Center for Environmental Health Sciences

Human health is dependent upon our relationship with the environment. The Center for Environmental Health Sciences (CEHS) predicts and elucidates the ways that chemical and biological agents in the environment affect our health, as well as the health of the ecosystem that supports all life. In addition to identifying toxic chemicals and hazardous organisms in our environment, CEHS research develops methods to detect them, shows mechanistically how these agents affect health at the cellular, tissue, individual, and population levels, and helps to create new technologies that allow us to live longer and healthier lives.

The Center acts as a nexus for a diverse group of environmental scientists, engineers, and policy experts from nine departments across the Institute. It brings their collective expertise to bear on both domestic and global environmental threats ranging from industrial pollution to the emergence of new infectious agents. CEHS complements its talented human resource pool with a toolbox of state-of-the-art technologies, thereby making headway on problems too large to be tackled by any individual laboratory. In this way, CEHS promotes partnerships between people and technology, leading to solutions to important environmental problems. CEHS comprises approximately 38 laboratories with various areas of expertise. However, the labs most in alignment with CEHS's mission share the following values:

- Knowledge of the chemistry and transport of pollutants in soil, water, and the atmosphere
- Knowledge of the pathways by which cells and organisms respond to toxic agents in the environment (reflected by expertise in DNA damage and repair, genomic instability, proteomics, metabolomics, and gene expression analysis)
- Knowledge of the ways in which microbes (as individual agents or collectively as microbiomes) affect health and disease
- Knowledge of the roles that the immune system and inflammation play as promoters of many environmental diseases
- Knowledge of bioengineered cellular, tissue, and whole-organism systems that enable next-generation testing of environmental hazards and development of disease-prevention strategies
- Creation of technologies that enable physical detection of contaminants and analysis of biological processes relevant to environmental health

Organization

CEHS is funded primarily by the National Institute of Environmental Health Sciences (NIEHS)—of the National Institutes of Health (NIH)—as one of the 22 Center Core grant recipients focusing on environmental health. Fulfilling the requirements of the NIEHS, the CEHS is composed of an administrative core, a community outreach education and engagement core (COE²C), a career development program, a pilot project program

(including both basic and translational pilot projects), and a global environmental health sciences program. In addition, the CEHS has four research facilities cores, including a mandated integrative health sciences facilities core, which provides an interface with the local medical community.

The center's membership currently consists of 40 science and engineering faculty and four professional full-time senior researchers. Forty-three members are from MIT and one is from the University of Oxford in the United Kingdom (David Hunter, professor of epidemiology and medicine). Of the MIT members, the center has one senior research scientist and one principal research scientist. The director of CEHS and a member of the administrative core, which is charged with the center's overall operation, is John M. Essigmann, the William R. and Betsy P. Leitch Professor in Residence of Chemistry in the Department of Chemistry and professor of toxicology and biological engineering in the Department of Biological Engineering. Members of the administrative core also include Professor Bevin P. Engelward, deputy director; Amanda Tat, administrative officer; Sophea Chan Diaz, fiscal officer; Kimberly J. Bond Schaefer, administrative assistant; Gianna Hernandez-Figueroa, events and administrative assistant; and Tobias Novak, financial assistant. The community outreach education and engagement core helps communities avoid exposures to environmental hazards that can adversely affect public health. In this broad mission, COE²C partners with three MIT departments: the MIT Museum to reach the general public, the Edgerton Center to reach students and teachers, and the MIT Clinical Research Center to reach healthcare professionals. The COE²C is led by Kathleen Vandiver and Professor Engelward, with support from Amy Fitzgerald and Amanda Gruhl.

CEHS continues a long tradition of providing its membership with excellent research facilities that reflect, nurture, and support the center's research directions. CEHS researchers use four facilities cores, each of which contribute to the research efforts of at least 10 center members. The cores include the animal models facilities core (AMFC), the bioimaging and chemical analysis facilities core (BCAFC), the genomics facilities core, and the integrative health sciences facilities core(IHSFC).

