# sustain

VOLUME 40
SPRING/SUMMER 2019

## Our Envirome

The Human Envirome: A Conceptual Framework for Understanding the Influence of the Environment on Health *p.4*

Christina Lee Brown
ENVIROME
INSTITUTE

**Editor**
Allan E. Dittmer

**Assistant Editor**
Lauren Beth Anderson

**Design/Layout**
Nick Dawson
University of Louisville
Design & Printing Services

The Envirome Institute was created in June, 2018, within the University of Louisville to support and promote research on the impact of the environment on human health.

The Envirome Institute pioneers a new, interdependent vision of health, supports research on the effects of the environment on health, and promotes holistic scholarship, locally and globally. The envirome is the personal, social and natural environment that impacts human development, growth, and disease. Envirome provides an infrastructure for transdisciplinary knowledge, bridging academic research with community engagement.

The Enirome Institute, directed by Dr. Aruni Bhatnagar, brings together 9 centers including: Superfund Basic Research; Diabetes & Obesity; Healthy Air, Water & Soil; Integrative Environmental Health Science; Environmental & Occupational Health Science; Environmental Policy & Management; Kentucky Pollution Prevention; Environmental Engineering; and American Heart Association Tobacco Regulation & Addiction Center.

Sustain is published semi-annually by the:

**Envirome Institute**
Cardiovascular Institute
302 E. Muhammad Ali Blvd.
Louisville KY 40292

Send electronic correspondence to
Dr. Ted Smith, ted.smith@louisville.edu

UNIVERSITY OF LOUISVILLE

This publication is printed on recycled paper.

For previous issues of Sustain Magazine, please visit: **partnershipgreencity.wixsite.com/greencitypartnership**

Christina Lee Brown ENVIROME INSTITUTE

# Introducing the Christina Lee Brown Envirome Institute Sustain Magazine

**by Christina Lee Brown**

Christina Lee Brown, image captured by Mike Wilkinson

Forty years ago, the eminent Kentucky philosopher, farmer, author, and poet gave us what might be the closest thing we have to a medical disease diagnostic for all forms of our individual, family, and institutional health. Here's what he wrote:

> *A healthy culture is a communal order of memory, insight, value, work, conviviality, reverence, and aspiration. It reveals the human necessities and the human limits. It clarifies our inescapable bonds to the earth and to each other.*

As a kind physician might say, the good news is we have tremendous room for improvement. Wendell Berry reminds us of our "inescapable" communion with the earth and with each other. This recognition, he implies, is the pathway to robust overall health. Berry is simply reminding us of the very premise of the science of ecology: We are all interconnected!

Humans live in complex environments that include physical elements of geography, ecology as well as large social networks fashioned by unique combinations of history and culture. The entirety of environmental factors that influence human health and disease risk could be understood collectively as the Envirome. The Envirome, analogous to the genome, is the total set of environmental conditions external to an individual that in concert with the genome enables development, and growth, and determines disease.

The Christina Lee Brown Envirome Institute, which I am so proud to support and to be associated with, is laying the groundwork to lead the scientific inquiry into human-environment interrelationships based on an expanded vision of health beyond genomics. Using Louisville as an urban laboratory, the Institute, which is based at the University of Louisville School of Medicine, will develop new partnerships and new knowledge to address the problems of urbanization. The Institute will create a new integrated curriculum in environmental health and invite leading experts from around the world to participate, bringing together scholars, educators, researchers and leaders in all forms of health from departments and schools across the globe and campus to help all learn to make decisions through the Lens of Health.

Somewhere along the way, our understanding of our health got trapped in the relatively narrow context of medicine. But health is about much more than not being sick. Health is indeed personal, but it is also social, cultural and environmental. And it all begins with the most basic elements: air, water and soil. And it begins at home.

A component of the Institute, the Center for Healthy Air, Water and Soil seeks to develop integrated knowledge of the relationships between human health and the environment through a model of multidimensional health. It incorporates community engagement and citizen science with Louisville as an "urban laboratory" to introduce a new approach to environmental health research. The goal is to connect all aspects of our city back to health. The work before us is to help everyone understand how our natural environment is the foundation that makes all life and good health possible.

Genomics has yielded miraculous insights, but it only offers a part of the health picture. For instance, where we live is often much more predictive of our health outcomes than our genes. In 2017, Louisville Metro's Department of Public Health and Wellness observed an 11-year difference in life expectancy between people living on east and west sides of Louisville. A person's zip code has a greater impact on a person's health than their genetic code because of how well their environment supports good health through things like clean air and water and access to good jobs and nutritious food. The Envirome Institute's research takes the multidimensional nature of heath into consideration when studying the effects of our environment on health and chronic disease.

Guiding my team's work to promote this vision of interconnected health in Louisville is a tool I developed called the Circle of Harmony and Health.


**The Circle of Harmony and Health is a model that deomnstrates a new vision of health where everyone can make decisions through a multifaceted lens of health.**

The Circle of Harmony and Health represents components of human health within our larger natural-social-cultural ecosystem. They are Nutritional, Economic, Environmental, Psychological, Intellectual, Spiritual, Cultural, and Physical Health. Each of these health areas is complex and dynamic individually, as well as interdependent with one another, requiring harmony and balance for a healthier community.

"Harmony" aspires to represent for human health what a national economic model does for our web of local and state economies. It inventories each of the individual components while also recognizing their interconnectedness and interdependence. Harmony shows us that our health ecosystem is far broader than we commonly acknowledge. All too often, we forget that we are part of nature ourselves. Harmony reminds us that we need to live and work where human health comes first, where our full selves can be expressed and nurtured, and where caring is integrated into the fabric of everything.

Harmony also gives us a comprehensive diagnostic tool. And it ensures that we see and address the relationships among those factors. Are they undercutting each other to diminish human health, or are they working in harmony to improve it? At the core of the circle are healthy air, water and soil, underscoring the centrality of the natural environment to sustaining human life. It is closely informed by a landmark study overseen by HRH the Prince of Wales entitled *Harmony: A New Way of Looking at Our World* (2010). The work depicts the interdependent relationships in the natural life cycle, bound in a balanced, rhythmic web of connections, relationships and flows of energy that Prince Charles calls "undoubtedly the greatest marvel ever placed before us."

The Circle of Harmony and Health helps to remind us that human health management is an individual, community, and even global responsibility. When it becomes our purpose, we are in tune with nature, building a lifestyle, a culture, and a global society each of which represents the fulfillment of human life, the point at which we can say with conviction, that we are, along with everything else, nature. And we are making decisions through our lens of all forms of Health so as to create that much needed new vision of Health.

## References

Berry, Wendell. *The Unsettling of America: Cluture and Agriculture.*New York: Avon, 1977. 43-44

Charles, Prince of Wales. *Harmony, A New Way of Looking at Our World.* New York: Harper, 2010

# The Human Envirome: A Conceptual Framework for Understanding the Influence of the Environment on Health

by Aruni Bhatnagar, Ph.D.
Christina Lee Brown Envirome Institute

## Introduction

A large body of empirical evidence supports the notion that the environment is an essential determinant of human survival, growth, disease risk, aging and evolution. Like all other life forms, humans depend upon the environment for food, oxygen and sunlight and only a narrow range of environmental conditions are capable for supporting biological life. Even within this narrow range, variations in physical and geographic characteristics such as temperature, altitude, and sunlight, profoundly affect human physiology and specific genetic and cultural adaptations are required for continued survival and growth. Human survival and evolution also depends upon other life forms. Humans need plants for food and shelter as well as for making built structures and tools. Moreover, human health and well-being is profoundly affected by the presence of microorganisms and marcofauna, which threaten human survival as pest, predators, parasites and infectious agents or serve as sources of food, agriculture and transport. In recent evolutionary history, the development and construction of cultural artifacts, built environments, and industrial production have significantly affected human environments by producing pollutants, contaminants and toxins, which now exert an important influence on human health and disease risk. Given the complex and complicated domains of human environments and the myriad features of the environment that affect humans, it is critical to develop a systematic understanding of these environments, not only to assess the impact of the environment on human health, but also to mitigate the adverse health effects and to create healthier environments in the future. This is particularly important in current societies, in which the decrease in infectious disease has been accompanied by an ominous rise in the incidence of non-communicable diseases such as cancer, diabetes, obesity, neurodegenerative disease, depression and cardiovascular disease, which threaten to erode recent gains in economic prosperity and human health across the globe. A vast majority of such non-communicable diseases could be attributed either to living in unconducive environments or in a state of dyssynchrony with the environment. Hence, it is imperative to reevaluate the concept of health and its relationship with the environment.

## Understanding Health

In current medical practice, health is understood as the absence of disease. In keeping with this understanding, contemporary medicine is focused on disease treatment and management. It is engaged in tracing etiologies, identifying symptoms, classifying conditions, and studying pathology. This approach has led to the development of increasingly complex, sophisticated, and costly treatments focused on minimizing pain, slowing disease progression, and decreasing disease-associated disability and mortality. In all such activities, there is a strong emphasis on effecting or finding a cure and restoring health.

This disease-focused approach of modern medicine stems in part from the legacy acquired from fighting infections. Infectious diseases have an identifiable cause, a pathogen, which when eliminated, restores the individual to health. If the right drugs and treatments are available, then the therapy is straightforward. The primary objective is to remove microbes and to minimize their pathogenic effects. While this model works for infectious diseases, non-communicable diseases are different. In non-infectious diseases, there is no single, offending pathogen. The disease is usually localized to the tissue, and therefore cannot be readily removed from its site to restore health. The pathology is native to an individual and not a foreign invasion, and therefore, the disease cannot be readily exorcised from the afflicted, leaving tissues to spontaneously revert to health.

Non-communicable diseases such as cancer, diabetes, and heart disease, cannot yet be cured, but simply managed. Therefore, health in the context of non-communicable disease is not simply a state that exists when a pathogen is absent, but a predisposition that may or may not progress to disease. That such a predisposition might exist leads to the question whether health is a steady state condition or whether it is a graded state or potential that could be enhanced or diminished even without a pathogenic insult. Such questions are difficult to answer. Old models of health and disease appear not to be entirely applicable, but no new paradigms have emerged. Meanwhile, the global burden of non-communicable disease continues to grow, even in the United States and Europe, where a dazzling array of medical treatments and procedures are widely available. It is evident that we have to develop a new understanding of health, not to just passively prevent disease, but to actively promote health and to realize health as an actionable goal.

The World Health Organization in the preamble to its constitution in 1946, defined health "*as a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity*." This definition, while extending the concept of health beyond disease, could be faulted for its descriptive ambiguity and a lack of clarity. No one can define or quantify "complete" physical, mental and social well-being, the quality of completeness is not only unattainable (or only temporarily achievable), but it may also be different for different people. The ambiguity is further compounded by the concept of well-being, which is subjective and non-quantifiable, and as a result, non-actionable. Clearly, a new definition is needed.

The deficiencies of the WHO definition have been widely recognized. To address such criticism, the WHO redefined health as "*the extent to which an individual or a group is able to realize aspirations and satisfy needs and to change or cope with the environment*." The definition succeeds in emphasizing health as a means, not an end. It also correctly views health as a resource - an ability to maintain homeostasis, and to withstand stress and recover from insults. In this concept, a person who can handle stress, maintain productive social relationships, and achieve self-prescribed goals is considered healthy. However, even though this view accommodates the possibility that health could be improved or strengthened, it does not explain how health could be assessed or measured. More importantly, it localizes health to the individual, seen as a discrete entity. In this concept, health is viewed as an ability or quality characteristic of a specific person, an entity distinct from other members of the society, and separate from the surrounding environment.

This localization of health to an individual overlooks that fact that humans exist, not as isolated independent entities, but as parts of elaborate social networks. These large and complex networks have their own identity, and are fashioned by their own unique history and culture. Moreover, these networks are embedded in specific ecosystems to which they have variably adapted during the course of evolution. Therefore, human health, like human identity, cannot be understood as an entity separate from the identity and the health of the ecological and social networks to which they belong. The resilience of an individual to disease is derived, at least in part, from a larger pool of social and natural resources, and is defined by elements that belong to the larger environmental context, often outside an individual's reach or control.

## Envirome and Health

One way to formulate an inclusive concept of an individual within a specific environment, is to adopt the omics approach developed by geneticists and psychologists. Using this approach, we could construct an inclusive model comprised of different environmental factors as an *envirome* to reflect the totality of environmental conditions that affect an individual. The envirome could be understood as the sum of all external conditions that effectuate and regulate the translation of the genome to the phenome throughout the lifespan of an individual. It comprises interdependent sets of natural, social and personal domains (Figure 1) that collectively permit the expression of the genome and thereby regulate human development, health and disease susceptibility.[1]

Although features of individual enviromes may be shared by many individuals that live within a specific set of social conditions or ecological niches, the envirome, like the genome is unique to each individual. This specificity of the envirome distinguishes it from current models of the social determinants of health, which often do not account for the personal microenvironments created and populated by lifestyle choices and living conditions specific to a person. These microenvironments distinguish an individual's experience and conditions from those of other members living within similar geographic and social conditions. It facilitates the understanding of social influences and how they are filtered, selected, and rectified by the personal domains of an individual's envirome. Moreover, the social determinants of health, considered in isolation, often do not account for the effects of the natural environment or how geographic features affect the evolution of societal structures and the health of specific individuals within that specific society. Because the social, personal, and natural domains of the envirome are inextricably intertwined, they cannot be readily unwoven without losing the pattern intrinsic to the weave. It is, therefore, important to understand collectively the natural, social, and personal determinants of health within the same framework so that comprehensive diagnoses and remediative solutions can be targeted to this pattern, and not just to the most directly accessible and readily identifiable strands of influence.

