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, or population level; and helps to create new technologies to live longer and healthier lives. As a federally funded center, we do this while following 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. The center 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 that enables quick headway to be made on high-impact problems 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. Approximately 42 laboratories of CEHS have many areas of expertise, and these contribute to the overall CEHS mission by providing the following:

- 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
- 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 Core Centers (the P30 Program) focusing on environmental health. Fulfilling the requirements of the NIEHS P30 Program, CEHS is composed of an Administrative Core, a Community Outreach

Education and Engagement Core, a Pilot Project Program (including both basic and translational pilot projects), and a Global Environmental Health Sciences Program. In addition, CEHS has four research facilities cores, including a mandated Integrative Health Sciences Facilities Core, which provides an interface with the local medical community.

CEHS membership currently consists of 40 science and engineering faculty, three emeritus faculty, and six professional full-time senior research members. Forty-eight members are from MIT and one is from the Broad Institute (Professor Paul Blainey). The members of the Administrative Core, which is charged with the center's overall operation, include Director Jacquin C. Niles, professor of biological engineering; Deputy Director John M. Essigmann, the William R. and Betsy P. Leitch Professor in Residence, and professor of chemistry, toxicology, and biological engineering; 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 (COE^{2}C) educates communities about environmental hazards that can adversely affect public health and helps communities take preventive measures. In a broad mission to environmental justice communities located in the urban Boston area, COE^{2}C partners with Mystic River Watershed Association and the Friends of the Malden River. The COE^{2}C also works with four Abenaki Tribal Nations in northern Maine, collaborating directly with tribal educational and environmental departments. Internally, COE^{2}C 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. The COE^{2}C is led by Kathleen Vandiver, director, and Professor Essigmann, co-director, with support from Amy Fitzgerald and - Amanda Mayer, outreach coordinators.

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 Bioanalytical 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 Bioanalytical Facilities Core provides 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 develop proficiency in biological mass spectrometry, other modern analytical methods, and sophisticated imaging tools. With the Orbitrap Q Exactive mass spectrometer in operation, our portfolio now includes a proteomics add-on functionality. The mass spectrometer gives us the ability to analyze how protein networks change over time in response to foreign agents (toxicants, infectious agents, and drugs) and lets us see changes in real time of conventional small-molecule metabolites of cells treated with the same agents. The Bioanalytical Facilities Core, which was renamed this year to the 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

and transitioned to Michael DeMott and Bogdan Fedeles as managers. DeMott, an expert in analytical mass spectrometry, had previously been involved in managing day-to-day core operations. Fedeles, a new addition to the core management team, is an expert in analytical biochemistry. This team has 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, directed by Stuart Levine, 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 biostatistics support 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. The DNA synthesizer from Biolytic 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 the epidemiology of mutagenic signatures in cancer and other diseases. In addition, the ability to incorporate nonstandard 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 community of scientists at MIT and beyond.

The Animal Models Facilities Core, directed by Professor James G. Fox, provides 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 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 David H. Koch Professor in Science Michael Yaffe and Professor Fox with the support of the hospital liaison program director, Catherine Ricciardi, and a cohort of clinical and translational consultants. Ricciardi has day-to-day management responsibility for the IHSFC, but Professor Yaffe (a practicing physician-scientist) and Professor 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 at Harvard and the Harvard-MIT Program in Health Sciences and Technology. This connection with the MIT Catalyst Clinical Research Center provides access to 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. The 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, with Professor Essigmann and Underwood-Prescott Professor of Biological Engineering Peter Dedon as co-directors. This program focuses on developing collaborative relationships among 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. At present, our global efforts focus on Thailand and Singapore. One example of the impact of this work is recent discoveries on the mechanism by which paraquat—an herbicide still used in the developing world—causes oxidative stress that can lead to neurological diseases such as Parkinson's disease. Our work in Thailand has expanded to include arsenic, a widespread environmental toxicant. In Singapore, our efforts helped with the development of a therapy for dengue fever, which was recently approved by regulatory authorities in that country.

