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 of detection; delineates the mechanisms through which these agents affect health at the cellular, tissue, individual or population levels; and helps to create new technologies that allow us to live longer and healthier lives. As a federally funded center, we do the above 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. The center 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—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 solutions for important environmental problems. Approximately 42 laboratories across many areas of expertise contribute to the overall center mission by providing knowledge and technologies impinging on:

- Chemistry and transport of pollutants in the atmosphere, water, and soil
- 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)
- Ways that microbes as individual agents or collectively as microbiomes affect health and disease
- Immune system and inflammation as promoters of many environmental diseases
- Use of engineered cellular, tissue, and whole-organism systems to enable next-generation testing of environmental hazards and development of disease-prevention strategies
- 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 26 Core Centers (the P30 Program) focusing on environmental health. Fulfilling the requirements of the NIEHS P30 Program, the center is composed of an Administrative Core, a Community Outreach Education and Engagement Core (COE^{2}C), 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—Paul Blainey, Associate Professor of Biological Engineering (BE). The members of the administrative core, which is charged with the center's overall operation, include Professor of Biological Engineering Jacquin C. Niles, director; Professor of Chemistry, Toxicology and Biological Engineering John M. Essigmann, deputy director; Amanda Tat, administrative officer; Gabrielle Stump Ceriales, fiscal officer; as well as a financial assistant, an administrative assistant, and event assistant.

The 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 tribes 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 healthcare professionals with instructional environmental health materials. The COE^{2}C is led by Dr. Kathleen Vandiver, director, and John 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. The center's researchers use four facilities cores; each core contributes to the research efforts of at least 10 center members. The cores include the Bioanalytical Facilities Core, the Genomics and Informatics Facilities Core, the Animal Models Facilities Core, and the Integrative Health Sciences Facilities Core.

The Bioanalytical 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. This 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 Q Exactive mass spectrometer in operation, a proteomics add-on functionality was 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 additionally lets us see changes in real time of conventional small-molecule metabolites of cells treated with the same agents. The Bioanalytical Facilities Core has been heavily used by CEHS labs and the broader MIT community. The management team includes Michael DeMott and Bogdan Fedeles; DeMott is an expert

in analytical mass spectrometry, and Fedeles is an expert in analytical biochemistry. This team has implemented several 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 Animals Models Facilities Core and Integrative Health Sciences Facilities Core (IHSFC) in providing 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. 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 understanding 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 Dr. James G. Fox, professor post-tenure of BE and a doctor of veterinary medicine—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 Dr. Michael Yaffe—David H. Koch Professor in Science, Professor of Biology, Professor of BE, and a practicing physician-scientist—and James G. Fox with the support of the Hospital Liaison Program director, Catherine Ricciardi, along with a cohort of clinical and translational consultants. Ricciardi continues to have day-to-day management responsibility for the IHSFC, but Yaffe and Fox have faculty-level responsibility for human and animal translational studies, respectively. Ricciardi is an expert in the preparation of MIT Institutional Review Board proposals for the use of human subjects in experimentation; she is also our liaison to the Tufts Clinical and Translational Science Institute (CTSI). The CTSI network is comprised of clinical and translational science experts including 40 medical, academic, industry, and community partners and collaborators. This connection with the MIT 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 the center's members translate their research activities for the clinical and epidemiological realms.

Another major program in the center is the Global Environmental Health Sciences Program (GEHSP), led by Essigmann and Dr. Peter Dedon, Underwood-Prescott Professor and Professor of Toxicology and BE. 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 and Singapore. One example of the impact of this work is recent discoveries on 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. Another global effort is in Singapore, which helped with the development of a therapy for Dengue fever that was recently approved by the Singaporean FDA.

The center has a long-standing commitment to fostering the careers of its young scientists and junior faculty, 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 include:

- 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 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 COE^{2}C 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 mentioned above, 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. 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 Vilma Kinney has enabled this new direction for the center.

Accomplishments

An important role of CEHS is to help nucleate research that integrates basic science and engineering towards solving real world problems, an example of which is highlighted below. 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, one of which is 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 a range 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, The center's members Timothy Swager and John 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 and 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 toward safeguarding human health by providing information to factory workers and communities on possible exposures, and to regulators seeking to understand the effectiveness of policies and engineering controls implemented to minimize exposure. This work is also part of a larger SRP led by CEHS member Bevin Engelward, Professor of BE, to study the health effects of hazardous industrial waste on affected communities.

The center has maintained an extremely strong volume of research support, totaling over $11.9 million in fiscal year 2021 and resulting in at least 342 publications. These research projects are funded through a variety of sources, including the NIH (National Cancer Institute, National Institute of Allergy and Infectious Diseases, National Institute of Biomedical Imaging and Bioengineering, National Center for Advancing Translational Sciences, and National Institute of Environmental Health Sciences), the 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 47th year, reflects the broadening of CEHS to include many faculty members, mainly engineers

from outside of the Department of Biological Engineering (BE). The Training Grant now supports predoctoral and postdoctoral trainees in many disciplines and has fostered interdisciplinary research. To keep the Training Grant grounded in the field of toxicology, Essigmann and John Groopman of Johns Hopkins University teach an intensive course entitled 20.S949 Fundamentals of Environmental Toxicology, which is required of Center Trainees and all Trainees on the SRP, as well as other interested parties at MIT.