The envirome model offers a fresh perspective of both human health and disease. In this view, health could be considered as a

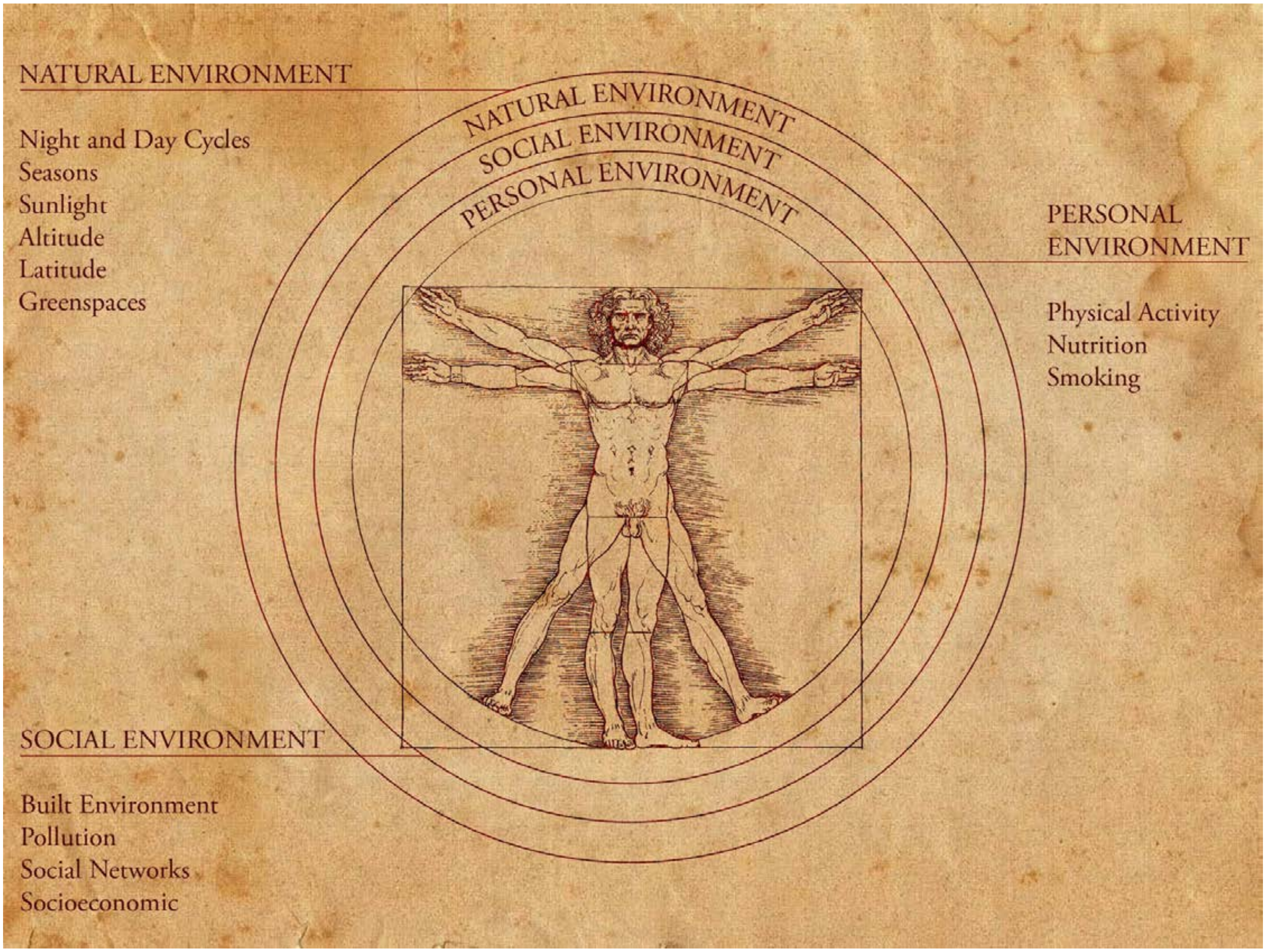



**Figure 1: Different domains of the human envirome.**

state of equilibrium between the envirome and the genome and disease as a mismatch between the two. During the life course of an individual, external challenges from the envirome could be mitigated if there is individual (genetic or cultural) capacity to withstand and counter such insults. For instance, detrimental outcomes of bacterial or viral infections can be avoided, if an individual has innate immunity against such pathogens. Likewise the effect of toxic exposures could be alleviated, if there are genetic resources to counter such insults. In addition to such intrinsic capacity, health could also be seen as genomic concordance with the natural and social domains of the environment. For instance, Tibetans living in the Tibetan plateau are healthy, despite the high altitude, because they have developed genomic resilience to live in such harsh conditions.[2] Such resilience or health may also be due to living in favorable environments – for example individuals living in areas with high access to walkable areas are likely to be less susceptible to obesity and those living near the equator may be more resistant to hypertension (because of greater exposure to UV radiation from the sun).[2]

The concept of the envirome also enables us to examine health as a more inclusive concept. If we consider a person to be a part of a complex envirome, then health relates not only to the ability of a specific individual, but also to the health of his or her envirome. For the natural domain of the envirome, this would include the health of the natural environment as it relates to greenness, biodiversity, climatic conditions and pollution - factors that have been found to exert an important influence on human health, disease susceptibility and longevity.[2] In the social domain, health would relate to the cultural and economic health of the society, as well as the technological and nutritional resources that these societal factors provide.

Could adopting the envirome model change current views of health and disease? Potentially. If we view an individual to be a part of his or her envirome, health could be enhanced as effectively by targeting the envirome as by targeting the individual. By accepting that the health of the natural environment is inextricably linked to the health of the individual, we can enhance human health by decreasing pollution, planting trees, or promoting biodiversity. We can also prevent disease by creating healthier urban and rural environments, building cities that are conducive to walking and physical activity and those that support social networks, which promote social cohesion, and minimize social and personal conditions that promote aggression, violence, addiction, discrimination, and economic disparities. We can encourage the construction of personal environments that empower individuals and communities, and encourage lifestyles that favor healthier choices in nutrition, education, and physical activity. Even when preventive efforts are targeted to the individual, we can see that much may be gained by understanding that lifestyle choices of individuals are, to a large extent, shaped by the natural domain of the environment as well as social norms and prevailing culture. For instance, lifestyle choices such as those related to nutrition, physical activity, chemical use, and addiction are constrained or abetted by social conditions, such as advertising as well as the availability of drugs, cigarettes, and alcohol in specific neighborhoods.

Even though attribution of lifestyle choices to the social environment does not minimize personal responsibility, it does delineate the extent to which both - individual initiative and social acceptance contribute to these choices. Once the contribution of both individual and social factors is delineated, we can target their confluent effects and thereby maximize prevention by not targeting individuals when social influences are strong or trying to effect social change when a change in the behavior of a few individuals would suffice. We can create an appropriate choice architecture that makes making healthier choices easier or preferable.[3] For instance, rates of smoking could be decreased not only by educating individuals about the dangers of smoking, but also increasing taxes on tobacco, decreasing cigarette advertising, prohibiting sales to minors, banning public smoking, and de-normalizing smoking.[4] Similar approaches targeting both the social and personal domains of the envirome could be adopted to promote other health behaviors such as those relating to nutrition, drug use, and physical activity.

By viewing health as a modifiable ability, we can change medical practice, by looking at the root causes of diseases beyond the individual to his or her envirome. For instance, some of the risk of diabetes and heart disease could be diminished by regulating sleep or synchronizing the circadian rhythm of an individual with the diurnal cycle of night and day.[2] The outcomes of stroke and heart failure could be improved by decreasing exposure to air pollution.[5] And the need for pain medication after surgery could be reduced simply by housing patients in rooms with a view of green scenery.[6] For all of this to happen, we need to develop a much wider evidence base as well as quantitative measures of health understood within the context of the envirome. A more robust evidence base to support this model would require extensive new research into the relationship between different domains of the environment and individual health. More work will also be required to determine how well individual genomes match with the individual enviromes and whether there are discordant factors in the personal, social or natural environments that could be altered to minimize this mismatch. But before we can do that, we will have to develop validated scales that measure health in all its forms. Even if we succeed in redeeming, in small measures, the promise of this approach, we will impact, more significantly, the growing burden of disease in contemporary societies and enhance, more effectively, the health of human populations and their environments.

## Acknowledgement

This work was supported in part a grant from the National Institute of Environmental Health Sciences (ES 029846) and The Nature Conservancy.

Reprinted from Circulation Research with permission

## References

1. Riggs DW, Yeager RA, Bhatnagar A. Defining the human envirome: An omics approach for assessing the environmental risk of cardiovascular disease. *Circ Res*. 2018;122:1259-1275

2. Bhatnagar A. Environmental determinants of cardiovascular disease. *Circ Res*. 2017;121:162-180

3. Thaler RH, Sunstein CR. *Nudge: Improving decisions about health, wealth, and happiness*. Penguin; 2009.

4. Bhatnagar A, Whitsel LP, Blaha MJ, Huffman MD, Krishan-Sarin S, Maa J, et al. New and emerging tobacco products and the nicotine endgame: The role of robust regulation and comprehensive tobacco control and prevention: A presidential advisory from the american heart association. *Circulation*. 2019:CIR0000000000000669

5. Bhatnagar A. Environmental cardiology: Studying mechanistic links between pollution and heart disease. *Circ Res*. 2006;99:692-705

6. Ulrich RS. View through a window may influence recovery from surgery. *Science*. 1984;224:420-421

# Superfund Research Programs

**by Lauren Anderson, MPA and Ted Smith, Ph.D.**
**University of Louisville Superfund Research Program**
**Christina Lee Brown Envirome Institute**

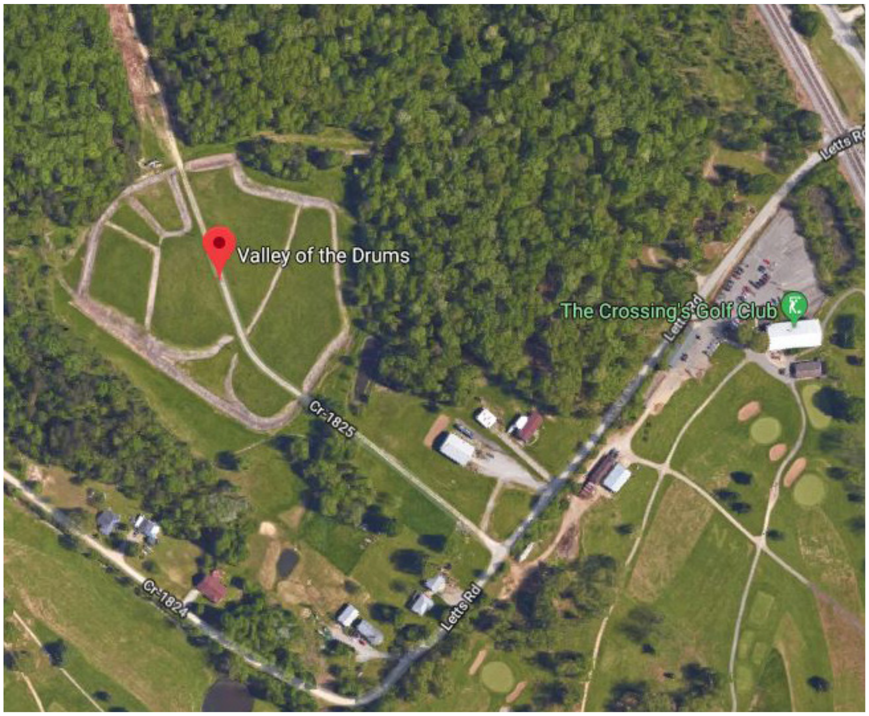
In November 2017, the University of Louisville was awarded a $6.7 million grant from the National Institutes of Health to become one of 23 Superfund Research Programs (SRP) in the United States. The University of Louisville joins partners like Massachusetts Institute of Technology, Columbia University and Duke University in the Superfund Research Program cohort. “This is a very prestigious grant for the university and will help raise the awareness of environmental issues as they relate to health, and train the next generation of environmental scientists,” said Sanjay Srivastava, Ph.D., a professor and researcher in cardiovascular medicine at the UofL School of Medicine who leads the project. In Louisville, Superfund researchers will study how chemical exposures, particularly to chemicals known as volatile organic compounds (VOCs), contribute to the incidence, prevalence, and severity of chronic diseases like diabetes, obesity, and cardiovascular disease.

Nationally, the Superfund Research Program (SRP) provides practical, scientifically-proven solutions to protect human health and improve hazardous environmental conditions. Superfund research contributes to a growing body of scientific knowledge about how to protect the public from exposure to hazardous volatile organic compounds like arsenic and benzene and heavy metals like lead and mercury that contaminate air, water, and soil in former industrial waste disposal sites. Exposure to emissions from more than 1,700 Superfund sites can cause respiratory distress and higher rates of cancer, heart disease, diabetes, and obesity for the people who live near them (NIEHS 2018).

### The First Superfund Sites

In 1980, the discovery of a massive chemical waste disposal site at the Love Canal (Fig.1; Google Maps 2019) in Niagara Falls, New York put the legacy of many years of unsustainable industrial practices on the public agenda. The Love Canal, a section of waterway between Lake Erie and Lake Ontario, was used by the Hooker Chemical Company as a dump site for toxic waste. The canal was covered with a clay seal in 1953 and homes and a school were built on top it. By 1976, toxic sludge


**Figure 1. The Love Canal, a massive chemical waste disposal site.**




made up of about 21,000 tons of chemicals would bubble up into the basements of the homes built on the clay cap. These discarded chemicals were linked to a high rate of miscarriages, birth defects, and other health disorders in surrounding neighborhoods (Landrigan et al. 2015).

Within a few years another major investigation discovered a second waste site near Louisville, Kentucky called the "Valley of the Drums." (Fig.2; Google Maps 2019.) When Kentucky's Department of Natural Resources and Environmental Protection investigated the site in 1978, they found more than 27,000 55-gallon drums full of chemical waste buried and seeping toxic contaminants into the nearby watershed (Landrigan et al. 2015).

By then, it was clear that unsustainable hazardous waste disposal practices were creating environmental and public health emergencies. In December 1980 Congress passed what would become the Superfund Act. The Superfund Act created a tax-supported fund to clean up sites contaminated with industrial pollutants, paid for by chemical manufacturing and petroleum industries. The Superfund tax on oil and chemical industry expired in 1995. Currently, cleanup of hazardous waste sites is funded through general tax revenue (Landrigan et al. 2015).

## Superfund Research Programs

The Superfund Research Program, as it is known today, launched in 1987 to provide scientific support for the Federal Environmental Protection Agency's hazardous waste programs. The SRP mission is to "seek solutions to the complex health and environmental issues associated with the nation's hazardous waste sites with the ultimate goal of improving public health" (NIEHS 2018).

In order to achieve this mission, to find solutions that protect public health from hazardous waste sites, SRPs are charged with the responsibility to develop;

- Methods and technologies to detect hazardous substances and assess their toxicity,
- Methods and technologies to assess and evaluate the risk to human health posed by environmental pollutants, and
- Innovative biological, chemical, and physical methods to remediate toxic waste sites to reduce human exposure to hazardous substances (NIEHS 2018).