CEHS has a long-standing commitment to supporting the careers of its young scientists and junior faculty, providing a broad range of opportunities for advancement at all stages of their careers. The center provides opportunities and resources that promote success and enable community engagement in environmental health, including the following:

- Mentoring
- Financial and research administration support
- Research resources
- Speaking opportunities for junior faculty
- New Frontiers Transition 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 Pilot Project Program, funded by the NIH and privately, which is overseen by the CEHS 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 COE^{2}C activities arising directly from the research of our center members.

The Translational Pilot Project Program, an offshoot of the 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 Translational Pilot Project Program continues to partner 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. This new direction was enabled by a gift from Vilma Kinney.

Accomplishments in 2019–2020

An important role of CEHS is to help nucleate research that integrates basic science and engineering toward solving real-world problems. For example, the former Olin Chemical Corporation plant in Wilmington, Massachusetts, is a designated Superfund site. Five of the town's municipal wells were contaminated with a wide range of chemicals, including N-nitrosodimethylamine (NDMA). NDMA is a cancer suspect agent found with increasing frequency in waters, foods, tobacco products, and as byproducts of the manufacture of an array of pharmaceutical products used for cardiovascular disease, acid reflux, and diabetes. This broad range of environmental exposures calls for a nimble technology that is fast, accurate, and sensitive. To this end, CEHS member John D. MacArthur Professor of Chemistry Timothy Swager and Professor Essigmann collaborated to develop the first carbon nanotube sensors for detecting *N*-nitrosamines in air. Traditionally, *N*-nitrosamines are measured using a laborious process requiring sophisticated and expensive instrumentation. These newly developed carbon nanotube sensors eliminate the tedious and costly procedures associated with traditional analysis and provide inexpensive, real-time, sensitive measurement of *N*-nitrosamines in air. They can also be integrated into field-deployable devices to provide measurements via computer or smartphone. These features create an opportunity for spatiotemporal mapping of *N*-nitrosamine levels in contaminated areas, which could safeguard human health by providing information to factory workers and communities on possible exposures, as well as to regulators seeking to understand the effectiveness of policies and engineering controls implemented to minimize exposure. This work is also part of a larger Superfund Research Project led by CEHS member Bevin Engelward (professor of biological engineering), to study the health effects of hazardous industrial waste on affected communities.

CEHS has maintained an extremely strong volume of research support, totaling over $11.7 million in FY2020, and resulting in at least 331 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, and NIEHS), 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 46th year, reflects the broadening of CEHS to include many faculty members, mainly engineers from outside the Department of Biological Engineering. The grant now supports predoctoral researchers and postdoctoral trainees in many disciplines and has fostered interdisciplinary research. To keep the Training Grant grounded in the field of toxicology, Professor Essigmann and John Groopman (of Johns Hopkins University) teach an intensive course called

Fundamentals of Environmental Toxicology (MIT subject 20.S949), which is required of center trainees and all trainees on the Superfund Research Program and is available to other interested parties at MIT.

A strength of CEHS is its ability to integrate with other organizations on campus, including departments with shared interests. CEHS has been awarded the Superfund Research Program (a P42 Program) grant. The leaders of this program are Professor Engelward (director) and Associate Professor Noelle Selin (co-director). Additionally, COE²C director Vandiver plays a critical role by making connections to stakeholders in nearby communities in Massachusetts and Maine for the Superfund Community Engagement Core. An important strength of the funded 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 (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. Four cores supporting key aspects are shared by all of the projects: Administrative, Research Translation, Community Engagement, and Training. A key aspect of the program is bringing together research leaders to focus on specific contaminants and to develop strong synergies. All members of the SRP are CEHS members, making this program a great asset.

