

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 cell, tissue, individual, and population levels; and helps to create new technologies that allow us to live longer and healthier lives. As a federally funded center, we engage in these activities in a manner that responds to our mandate to interact bidirectionally with our local community.

CEHS acts as a nucleation point for a diverse group of environmental scientists, engineers, historians, and policy experts from 11 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 an equally impressive toolbox of state-of-the-art technologies enabling quick headway to be made on high-impact problems—problems that are larger than those that could be realistically tackled by any individual laboratory. In this way, CEHS enables synergistic partnerships of people and technologies, leading to the solution of important environmental problems. There are approximately 38 laboratories that participate in the Center for Environmental Health Sciences with various areas of expertise, but the expertise most in alignment with the center’s mission include:

- Knowledge of the chemistry and transport of pollutants in the atmosphere, water, and soil
- Knowledge of the pathways by which cells and organisms respond to toxic agents in the environment (reflected by our expertise in DNA damage, DNA repair, genomic instability, proteomics, metabolomics and gene expression analysis)
- Knowledge of the ways that 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 20 core centers focusing

on environmental health. CEHS is composed of an Administrative Core, the Community Outreach Education and Engagement Core, the Career Development Program, the pilot project program (including both basic and translational pilot projects), and the Global Environmental Health Sciences Program. In addition, CEHS has four research facility cores, including a mandated Integrative Health Sciences Facilities Core that provides an interface with the local medical community.

The CEHS membership currently consists of 36 science and engineering faculty, five emeritus faculty, and four professional full-time senior researchers. Forty-four members are from MIT and one is from the Broad Institute (Professor Paul Blainey). Of the MIT members, the center has one senior research scientist emeritus and one principal research scientist. The members of the Administrative Core, which is charged with the center's overall operation, include Professor of Biological Engineering Jacquin C. Niles, director; William R. and Betsy P. Leitch Professor in Residence and Professor of Chemistry, Toxicology, and Biological Engineering John M. Essigmann, deputy director; Amanda Tat, administrative officer; Gabrielle Stump Ceriales, fiscal officer; Tainara Candido, financial assistant; and an administrative assistant and event assistant. The Community Outreach Education and Engagement Core (COE²C) educates communities about environmental hazards that can adversely affect public health and helps communities take preventive measures. In a broad mission to assist environmental justice communities in the urban Boston area, COE²C partners with the Mystic River Watershed Association and the Friends of the Malden River. COE²C also works with four tribes in northern Maine, collaborating directly with tribal educational and environmental departments. Internally, COE²C partners with the MIT Edgerton Center, the MIT Clinical Research Center, and the MIT Superfund Research Program (SRP) to reach out nationally to science teachers and health care professionals with instructional environmental health materials. COE²C is led by Kathleen Vandiver, director, and John Essigmann, co-director, with support from outreach coordinators Amy Fitzgerald and Amanda Mayer. Essigmann has a strong interest in these programs and is actively engaged with them.

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: the Bioimaging and Chemical Analysis Facilities Core, the Genomics and Informatics Facilities Core, the Animal Models Facilities Core, and the Integrative Health Sciences Facilities Core. Each core contributes to the research efforts of at least 10 center members.

The Bioimaging and Chemical Analysis Facilities 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 to DNA, RNA, and protein, and state-of-the-art proteomics and metabolomics research capabilities. In addition, this core offers a variety of sophisticated quantitative imaging technologies. The core operates as a resource for the center—as well as 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 Orbitrap Exactive Q mass spectrometer in operation, proteomics add-on functionality has been added to our portfolio. This instrument gives us the ability to analyze how protein networks change over time in response to foreign agents

(toxicants, infectious agents, and drugs) and also allows us to see changes in real time in conventional small-molecule metabolites of cells treated with the same agents. The recently restructured Bioimaging and Chemical Analysis Facilities Core has been heavily used by CEHS labs and the broader MIT community. The management team has evolved over the past year. Mohanraja Kumar, an expert in analytical chemistry, was previously hired jointly between the center and the Department of Chemistry to manage CEHS and chemistry core operations. Increased needs in the Department of Chemistry, however, led to Kumar transitioning to full-time work there in early spring 2019. Michael DeMott and Bogdan Fedeles have since been serving as managers of this CEHS core. DeMott, previously involved in managing day-to-day core operations, is an expert in analytical mass spectrometry. Fedeles, a new addition to the core management team, is an expert in analytical biochemistry. The team has already implemented a number of improvements in user training, scheduling, instrument maintenance, and billing practices that are allowing the core to function more efficiently while providing strong user support.