Today, SRP supports research in 23 university-based Centers across the United States. SRPs practice integrated research, each Center must have projects that include at least two biomedical projects and two environmental science or engineering projects (Suk and Anderson 1999). The graphic below shows the distribution of these 1,700 Superfund sites and the places where research is being done (Fig.3) (NIEHS 2018).

## Protecting Human Health through Biomedical Projects

Human health is tied directly to the health of the environment. Increased exposure to industrial solvents and other pollutants increases people's risk for developing chronic diseases like heart disease, cancer, obesity, and diabetes. It is challenging for researchers to identify all the potential harms and exposure threats at Superfund waste sites because they often contain complex mixtures of chemicals which cause unexpected interactions can lead to other unforeseen forms of toxicity. However, SRP research has led to improved understanding of how certain contaminants react to others, how people are exposed to them, and the dangers exposure creates. For example, Superfund researchers have discovered;

- Exposure to acrolein exacerbates cardiovascular toxicity (Dejarnett et al. 2014, and Srivastava et al. 2011)
- Links between arsenic in drinking water and diminished intellectual function (Wasserman et al. 2014).
- Early-life exposure to polybrominated diphenyl ether, a common flame retardant, may be linked to changes in physical activity, fear, and anxiety (Macaulay, et al. 2015).
- Associations between early-life exposure to perchloroethylene, and elevated risk of mental illness and teenage drug use (Gallagher et al. 2017).

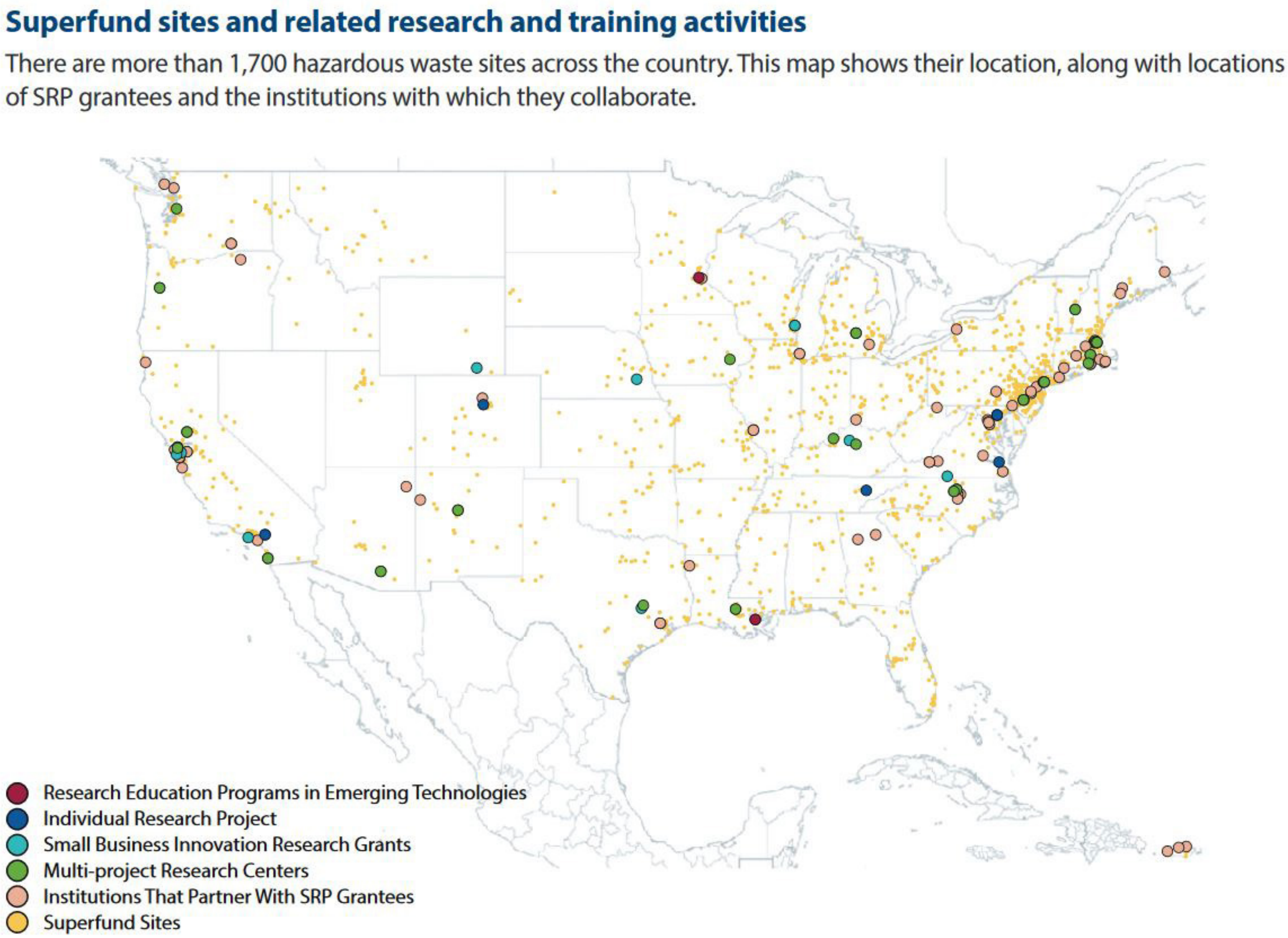



**Figure 3. Superfund sites in the United States.**
*Credit: National Institute of Environmental Health Sciences, Superfund Research Program Fact Sheet. March 2018.*

- Genetic links that may explain why some people exposed to arsenic develop skin lesions and get sick while others do not (Kibriya et al. 2017).
- Consuming activated carbon may reduce the health risks associated with exposure to dioxins which are known carcinogens (Boyd at al. 2017).
- Ways that liver inflammation promotes cancer and suggest novel targets that could lead to new cancer therapies (Shalapour et al. 2017).
- Exposure to vinyl chloride is associated with liver disease (Cave et al. 2010; and Lang et al. 2018)
- Benzene exposure is associated with insulin resistance and cardiovascular disease (Abplanalp et al. 2017, and Abplanalp et al. 2019)

## Reducing Contamination through Environmental Science and Engineering Projects

During a time of rapid development in the early 20th century, unsustainable methods of generating and disposing of industrial chemicals was common. This led to pollution of the air, water, and soil across the United States. Now, SRP research has identified ways to reduce and remediate the pollution of the past such as;

- Using Switchgrass and its associated bacteria to remove polychlorinated biphenyls (PCBs) from soil (Liang, et al. 2014).
- Methods to clean up chlorinated contaminants like trichloroethylene from groundwater using solar power (Fallahpour, et al. 2016).
- Microbes that enhance the ability of poplar trees to remove chlorinated contaminants from the soil and degrade them (Doty, et al. 2017).

- A novel process that binds heavy metals in soil cementing them together so they cannot contaminate groundwater (Biocement Technologies 2017).
- Methods to remove perchlorate and nitrate from contaminated water and provide safe drinking water to California communities (Biocement Technologies 2017).

### Administrative Structure

Every SRP is administratively structured in the same way. Each Center has a(n);

- Administrative Core that provides oversight and manages cross-disciplinary partnerships between centers, University departments, and external entities,
- Research Translation Core that shares information with the scientific community, SRP network, policy makers, and the public in order to guide site remediation and disease risk mitigation.
- Community Engagement Core that works to encourage participation in research by people who are affected by Superfund sites, and a
- Training Core that develops young scientists experience in interdisciplinary research.

A few examples of these core's work highlights SRP's interdisciplinary framework that supports the development and use of innovative tools for research translation, community-engaged research, and investigator training.

- Research Translation: The University of Arizona SRP in collaboration with a local group of Hispanic community health workers created freely available training modules that provide information to communities on how to understand and reduce exposures to toxicants (University of Arizona 2015).
- Community Engagement Boston University's SRP created a guide for community groups that helps communities decide whether a health study is an appropriate strategy for addressing their concerns. It includes contributions by residents living near contaminated sites, community and agency partners, and SRP investigators (Scammell and Howard 2015).
- Investigator Training: Each SRP University supports graduate and postdoctoral-level training in environmental health, science, and engineering. As of 2015, Superfund programs trained over 1,504 students. Scientists and engineers who have finished their training have pursued a range of careers in academia, in government, 192 in industry and other fields (Landrigan et al. 2015).

### Impacted Populations

Although hazardous waste is much better controlled in the United States today than in the past, it still requires study and attention. New chemicals, new technologies, and new forms of waste are created every year (Landrigan and Goldman 2011). The populations at greatest risk of exposure to toxic chemicals are those who live or work near industry and hazardous waste sites;

- 11 million people who live within 1 mile of a federal Superfund site, those who live close to state Superfund sites, and the many thousands of people who are employed by chemical manufacturers or the hazardous waste disposal industry, or as emergency responders (U.S. EPA 1996).
- Children living near hazardous waste sites and industrial complexes have heightened biological vulnerability as they develop and are at especially high risk of experiencing adverse health effects (Landrigan and Suk 1999).
- Poor and minority populations are at high risk of exposure because hazardous waste sites and industrial complexes are disproportionately located in neighborhoods with minority and black populations and lower socioeconomic status (Faber and Krieg 2002).

### Superfund Research Programs, Global Applications

Hazardous waste and chemical pollution is a global issue. Chemical manufacturing industry, chemical use, and hazardous waste burdens are migrating to low- and middle-income countries where labor costs are low and environmental protections often few (Goldstein et al. 2013) (Caravanos et al. 2011). At the same time, exports to low-income countries of hazardous materials such as asbestos, banned pesticides, and e-waste are accelerating (World Health Organization 2014) (Smith et al. 2008). These conditions are a major, although insufficiently recognized, contributor to the burden of disease in these places (Chatham-Stephens et al. 2013).

Other countries are learning the same difficult lessons around human exposure to toxic chemicals because of the migration of chemical manufacturing industry to developing countries. One example is the Bhopal disaster in India, where thousands of people were exposed to methyl isocyanate after an explosion in a pesticide manufacturing facility resulting in hundreds of deaths and injuries. Other examples are just as tragic, but not as dramatic. Currently, more than one million people in China, South and Southeast Asia, and sub-Saharan Africa are exposed to dangerous chrysotile asbestos every day Dhara et al. 2002) (Frank and Joshi 2014).

SRP is dedicated to studying environmental exposure and related human health outcomes all over the world. These efforts occur through partnerships between domestic universities and government agencies and civil society organizations aimed to remediate issues of toxic waste and exposure to harmful chemicals in developing countries.

1. UC San Diego SRP represents SRP on the Good Neighbor Environmental Board (GNEB), an independent federal advisory committee that provides guidance to the President and the Congress on environmental challenges along the U.S.–Mexico border (U.S. EPA 2014).

2. Columbia University SRP studies the epidemiology and toxicology of arsenic in Bangladesh (U.S. EPA and Secretaría de Medio Ambiente y Recursos Naturales 2012).

3. UC Berkeley SRP has studied the hematopoietic toxicity of benzene in China (Ahsan et al. 2006).

## 39 Years of Scientific Discovery

The United States Congress created the Superfund Program 39 years ago in response to a public health emergency created by unsustainable industrial waste disposal. People were at risk of experiencing serious adverse consequences of hazardous chemicals that were contaminating community's water and soil quality. Since the 1980's, the Superfund Research Program has grown and expanded its scope to create new technologies and train scientists of the future. This growth has cemented the program's scientific credibility and impact not only in the Unites States but around the world because of three key factors;

1. Diversification in SRP activities; facilitating innovation for human health research, developing new technologies to remediate environmental toxicants, and translating research to affected communities, industry, municipal decision makers, and federal regulation agencies.

2. Research focus on the connections between public health and environmental exposures; without the SRP program it is likely that rigorous scientific research on the health and environmental effects of hazardous waste and unsustainable development practices would have been neglected until much later in time, causing many unknown detrimental health outcomes.

3. Promotion and importance of transdisciplinary research; Superfund Research Programs gather the best minds from across the United States to participate in collaborative environmental research. Biomedical researchers and engineers, ecologists, earth scientists, social scientists, and evolutionary biologists bring expertise from diverse fields and improve scientific processes and outcomes.

SRP's first 39 years have provided a firm foundation to continue to develop better science to solve one of the world's most difficult problems – how we can sustainably move forward and develop as a society and not harm human health in the process.

## References

Ahsan H, Chen Y, Parvez F, Argos M, Hussain AI, Momotaj H, et al. Health Effects of Arsenic Longitudinal Study (HEALS): description of a multidisciplinary epidemiologic investigation. J Expo Sci Environ Epidemiol. 2006;16:191–205. [PubMed] [Google Scholar]

Boyd SA, at al. 2017. Sequestration of 2,3,7,8-tetrachlorodibenzo-p-dioxin by activated carbon eliminates bioavailability and the suppression of immune function in mice. Environ Toxicol Chem 36(10):2671-2678.

Caravanos J, Clark E, Fuller R, Lambertson C. Assessing worker and environmental chemical exposure risks at an e-waste recycling and disposal site in Accra, Ghana. J Health Pollution. 2011;1:16–25.[Google Scholar]

Doty SL, et al. 2017. Enhanced degradation of TCE on a Superfund site using endophyte-assisted poplar tree phytoremediation. Environ Sci Technol 51(17):10050-10058.

Faber DR, Krieg EJ. Unequal exposure to ecological hazards: environmental injustices in the Commonwealth of Massachusetts. Environ Health Perspect. 2002;110(suppl 2):277–288.[PMC free article] [PubMed] [Google Scholar]

Fallahpour N, et al. 2016. Hydrodechlorination of TCE in a circulated electrolytic column at high flow rate. Chemosphere 144:59-64.

Frank AL, Joshi TK. The global spread of asbestos. Ann Glob Health. 2014;80(4):257–262. [PubMed] [Google Scholar]

Gallagher LG, et al. 2017. Exploring associations between prenatal solvent exposures and teenage drug and alcohol use: a retrospective cohort study. Environ Health 16(1):26.

Goldstein BD, Banda S, Cairncross E, Jiang G, Massey R, Miglioranza K, et al. Nairobi, Kenya: United Nations Environment Programme, 37–51; 2013. Reaching for the 2020 goal: the need for better information and sound management to minimize chemical risks. In: UNEP Year Book 2013: Emerging Issues in our Global Environment. [Google Scholar]

Kibriya MG, at al. 2017. Association between genome-wide copy number variation and arsenic-induced skin lesions: a prospective study. Environ Health 16(1):75.

