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 athe cellular, tissue, individual, and population levels, and helps to create new technologies that allow us to live longer and healthier lives.

The CEHS acts as a nucleation point for a diverse group of environmental scientists, engineers, and policy experts from eight 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 that enables quick headway to be made on high-impact problems—such as those larger than 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 40 laboratories of CEHS have many areas of expertise but the ones most in alignment with the CEHS mission are:

- 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 and 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
- Bioengineered cellular, tissue, and whole-organism systems that enable nextgeneration testing of environmental hazards and development of diseaseprevention strategies

Organization

CEHS is funded primarily by the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health as one of the 22 Core Centers 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 CEHS membership currently consists of 44 science and engineering faculty and five professional full-time senior researchers. Forty-three members are from MIT and one is from Harvard University (epidemiologist, Professor David Hunter). Of the MIT members, the center has one senior research scientist and two principal research scientists. The members of the Administrative Core, which is charged with the center's overall operation, include William R. and Betsy P. Leitch Professor of Chemistry and Biological Engineering John M. Essigmann, director; Professor of Toxicology and Biological Engineering Bevin P. Engelward, deputy director; Amanda Tat, administrative officer; Sophea Chan Diaz, financial administrator; Kimberly J. Bond Schaefer, senior administrative assistant; and an event coordinator. 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 MIT Edgerton Center to reach students and teachers, and the MIT Catalyst Clinical Research Center to reach health professionals. The COE²C is led by Dr. Kathleen Vandiver, director, and Professor Bevin Engelward, co-director, with support from Amy Fitzgerald and Dr. Amanda Gruhl, outreach coordinators.

The CEHS continues a long tradition of providing its membership with excellent research facilities that reflect, nurture, and support the center's research directions. The CEHS 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 Imaging Facilities Core, the Animal Models Facilities Core, and the Integrative Health Sciences Facilities Core.

Under the supervision of Drs. John Wishnok (director) and Koli Taghizadeh (codirector), 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 of cellular molecules such as DNA, RNA, and protein—as well as 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 and other modern analytical methods. In 2015, the center purchased an inductively coupled plasma mass spectrometry with support from the Office of the Vice President for Research. This instrument allows center members and others in the MIT community to measure trace amounts of a host of inorganic compounds, including toxic metals. This year the center purchased a new Thermo Fisher Q Exactive Hybrid Quadrupole-Orbitrap mass spectrometer, again with the support of the Vice President for Research and the Departments of Biological Engineering and Chemistry. This instrument will enhance our ability to do proteomics and small molecule drug and foreign compound metabolism studies.

Drs. Stuart Levine and Robert G. Croy oversee the Genomics and Imaging Facilities Core, which provides center members with a variety of sophisticated quantitative imaging technologies and an integrated facility for DNA sequencing and analysis, data storage and management, data mining, biostatistics, and modeling. These tools are critical to the

goal of moving CEHS research to higher levels of complexity in an attempt to understand the response of an organism to environmental influences at the systems level.

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.

Starting April 2016, the Integrative Health Sciences Facilities Core (IHSFC) leadership has been reorganized. It is now led by Professors Michael Yaffe and James G. Fox with the support of the Hospital Liaison Program director (Dr. Catherine Ricciardi) along with a cohort of clinical and translational consultants (John J. and Dorothy Wilson Professor Sangeeta Bhatia; Professor David Hunter; Professor Peter Dedon; Associate Professor Jacquin Niles; Ravi Thadhani; Susan Erdman; and Avrum Spira); this team is composed of MD and DVM clinical specialists. The IHSFC was developed to help CEHS members translate their research activities for the clinical and epidemiological realms. This reorganization involved formalizing a relationship between CEHS and the MIT Catalyst 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 program in the CEHS is the Global Environmental Health Sciences Program, led by co-directors Gerald Wogan 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 and Singapore; in the past they have included studies in China, Vietnam, and various countries in South America and Africa.

The CEHS has a long-standing commitment to fostering the careers of its young scientists and junior faculty. The Career Development Program, directed by Professors Bevin Engelward and Leona Samson, 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, the CEHS provides resources that promote success and enable community engagement in environmental health. These types of opportunities and resources are:

- Mentoring
- Financial and administrative support
- Research resources
- Speaking opportunities for junior faculty
- New Frontiers seminar series for postdocs

- Translational research support
- Outreach opportunities
- Global program in public health
- Responsible conduct of research training

The center continues its successful and popular National Institute of Health (NIH) and privately funded Pilot Project Program, which is overseen by the center director and the 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 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 last year, 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 CEHS. The first Theron G. Randolph Translational Pilot Project was awarded in 2015 to Associate Professor Katharina Ribbeck.