The decision was made last year by the CEHS Internal Advisory Committee to consolidate the important but financially challenged bioanalytical core with our imaging core and to reach out to other departments at MIT to share costs, help jointly manage the combined cores, and expand CEHS's user base. This reorganization occurred in the first quarter of 2017 under the leadership of Professors Peter Dedon, Bevin Engelward, and John Essigmann. Drs. Michael DeMott, Stephen Slocum, and Robert Croy are assisting them temporarily in the management of this new core, the bioimaging and chemical analysis facilties core. This is a significant revision to the structure of our center, but it is one that we believe is practical and will foster collaborations with other departments. The bioimaging and chemical analysis facilties core provides center members with the latest tools, techniques, and expertise in the characterization and quantification of almost any molecule in a biological system—including modifications of cellular molecules such as DNA, RNA, and protein—as well as state-of-the-art proteomics and metabolomics research capabilities. In addition, this core offers a variety of sophisticated quantitative imaging technologies. It operates as a resource for the center, as well as for

all of MIT, and provides invaluable training for students and postdoctoral scholars to become proficient in biological mass spectrometry, other modern analytical methods, and sophisticated imaging tools. With the new Thermo Fisher Q Exactive Hybrid Quadrupole-Orbitrap mass spectrometer in operation, a proteomics add-on functionality was critical to perform proteomic analysis to assess changes in metabolic networks. Therefore, with the joint support of the Departments of Biological Engineering and Chemistry, CEHS was able to recently purchase a refurbished Thermo Fisher EASY-nLC 1000 Liquid Chromatography system which provides effortless nanoflow ultra-high performance liquid chromatography. We expect this proteomics add-on capability to be fully functional by the fall. This instrument enhances our ability to do proteomics and small molecule drug and foreign compound metabolism studies. In addition, as a costcontrol measure for the entire facility, CEHS purchased a liquid nitrogen generator the cost of which will be fully recovered within two to three years. This device will significantly reduce the amount of liquid nitrogen needed to run the instruments in the core. As an additional cost-control measure, we have agreed to partner with the Department of Chemistry by sharing a research scientist who will manage the BCAFC. This collaboration was enthusiastically embraced by both administrative units.

In parallel with the consolidation of our bioanalytical and imaging assets, the Genomics and Imaging Facilities Core was also restructured. Because genomics and informatics have been growing rapidly at MIT and elsewhere, we are reconfiguring our genomics operation as a stand-alone unit under the leadership of Stuart Levine. This core, renamed the genomics facilities core, provides center members with an integrated facility for transcriptomics, next generation sequencing capabilities, data storage, database management, and data mining and modeling. It overlaps with our animal models and integrative health sciences facilities cores in providing a biostatistics support unit for CEHS. These physical, computational, and statistical tools are critical to the goal of moving center research efforts to higher levels of sophistication in our attempt to understand the response of the whole organism to environmental agents. In an effort to expand on next generation sequencing capabilities, CEHS purchased a new DNA fragment analysis instrument from Advanced Analytical Technologies, Inc. (AATI). The FEMTO *Pulse* is a brand-new instrument that provides a remarkable upgrade over the existing AATI Fragment Analyzer and Agilent BioAnalyzer technologies that have been in use in CEHS for many years. The FEMTO *Pulse* adds a pulse field generator to allow the capillary electrophoretic separation and characterization of significantly longer molecules, out to 200,000 base pairs of DNA. Additionally, the FEMTO Pulse has significantly improved optics that allow several orders of magnitude of additional sensitivity. While the AATI Fragment Analyzer bottoms out at a sensitivity of 2-3 pg/ μ L, the FEMTO *Pulse* has nearly 1,000x improved sensitivity, which may enable this instrument to directly observe molecular reactions without the need for amplification or modification with radioactive nucleotides. With the purchase of this new instrument, CEHS members will be able to efficiently prepare DNA fragments for next generation DNA sequencing.

The animal models facilities core, directed by Professor James G. Fox, provides center members with the latest technologies 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 tissues by histological and image analysis. The animal models facilities core maintains cutting-edge technology, including the rapid production of mouse mutants using CRISPR/Cas9.

The integrative health sciences facilities core is led by Professors Michael Yaffe and James Fox with the support of Dr. Catherine Ricciardi, the Hospital Liaison Program director, along with a cohort of clinical and translational consultants. Dr. Ricciardi will continue to have day-to-day management responsibility for the IHSFC, but Professors Yaffe (a practicing physician-scientist) and Fox (a doctor of veterinary medicine, and director of the Division of Comparative Medicine) have faculty-level responsibility for human and animal translational studies, respectively. Dr. Ricciardi is an expert in the preparation of institutional review board proposals for the use of human subjects in experimentation. She is also our liaison to the Harvard Catalyst network of clinical experts and the Harvard-MIT Program in Health Sciences and Technology. The IHSFC was developed to help CEHS members translate their research activities for the clinical and epidemiological realms. This reorganization in 2016 involved formalizing a relationship between CEHS and the MIT Clinical Research Center to develop a facilities core that would provide services to CEHS members involved in human health research, particularly studies with human clinical samples, clinical trials, and statistics for human population-based studies and other activities.