The Genomics and Informatics 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 offering biostatistics support for CEHS. The core's 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 late 2018, we added a DNA synthesizer from Biolytic to the core. This instrument enables highly parallel DNA and RNA synthesis using both standard and modified nucleotides. These modified nucleotides can be highly unstable or mutagenic by-products of chemicals in the environment that are associated with disease. Being able to produce DNA and RNA with these modifications on demand and on site should allow more robust testing of a broad spectrum of different basic and applied biological questions, including DNA repair mechanisms and improved understanding of the epidemiology of mutagenic signatures in cancer and other diseases. In addition, the ability to incorporate non-standard nucleotides is critical in using DNA and RNA as structural molecules in state-of-the-art techniques such as DNA origami and DNA data storage. This example shows how service facilities work with our basic science community to develop advanced technology that will benefit a broad range of scientists at MIT and beyond.

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. This core also does state-of-the-art research on the role that microbes play in accelerating the development of diseases such as cancer.

The Integrative Health Sciences Facilities Core (IHSFC) is led by Professors Michael Yaffe and James Fox, with the support of the Hospital Liaison Program director (Dr. Catherine Ricciardi) and a cohort of clinical and translational consultants. Ricciardi continues to have day-to-day management responsibility for 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. 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 Division of Health Sciences and Technology. This connection with the MIT Catalyst Clinical Research Center provides access to services for CEHS members engaged in human health research, particularly studies involving human clinical samples, clinical trials, and population-based studies. IHSFC was developed to help CEHS members translate their research activities for the clinical and epidemiological realms.

Another major program in CEHS is the Global Environmental Health Sciences Program, led by co-directors 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. One example of the impact of this work is recent discoveries regarding the mechanism by which paraquat, a herbicide still used in the developing world, causes oxidative stress that can lead to neurological diseases such as Parkinson's disease. Our efforts in Thailand have recently expanded to include arsenic, a widespread environmental toxicant. Our Singapore program helped with the development of a therapy for dengue fever that was recently approved by the Singaporean government. Similar translational studies on Zika virus are also under way.

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

- Mentoring
- Financial and research administration support
- Research resources
- Speaking opportunities for junior faculty
- New Frontiers Seminar Series for postdocs
- Translational research support
- Engagement opportunities
- 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, 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 applications. The importance of this type of research warrants special funding outside of the regular pilot project program. Established in 2015, the translational pilot project program has partnered with the Theron G. Randolph Translational Pilot Project 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 Vilma Kinney has enabled this new direction for the Center for Environmental Health Sciences.

Accomplishments in 2018–2019

Many of our accomplishments this past year stem from our superb instrumentation stock in our facilities cores. Matthew Shoulders is providing new insights into protein evolution during viral attacks, and Professor Elizabeth Nolan is helping to increase knowledge of how infectious agents acquire metals needed for their normal biology (and pathobiology). Shoulders' work illustrates how viruses such as HIV rapidly evolve drug resistance, and Nolan's work guides us toward new drugs that could limit metal nutrients needed for pathogen growth. The Orbitrap proteomics instrumentation is critical to Shoulders' work and the inductively coupled plasma mass spectrometer (ICP-MS) is critical to the work done by Nolan. These new pieces of CEHS equipment have enabled many groundbreaking discoveries in a short period of time. More than 70 investigators in several dozen laboratories at MIT use the ICP-MS.