Landrigan PJ, Goldman LR. Children's vulnerability to toxic chemicals: a challenge and opportunity to strengthen health and environmental policy. Health Aff

(Millwood) 2011;30(5):842–850. [PubMed] [Google Scholar]

Landrigan, P. J., Wright, R. O., Cordero, J. F., Eaton, D. L., Goldstein, B. D., Hennig, B., … Tukey, R. H. (2015). The NIEHS Superfund Research Program: 25 Years of Translational Research for Public Health. Environmental health perspectives, 123(10), 909–918. doi:10.1289/ehp.1409247

Liang Y, et al. 2014. Enhanced polychlorinated biphenyl removal in a switchgrass rhizosphere by bioaugmentation with Burkholderia xenovorans LB400. Ecol Eng 71:215-222.

Macaulay LJ, et al. 2015. Persisting effects of a PBDE metabolite, 6-OH-BDE-47, on larval and juvenile zebrafish swimming behavior. Neurotoxicol Teratol 52(Pt B):119-126.

Microvi Biotechnologies, Inc. 2017. NIEHS grantee webpage. Available: https://tools.niehs.nih.gov/srp/programs/Program_detail.cfm?Project_ID=R41ES026541 [accessed 31 January 2018].

NIEHS (National Institute of Environmental Health Sciences, U.S. Department of Health and Human Services) Superfund Research Program Fact Sheet. March 2018. Accessed 3/22/19 https://www.niehs.nih.gov/research/supported/centers/srp/assets/docs/srp_fact_sheet_508.pdf

NRC (National Research Council). Pesticides in the Diets of Infants and Children. Washington, DC:National Academies Press. 1993. Available: http://www.nap.edu/openbook.php?record_id=2126[accessed 9 December 2014]

Scammell MK, Howard GJ. Is a Health Study the Answer for Your Community? A Guide for Making Informed Decisions. Boston, MA:Boston University Superfund Research Program. 2015. Available:http://cityofportsmouth.com/publicworks/cabhw/HSG_5-14-2015_nocover.pdf [accessed: 17 September 2014]

Shalapour S, et al. 2017. Inflammation-induced IgA(+) cells dismantle anti-liver cancer immunity. Nature 551(7680):340–345.

Smith C, Kerr K, Sadripour A. Pesticide Exports from U.S. ports, 2001–2003. Int J Occup Environ Health. 2008;14:167–186. [PubMed] [Google Scholar]

Suk WA, Anderson BE. A holistic approach to environmental health research [Editorial]. Environ Health Perspect. 1999;107:A338–A339. [PMC free article] [PubMed]

Suk WA, Anderson BE, Thompson CL, Bennett DA, VanderMeer DC. Creating multidisciplinary research opportunities: a unifying framework model helps researchers to address the complexities of environmental problems. Environ Sci Technol. 1999;33(11):241A–244A. [PubMed]

U.S. EPA. Environmental Health Threats to Children. EPA 175-F-96-001. Washington, DC:U.S. EPA. 1996. Available: http://www2.epa.gov/sites/production/files/2014-05/documents/national_agenda_to_protect_childrens_health_from_environmental_threats.pdf [accessed 12 December 2014]

U.S. EPA, Secretaría de Medio Ambiente y Recursos Naturales. Border 2012 Accomplishments Report (2010–2012). U.S.-Mexico Environmental Program. 2012. Available:http://www2.epa.gov/border2020/border-2012-bi-national-success-story [accessed 17 September 2014]

U.S. EPA. The Good Neighbor Environmental Board. 2014. Available: http://www.epa.gov/ocem/gneb/[accessed 7 December 2014]

United Church of Christ Commission for Racial Justice. New York: United Church of Christ; 1987. Toxic Wastes and Race in the United States: A National Report on the Racial and Socio-Economic Characteristics of Communities with Hazardous Waste Sites. [Google Scholar]

University of Arizona. Dean Carter Binational Center for Environmental Health Sciences Homepage. 2014. Available: http://binational.pharmacy.arizona.edu/ [accessed 7 December 2014]

University of Arizona, Superfund Research Program. Promoter Modules. 2015. Available:http://superfund.pharmacy.arizona.edu/learning-modules/promotor-modules [accessed 23 April 2015]

Wasserman GA, et al. 2014. A cross-sectional study of well water arsenic and child IQ in Maine schoolchildren. Environ Health 13(1):23.

World Health Organization. Asbestos: Elimination of Asbestos-Related Diseases. Fact sheet No. 343. 2014. Available: http://www.who.int/mediacentre/factsheets/fs343/en/index.html [accessed 17 September 2014]

Chatham-Stephens K, Caravanos J, Ericson B, Sunga-Amparo J, Susilorini B, Sharma P, et al. 2013Burden of disease from toxic waste sites in India, Indonesia, and the Philippines in 2010. Environ Health Perspect 121791–796.; 10.1289/ehp.1206127 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Dhara VR, Dhara R, Acquilla SD, Cullinan P. Personal exposure and long-term health effects in survivors of the Union Carbide disaster at Bhopal. Environ Health Perspect. 2002;110:487–500.[PMC free article] [PubMed] [Google Scholar]

# The University of Louisville Superfund Research Program

**by Millicent G. Winner and Sanjay Srivastava, Ph.D.**
**University of Louisville Superfund Research Program**
**Christina Lee Brown Envirome Institute**

The overarching theme of the University of Louisville Superfund Center addresses the cardiometabolic effects of hazardous chemicals relevant to the Superfund Research Program (SRP). Within this theme, the Center examines the relationship between cardiometabolic disease (CMD) and exposure to specific volatile organic chemicals (VOCs) in populations living and working in areas impacted by these hazardous substances. The Center engages the local community, including relevant stakeholders, to develop a clear understanding of the health effects of environmental pollutants in residential neighborhoods in South Louisville and a Superfund Site (Lee's Lane). Our collaborative and internationally recognized investigators in CMD also examine how nutrition and obesity influence susceptibility to environmental exposure and how nutritional interventions might mitigate or attenuate this risk.

CMD, contributing to the development of obesity, type-2-diabetes (T2D), fatty liver disease (FLD) and cardiovascular disease (CVD), is the leading cause of death worldwide. It kills twice as many people as infectious and parasitic disease, and three times as many people as all forms of cancer combined.[1, 2] In the U.S., CMD burden is particularly high among socially disadvantaged populations –populations that are also more likely to live near Superfund sites and more likely to be exposed to hazardous chemicals both in residential and in occupational settings. Moreover, individuals with low socioeconomic status are also more prone to obesity, T2D, and CVD.[3, 4] It is therefore not surprising that a poor state like Kentucky leads the country in both childhood obesity and coronary heart disease prevalence (CDC, 2012). Although recent medical advances have decreased CVD mortality, its prevalence remains high and the American Heart Association (AHA) estimates that overall CVD prevalence will increase from 36.9% in 2010 to 40.5% in 2030, and the medical costs of CVD will triple (from $275 to $818 billion), *if the status-quo in CVD prevention and treatment is maintained*.[5] This increase in CVD prevalence is fueled in part by a progressively aging population and an increase in the incidence of obesity, FLD, and T2D. Between 2000-2005, the number of morbidly obese individuals (BMI > 50Kg/m$^2$) in Europe and the U.S. has increased by an astonishing 75%,[6] and currently 68% of the US population is either overweight or obese. T2D is now an epidemic even in children, and it is estimated that between 25-30 % of U.S. adults have FLD. Moreover, children now have both FLD and the more serious form, non-alcoholic steatohepatitis (NASH). This may lead to an increased need for liver transplantation. As a result, for the first time since the Industrial Revolution, our children are threatened with a life expectancy shorter than that of their parents. Although the rate of increase in BMI may be slowing, the incidence of obesity is likely to increase once again with the maturation of the current cohort of U.S. children, among whom obesity rates are at a historical high.[7] Studies using the CHD Policy Model forecast that by 2035, current adolescents overweight will increase future adult obesity by 5-15%, resulting in >100,000 excessive CHD prevalence cases[8], and the associated cost will increase by another $254 billion[9]. Because cardiometabolic defects affect such large sectors of populations, for any current or future evaluation of the health effects of hazardous chemicals, it is imperative to understand how toxic chemicals affect CMD, and how CMD alters the susceptibility to and toxicity of hazardous substances. Moreover, it is of high importance to know whether the current explosion in the rates of obesity and diabetes could be in part related to increased exposure to environmental chemicals.

While the specific cause(s) of CMD or its recent extensive spread remain unclear, current strategies to prevent or treat CMD are based on the concept of risk factors, as well as primary and secondary prevention strategies. These risk factors are common to T2D, FLD, and CVD, suggesting that these diseases share similar etiologies (the "common soil" hypothesis)[10] and overlapping, if not identical, mechanisms. These similarities indicate that in essence diabetes is a cardiovascular disease and that the degenerative changes associated with atherosclerosis or microvascular disease result from "diabetic" changes, such as insulin resistance, even in patients not traditionally considered diabetic. These common risk factors constitute a constellation of features that contribute to overall CMD with insulin resistance as the underlying biochemical defect.

Therefore, assessments of the impact of hazardous chemicals on insulin resistance, and understanding the underlying cellular and molecular mechanisms are informative avenues for assessing the cardiometabolic burden of environmental exposures. To begin to understand the cardiometabolic effects of chemical exposure, the Center investigators examine the effects of VOCs. Not only are these chemicals the most important and abundant at Superfund sites, industrial locations and waste sites, but importantly, there is extensive literature suggesting that cardiometabolic processes are uniquely vulnerable to these pollutants.

This high vulnerability of cardiometabolic processes to hazardous substances and chemicals is underscored by studies demonstrating the cardiometabolic effects of ambient air pollution,[11] which is a variable mixture of VOCs, gases, and particles. These studies, representing data collected from >100 million people in 119 cities in the U.S. and Europe, show that short-term exposure is associated with an increase in myocardial infarction, arrhythmias, endothelial dysfunction, stroke, thrombosis, vascular inflammation and cardiovascular mortality. [12,13] Acute exposure to ambient air pollution reduces metabolic insulin sensitivity in healthy adult humans.[14] Chronic exposure to pollutant levels has also been linked to premature mortality[15], mostly (>70%) due to cardiovascular deaths.[16] Compared with non-diabetics, individuals with T2D are more susceptible to the effects of air pollution[17-19] and have greater risk of death when exposed to high levels of ambient pollutants.[20] Data from animal studies support the concept that chronic exposure to air pollution increases atherogenesis,[21-23] insulin resistance, and visceral adiposity.[24] Recent studies have also shown that exposure to pollutants, especially traffic-related pollutants, increases T2D risk[25,26] and that high levels of ambient air pollution are associated with an increase in T2D prevalence in different counties across the U.S.[27]

Although the cardiometabolic toxicity of most Superfund chemicals has not been studied, excessive rates of T2D and stroke have been found in an evaluation of 720,000 individuals living within a half-mile of 258 Superfund sites that were associated with excessive VOCs in the drinking water.[28] These rates correspond to roughly 8,600 excessive T2D cases and 8,600 excessive stroke cases with an estimated total annual cost of $160 million for long-term care and lost productivity.[28] Clearly, rigorous and comprehensive studies are needed to identify specific hazardous chemicals that elevate CMD risk and to understand their toxicology and mode-of-action. While no data are available to directly link VOC exposure to CVD, an assessment of excessive CVD mortality shows that in a single-pollutant model, propylene, benzene, and xylene are all significantly associated with CVD mortality.[29] In a cohort study of intra-urban variation in VOCs and mortality, similar associations were found between CVD mortality and exposure to benzene, hexane, and total hydrocarbon.[30] Nevertheless, specific VOCs that contribute to CVD risk have yet to be identified, and it is unclear whether VOCs identified in epidemiological studies directly cause adverse health effects, or whether they are mere indicators of exposure to traffic pollution or other environmental pollutants. Therefore, the Center will conduct studies to determine whether VOC exposure is associated with an increased CVD risk in humans. Moreover, to establish biological plausibility of such associations our investigators will conduct pre-clinical studies to establish whether these VOCs can directly trigger or exaggerate CMD.

Results of previous population studies have shown that workplace exposure to VOCs, such as vinyl chloride, benzene, and butadiene, increases CVD risk. In a cohort analysis of 1,658 male workers in Italy, exposure to vinyl chloride (VC) was associated with excessive CVD (relative risk, RR=2.25).[31] Similarly, occupational exposure to benzene has been associated with increased prevalence of arterial hypertension,[32, 33] rhythm abnormalities,[32] and CVD risk.[34] Analysis of mortality data collected from over 12,000 workers at 8 butadiene-styrene polymer manufacturing plants from 1943-1982 shows a significant increase in atherosclerotic heart disease (standard mortality ratio, SMR=1.48).[35] A similar increase in SMR for CVD has also been reported in another study of 2,800 workers.[36] Nevertheless, it remains unclear whether this increase in CVD mortality is directly due to exposure and whether it is associated with cardiometabolic dysfunction. Our Center investigators have found that among highly exposed VC workers the prevalence of steatohepatitis was 80%, indicative of what we have termed, toxicant-associated steatohepatitis (TASH), which is characterized by insulin resistance, elevated proinflammatory cytokines but normal liver enzymes.[37] The liver is the principal organ for xenobiotic detoxification. Our human research regarding human hepatic steatosis clearly indicates that despite the absence of obesity (BMI 25), workers highly exposed to vinyl chloride, as well as other VOCs, developed fatty liver with TASH, insulin resistances, and reduced adiponectin levels.[37] These findings suggest that the disruption of cardiometabolic processes may be an important feature of VOC toxicity, but that further studies are required to determine the effects of VOCs in animal models and to understand their mechanism(s) of toxicity.

Research in the laboratories of our Center investigators has shown that in mouse models, exposure to acrolein induces both vascular [38, 39] and myocardial[40, 41] dysfunction, as well as endothelial activation,[42] and abolishes the cardioprotective effects of ischemic preconditioning.[43] We have also found that acrolein exposure induces dyslipidemia[44] and platelet activation,[45] increases atherogenesis,[46] and causes destabilization of atherosclerotic plaques.[47] Significantly, we have found that exposure to acrolein suppresses circulating endothelial progenitor cell (EPC) levels in both animals[48] and humans,[49] suggesting that this and potentially other VOCs, could suppress responses that contribute to wound healing, angiogenesis and tissue regeneration.