Another major CEHS program is the Global Environmental Health Sciences Program, co-led by John Essigmann and Peter Dedon. 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 at present focus on Thailand, Singapore, and South America.

CEHS has a long-standing commitment to fostering the careers of its young scientists and junior faculty. The Career Development Program, directed by Bevin Engelward, provides a broad range of opportunities for the advancement of its members at all stages of their careers. From research resources to career coaching to global opportunities for outreach, CEHS provides resources that promote success and enable community engagement in environmental health. These types of opportunities and resources are as follows:

- Mentoring
- Financial and administrative support
- Research resources
- Speaking opportunities for junior faculty
- New Frontiers Transition Seminar series for postdocs
- Translational research support
- Engagement opportunities

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- Global program in public health
- Responsible conduct of research training

The center continues its successful and popular NIH and privately funded Pilot Project Program, which is overseen by the center director and deputy director, along with the Internal Advisory Committee. This program provides initial support for early-stage investigators and support for senior investigators who wish to establish new lines of research in environmental health sciences and toxicology. The program also motivates investigators from other fields of research to apply their expertise to environmental health research and promotes the development of novel COE²C activities arising directly from the research of our center members.

Finally, the Translational Pilot Project Program, which is an offshoot of the regular Pilot Project Program, was created to encourage CEHS members and others to pursue translational research in which fundamental research activities are moved progressively from cell-based systems to animal models and ultimately into human epidemiological and clinical application. The importance of this type of research warrants special funding outside of the regular Pilot Project Program. The joint partnership established in 2015, the Translational Pilot Project Program has partnered with the Theron G. Randolph Translational Pilot Project gift to encourage investigators to take basic environmental health research to the translational level, especially in the areas that connect environmental exposures to allergy and immunity. A gift from Ms. Vilma Kinney has enabled this new direction for the CEHS. The current Theron G. Randolph Translational Pilot Project was awarded in 2016 to Professor Elizabeth Nolan.

Accomplishments

Accomplishments this past year include the reorganization and expansion of the equipment of the facilities cores, the establishment of a new NIEHS Superfund Research Center; hosting the External Advisory Committee meeting in January 2017; and the modernization of the CEHS newsletter to a web-based format. CEHS has maintained a strong volume of research support, totaling over \$9.7 million in FY2017 and resulting in at least 279 publications. These research projects are funded through a variety of sources, including the National Institutes of Health, the National Science Foundation, the Department of Defense, the Food and Drug Administration, the Singapore-MIT Alliance for Research and Technology, and various foundations and industries. Our institutional Training Grant in Toxicology, now in its 43rd year, reflects the broadening of CEHS to include many faculty members (mainly engineers) from outside of the Department of Biological Engineering. The training grant now supports pre and postdoctoral trainees in many disciplines and has fostered interdisciplinary research. To keep the training grant grounded in the field of toxicology, Professors John Essigmann and John Groopman (visiting professor from Johns Hopkins University) taught an intensive course during MIT's Independent Activities Period titled Fundamentals of Environmental Toxicology (20.S949).

A strength of CEHS is its ability to integrate with other organizations on campus, including departments with shared interests. As indicated above, CEHS has been

awarded a center grant under the Superfund Research Program. The leaders of this program are Professors Engelward and Essigmann. Additionally, Kathleen Vandiver played a critical role by making connections to stakeholders in nearby communities in Massachusetts and Maine. An important strength of the funded Superfund Research Program is its focus on alkylating agents and polycyclic aromatic hydrocarbons, which are chemicals in our environment that can cause mutations and cancer. Within the program, there are five research projects, each with multiple investigators from seven departments (Earth Atmospheric and Planetary Sciences; Institute for Data, Systems, and Society; Civil and Environmental Engineering; Chemical Engineering; Chemistry; Biological Engineering; and Biology). The projects focus on water pollution, air pollution, genetic susceptibility factors for disease, mutational spectrometry, and complex systems-level responses to exposures. Further, there are four cores that support key aspects that are shared by all of the projects. The foci of these four cores are administrative, research translation, community engagement, and training. In addition, the preparation of the proposal brought 11 CEHS members together and thus has fostered new collaborations and research aimed at problems in environmental health. A key aspect of the program that was critical to it being funded was the coming together of research leaders to focus on specific contaminants and to develop meaningful and lasting collaborations. All of the research projects benefit from all of the cores, making this a highly cohesive program. Finally, all members of the Superfund Research Program are also CEHS members, making this new program a great asset to CEHS.