Accomplishments in AY2016

Our principal accomplishment this past year was the renewed funding for five years of our Core Center by the NIEHS. The CEHS has maintained a strong volume of research support, totaling over \$8.1 million in FY2016 and resulting in at least 370 publications. These research projects are funded through a variety of sources, including the National Institutes of Health (NCI, NIAID, NIBIB, and NIEHS), 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 Environmental Toxicology was moved this year from its original home in the Department of Biological Engineering into CEHS. This move, which was encouraged by the NIEHS, reflects the broadening of CEHS to include many faculty members, mainly engineers, from outside Biological Engineering. The training grant now supports students and postdoctoral fellows 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 now teach an intensive independent activities course entitled "Fundamentals of Toxicology and Environmental Health."

Community Outreach Education and Engagement Core

The National Institutes of Environmental Health Sciences mandates that each of its Core Centers participates in a program for community engagement and outreach. The goals are to develop partnerships with community members to translate and disseminate the center's research science, evaluate outreach models, disseminate the results at local and national levels, and promote models for national implementation.

Our COE²C has three major focus areas: (1) outreach to underserved communities that are also designated as environmental justice (EJ) communities; (2) innovative technologies for conveying key concepts relevant to environmental health to children and lay people; and (3) workshops that serve key members of our community in order to teach about environmental health.

COE²C has two EJ communities: (1) immigrant populations living along the urban shores of the Mystic River watershed, which flows through over 22 communities in the greater Boston area; and (2) Native Americans living on Tribal lands in northern Maine. Our challenge is how best to inform, advise, listen to, and work with partner organizations in these communities to mitigate the human health effects of industrial pollution and unhealthy lifestyles. An annual visit by CEHS to Tribal lands to meet with the Tribal environmental officers has increased our understanding of the issues facing indigenous peoples. These regular visits along with our invited participation at the 2015 Environmental Protection Agency Region 1 Tribal Environmental Summit, has helped to establish an excellent working relationship. COE²C director Dr. Vandiver has also shared science curricula for youth, collaborating with tribal earth camp educators and with science teachers in the Maine Indian Ed (MIE) schools. Closer to home in Malden, MA, COE²C has provided timely leadership through the Mystic River Watershed Association and its sister organization the Friends of the Malden River in EJ matters relating to safe public access to the Malden River. Plans for the development of real estate along the river are moving rapidly with COE²C support. COE²C recognizes the need for public access to clean water and the need for access to water and open green spaces to promote health and well-being for all.

COE²C has made significant progress this year in the development of innovative teaching tools that are being used to convey important concepts in environmental health. For many years we have used LEGO-based kits that were created in CEHS as teaching tools to inform our target communities about the biological impact of environmental exposures as well as the chemical processes related to the generation of greenhouse gases. COE²C uses these hands-on tools for workshops to directly reach out to our stakeholders, as well as for supporting teachers and nurses to be able to use the kits to inform their students and patients. Recently, COE²C invented an alternative approach that serves the same functions but does not use LEGO bricks. Importantly, a grant from the J. M. R. Barker Foundation has made possible the fabrication of production molds for our molecular biology sets. We designed the molds and the models in partnership with the MIT Edgerton Center. The first shipment of the models—one ton worth of plastic—arrived in June 2016 to much excitement. The Barker Foundation grant will provide molecular sets and teacher-training workshops to all 34 Boston Public High Schools. Additionally, nursing schools have found COE²C teaching methodology to be of interest

in the training of nurses. Dr. Vandiver co-authored "Building Genetic Competence through Partnerships and Interactive Models," an article published in the May 2016 issue of the Journal of Nursing Education, describing how the prototype models were utilized to increase competence in the field of genetics among nurses. A design patent has been issued to MIT for the DNA and RNA set this past year and we expect additional patents to be filed in the future. The other major outside grant benefiting COE²C this past year is an EPA project that is just getting underway. Specifically, Associate Professor Jesse Kroll is building an air sensor network to monitor volcanic emissions in Hawaii. The nodes in the sensor network will be sited in school community gardens all around the island. COE²C's major role will be to provide teacher training workshops for the science kits designed to teach students about climate change and air pollution.

COE²C has also made significant progress this year in reaching out directly to our stakeholders. COE²C has participated in science festivals, including the Beijing Science Festival, the Cambridge Science Festival, and the MIT Open House in April 2016. Our Beijing sponsors were pleased that we chose to create a booth that, in addition to highlighting the molecular consequences of exposures, also teaches about both climate change and air pollution. In an effort to effectively communicate to a large number of people, COE²C trained more than 60 bilingual Chinese school children to be the explainers at the MIT booth in Olympic Park. Our next festival was the Cambridge Science Festival (CSF). Our event took place in the Cambridge Public Library where we celebrated the CSF's 10th anniversary and our 10th year of participation. The very next weekend was the MIT Open House where MIT graduate and undergraduate students volunteered to teach about DNA and air pollution using our new interactive models. Taken together, this past year, we have successfully reached out to hundreds of people using innovative CEHS-supported technologies that teach about air pollution and climate change, and about the impact of our environment on our health.