A strength of the center is its ability to integrate itself with other organizations on campus, including departments with shared interests. As indicated above, CEHS has been awarded the SRP grant, a P42 Program. The leaders of this program are Engelward, director, and Noelle Selin, co-director, professor of Earth, Atmosphere and Planetary Sciences (EAPS), and associate director, Institute for Data, Systems, and Society (IDSS). Additionally, Vandiver plays a critical role by making connections to stakeholders in nearby communities in Massachusetts and Maine for the SRP Community Engagement Core. An important strength of the funded SRP 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 (EAPS, IDSS, Civil and Environmental Engineering, Chemical Engineering, Chemistry, BE, 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 shared by all projects. The foci of these cores are Administrative, Research Translation, Community Engagement, and Training. A key aspect of the program was bringing together research leaders to focus on specific contaminants and to develop strong synergies amongst each other. Finally, all members of the SRP are also center members, making this program a great asset to CEHS.

Community Outreach Education and Engagement Core

High school educators across the country struggled with teaching science during the pandemic, and vulnerable students were at increased risk of losing access to vital summer enrichment activities. Vandiver collaborated with three NIH-funded programs to support underrepresented minority youth in STEM enrichment summer programs that might otherwise have been cancelled. Three highlights wherein the CEHS COE^{2}C created and shared new teaching methods are described below.

First, COE^{2}C collaborated with the LEAH Knox Scholars Program, an NIH Science Education Partnership Award grant program for Boston Public High School students in biotechnology. In preparation for intensive lab work conducted in the MIT Department of Biology Teaching Labs, COE^{2}C assisted Boston High School students by teaching a two-day molecular biology class. Learning materials, including DNA modeling kits, were delivered to participating students along with an inexpensive videocam to allow instructors to interactively observe and coach students. To facilitate interactions during virtual breakout sessions, COE^{2}C instructors Vandiver and Mayer trained four MIT Biology Teaching Assistants. This team led students through modeling cellular processes and teaching laboratory molecular techniques. Student feedback highlighted the hands-on course as an incredible learning experience.

Second, COE²C worked with the Texas A&M University's Summer Environmental Health Institute for Science Teachers program to quickly pivot from in-person to virtual programming within a two-week timeframe. Vandiver and Mayer quickly adjusted their curricular activities and led a teachers' workshop that used a combination of short lectures, model-based demonstrations, and pedagogical training videos that also fulfilled Texas' accreditation requirements. These videos are now freely available on the MIT Edgerton Center's YouTube playlist.

Third, CEHS initiated a collaboration with Professor Christa Wright, who leads the Georgia State University undergraduate program in public health and works with high school biology teachers in Atlanta. The COE²C provided a professional development workshop for teachers and assisted in coaching an undergraduate capstone team project. This included giving a presentation to engage a high school biology class in understanding more about pesticide toxicity and environmental health.

Last, through the NIH Partners in Environmental Public Health Webinar held in September 2020, the MIT COE²C shared instructional expertise and online educational resources with organizations across the country in a presentation titled, "MIT DNA and Protein Models Adapt to Covid-Times: Teaching Hands-on Biology via Online Instruction."

Annual Poster Session

The CEHS poster session was postponed due to the pandemic.

Lecture Series

The lecture series schedule was curtailed due to the pandemic. CEHS co-hosted three virtual joint Friday Forum lectures with the Superfund Research Program (SRP) Friday Forum. 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, Pilot Project award recipients, and Superfund members and centers gave presentations. The format of the seminar series includes opportunities for socializing both before and after the seminar. These opportunities for mingling among the center and SRP members have 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, Boston University, Brown University, Harvard University, Northeastern University, Tufts University, UMass Medical School in Worcester, and Yale University. The DRAM seminar has become a vibrant part of the center's 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 practice their job talk and receive feedback. Talks are advertised

to the entire CEHS community, which allows questions and offers advice to help in preparation for the postdoc's job interviews. Following presentations, there is a private meeting between faculty members and the postdoc speaker at which there is a detailed discussion of speaking strategy, organization, and clarity. This format provides valuable feedback for postdocs, enabling them to hone their slides and talks in preparation for a competitive job market.

Lastly, the center continues to co-sponsor three named lectureships with BE: the Robert S. Harris, Gerald N. Wogan, and David B. Schauer Lectures. The Wogan and Harris Lectures were not held due to the pandemic, while Professor Cynthia L. Sears from the Johns Hopkins University presented the David B. Schauer lecture "Is it Group or Solo Microbial Colon Cancer Promotion?" in March 2021.

Plans for 2021–2022

In the upcoming year, the CEHS leadership will be actively engaged in strategic planning discussions to reflect the evolution of the center's leadership, membership, and organizational chart. The center plans to host a virtual or in-person External Advisory Committee meeting to aid this process. The center director and deputy director will focus on the following goals for 2021–2022:

1. Re-assessment of center membership, with the objective of attracting more junior faculty and fostering relationships, where possible, between scientists and engineers
2. Stimulating center members' participation in the GEHSP, as environmental pollution ignores geopolitical boundaries and diseases of the developing world indirectly impact the United States
3. 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
4. Re-examination of the IHSFC to make sure they are in concert with best practices in our field
5. Continue our dialogue with members of the External Advisory Committee
6. 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
7. Evaluate management needs of the Bioanalytical Facilities Core to develop a 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 for users of the core

As always, the CEHS leadership will continue efforts to engage the broader MIT community and our academic neighbors in research activities related to environmental health sciences and engineering.

We plan to continue to create and publish additional educational curricula in environmental health sciences in partnership with the MIT Edgerton Center. In the coming year, we expect to publish two additional instructional booklets: *Genes, Proteins and Health*, aimed at teaching health professionals about genetic susceptibilities to environmental exposures, and *DNA and Biotechnology*, aimed at teaching about molecules evaluated in biotech lab procedures.

CEHS will continue its global collaborative research activities 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, up to three students from the Chulabhorn network may be selected for 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 CEHS' research in the infectious disease arena. International partnerships continue to be critical to our translational mission.

Jacquin C. Niles
Director
Professor of Biological Engineering

John M. Essigmann
Deputy Director
Professor of Biological Engineering and Chemistry