Community Outreach Education and Engagement Core

The National Institutes of Environmental Health Sciences mandates each core center to have community engagement programs to improve environmental health. The goal is to develop partnerships with community members by working together on local environmental health challenges, translating and disseminating the center's research science, disseminating methods of public engagement at local and national levels, and evaluating and promoting models for national implementation. Our COE²C focuses on engagement to underserved populations that are designated as environmental justice (EJ) communities; innovative technologies for conveying to children and lay people key concepts relevant to environmental health; and workshops that serve key members of our community by teaching about environmental health.

MIT COE²C has chosen to serve two regions in New England. The first is the Mystic River watershed, which flows through 22 Boston-area communities and includes immigrant populations and EJ communities along the Malden River—a tributary of the Mystic River. The second regional focus is on Native Americans living on tribal lands in northern Maine. Our challenge is how best to inform, advise, listen to, and work with partner organizations within these communities to mitigate the human health effects of industrial pollution and unhealthy lifestyles. To meet this challenge, COE²C annually travels to tribal lands in Maine to listen to and talk with tribal environmental officers. These visits have increased our understanding of the issues facing indigenous peoples. This dialogue along with our invited annual participation at the Environmental Protection Agency (EPA) Region 1 Tribal Environmental Summit, hosted by the Mashpee Wampanoag tribe this past year, has helped to establish a strong working relationship. Dr. Vandiver has also shared science curricula for American Indian youth, collaborating with tribal earth camp educators and science teachers in the Maine Indian Education schools again this year.

In Massachusetts, COE²C has provided timely leadership to the communities of Malden, Everett, and Medford via the Mystic River Watershed Association (MyRWA) and its sister organization, the Friends of the Malden River. COE²C recognizes the need for public access to clean water and open green spaces to promote healthy living for all. To broaden participation and gather public comment on river greenway design, the COE²C encouraged EJ community groups such as the Chinese Culture Connection, providing informational sessions and inviting Chinese translators to attend. This past year, the MyRWA spearheaded a major greenway planning effort to create public access, walking paths, and park amenities along the length of the Malden River. The river's edge is currently inaccessible and lined primarily by commercial parking lots. Along with other community partners, MIT is assisting in the production a human health risk study for the Malden River. This research report will provide the local municipalities with the information needed to make objective decisions for the river's potential recreational use.

In the education field, COE²C has continued to make strides in disseminating innovative teaching tools for molecular biology, funded in part by a generous grant from the J. M. R. Barker Foundation. In March 2017, working together with the MIT Edgerton Center, COE²C delivered 14 DNA and protein classroom sets to 14 of the 34 Boston Public High Schools. The remainder of the schools will receive sets after their teachers participate in the required teacher training workshop this fall. Overall, educators find that the DNA and protein sets make learning the key concepts in science, technology, engineering, and math intuitive and memorable. COE²C continues to lead workshops both nationally and internationally to support teachers while working to create the necessary online instructional materials required for the anticipated global distribution. A second US patent was issued this year for amino acids with their transport molecule tRNA, thanks to the MIT Technology Licensing Office. The US design patents were issued last year for the MIT DNA nucleotide models.

COE²C continues to participate in science festivals designed for the general public, such as the annual Cambridge Science Festival and the American Lung Association's annual Lung Force Walk on the Boston Common. Last October, COE²C was tapped to contribute to MIT's Better World Campaign event in New York City, where alumni and guests enjoyed building DNA helices with our model sets. We have been invited to bring this unique, hands-on display back to the campaign event in Boston this fall. In summary, we have successfully reached out to hundreds of people with our educational tools, using innovative CEHS-supported technologies that teach about the impact of our environment on health, about air pollution, and climate change.

Annual Poster Session

For the 13th consecutive year, the center offered its popular CEHS Poster Session in January 2017. This event has attracted more than 100 participants, including CEHS members, faculty, students, postdoctoral scholars, scientists, and staff. The Myriam Marcelle Znaty Research Fund, administered by Professor Steven Tannenbaum, continues to sponsor the cash prizes for the best poster presentations in both graduate student and postdoctoral scholar categories. The poster session receives overwhelmingly positive feedback in terms of promoting scientific exchange and collaborations, as well as introducing CEHS to the broader MIT community.