Community Outreach Education and Engagement Core

A highlight this year was winning the Norman B. Leventhal Cities Prize ($100,000), created by the Leventhal Center for Advanced Urbanism. Led by Vandiver, the Malden River Works (MRW) for Waterfront Equity and Resilience project built upon and substantially extended CEHS work supported by the NIEHS. Designed to build civic leadership capacity for people of color and benefit the entire city, this project is closely guided by a steering committee of Malden residents. The goal is to transform a parcel of publicly owned land abutting the Malden River (the Malden City Yard) into a vibrant riverfront park. Designs are actively shaped by public input through online surveys in multiple languages, town-wide public meetings, and community dialogue. Based on these inputs, the desire for open green space and recreational boating is clear. MIT's contribution to the MRW Project Team is to provide technical and planning expertise in areas related to Malden's climate vulnerability and disaster preparedness plans for the park, green infrastructure for flood prevention, and heat island dissipation.

Annual Poster Session

The CEHS poster session was postponed due to the pandemic.

CEHS-Sponsored and Co-Sponsored Lecture Series

While the lecture series schedule was curtailed due to the pandemic, CEHS did host six Friday Forum lectures and two Superfund Friday Forums. 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 members, potential members, Pilot Project award recipients, and SRP/CEHS members gave presentations. The format of the seminar series includes opportunities for socializing among CEHS and SRP members, which has been a constant source of new scientific collaborations.

CEHS also sponsored 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 MIT, UMass 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 CEHS culture.

In addition, CEHS 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 seminar series is specifically aimed at providing postdocs with the opportunity to give and get feedback on their job talk. Talks are advertised to the entire CEHS community, which asks questions and offers advice that helps in preparation for the postdoc's job interviews. Importantly, following the presentation, faculty members and the postdoc speaker meet privately for a detailed discussion of speaking strategy, organization, and clarity. This format provides postdocs valuable feedback, enabling them to hone their slides and talks in preparation for a competitive job market.

Further, 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. The Wogan and Harris Lectures, originally scheduled for May 2020, were postponed due to the pandemic. The postponed Wogan Lecture speaker was Dr. Janet Woodcock from the US Food and Drug Administration, while the Harris Lecture speaker had been Professor Susan M. Rosenberg from Baylor College of Medicine.

Plans for 2020–2021

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 as well as the CEHS organizational chart. CEHS plans to host a virtual External Advisory Committee meeting in fall 2020 to assist with this discussion. The CEHS director and deputy director will focus on the following goals for 2020–2021:

- Reassessment of center membership, with the objective of attracting more junior faculty and fostering relationships, where possible, between scientists and engineers
- Stimulating center members' participation in the Global Environmental Health Sciences Program as environmental pollution ignores geopolitical boundaries and diseases of the developing world indirectly impact the United States
- Expanding CEHS activities to more broadly examine the impact of microbial systems on human health, with emphasis on how these modulate susceptibility to environmental exposures

- Reexamination of the Integrative Health Sciences Facilities Core to make sure it aligns with best practices in our field
- Continue our dialogue with members of the External Advisory Committee
- Continue to make use of the Community Outreach Education and Engagement Core to showcase some of the exceptional research performed by center members
- Evaluate current management of the Bioanalytical 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 its high-quality and expert service, instrumentation readiness, and training, given time and personnel constraints. As always, the CEHS leadership will continue efforts to engage the broader MIT community and academic neighbors in research activities related to environmental health sciences and engineering.

The CEHS COE^{2}C will continue to be involved in year two of the Malden River Works. The COE^{2}C has been invited to participate in and contribute to the Leventhal Center for Advanced Urbanism's international conference on Equitable Resilience, planned for Boston in 2021. Additionally, our MRW Project Team expects to dedicate considerable time and energy to grant writing. We will be responding to solicitations offered by government agencies and foundations to support the construction phase of the Malden Park and translate Malden's collective vision into a public riverfront amenity.

With regard to global research efforts, CEHS will continue its 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. At any time, one to three students from the Chulabhorn network may be selected for MIT internships in CEHS laboratories. As some of that research is relevant to our Superfund efforts, our global program is formally connected to the Superfund Training Core. Several center members have laboratories and strong commitments in Singapore as well, which is the locus of much of CEHS' research in the infectious disease arena. International partnerships give us access to affected populations, which is critical to our translational mission.

Jacquin C. Niles
Director
Professor of Biological Engineering

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