Annual CEHS Poster Session

For the 12th consecutive year, the center offered its popular CEHS Poster Session in May 2016. This event has attracted over 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 CEHS Poster Session receives overwhelmingly positive feedback in terms of promoting scientific exchange and collaborations, as well as introducing the CEHS to the broader MIT community.

CEHS Sponsored and Co-Sponsored Lecture Series

In the past year, the center hosted eight 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 both before and after the seminar. These opportunities for mingling among CEHS members 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 evening seminar series draws students, postdocs, and faculty from Boston University, Brown, Harvard, Northeastern, Tufts, Yale, and the UMass Medical School in Worcester. The DRAM seminar has become a vibrant part of the CEHS culture.

In addition, the center has continued to offer the New Frontiers Seminar Series for postdocs transitioning into the workforce. 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 receive feedback on their job talk. Talks are advertised to the entire CEHS community, which asks questions and offers advice that help in preparation for future job interviews. Importantly, following the presentation, there is a private meeting between faculty 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 presentations in preparation for a competitive job market.

In addition, 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. Professor Daniel C. Liebler presented the Gerald N. Wogan Lecture, "Proteogenomic Analysis of Human Cancer," in April 2016. Dr. Michael Rosenblatt presented the David B. Schauer Lecture, "Drug Invention and Access to Innovation: What will it really take to improve health?," in February 2016. And Professor Li-Huei Tsai presented the Robert S. Harris Lecture in December 2016.

A strength of the CEHS is its ability to integrate with other organizations on campus, including departments with shared interests. This year, we put significant effort into the possible creation of a new center, which if funded, will be embedded within CEHS. Specifically, we applied to the NIH to designate a center under the Superfund Research Program. The application process required coordination among about a dozen faculty from many different departments and aims to address problems created by environmental contaminants from prior industrial activity in the greater Boston area. The leaders for this process were Bevin Engelward, director; John Essigmann, co-director; and Amanda Tat administrative officer. Additionally, Kathleen Vandiver, director of the CEHS COE²C, played a critical role by making connections to stakeholders in nearby communities. The proposed Superfund Research Program homes in on alkylating agents, which are chemicals in our environment that can cause mutations and cancer. Within the program, there are four major projects, each with multiple investigators, that are focused on water pollution, air pollution, susceptibility factors, mutations, 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 to the possibility of funding, the preparation of the proposal

brought CEHS members together and thus has supported new collaborations and research aimed at problems in environmental health.

Plans for AY2017

In the next year, the CEHS leadership will be actively engaged in strategic planning discussions to reflect both the evolution of the center membership as well as the center organizational chart. We are planning a retreat and poster session to be scheduled in late January 2017 with an External Advisory Committee meeting following the day after. The CEHS center director and the deputy director will focus on the goals for AY2017, which are: (1) to reassess the center membership, with the specific goal of attracting additional junior faculty and to help foster relationships where possible between scientists and engineers; (2) to stimulate center members' participation in the Global Environmental Health Sciences Program, because 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 restructure our Bioanalytical and Imaging Facilities Cores to put them more in-line with the evolving research mission of CEHS. As always, the CEHS leadership will continue efforts to engage the broader MIT community, including the newly formed Environmental Solutions Initiative and the MIT Energy Initiative, in research activities related to environmental health sciences.

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

Our Career Development Program conducts mentoring activities for junior members of the center that will complement departmental mentoring efforts and enhance the participation of junior members in the center activities. For many years, the faculty members of the Training Grant in Environmental Toxicology (Professor Essigmann is the PI and Professors Dedon, Engelward, and Forest White serve on the Executive Committee) have run a series on Responsible Conduct of Research for the pre and postdoctoral trainees. We have opened this series to all faculty members of the center and other groups around the Institute. This training is central to the development of young scientists. Junior faculty are also the primary presenters in our Friday Forum series, which recruits in part from previous awardees of our Pilot Project Programs. The opportunity to present in front of senior colleagues in this well-attended series gives excellent opportunities for career feedback. Finally, the online series of lectures to graduate students, postdocs, and junior faculty offered as part of the Responsible Conduct of Research Program will be expanded by two sessions. The center will continue the New Frontiers Seminar Series in addition to the new Grant Proposal

Writing Workshop and the Page One Program, in which senior faculty evaluate the Specific Aims and Introduction sections of grant proposals by junior faculty to help craft competitive proposals.

John M. Essigmann Director Professor of Biological Engineering and Chemistry

Bevin P. Engelward Deputy Director Professor of Toxicology and Biological Engineering