stages of preimplantation embryos.

Plans for 2008–2009

This past year, the CEHS leadership has actively engaged in strategic planning discussions reflecting both the evolution of the center membership and the new mandates of the NIEHS, which provides the major funding to support the CEHS. There are three major objectives in the strategic planning process. Our current plan is to reorganize the research cores along research themes rather than the current disciplinary lines. This is designed to foster greater interaction among the diverse center membership and bring their various talents to bear on specific biomedical problems, such as inflammation, liver disease, and other human conditions related to environmental exposures. A second major effort is under way to create a new program in global environmental health sciences that focuses on developing collaborative relationships between the CEHS members and international researchers in environmental health, and also on developing research training and education exchange programs for graduate students and postdoctoral scholars. This global effort has begun with strong interactions between the Chulabhorn Research Institute and the MIT CEHS. Finally, the CEHS will also create a new Integrative Human Health Science facilities core to help center members translate their research activities into the clinical and epidemiological realms. This effort, as discussed earlier, required formalizing a relationship between the MIT CEHS and the MIT Clinical Research Center to develop a facilities core. This core will provide services to the CEHS members involved in human health research, particularly those involved in studies with clinical human samples, clinical research, statistics for human population-based studies, and other activities.

In the next year, we will formalize these initiatives as we continue to evaluate the changing needs of the CEHS members, as well as provide an opportunity to recruit new faculty whose research is relevant to the environmental health sciences.

Pilot Projects and Career Development Program

We anticipate disseminating a call for proposals in February 2009 for funding beginning April 2009. It is anticipated that the CEHS will provide \$15,000–\$25,000 in direct costs

funding for five to seven 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.

Community Outreach and Education Core Activities

The COEC will continue the activities described earlier in conjunction with the Edgerton Center staff. These activities include the MIT Museum events, teacher's workshops, and after-school science lessons from Summerbridge Cambridge. Summerbridge provides year-round academic enrichment for middle school children. We plan to begin a new workshop series in collaboration with the MIT Clinical Research Center that will offer continuing education credits for nurses, updating their knowledge in basic cell biology. Modern medical practice is becoming more molecularly based.

Friday Forum

The CEHS will continue the highly successful Friday Forum 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 anticipate sending a draft of the CEHS Core Competitive Renewal Grant to our External Advisory Committee in November 2008 to receive their constructive comments for submission in February 2009.

Poster Session

We will continue this successful activity again in 2008–2009.

Newsletter

Only one edition of the CEHS Newsletter was published this year because of the change in administrative officer from Jacqueline Breen to Amanda Tat. The spring 2008 issue was published in January 2008, highlighting the article "Taking on Global Health Issues: CEHS and Thailand Researchers Identify the Genome-wide Impact of Prenatal Arsenic Exposure in Newborns." All editions of the newsletter were 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/>.