The center has maintained an extremely strong volume of research support, totaling over \$13.7 million (the highest volume to date) in FY2019 and resulting in approximately 300 publications. These research projects are funded through a variety of sources, including the National Institutes of Health, National Cancer Institute, National Institute of Allergy and Infectious Diseases, National Institute of Biomedical Imaging and Bioengineering, National Center for Advancing Translational Sciences, National Institute of Environmental Health Sciences, National Science Foundation, Department of Defense, 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 45th year, reflects the broadening of CEHS to include many faculty members, mainly engineers from outside the Department of Biological Engineering. The training grant now supports predocs and postdoctoral trainees in a number of disciplines and has fostered interdisciplinary research. To keep the grant grounded in

the field of toxicology, Professor Essigmann and John Groopman (of Johns Hopkins University) teach 20.S949 Fundamentals of Environmental Toxicology, an intensive course required of center trainees and trainees in our new Superfund Research Program.

A strength of the center is its ability to integrate with other organizations on campus, including departments with shared interests. CEHS has been awarded a center grant under the Superfund Research Program (the P42 SRP Program), led by Bevin Engelward (director) and Noelle Selin (co-director). Additionally, Kathleen Vandiver plays a critical role by making connections with stakeholders in nearby communities in Massachusetts and Maine for the SRP Community Engagement Core. An important strength of the Superfund Research Program is its focus on DNA 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 and institutes (Earth, Atmospheric, and Planetary Sciences; the 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. Furthermore, there are four cores (administrative, research translation, community engagement, and training) that support key aspects shared by all of the projects. A key element of the program was to bring together research leaders to focus on specific contaminants and to develop strong synergies. Finally, all members of the Superfund Research Program are also CEHS members, making this program a great asset to the center.

Community Outreach Education and Engagement Core

Our funding agency, the National Institute of Environmental Health Sciences, mandates that all 20 of its extramural research centers engage in community-based programs to improve public health. The CEHS COE²C provides (1) outreach to underserved communities designated as environmental justice communities, (2) innovative educational tools to convey key concepts relevant to environmental health for adults as well as children, and (3) workshops for educators, including instructors in nursing schools who can be instrumental in improving environmental health literacy.

The MIT COE²C selected two geographic regions in New England for their work. The first is the urban Mystic River Watershed. The Mystic River flows through 22 Boston-area communities and includes immigrant populations in environmental justice communities along the Malden River. The second region is made up of Native Americans living on tribal lands in rural northern Maine. Our challenge is finding the best way to inform, advise, listen to, and work with partner organizations in these communities to mitigate the human health effects of pollution and unhealthy lifestyles.

Highlights from the past year include an informal educators' workshop for Native Americans in partnership with the Wabanaki Youth in Science (WaYS) Program in Maine and a human health risk study for boating on the Malden River. Also, we received a one-year NIEHS-funded research award to study environmental health education with nursing students in tribal communities.

CEHS agreed to support WaYS, an ambitious National Science Foundation program at the University of Maine. As part of this ongoing collaboration, Kathleen Vandiver led a daylong train-the-trainer science workshop in Orono, ME, for Native American scientists and teachers. An MIT undergraduate student interested in working with native communities assisted with the workshop.

COE²C and two community partners (the Mystic River Watershed Association and the Gradient Corporation) participated in sampling the Malden River and produced a human health risk study for boating. The study revealed that the health risk is minimal for recreational purposes such as rowing and kayaking. This news came as a major surprise to municipal and state officials, since much of the river remains fenced off to protect people from legacy industrial waste. Kathleen Vandiver delivered a clear and convincing presentation about the results to the Malden City Council in a televised session in April 2019. Her presentation materials were also used at Massachusetts state senator Jason Lewis's Malden River Forum. The CEHS COE²C is pleased to have played a key role in promoting healthy public use of the Malden River.

This past year, COE²C undertook a new challenge to obtain an NIEHS supplemental grant to demonstrate the efficacy of our hands-on models for teaching nursing students in tribal communities about environmental health. Studies were implemented with the assistance of the Ramapo Tribe in New Jersey and the Cheyenne River Sioux Tribe in South Dakota. The favorable study results were analyzed in collaboration with three universities. Overall, COE²C has continued to make strides in disseminating innovative teaching tools for molecular biology and, most recently, has extended the application to health professionals.

Annual Poster Session

Due to the transition in the center's directorship, the CEHS poster session has been postponed to fall 2019. Our hope is that the event can be aligned with the External Advisory Committee meeting.