The University of Louisville Superfund Research Center supports two biomedical research projects (Research Projects 1 and 2), two non-biomedical research projects (Projects 3 and

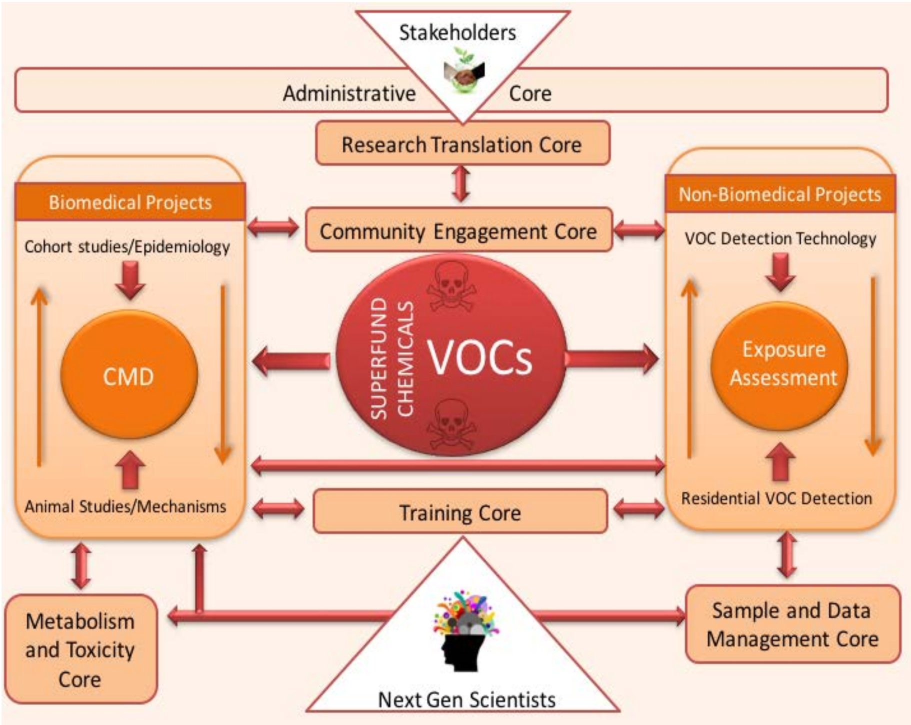



**Fig. 1: Organizational Structure of the Center**

4), an Administrative Core (Core A), Training Core (Core B), Community Engagement Core (Core C), Research Translation Core (Core D), Bioanalytics and Toxicity Core (Core E), and Sample and Data Management Core (Core F). Cores provide technical support to individual projects, but also function as research cores that conducts research independent of the individual projects. The reach of our different projects and cores extends from chemistry and chemical engineering, through basic toxicology, cardiometabolic research and biomarker identification all the way to community engagement and research translational activities that will involve government agencies and SRP stakeholders. The Center organization is specifically designed to accommodate optimal flexibility, integration, and interaction (**Fig. 1**), as well as depth and range, allowing it to respond quickly to SRP needs in most aspects of environmental pollution and cardiometabolic toxicity, as well as contributing to the development of new science and expertise in this area.

The goals of the Center are closely aligned with the Superfund mandate of supporting hazardous substance research and training programs. Within the overarching theme, specific projects and cores of the Center are integrated to address the central problem of cardiometabolic toxicity of hazardous substances. The theme of the Center addresses a major gap in our current understanding of the health effects of toxic substances. Center investigators have unique expertise in atmospheric science, chemistry, chemical engineering, environmental cardiology, gastroenterology, diabetes, obesity and nutrition, and bring to the program extensive and unduplicated experience in studying the cardiometabolic effects of toxic substances. Center investigators conduct mode-of-action research to unravel critical pathways of toxicity and to identify toxicological end-points (cardiometabolic changes) of chemicals (VOCs) found at Superfund and related sites. Using high throughput metabolomic and mass spectrometry approaches, animal experiments and human population studies, Center investigations aid in the discovery and validation of novel biomarkers of both exposure and cardiometabolic injury that would lay the foundation for future remediation strategies. These studies employ state-of-the-art tools to develop pollutant atmospheres for animal exposure and to measure unique and sensitive biological endpoints reflective of cardiometabolic injury. Work supported by the Center is likely to lead to the development of new methods and devices for quantifying atmospheric levels of VOCs that will employ advanced technologies and offer precise, but low-cost measurements of hazardous waste sites.

The findings of the Center's studies will contribute to both the discovery and the validation of sensitive and robust biomarkers that could be used to assess the extent of exposure, metabolism and toxicity. Center investigators are working to create new technologies for detecting VOCs at low environmental levels to enable future exposure assessment activities. Senior Center members educate and train junior investigators, graduate students, and post-doctoral Fellows in the field of environmental science, and promote relevant community awareness and participation to enhance mutual bidirectional understanding of exposure risk and the health effects of exposure. The findings and discoveries of the Center will be transferred to affected communities, end users in public and private sectors, and other stakeholders.

## References


1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D and Turner MB. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2-e220.

2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Franco

S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Magid D, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Nichol G, Paynter NP, Schreiner PJ, Sorlie PD, Stein J, Turan TN, Virani SS, Wong ND, Woo D and Turner MB. Heart disease and stroke statistics--2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6-e245.

3. Kaplan GA and Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation*. 1993;88:1973-98.

4. Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, Sorlie P, Szklo M, Tyroler HA and Watson RL. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med*. 2001;345:99-106.

5. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khera A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PW and Woo YJ. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123:933-44.

6. Sturm R. Increases in morbid obesity in the USA: 2000-2005. *Public Health*. 2007;121:492-6.

7. Stewart ST, Cutler DM and Rosen AB. Forecasting the effects of obesity and smoking on U.S. life expectancy. *N Engl J Med*. 2009;361:2252-60.

8. Bibbins-Domingo K, Coxson P, Pletcher MJ, Lightwood J and Goldman L. Adolescent overweight and future adult coronary heart disease. *N Engl J Med*. 2007;357:2371-9.

9. Lightwood J, Bibbins-Domingo K, Coxson P, Wang YC, Williams L and Goldman L. Forecasting the future economic burden of current adolescent overweight: an estimate of the coronary heart disease policy model. *Am J Public Health*. 2009;99:2230-7.

10. Stern MP. Diabetes and cardiovascular disease. The "common soil" hypothesis. *Diabetes*. 1995;44:369-74.

11. Brook RD, Rajagopalan S, Pope CA, 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC, Jr., Whitsel L and Kaufman JD. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331-78.

12. Katsouyanni K, Touloumi G, Samoli E, Gryparis A, Le Tertre A, Monopolis Y, Rossi G, Zmirou D, Ballester F, Boumghar A, Anderson HR, Wojtyniak B, Paldy A, Braunstein R, Pekkanen J, Schindler C and Schwartz J. Confounding and effect modification in the short-term effects of ambient particles on total mortality: results from 29 European cities within the APHEA2 project. *Epidemiology*. 2001;12:521-31.

13. Samet JM, Dominici F, Curriero FC, Coursac I and Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. *N Engl J Med*. 2000;343:1742-9.

14. Brook RD, Xu X, Bard RL, Dvonch JT, Morishita M, Kaciroti N, Sun Q, Harkema J and Rajagopalan S. Reduced metabolic insulin sensitivity following sub-acute exposures to low levels of ambient fine particulate matter air pollution. *Sci Total Environ*. 2013;448:66-71.

15. Dockery DW, Pope CA, 3rd, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG, Jr. and Speizer FE. An association between air pollution and mortality in six U.S. cities. *N Engl J Med*. 1993;329:1753-9.

16. Pope CA, 3rd, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D and Godleski JJ. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. *Circulation*. 2004;109:71-7.

17. Goldberg MS, Burnett RT, Yale JF, Valois MF and Brook JR. Associations between ambient air pollution and daily mortality among persons with diabetes and cardiovascular disease. *Environ Res*. 2006;100:255-67.

18. Frampton MW, Bausch J, Chalupa D, Hopke PK, Little EL, Oakes D, Stewart JC and Utell MJ. Effects of outdoor air pollutants on platelet activation in people with type 2 diabetes. *Inhal Toxicol*. 2012;24:831-8.

19. Dubowsky SD, Suh H, Schwartz J, Coull BA and Gold DR. Diabetes, obesity, and hypertension may enhance associations between air pollution and markers of systemic inflammation. *Environ Health Perspect*. 2006;114:992-8.

20. Bateson TF and Schwartz J. Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. *Epidemiology*. 2004;15:143-9.

21. Araujo JA, Barajas B, Kleinman M, Wang X, Bennett BJ, Gong KW, Navab M, Harkema J, Sioutas C, Lusis AJ and Nel AE. Ambient particulate pollutants in the ultrafine range promote early atherosclerosis and systemic oxidative stress. *Circ Res*. 2008;102:589-96.

22. Sun Q, Wang A, Jin X, Natanzon A, Duquaine D, Brook RD, Aguinaldo JG, Fayad ZA, Fuster V, Lippmann M, Chen LC and Rajagopalan S. Long-term air pollution exposure and acceleration of atherosclerosis and vascular inflammation in an animal model. *Jama*. 2005;294:3003-10.

23. Suwa T, Hogg JC, Quinlan KB, Ohgami A, Vincent R and van Eeden SF. Particulate air pollution induces progression of atherosclerosis. *J Am Coll Cardiol*. 2002;39:935-42.

24. Sun Q, Yue P, Deiuliis JA, Lumeng CN, Kampfrath T, Mikolaj MB, Cai Y, Ostrowski MC, Lu B, Parthasarathy S,

Brook RD, Moffatt-Bruce SD, Chen LC and Rajagopalan S. Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. *Circulation*. 2009;119:538-46.

25. Coogan PF, White LF, Jerrett M, Brook RD, Su JG, Seto E, Burnett R, Palmer JR and Rosenberg L. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. *Circulation*. 2012;125:767-72.

26. Andersen ZJ, Raaschou-Nielsen O, Ketzel M, Jensen SS, Hvidberg M, Loft S, Tjonneland A, Overvad K and Sorensen M. Diabetes incidence and long-term exposure to air pollution: a cohort study. *Diabetes Care*. 2012;35:92-8.

27. Pearson JF, Bachireddy C, Shyamprasad S, Goldfine AB and Brownstein JS. Association between fine particulate matter and diabetes prevalence in the U.S. *Diabetes Care*. 2010;33:2196-201.

28. Lybarger JA, Lee R, Vogt DP, Perhac RM, Jr., Spengler RF and Brown DR. Medical costs and lost productivity from health conditions at volatile organic compound-contaminated superfund sites. *Environ Res*. 1998;79:9-19.

29. Tsai DH, Wang JL, Chuang KJ and Chan CC. Traffic-related air pollution and cardiovascular mortality in central Taiwan. *Sci Total Environ*. 2010;408:1818-23.

30. Villeneuve PJ, Jerrett M, Su J, Burnett RT, Chen H, Brook J, Wheeler AJ, Cakmak S and Goldberg MS. A cohort study of intra-urban variations in volatile organic compounds and mortality, Toronto, Canada. *Environ Pollut*. 2013.

31. Gennaro V, Ceppi M, Crosignani P and Montanaro F. Reanalysis of updated mortality among vinyl and polyvinyl chloride workers: Confirmation of historical evidence and new findings. *BMC Public Health*. 2008;8:21.

32. Kotseva K and Popov T. Study of the cardiovascular effects of occupational exposure to organic solvents. *Int Arch Occup Environ Health*. 1998;71 Suppl:S87-91.

33. Wiwanitkit V. Benzene exposure and hypertension: an observation. *Cardiovasc J Afr*. 2007;18:264-5.

34. Zoloth SR, Michaels DM, Villalbi JR and Lacher M. Patterns of mortality among commercial pressmen. *J Natl Cancer Inst*. 1986;76:1047-51.

35. Matanoski GM, Santos-Burgoa C and Schwartz L. Mortality of a cohort of workers in the styrene-butadiene polymer manufacturing industry (1943-1982). *Environ Health Perspect*. 1990;86:107-17.

36. Divine BJ and Hartman CM. Mortality update of butadiene production workers. *Toxicology*. 1996;113:169-81.

37. Cave M, Falkner KC, Ray M, Joshi-Barve S, Brock G, Khan R, Bon Homme M and McClain CJ. Toxicant-associated steatohepatitis in vinyl chloride workers. *Hepatology*. 2010;51:474-81.

38. Tsakadze NL, Srivastava S, Awe SO, Adeagbo AS, Bhatnagar A and D'Souza SE. Acrolein-induced vasomotor responses of rat aorta. *Am J Physiol Heart Circ Physiol*. 2003;285:H727-34.

39. Awe SO, Adeagbo AS, D'Souza SE, Bhatnagar A and Conklin DJ. Acrolein induces vasodilatation of rodent mesenteric bed via an EDHF-dependent mechanism. *Toxicol Appl Pharmacol*. 2006;217:266-76.

40. Luo J, Hill BG, Gu Y, Cai J, Srivastava S, Bhatnagar A and Prabhu SD. Mechanisms of acrolein-induced myocardial dysfunction: implications for environmental and endogenous aldehyde exposure. *Am J Physiol Heart Circ Physiol*. 2007;293:H3673-84.

41. Ismahil MA, Hamid T, Haberzettl P, Gu Y, Chandrasekar B, Srivastava S, Bhatnagar A and Prabhu SD. Chronic oral exposure to the aldehyde pollutant acrolein induces dilated cardiomyopathy. *Am J Physiol Heart Circ Physiol*. 2011;301:H2050-60.

42. Haberzettl P, Vladykovskaya E, Srivastava S and Bhatnagar A. Role of endoplasmic reticulum stress in acrolein-induced endothelial activation. *Toxicol Appl Pharmacol*. 2009;234:14-24.

43. Wang GW, Guo Y, Vondriska TM, Zhang J, Zhang S, Tsai LL, Zong NC, Bolli R, Bhatnagar A and Prabhu SD. Acrolein consumption exacerbates myocardial ischemic injury and blocks nitric oxide-induced PKCepsilon signaling and cardioprotection. *J Mol Cell Cardiol*. 2008;44:1016-22.

44. Conklin DJ, Barski OA, Lesgards JF, Juvan P, Rezen T, Rozman D, Prough RA, Vladykovskaya E, Liu S, Srivastava S and Bhatnagar A. Acrolein consumption induces systemic dyslipidemia and lipoprotein modification. *Toxicol Appl Pharmacol*. 2010;243:1-12.

