

Addressing Environmental Health Disparities

Strategic Plan Theme: Sustainable Health

Funding Level: More than \$5 million

Facility Needs: Adjustments to existing facilities will be needed

Submitting Unit: Natural Sciences/Biochemistry & Molecular Biology/Institute for Integrative Toxicology

Collaborating colleges/departments/units involved with this proposal.

Key collaborators include IIT faculty representing 7 colleges (Education, Natural Science, Human Medicine, Osteopathic Medicine, Engineering, Social Sciences, Veterinary Medicine). Environmental health research will also involve using the rich infrastructure and resources available at MSU such as the cores in the Research Technologies Support Facilities (RTSF), the Institute for Cyber-Enabled Research (ICER), and the Center for PFAS Research (Dr. Murphy, Fisheries and Wildlife).

What is the proposal's big theme or idea?

Economically disadvantaged and underserved communities are disproportionately burdened by exposure to environmental contaminants and industrial chemicals. In response to growing awareness of the potential adverse health outcomes associated with continuous exposure, communities and advocates are demanding a greater voice in the curtailment of environmental contaminant and industrial chemical exposure and remediation efforts. In Michigan alone, there is heightened concern regarding (i) the lead in Flint and Benton Harbor drinking water, (ii) the discovery of per/polyfluorinated alkyl substances (PFAS) – “forever chemicals” - in Michigan ground and surface waters, and (iii) the legacy of “dioxins” in the Tittabawassee River floodplains from Midland to Saginaw. These examples illustrate the need for a greater understanding of the impact of environmental contaminant and industrial chemical exposures on human health, and is magnified by the fact that even low-levels enhance disease development and progression.

The emergence of transcriptomic, epigenomic, metabolome and microbiome technologies has led to unprecedented opportunities to investigate underlying mechanisms, interactions between organ systems, and identify markers of susceptibility, exposure and disease outcome.

What is the proposal's goal?

Our overall GOAL is to address the environmental health disparities and advance environmental health equity associated with chronic exposure to environmental contaminants and industrial chemicals that contribute to disease development and progression. A critical component to the success of this effort is the establishment of effective communication strategies to gain the trust of affected communities. This proposal will solidify MSU's enormous strengths to address complex environmental and public health issues, as well as enhance MSU's leadership in providing real world solutions to local and global environmental health disparities. We will achieve this goal by leveraging existing MSU resources, infrastructure and expertise across diverse colleges, departments, institutes, centers and facilities while supplementing with targeted recruiting to fill critical infrastructure and expertise gaps.

To maximize these possibilities, the four critical gaps need to be addressed.

Environmental Justice Communication: Dr. Hamm (School of Criminal Justice) has exposed the gross disconnect between research, affected communities, regulatory agencies and polluters. It is essential to engage all stakeholders to establish trust and cooperation between all stakeholders to maximize the impact

of environmental health research and mitigation efforts. This position will develop communication training programs for investigators and trainees, and serve as a facilitator between stakeholders.

Data Science: This type of research generates big datasets. Funding agencies and journals are requiring all data and analysis strategies to be findable, accessible, interoperable and re-usable (the FAIR guidelines). This is expected to accelerate discovery, reduce animal use, increase transparency and enhance research integrity. It also provides datasets for independent investigation (i.e., Krishnan (Computational Mathematics, Science & Engineering (CMSE)), Mias (CMSE/BMB), Bhattacharya (Biomedical Engineering), Maiti (Statistics & Probability). Most research programs lack the skills to comply with the FAIR guidelines.

Human Models: A limitation in environmental health science research is the ability to predict human responses. Moreover, there is growing pressure to reduce animal use with the European Community and US Environmental Protection Agency phasing out animal testing. MSU could be at the forefront of environmental health science research by recruiting expertise in human organoid models. For example, Dr. Johnson (BME) is developing in vitro systems to investigate signaling between different organoids to mimic systemic interactions between organs.

Exposure Science: The accurate assessment of environmental and tissue levels of contaminants and chemicals is a critical data gap. This is further complicated due to exposure to complex contaminant and chemical mixtures. To maximize the impact of environmental health research at MSU, exposure science expertise is required.

Define the significance, or impact of your big idea.

For many environmental contaminants and industrial chemicals, the concentrations in air, water or food are quite small (ppm to ppt), raising questions regarding the effects of low levels of persistent exposures to healthy individuals. Epidemiology and environmental health studies suggest low-level exposures have the potential to initiate adverse health consequences in susceptible individuals and/or exacerbate underlying disease. It has been proposed that chronic exposure to environmental contaminants and industrial chemicals are important factors in disease susceptibility and severity. Advancing our mechanistic understanding of chronic diseases associated with contaminant and chemical exposure is essential to communicate the potential risks to affected communities.