CEHS Sponsored and Co-Sponsored Lecture Series

Over the past year, the center hosted six Friday Forum lectures and two Superfund Friday Forum events. The long-standing series of Friday Forum 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, pilot project award recipients, and Superfund members all gave presentations. The format of the seminar series includes opportunities for socializing both before and after seminars. These opportunities for mingling have been a constant source of new scientific collaborations.

Another CEHS-sponsored monthly seminar series is the Boston DNA Repair and Mutagenesis (DRAM) Seminar Series. For many years, 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 evening seminar series draws students, postdocs, and faculty from the University of Massachusetts Medical School in Worcester, Northeastern

University, Harvard University, Boston University, Yale University, Tufts University, and Brown University. The DRAM seminar has become a vibrant part of the CEHS culture.

In addition, the center has continued to offer the New Frontiers Postdoctoral Transition Seminar Series. The center recognizes the importance of having a great seminar for job interviews, and this 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 asks questions and offers advice. Importantly, following the presentation, there is a private meeting between faculty members and the postdoc speaker that includes a detailed discussion of speaking strategy, organization, and clarity. This format provides valuable feedback for postdocs, enabling them to hone their presentations in preparation for a competitive job market.

Lastly, the center 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. Dartmouth College professor Mary Lou Guerinot presented the Robert S. Harris Lecture (“Ionome to Genome: Tales of Gene Discovery”) in September 2018, ETH Zurich professor Shana J. Sturla presented the Gerald N. Wogan Lecture (“How Chemistry Can Change Your Fate: From Microbiome Metabolism to Genome-Wide Damages?”) in November 2018, and MIT professor Ram Sasisekharan delivered the David B. Schauer Lecture (“At the Interface of Regulatory Sciences and Global Health: A Perspective”) in May 2019.

Plans for 2019–2020

In the upcoming year, the CEHS leadership will be actively engaged in strategic planning discussions to reflect the evolution of the center’s leadership and membership. The center plans to host an External Advisory Committee meeting in fall 2019 to assist with these discussions; during the meeting, we will receive input on the center’s competing renewal due in spring 2020. The center leadership expects to focus on the following goals for 2019–2020:

- Reassessing the center’s membership with the objective of attracting more junior faculty and fostering relationships between scientists and engineers where possible
- Stimulating members’ participation in the Global Environmental Health Sciences Program, as environmental pollution ignores geopolitical boundaries and diseases of the developing world indirectly affect the United States
- Expanding CEHS activities to more broadly examine the impact of microbial systems on human health, with an emphasis on how these systems modulate susceptibility to environmental exposures
- Reexamining the Career Development Program and the Integrative Health Sciences Facilities Core to make sure they are in concert with best practices in our field
- Continuing to make use of the Community Outreach Education and Engagement Core to showcase some of the exceptional research performed by center members

- Evaluating current management of the Bioimaging and Chemical Analysis Facilities Core to develop a more sustainable management plan. Continuously increasing user volume across the range of analytical services provided in this core poses an ongoing challenge with respect to maintaining high-quality and expert service, instrumentation readiness, and training given constraints on the degree of effort current managers can provide.

The COE²C plans for 2019–2020 include (1) completing the NIEHS supplemental grant to demonstrate the efficacy of teaching nursing students about gene-environment interactions with our materials and submitting a journal article about this research and (2) producing a new biology toolkit. The chromosome models are currently in production, and the next task is to create the accompanying curriculum materials to teach the basics about genetic variations and chromosomes.

The Community Outreach Education and Engagement Core successfully reached out to hundreds of people with its educational activities this past year, using innovative CEHS-supported technologies to teach about the impact of our environment on health, including examples of air pollution, climate change, and DNA damage.

With regard to global research efforts, CEHS will continue its ongoing collaboration with the Chulabhorn Research Institute in Bangkok, which has been a world hub for environmental health research and training for many years. At any given time, one to three students from the Chulabhorn network participate in internships at MIT in CEHS laboratories and some of that research is relevant to our Superfund efforts. Hence, our global program is formally connected to the Superfund Training Core. In addition, several center members have laboratories and strong commitments in Singapore, which is the locus of much of the center's research in the infectious disease arena. International partnerships give us access to diverse populations, which is critical to our translational mission.

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