45. Sithu SD, Srivastava S, Siddiqui MA, Vladykovskaya E, Riggs DW, Conklin DJ, Haberzettl P, O'Toole TE, Bhatnagar A and D'Souza SE. Exposure to acrolein by inhalation causes platelet activation. *Toxicol Appl Pharmacol*. 2010;248:100-10.

46. Srivastava S, Sithu SD, Vladykovskaya E, Haberzettl P, Hoetker DJ, Siddiqui MA, Conklin DJ, D'Souza SE and Bhatnagar A. Oral exposure to acrolein exacerbates atherosclerosis in apoE-null mice. *Atherosclerosis*. 2011;215:301-8.

47. O'Toole TE, Zheng YT, Hellmann J, Conklin DJ, Barski O and Bhatnagar A. Acrolein activates matrix metalloproteinases by increasing reactive oxygen species in macrophages. *Toxicol Appl Pharmacol*. 2009;236:194-201.

48. Wheat LA, Haberzettl P, Hellmann J, Baba SP, Bertke M, Lee J, McCracken J, O'Toole TE, Bhatnagar A and Conklin

DJ. Acrolein inhalation prevents vascular endothelial growth factor-induced mobilization of Flk-1+/Sca-1+ cells in mice. *Arterioscler Thromb Vasc Biol*. 2011;31:1598-606.

49. DeJarnett N, Conklin DJ, Riggs DW, Myers JA, O'Toole TE, Hamzeh I, Wagner S, Chugh A, Ramos KS, Srivastava S, Higdon D, Tollerud DJ, DeFilippis A, Becher C, Wyatt B, McCracken J, Abplanalp W, Rai SN, Ciszewski T, Xie Z, Yeager R, Prabhu SD and Bhatnagar A. Acrolein exposure is associated with increased cardiovascular disease risk. *J Am Heart Assoc*. 2014;3.

# The University of Louisville Superfund Research Center Training Core

by Jonathan H. Freedman, Ph.D. and David W. Hein, Ph.D.
University of Louisville Superfund Research Program
Christina Lee Brown Envirome Institute

### University of Louisville SRP Trainees

The University of Louisville Superfund Research Program (SRP) was established in 2017 with the goal of connecting human health outcomes with exposure to volatile organic chemicals (VOCs) such as trichloroethylene, xylene, benzene and acrolein. At the University of Louisville, our researchers believe that an essential component to a more robust and detailed understanding of the cardiometabolic effects of VOC exposure is training new scientists. The University of Louisville's SRP Training Core engages our pre- and post-doctoral fellows in laboratory-based research and effective communication of the Program's findings.

Building on the expertise at the University of Louisville and Washington University, a partner in University of Louisville's SRP Projects 3 and 4, trainees are exploring the cardiometabolic effects, and developing and validating sensitive biomarkers of VOC exposure. Trainees develop their specific project to translate research findings into concepts that can be transmitted effectively to the community, various local/state/federal agencies and university audiences. Additionally, trainees interact frequently with faculty and students, providing the latest information about the chemistry and human health effects of VOCs through a variety of methods.

Beyond project-based bench science, trainees receive scientific instruction from project cores. Through the Community Engagement Core, trainees are developing the skills required to communicate and engage with relevant stakeholders; including community, government leaders and healthcare professionals; regarding the importance of their research and the Superfund Program. This is being accomplished through traditional methods

**Trainees Austin Zachary and Lindsey Wood participate in a HEAL Health Study event for the Green Heart project.**

such as didactic lectures, participation in local and national workshops, meetings and presentations. Through the Research Translation Core, trainees participate in projects like Green Heart. For this wide-ranging project, trainees have coordinated outreach efforts. This includes recruiting study participants and communicating with enrolled participants in the consent and measurement collection processes at HEAL Community Health Study site visits.

The University of Louisville's SRP is nested within the Christina Lee Brown Envirome Institute with several partnering research centers that include VOCs as toxicants of interest: the American Heart Association Tobacco Regulation and Addiction Center (A-TRAC); Center for Integrative Environmental Health Science, Center for Healthy Air, Water and Soil; Center for Environmental Policy and Management; and the Diabetes and Obesity Research Center. Trainees participate and increase their scientific experience by working within each of these centers, which can include wet-bench research, human health studies and epidemiology.

A unique aspect in the education of our SRP trainees is their integration into other environmental research and educational programs within the University. The SRP Training Core interacts closely with two NIEHS funded T32 and T35 training programs in environmental health sciences. The initiation of the University of Louisville SRP provides an opportunity to synergize the SRP with these training programs.


**Trainees from University of Kentucky and University of Louisville at an Engagement and Communication Training Workshop in Louisville Kentucky. Pictured from left to right; Irfan Ahmad (UK), Mohammad Islam (UK), Michael Detisch (UK), Rishabh Shah (UK), Shuo Tang (UK), Elham Shirazi (UK), Chunyan Wang (UK), Banrida Wahlang (UofL), Stacey Konkle (UofL), Mike Petriello (UK), and Pan Deng (UK)**

The T32 training grant in environmental health sciences, continuously funded since 2004 under the direction of Professor David Hein, was the first institutional pre-doctoral training grant awarded to the University of Louisville. Postdoctoral training was added in the first competitive renewal funded in 2009. During the past 15 years, this program has supported 34 pre-doctoral trainees who completed Ph.D. degrees in Biochemistry & Molecular Biology, Pharmacology & Toxicology and Public Health/Environmental & Occupational Health Sciences. Currently there are nine pre-doctoral fellows pursuing Ph.D. degrees in these programs, including a Superfund trainee. The T32 program has also supported ten post-doctoral fellows based in the Departments of Pathology & Laboratory Medicine, Pharmacology & Toxicology, Environmental & Occupational Health Sciences, Internal Medicine and the Birth Defects Center. Currently there are two postdoctoral fellows in training, one of whom is also a Superfund Trainee. Graduates of this program are now faculty and principal investigators with federal research grants at University of Louisville and other universities or employed in senior research leadership positions at the University of Louisville and in major administrative and research positions in government and industry.

The T35 summer environmental health sciences training program, which supports research projects for medical students, began in 2006 under the direction of Professor Russell Prough. SRP trainees together with T32 trainees, and to some extent T35 trainees, hold joint trainee-led meetings, workshops and field trips. The group is currently organized and directed by SRP and T32 post-doctoral trainees.

**Trainees from University of Kentucky and University of Louisville at an Engagement and Communication Training Workshop in Louisville Kentucky.**

## Workshops, Events and Tours

Since the beginning of the University of Louisville SRP Training Core our trainees have participated in local workshops, community events, disaster training and a field trip to a local Superfund site.

## University of Louisville and University of Kentucky SRP Trainee Workshop

The University of Louisville SRP Training Core held an Engagement and Communication Training Workshop with the University of Kentucky SRP in downtown Louisville, KY. The event was hosted by the University of Louisville trainee leaders, Dr. Banrida Wahlang, a former University of Kentucky trainee, and Dr. Marina Malovichko. The workshop was a cross-center event with the active participation of trainees from both SRPs. Dr. Mike Petriello, trainee leader of the University of Kentucky SRP, started the workshop with a brief introduction about their SRP and its team members. The highlight of the workshop was an enthusiastic and informative talk by Dr. Anna Hoover, Assistant Professor and co-leader of the University of Kentucky SRP Research Translation Core. Dr. Hoover discussed the importance of effective communication, not only in research, but also with community members, policy makers and stakeholders. Other notable speakers included Drs. Kandi Walker and Joy Hart from the University of Louisville Department of Communication, who described how trainees can use creative methods to communicate their science; Dr. Lauren Heberle, Director of the Center for Environmental Policy and Management, stressed the need for community-engagement; and Dr. Rachel Keith and Lori Clark from the Green Heart Project and Dr. Jonathan Freedman, co-leader of the University of Louisville SRP Training Core. Trainees gained a better understanding of the goals and objectives of the two SRP, along with how to be better spokespersons to targeted audiences. The workshop was a success, with trainees enjoying the opportunity to network and compare notes about their own SRPs and research projects. In the future, they intend to foster successful research collaborations between the two centers.


**Stacey Konkle (left) and Lindsey Wood (right) attended a disaster response research training hosted by Texas A&M.**

## Disaster Research Training Workshop at Texas A&M

Two of our epidemiology Ph.D. trainees, Stacey Konkle; under the supervision of Dr. Bhatnagar, and Lindsey Wood; under the supervision of Drs. Hart and Kandi, and Katlyn McGraw , a superfund and T32 trainee, attended the first Disaster Research Training Workshop, a two-day workshop held at the Texas A&M University's Engineering Extension Service (TEEX) Disaster City in College Station, TX. Prior to the event, trainees were taught Incident Command Systems and National Response Frameworks. The workshop was led by government officials, NGO scientists and industry workers. They instructed the trainees on incident command systems, communicating through mass media, safety in field research, field sampling and human studies during and after environmental emergencies. There were spirited debates and a clear difference of opinions between national responders, government officials and industry leaders. Attendees varied from coastal universities to Superfund Research Program investigators. The workshop gave a great background on first responders' command system and the role of researchers in that command system. It also provided resources and information on how to be best prepared for immediate research roll-out during or after a disaster or environmental emergency. The representation from various fields offered an advantage to the discussion. After attending the workshop, Stacey and Lindsey presented highlights of their training at the monthly UofL SRP meeting. They made well received recommendations to the leadership regarding the implementation of a disaster response program for the region that aligned with the goals and expertise of the SRP. They have established a University of Louisville Disaster Research working group, whose goal is to establish the capacity to respond to and

**Trainees (from left to right) Jack Pfeiffer, Banrida Wahlang, Lindsey Wood, Jennifer Toyoda, Jamar Wheeler, Marina Malovichko, Stacey Konkle, Jordan Finch, Rachel Speer, Christine Kim, and Katlyn McGraw tour Rubbertown in Louisville with Dr. Russ Barnett.**


**University of Louisville's Dr. Lauren Heberle (left) and trainees Jamar Wheeler (center) and Lindsay Tompkins (right) presenting a poster at the 2019 Superfund Annual Meeting in Sacramento, California.**


**Trainees Katlyn McGraw (left), Anuradha Kalani (center) and Marina Malovichko (right) presenting a poster at the 2019 Superfund Annual Meeting in Sacramento, California.**

conduct disaster research within the scope of the University of Louisville SRP. They are establishing an umbrella IRB and developing a team capable for rapid response research in the event of a local environmental disaster.

## Tour of the Lee's Lane Superfund site

University of Louisville SRP and T32 trainees, staff and faculty toured the Lee's Lane Superfund site to better understand and appreciate health concerns of residents in the adjacent community of Riverside Gardens. Lee's Lane was listed as a Superfund site in 1983 and is one of the nation's first Superfund cleanup sites. Lee's Lane and the adjacent Riverside Gardens is a focus area of the University of Louisville's SRP. Trainees met with Donna Seadler, EPA Region 4 Site Coordinator and Christoph Uhlenbruck, Kentucky Federal Superfund Branch Manager. During the visit, government personnel were installing soil gas monitors along the site perimeter that will be used to determine if VOC's are infiltrating into adjacent homes from contaminated groundwater.

The community, which was built in 1929 and predates the operation of the landfill, is located in a perfect storm of environmental risks. It is adjacent to the former coal-fired electric power plant (coal-fired from 1954-2015, now a natural gas combined cycle plant), a large chemical complex (Rubbertown), contaminated alluvial groundwater and the Lee's Lane landfill. Most residents have lived in Riverside Gardens their entire lives and are trapped financially. There is no market for these homes, and ethically the residents are reluctant to sell due to potential future health problems. Although, after 70 years, most of the waste in the landfill is not measurably posing future risks.

The tour also stopped in Rubbertown to understand what products the complex produced and the history of vinyl chloride exposure to workers at the former B.F. Goodrich plant, and to appreciate the progress made over the last 20 years to reduce VOC emissions through pollution prevention efforts and local regulatory programs, developed by and promoted by community residents.

## 2019 Annual Superfund meeting

Each year the Superfund Centers from around the country come together for their national meeting. This year's meeting will take place in Seattle WA, and be hosted by the Universities of Washington and Louisville. It is a time for the host SRP's to highlight their accomplishments and for trainees to learn about other SRP programs. A large portion of the meeting is dedicated to the trainees; with poster sessions, plenary talks, roundtable discussions and opportunities to network with other scientists. The Training Core sessions are being organized by the University of Louisville SRP trainees Marina Malovichko and Banrida Wahlang. To further strengthen the links between the University of Louisville SRP and T32 training program, Jamie Young, a T32 trainee is also a member of the committee. They will be collaborating with their University of Washington counterparts and the NIEHS during the next several months to organize sessions, invite speakers and finalize the agenda.

## Trainee Highlights

***Prasadanie Karunarathna Adhihetty, Ph.D. Candidate***

Department of Chemistry, College of Arts and Sciences

**Mentor:** Michael H. Nantz, Ph.D.

**Research Project:**

Development of Novel Ultrasensitive Devices for Measurement of VOCs. This project is focused on development of gas sensor array technology for measurement of target Volatile Organic Compounds (VOCs). Her goal is to develop novel technologies for quantitative analysis of VOCs to improve both lab and on-site measurements of toxic VOCs. Since this interdisciplinary project demands knowledge of various fields like Chemistry, Nanotechnology and Chemical analysis, this project provides her the perfect opportunity to develop her research skills.

***Audrey Dang, Ph.D. Candidate***

Department of Energy, Environmental, and Chemical Engineering, McKelvey School of Engineering, Washington University

**Mentor:** Brent Williams, Ph.D.

**Research Project:**

Developing a Portable, Multichannel Gas Chromatography-Mass Spectrometry Instrument for Characterizing Urban- and Finer-Scale Spatial Variability for Select VOC Superfund Compounds. A novel portable, multichannel gas chromatography-mass spectrometry (GCMS) instrument is being developed for high time resolution, mobile measurements of volatile organic compounds (VOCs). The instrument will be deployed to Louisville to understand the spatial variability of VOC Superfund Chemicals throughout neighborhoods.