Lecture Series

In the past year, the center hosted five Friday Forum lectures. This long-standing series of informal research seminars is one of the most popular CEHS-sponsored events and has stimulated significant collaboration in environmental health research with new center members. New center members, potential members, and Pilot Project–award recipients gave presentations. The format of the seminar series includes opportunities for socializing and mingling both before and after the seminar, which have been a constant source of novel scientific collaborations.

The second CEHS-sponsored monthly seminar series is the Boston DNA Repair and Mutagenesis (DRAM) Seminar Series. For many years, the DRAM seminars have brought together scientists from institutions throughout New England who share an interest in the mechanisms of genome maintenance and the consequences of mutations in humans and model organisms. This seminar series draws students, postdocs, and faculty from Boston University, Brown University, Harvard University, Northeastern University, Tufts University, Yale University, and the University of Massachusetts Medical School in Worcester.

In addition, the center has continued to offer the New Frontiers Postdoctoral Transition Seminar Series for postdocs transitioning into the workforce. The center recognizes the importance of providing a seminar for job interviews, and this seminar series is specifically aimed at providing postdocs with the opportunity to give and receive feedback on their job talk. Talks are advertised to the entire CEHS community, which allows for questions and advice to help in preparation for potential job interviews. Following the presentation, there is a private meeting between faculty members and the postdoc speaker with detailed feedback about speaking strategy, organization, and clarity. This format provides valuable information for postdocs, enabling them to hone their presentations in preparation for a competitive job market.

The center also continues to co-sponsor three named lectureships with the Department of Biological Engineering: the Robert S. Harris, Gerald N. Wogan, and David B. Schauer Lectures. Nobel Laureate and MIT alumnus Paul Modrich presented the Gerald N. Wogan Lectur, "*Mechanisms in Human DNA Mismatch Repair*" on November 17, 2016. Professor Leona Samson presented the Robert S. Harris Lecture "Biological Responses to Inflammation and Alkylation" on May 18, 2017. Dr. Julie Gerberding is scheduled to present the David B. Schauer Lecture in September 2017.

Future Plans

In the upcoming year, the CEHS leadership will be actively engaged in strategic planning discussions to reflect both the evolution of the center's leadership, membership, and organizational chart. We are planning a retreat (likely in the spring) and poster session (scheduled for April 2018). The CEHS director and the deputy director will focus on the goals for AY2018, which are (1) to reassess the

center membership, with the specific goal of attracting additional junior faculty and help foster relationships between scientists and engineers; (2) to stimulate center members' participation in the Global Environmental Health Sciences Program (since environmental pollution ignores geopolitical boundaries and the diseases of the developing world indirectly impact the United States); (3) to reexamine the Career Development Program and the integrative health sciences facilities core to make sure they are fully in concert with best practices in our field; (4) to continue our dialogue with members of the External Advisory Committee; (5) to continue to make use of the community outreach education and engagement core to showcase to our community some of the exceptional research performed by center members; and (6) to continue to assess the temporary management of the Bioimaging and chemical analysis facilities core to develop a permanent management plan for financial sustainability. As always, the CEHS leadership will continue efforts to engage the broader MIT community, including the Environmental Solutions Initiative and the MIT Energy Initiative, in research activities related to environmental health sciences.

With the newly funded NIEHS Superfund Research Program, CEHS plans to significantly expand activities and seminars to incorporate a separate focus specifically for this program. This program also includes work with American Indian communities in northern Maine and community work with various populations in the Boston area.

An EPA grant under center member Jesse Kroll includes a COE²C component, but the anticipated community work for this project was postponed by one year. The goal of this project is to build an air sensor network to monitor volcanic emissions on the Big Island of Hawaii. In January 2018, the team will begin to place sensor nodes in school community gardens throughout the island. COE²C's role will be to provide teacher training workshops for the science kits designed to teach about climate change and air pollution at the participating schools. The teacher workshop is scheduled to occur in late June 2018 and we look forward to working with Hawaiian Pacific Islanders alongside our local partner organization, The Kohala Center.

With regard to our global research efforts, CEHS will continue ongoing collaboration with the Chulabhorn Research Institute in Bangkok, which has been a developing world hub for environmental health research and training for many years. In addition, several center members have laboratories and strong commitments in Singapore, which is the locus of much of CEHS's research in the infectious disease arena. International partnerships give us access to populations, which is critical to our translational mission.

John M. Essigmann Director Professor of Biological Engineering and Chemistry

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