IIT will leverage our record of excellence in environmental health by increasing educational opportunities for high school, undergraduate, graduate and postdoctoral trainees. Environmental health education and training has been a MSU strength for nearly 5 decades. Campus-wide IIT efforts to have secured a National Institutes of Health/National Institute of Environmental Health Sciences (NIH/NIEHS) Multidisciplinary Training in Environmental Toxicology Training Grant (33 years of continuous funding - the longest standing NIH training grant at MSU), which supports dual majors in environmental health sciences in partnership with 17 academic programs. To date, IIT has trained 269 doctoral students, many of which are leaders in government, academia and industry. More recently, the graduate courses have been adapted and offered to undergraduate students through the Department of Pharmacology & Toxicology. In addition, IIT faculty routinely participate in the NIH/NIEHS R25-supported summer undergraduate research program and the BRUSH Summer Research Program. These undergraduate experiences encompass multiple themes, including public health, toxicology, chemicals as drivers of disease progression, and environmental health, and could be extended to include risk/safety assessments as well as environmental health science communication research.

Who will be impacted?

Our established strength is in the elucidation of underlying mechanistic role of environmental contaminants and industrial chemicals in disease. This includes:

Immune/inflammatory diseases: The immune system is exquisitely sensitive to contaminant and chemical exposure and plays a major role in the development of metabolic, cardiovascular and neurodegenerative disease. Existing strengths include the research programs of Drs. Rockwell and Kaminski (Pharmacology & Toxicology (P&T)) investigating the effects of food additives and cannabinoids on immune responses. Drs. Liby (P&T) and Doseff (Physiology) also examine the role of the immune system in cancer growth

and metastasis. Dr. Moore (Director, Precision Health Program, College of Human Medicine), focuses on how life style such as socioeconomic status, affects disease susceptibility. Additional opportunities related to inflammation and/or immunotoxicology are expected following COM's Applied Immunotherapeutics (AICER) cluster hire.

Neurodegenerative disease: Americans afflicted with Parkinson's and Alzheimer's Disease represent a devastating health, social and economic burden. Although the cause of these diseases remain to be determined, emerging evidence suggests environmental factors, including genetic-environment interactions, play a central role. The College of Human Medicine (CHM) has made extensive investment in diseases of aging, including neurodegenerative disorders such as Dr. Lipton's Translational Neuroscience Group (Grand Rapids Research Center). Specifically, Dr. Bernstein is exploring links between pesticide exposure and neurodegeneration.

Cardiometabolic Disease: Exposure to environmental contaminant and industrial chemicals occurs through the air we breathe, the water we drink and the food we eat. Cardiometabolic disease typically involves interactions between multiple organ systems resulting chronic diseases such as asthma, diabetes, hypertension and cancer. MSU has a impactful research history that includes discovering novel strategies to mitigate the effects of environmental contaminant and industrial chemical exposures. For example, Drs. Harkema and Luyendyk (Pathobiology & Diagnostic Investigation (PDI), College of Veterinary Medicine) as well as the recently awarded NIH program project grant headed by Dr. Watts (P&T) explore complementary aspects of respiratory disease. Similarly, Drs. Copple (P&T), LaPres (Biochemistry & Molecular Biology (BMB), Sen (Animal Science) and Zacharewski (BMB) investigate aspects of environmental contaminant and industrial chemical exposure on metabolic disease.

What does sustainability for your proposal look like?

IIT has a strong record of environmental health stewardship and sustainability. In addition to 33 years of continuous Multidisciplinary Training in Environmental Toxicology Training Grant funding, it is also the administrative home of the MSU Superfund Research Center (28 years of continuous funding) and the Center for Research on Ingredient Safety (CRIS). IIT has fostered numerous collaborative investigator-initiated National Institutes of Health funded RO1 proposals. This proposal will ensure the sustainability of these efforts by enhancing the competitiveness of externally funded proposals from traditional funding agencies, philanthropic foundations, and other affected stakeholders. For example, IIT investigators have successfully secured funding from non-traditional sources including the food and beverage industry (Kaminski) industrial trade organizations (Harkema, Zacharewski), pharmaceutical companies (Luyendyk, Kaminski) and the chemical manufacturing sector (Kaminski, Zacharewski).

Overall, this proposal has the potential to (1) provide new insights on how environmental contaminants and industrial chemicals contribute to disease processes, (2) address health disparities in economically disadvantaged and underserved communities by addressing environmental justice through targeted research and effective communication; and (4) provide training for the next generation of investigators and communication specialist that will inform the public to ensure responsible use of industrial chemicals and processes to maintain natural resources and human health while reducing the risk of adverse health consequences to vulnerable populations today and in the future.