**Honors/Awards:**

National Science Foundation Graduate Research Fellow

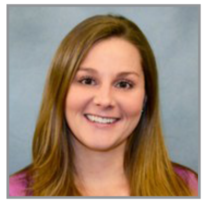
***Sujoy Halder, Ph.D. Candidate***

Department of Chemical Engineering, J.B. Speed School of Engineering

**Mentor:** Xiao-An "Sean" Fu, Ph.D.

**Research Project:**

Development of Ultrasensitive Devices for VOC Measurement. The goal of this project is to develop micropreconcentrator and microsensor array chip for quantitative analysis of trace amount of VOCs in air. The approach is to investigate chemoselective micropreconcentrators for capture of target VOCs by chemical reactions and to develop chemo-resistive gas sensor arrays for measuring the concentrations of target VOCs in air.



***Stacey Konkle, Ph.D. Candidate***

Department of Epidemiology, School of Public Health and Information Sciences

**Mentor:** Aruni Bhatnagar, Ph.D.

**Research Project:**

Volatile Organic Compound Exposure and Cardiometabolic Syndrome Risk In a Nationally Representative Cohort. My current projects focus on investigating associations of urinary volatile organic compound (VOC) metabolites with secular trends and measures of increased cardiovascular and metabolic risk among large complex survey study populations such as NHANES. My work will be used as a benchmark of national VOC exposures and outcomes, which will inform and compliment the University of Louisville VOC Superfund projects to break the link between chemical exposure and disease..

**Presentations:**

2018 Annual Meeting of the American College of Epidemiology, National Secular Trends in Ambient Air Volatile Organic Compound Levels and Biomarkers of Exposure in the United States, Poster

**Honors/Awards:**

Research! Louisville doctoral student poster winner

***Katlyn E McGraw, MPH; Ph.D. Candidate***

Department of Environmental and Occupational Health Sciences, Public Health Information and Health Sciences

**Mentor:** Aruni Bhatnagar PhD

**Research Project:**

Exposure to Environmental Chemicals Contributes to Cardiovascular Disease Gaseous co-pollutants such as volatile organic compounds are major components of indoor and outdoor air pollution. The project objective is to investigate cross-sectional associations between VOC exposure in a human cohort and further validate effects in an animal model.

**Presentations:**

2018 Kentucky Public Health Association, Exposure to Volatile Organic Compounds is Associated with Cardiovascular Disease, Poster.

2017 Research!Louisville, Exposure to Volatile Organic Compounds is Associated with Cardiovascular Disease, Poster.

2017 Superfund Research Program Annual Meeting, Exposure to Volatile Organic Compounds is Associated with Cardiovascular Disease, Poster.

2019 Society of Toxicology, Association of Volatile Organic Compound Exposure and Catecholamines, Poster

2018 Superfund Research Program Annual Meeting, Association of Volatile Organic Compound Exposure and Catecholamines, Poster

2018, Research!Louisville, Association of Volatile Organic Compound Exposure and Catecholamines, Poster

***Jack Anthony Pfeiffer, Ph.D. Candidate***

Department of Epidemiology, School of Public Health and Information Sciences

**Mentor:** Natalie DuPre, Ph.D.

**Research Project:**

Air Pollution Exposure and Community-Acquired Pneumonia Re-hospitalization and Mortality in Jefferson County Adults. This research project is designed to examine the relationship between exposure to multiple air pollutants and re-hospitalization and mortality in adults hospitalized with community-acquired pneumonia (CAP) in Jefferson County, KY. GIS will be used to interpolate air pollutant concentrations for individual participants based on existing datasets. The goal of the project is to determine if air pollution exposure can influence the occurrence of re-hospitalization or mortality from CAP.

**Presentations:**

Ohio Valley Society of Toxicology Annual Meeting 2018, Harm Perceptions of Tobacco Products and ENDS; Poster

American Public Health Association 146th Annual Meeting, Coal fly ash and wheezing among children 6-14 years old; Poster

Society of Epidemiological Research 2018 Meeting, Coal fly ash and asthma among children 6-14 years old; Poster

**Honors/Awards:**

APHA Environment Section Travel Scholarship

***Pradeep Prathibha, Ph.D. Candidate***

Department of Energy, Environmental, and Chemical Engineering, McKelvey School of Engineering, Washington University

**Mentor:** Jay R. Turner, Ph.D.

**Research Project:**

Hyperlocal Exposure Assessment to VOCs. This project aims to characterize intra-urban spatial variability to exposures of select VOC Superfund Chemicals through tools such as land use regression. This work combines mobile monitoring with modeling to characterize residential level outdoor exposures.

**Presentations:**

Can Urban Greening Improve Air Quality and Health?; Air & Waste Management Association, St. Louis Section; Invited Speaker

Quantifying the Impacts of Vegetation on Air Quality and Health; St. Louis Area Monitoring Agencies Meeting; Invited Speaker

Air Quality Measurements in Louisville: Louisville Superfund Research Program; Louisville Air Researchers Forum; Public meeting

**Honors/Awards:**

Best Presentation Award, 2018 Annual Mid-American Environmental Engineering Conference

***Daniel Riggs, MS; Ph.D. Candidate***

Department of Bioinformatics and Biostatistics, Public Health Information and Health Sciences

**Mentors:** Aruni Bhatnagar, Ph.D., Sanjay Srivastava, Ph.D., Shesh Rai, Ph.D.

**Research Project:**

Investigating the Role of Volatile Organic Compound Exposure on Biomarkers of Cardiovascular Disease. Volatile organic compounds (VOCs) are airborne toxicants abundant in outdoor and indoor air. Emerging data suggest that VOCs are associated with many adverse health outcomes, however, little is known about the effect of VOCs on cardiovascular disease. Therefore we are investigating whether VOC exposure is associated with biomarkers of CVD, such as circulating angiogenic cells, which have been shown to be predictive of cardiovascular mortality.

**Presentations:**

2017 American Heart Association, Volatile Organic Compounds in Tobacco Smoke are Associated with Cardiovascular Disease Risk, Poster

2018 Society of Toxicology, Volatile Organic Compounds in Tobacco Smoke are Associated with Cardiovascular Disease Risk, Poster

2018 Superfund Research Program Annual Meeting, Exposure to Volatile Organic Compounds Depletes Circulating Angiogenic Cells, Poster

2019 ICTXV Meeting, Exposure to Volatile Organic Compounds Depletes Circulating Angiogenic Cells, Poster

**Manuscripts:**

Keith RJ*, Riggs DW*, Conklin DJ, Lorkiewicz P, Srivastava S, Bhatnagar A, DeFilippis A. Nicotine Metabolism in Adults with Type 2 Diabetes. Nicotine Tob Res. ntx214, 2017.

Riggs DW, Yeager R, Bhatnagar A. Defining the Human Envirome: An OMICS Approach for Assessing the Environmental Risk of Cardiovascular Disease. Circ Res. 2018: 122:1259-1275.

***Tirtha Raj Sibakoti, Ph.D. Candidate***

Department of Chemistry, College of Arts and Sciences

**Mentor:** Michael H. Nantz, Ph.D.

**Research Project:**

Development Of Gold Nanoparticle Based Chemiresistors For The Detection Of Vocs. Our work is focused on the utilization of aminooxy chemistry and its chemo-selective reactions with aldehyde and ketones. For this, we first synthesized small (<2 nm) sized gold nanoparticles and functionalized them with the thiol ligand that has aminooxy functionality via place-exchange reaction. Thus, prepared aminooxy-functionalized nanoparticles will serve as a sensor for the detection of VOCs (aldehyde/ketones). We could also detect aromatic VOCs via this sensing approach

**Presentations:**

2018 Superfund Research Program Annual Meeting, Aminooxy-Functionalized Aminothiols as Ligands for Gold Nanoparticle Chemiresistors, Poster

***Lindsay Tompkins, M.S.; Ph.D. Candidate***

Department of Epidemiology and Population Health, School of Public Health Information and Health Sciences

**Mentor:** Joy Hart, Ph.D.

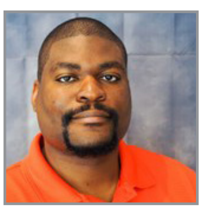
**Research Project:**

The Heart of the Matter: Research Translation with Youth in Louisville. This project aims to translate University of Louisville SRP-related findings to Louisville elementary, middle, and high school students, as well as university undergraduates. Translation activities being employed with area youth include science education and creative projects (e.g., art). Additionally, undergraduate teams are being included in translation activities by both learning about the science and how to communicate scientific information to youth.

**Presentations:**

2018 Superfund Research Program Annual Meeting, The Heart of the Matter: Research Translation with Youth in Louisville

2017 Superfund Research Program Annual Meeting, Capacity Building for Transdisciplinary Collaboration



***Jamar Wheeler, M.A.; Ph.D. Candidate***

Department of Sociology, College of Arts and Sciences

**Mentor:** Lauren Heberle, Ph.D.

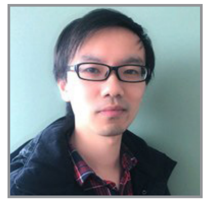
**Research Project:**

Building Community Engagement Capacity For Investigators And Community Residents. This project aims to augment community and investigator capacity for transdisciplinary research focused on exposure to Superfund contaminants. Project supports project- and core-specific community engagement activities as well as efforts to mitigate the effects of exposures to Superfund VOCs. The research focus is assessing change in perception and knowledge of community participants and investigators as a result of engaging in specific Superfund Center activities.

**Presentations:**

2018 Superfund Research Program Annual Meeting, The Role of Community Engagement in Building a Transdisciplinary Superfund Research Center

Facilitated numerous community engagement events known as Community Knowledge Exchange Sessions and presented at the Louisville Metro Air Pollution Control District's 'Clearing the Air' seminars.



***Qi Li, Ph.D. Graduate 2018***

Department of Chemical Engineering, J.B. Speed School of Engineering

**Mentor:** Xiao-An Fu, Ph.D.

**Research Project:**

A Microreactor Approach for Analysis of Aldehydes in Environmental Air. The aim of this project is to develop a microfabricated silicon reactor for capture of carbonyl compounds in environmental air. The captured carbonyl adducts were analyzed by UHPLC-MS. The concentrations of formaldehyde, acetaldehyde and acrolein were determined.

**Manuscript:**

Li, M., Li, Q., Nantz, M.H. and Fu, X-A (2018) Analysis of Carbonyl Compounds in Ambient Air by a Microreactor Approach, ACS Omega, 3, 6764-6769

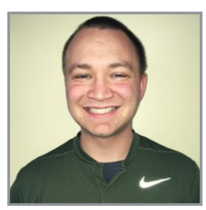
***Lindsey Wood, M.S. Candidate***

Department of Epidemiology and Population Health, School of Public Health and Information Sciences

**Mentor:** Kira Taylor, Ph.D.

**Research Project:**

Probability of conception after fertility counseling and the effects of sexually transmitted infection on conception in the LOUSSI Study. This project aims to determine the likelihood of conception and spontaneous conception through survival analyses among infertile women of whom may or may not be receiving ART treatments, as well as to identify significant predictors of conception and spontaneous conception. We also aim to determine the etiologic effects of history of STI and which specific STI have stronger associations with likelihood of conception and spontaneous conception.



***Austin Zachary, M.S. Candidate***

Department of Epidemiology, School of Public Health and Information Sciences

**Mentors:** Drs. Kandi Walker and Joy Hart

**Research Project:**

Research Translation and Youth. This project translates research findings on health and the environment to youth in focal communities. Several methodologies are used in our translation approaches. Although the translation efforts also reach adults, several of our initiatives involve youth, ranging from elementary to high school students

***Anuradha Kalani, Ph.D.***

Diabetes and Obesity Center, School of Medicine

**Mentor:** Sanjay Srivastava, Ph.D.

**Research Project:**

Molecular and Cellular Mechanisms of Cardiometabolic Toxicity of VOC. Anuradha project integrates her previous experience to elucidate the regulatory roles of cellular and molecular pathways triggered by exposure to VOCs and their impact on cardiometabolic injury. The long-term goal is to explore novel regulatory pathways and establish excellent therapeutic interventions against diabetes and cardiovascular diseases.

***Banrida Wahlang, Ph.D.***

Department of Pharmacology and Toxicology, School of Medicine

**Mentor:** Matthew C Cave, M.D.

**Research Project:**

Sex differences in environmental liver disease. Mechanistic studies pertaining to sex-based differences in environmental liver disease are currently insufficient to explain and prevent the higher prevalence of certain symptoms in women versus men and vice versa. In addition, epidemiologic studies have reported that exposure to environmental chemicals yield different health outcomes in men and women, and therefore, the current project aims to evaluate the underlying cellular mechanisms of volatile organic chemical exposures that are impacted by sexual dimorphism

**Presentations:**

2018 Digestive Disease Week, Molecular Mechanisms of PDE4 Inhibition on Alcohol-Induced ER Stress and Hepatocyte Survival in an Alcoholic Liver Injury Model, Oral and Poster

2019 Society of Toxicology Annual Meeting, Sex Differences in Persistent Organic Pollutant Levels and Liver Disease Biomarkers in the Anniston Community Health Survey Participants, Poster

Panelist, Community Knowledge Exchange: VOC Facts

**Manuscripts:**

Wahlang B. (2018) Exposure to persistent organic pollutants: impact on women's health. Rev Environ Health. 33(4):331-348

Wahlang B, McClain C, Barve S, Gobejishvili L. (2018)Role of cAMP and phosphodiesterase signaling in liver health and disease. Cell Signal. 49:105-115

**Honors/Awards:**

Basic Science Travel Award, Digestive Disease Week

Poster of Distinction, Digestive Disease Week

***Zhenzhen Xie, MS; Ph.D.***

Department of Chemical Engineering, J.B. Speed School of Engineering

**Mentor:** Xiaoan Fu, Ph.D.

**Research Project:**

Electronic Nose For Analysis Of Volatile Organic Compounds In Air And Exhaled Breath. This project aims to develop gold nanoparticle-based sensor arrays for analysis of VOCs in air and exhaled breath. Breath analysis can be used to identify cancer, diabetes by using a chemiresistor sensor array to detect biomarkers.

**Presentations:**

2018 Superfund Research Program Annual Meeting, Detection of volatile organic compounds by thiol functionalized gold nanoparticle

**Manuscripts:**

Xie Z, Ramakrishnam Raju MV, Stewart AC, Nantz MH, Fu XA. Imparting sensitivity and selectivity to a gold nanoparticle chemiresistor through thiol monolayer functionalization for sensing acetone. 2018 RSC Adv. 8; 35618-35624

Honors/Awards

Graduate Dean's Citation Award

University Scholarship and Tuition Award

***Jamie Lynn Young, MS; Ph.D. Candidate***

T32 Training Program, Department of Pharmacology & Toxicology, School of Medicine

**Mentor:** Lu Cai, M.D., Ph.D.

**Research Project:**

The effects of whole life, low dose cadmium exposure on high fat diet-induced NAFLD. This project will focus on the interactions between cadmium and high fat diet in the development of liver disease and the use of dietary zinc to stop disease initiation and progression. This project takes into consideration that environmental exposures are typically multigenerational and life-long, and that factors, such as diet, are involved in the development of disease. We propose whole life, low dose cadmium exposure will enhance metabolic syndrome associated with consumption of a high fat diet, resulting in liver disease and that zinc plays a key role in determining this outcome.

**Presentations:**

2019 The International Society for Trace Element Research in Humans XIII. The Role of Dietary Zinc in Cadmium-Enhanced Non-Alcoholic Fatty Liver Disease. Oral Presentation

2019 The XV International Congress of Toxicology. Poster Presentation. The Effects of Whole Life, Low Dose Cadmium Exposure on High Fat Diet-Induced Metabolic Disease and Its Modulation by Zinc. Poster

2018 10th Conference on Metal Toxicity and Carcinogenesis. Cadmium and High-Fat Diet Disrupt Renal, Cardiac and Hepatic Essential Metal Homeostasis. Oral and Poster Presentations.

2018 58th Annual Meeting of the Society of Toxicology. Sex-Dependent Effects of Early Life Cadmium Exposure and High Fat Diet on the Liver, Heart and Kidney. Poster.

2018 Research! Louisville, Effects of Whole Life Cadmium Exposure on the Development of Non-Alcoholic Fatty Liver Disease in Male and Female Mice. Poster.

2018 56th Annual meeting of the Society of Toxicology. Effects of Early Life Chronic Exposure to Arsenic and Cadmium on the Development of Adult Cardiometabolic Syndrome. Poster.

2018 Graduate Student Regional Research Conference. Effects of Early Life Chronic Exposure to Arsenic or Cadmium on the Development of Adult Metabolic Syndrome: Initial Characterization of Hepatic Changes. Oral Presentation.

2017 Annual Meeting of the Ohio Valley Chapter of the Society of Toxicology. Effects of Early Life Chronic Exposure to Arsenic or Cadmium on the Development of Adult Metabolic Syndrome: Initial Characterization of Hepatic Changes. Poster.

2017 Research! Louisville. Effects of Early Life Chronic Exposure to Arsenic and Cadmium on the Development of Adult Cardiometabolic Syndrome. Poster.

2018 Invited Seminar Department of Pediatrics, University of Louisville. Whole Life Exposure to Cadmium and Its Influence on Diet-Induced Liver Damage.

2018 Radio Show Interview, UofL Today with Mark Hebert. “How do arsenic and cadmium impact human health?

**Manuscripts:**

Impact of Prenatal Arsenic Exposure on Chronic Adult Diseases. Systems Biology in Reproductive Medicine. (2018) Accepted

**Honors/Awards:**

2017 Elected SOT Graduate Student Leadership Committee programming sub-committee secretary

2018 10th Conference on Metal Toxicology and Carcinogenesis Student Travel Award

2018 Ohio Valley Society of toxicology, 1st Place PhD poster

2018 Graduate Deans Citation, University of Louisville

2017 Research!Louisville, 2nd place poster in Masters Basic-Science

2017 Elected SOT Graduate Student Leadership Committee, programming sub-committee secretary

# What is Killing the Coho?

by Eric Wagner

Researchers are trying to determine which chemicals in stormwater are contributing to the deaths of large numbers of coho salmon in Puget Sound. It has prompted a larger question: What exactly is in stormwater anyway?

Jenifer McIntyre holds out a large Ziploc bag full of a mysterious black substance. "What do you think is inside?" she asks.

I take the bag and heft it, squeeze it. The material is fine and feels dry, lightweight, oddly synthetic. I hazard a guess. "Is it some kind of dust or dirt or something?"

McIntyre shakes her head. "Nope!"

I squeeze the bag again. "I don't know, compost? Coffee grounds, maybe?"

"Nope." McIntyre grins. "It's ground-up car tires." She takes the bag back and gives it an affectionate pat. "I've been waiting awhile to get this, so it's a good day."

**Dr. Jenifer McIntyre, an Aquatic Ecotoxicologist, standing in a stream.** *Photo courtesy: Washington State University*

McIntyre, an aquatic ecotoxicologist with Washington State University (WSU), is part of a broad coalition of scientists at groups including WSU, NOAA Fisheries, the U.S. Fish and Wildlife Service and the University of Washington working together to solve a longstanding mystery. The ground-up tires are for use in an upcoming study to see what chemicals might leach out of them during a rainstorm, as rain turns into urban stormwater. The results might help clarify what is killing large numbers of coho salmon in the waters of Puget Sound, a condition known as "pre-spawn mortality."

Stormwater may be Puget Sound's most well-known pollutant, and at the same time its least known. While the state has called stormwater Puget Sound's largest source of toxic contaminants, scientists are still having a tough time answering two basic questions about it: What is stormwater, exactly, and what does it do?

## Let it rain

Every year, the Puget Sound region receives up to forty inches of precipitation, most of it as rain. In the past, which is to say before the I-5 corridor became the bustling urban matrix it is today, much of that rain seeped into the soil or collected on leaves and grass and then evaporated back into the atmosphere; less than one percent was thereafter left to trickle into the Sound as surface runoff. But as humans altered the drainage basin of Puget Sound, so, too, did we alter the fate of the rains. Now, with more than 350,000 acres of impervious surfaces—streets, roads, highways, parking lots, building roofs, and so on—between twenty and thirty percent of precipitation turns into surface runoff. This translates into more than 370 billion gallons of stormwater per year pouring into Puget Sound.

As modern stormwater sluices downhill, it gathers whatever is in its path. By the time it becomes soundwater, it is a formidable toxic stew. According to a 2015 report from the Washington Department of Ecology, at least 33 pollutants have a 50% or greater detection frequency in stormwater, meaning that they are found in at least half of samples. The list includes almost everything from fecal coliform to polycyclic aromatic hydrocarbons, or PAHs, which are known carcinogens. On top of those pollutants, 16 others are found in at least 20% of samples, and hundreds of other chemicals also are present.

All of these pollutants and toxins can have profoundly negative effects on Puget Sound's biota, such as aquatic insects and, especially, salmon runs, several of which are federally listed as threatened. Nathaniel Scholz, a biologist with NOAA, and colleagues from several government agencies showed in 2011 that between 60 to 100 percent of coho salmon returning to some lowland urban streams in Puget Sound die before spawning. More recent work found that juvenile and adult coho salmon die within hours of exposure to untreated runoff from the 520 bridge between Seattle and the eastside of Lake Washington. And in a new paper in Ecological Applications, biologists from NOAA and the Washington Department of Fish and Wildlife found that across 40 percent of coho's Puget Sound range, returning spawners are being especially hard-hit in urban areas, primarily due to stormwater.

**Stormwater picks up contaminants from vehicles.**
*Photo: Daniel Parks (CC BY-NC 2.0)*

### A complex mixture

So which of the potentially thousands of chemical compounds found in stormwater might be killing the coho? That question is behind McIntyre's research today at the Washington Stormwater Center in Puyallup, and it is why she has waited so eagerly for the bag of tire shavings.

Among the biggest suspects, not surprisingly, are the millions of cars that pass nearby, shedding potentially toxic substances such as synthetic rubber from tires, motor oil, windshield washer fluid, transmission fluid, brake dust and automobile exhaust. Those and other substances are being tested at the lab.

If in fact the problem is cars, McIntyre wonders: "Could we find a vehicle pollutant source that is responsible for most of the toxicity?" And if so, could that help regulators deal with the issue?

For the study of the ground up tires, McIntyre will run water through the grounds — a process not unlike making a cup of coffee — and see whether the contaminants that leach out match the toxicity of urban stormwater runoff. Early results have been intriguing. Coho salmon have died when exposed to the leached chemicals, but other chemicals may have similar results and it's too early to say what role automobile tires might have in pre-spawn mortality of coho in the wild.

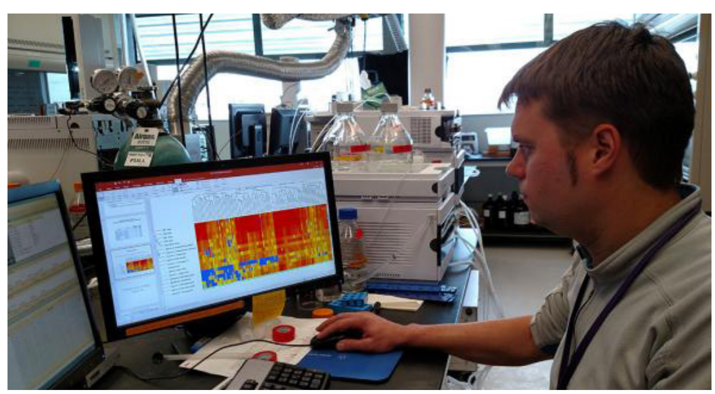
"Stormwater is a complex mixture," McIntyre says. It can vary by location (urban, rural), habitat type (forest, farmland), and season (winter, summer). As to its exact chemical makeup, she demurs. "That's probably a better question for someone like Ed Kolodziej," she says.

### New analysis

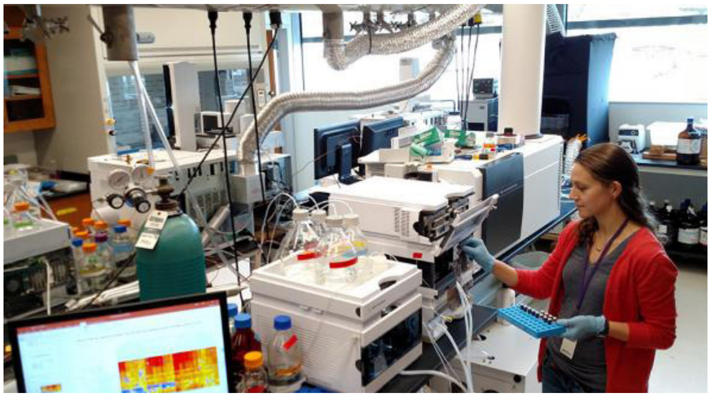
While McIntyre is doing the biology — by researching how salmon react to certain chemicals — Ed Kolodziej is looking deep into the chemistry of stormwater. When I find Kolodziej, he is at work in a backroom in the Department of Civil and Environmental Engineering, which serves as his makeshift office on the UW Seattle campus. He is just here for the day; he spends most of his time at the UW Tacoma Center for Urban Waters where he works with a series of specialized instruments that can measure the presence of molecules in a water sample in the parts per billion [Editor's note: The Center for Urban Waters is the parent group of the Puget Sound Institute, which publishes Salish Sea Currents].

Kolodziej is using a process known as high resolution mass spectrometry to understand stormwater's convoluted chemical makeup. If a particular chemical is in the water, the instruments at the lab are likely to find it. The proverbial needle in a haystack? No problem. But what if you don't know exactly what you are looking for? That's more difficult, and it's where Kolodziej's work may differ from that of other researchers.

Conventional diagnostic methods are best at finding known chemicals. Typically, when facing a sample, a researcher will come up with a list of toxicants they think they're likely to find, called targets, and then test for those substances.



**Dr. Ed Kolodziej analyzes mass spectrometry data in his lab at the Center for Urban Waters.** *Photo: Kris Symer*



**Dr. Kathy Peter loads samples into the mass spectrometry instrument at the Center for Urban Waters labs.** *Photo: Ed Kolodziej*

What Kolodziej is helping to develop is a method for testing urban stormwater that uses liquid chromatography coupled to high-resolution quadrupole time-of-flight mass spectrometry. (This goes by the equally formidable acronym LC-QTOF-MS.) He and his co-authors described the process last August in a paper in Environmental Sciences: Processes & Impacts. “Basically, I think of it as someone going fishing for a specific kind of fish, versus a trawler that pulls everything in and then sorts through the catch,” says Kathy Peter, Kolodziej’s postdoctoral scientist and one of the study’s co-authors. “When you run a stormwater sample, you might see 1,000 or 2,000 features, and each feature is a chemical. Some of them will be natural, but some will be synthetic compounds that you need to test.”

This sort of non-target analysis is good at uncovering what Kolodziej calls the unknown-unknowns of stormwater. “What are the emerging contaminants?” he says. “We’re good at building analytical methods for things we know about, but there’s tons of stuff we don’t know about.” To help assemble a wide array of urban runoff samples, he has enlisted citizen scientists. If someone sees a salmon die in a stream, they can take water and tissue samples. Kolodziej can then analyze the water that salmon was swimming in, and try to figure out what killed it.

**SR-520 bridge traffic in Seattle. Drain pipes visible at each column allow contaminated stormwater to flow directly from the roadway into Portage Bay, Union Bay, and Lake Washington.** *Photo: Kathy Peter*

Even as Kolodziej and his colleagues have identified possible toxins, their precise origin remains as murky as the stormwater itself, at least in the published literature. “But,” he says, “cars and trucks seem to be the biggest culprits.” Motor vehicles are always shedding little bits of themselves as they whiz down roads and highways: flakes of brake, tire dust, droplets of motor oil, antifreeze and gasoline. All of it adds up. The question is how might these different substances interact with one another. Can they become greater than the sum of their parts?

### Possible solutions

As for what to do about stormwater, McIntyre and her colleagues at the Washington Stormwater Center are testing a variety of possible solutions. With coho and the lethal stormwater cocktail streaming off the 520 bridge, McIntyre was able to reduce the runoff’s toxicity simply by running it through a vertical soil treatment column: essentially, a barrel full of sand, shredded bark, and compost. After that, the coho were basically fine. (An interesting quirk is that chum salmon—or, as McIntyre calls them, “zombie fish” — were essentially untroubled by what killed the coho. “They just swam right through it like nothing,” she says.) And in a greenhouse down the road, Ben Leonard, one of her graduate students, is testing different lengths of swale for the extra removal of metals, running gallons of stormwater over a mix of Dutch clover and red fescue. His goal is to learn what a minimum effective length of swale might be, so Washington Department of Transportation engineers know how much to plant next to roads.

“It’s an issue of horizontal versus vertical, and how long stormwater stays in contact with the media,” Leonard says. “Horizontal is better for roadways, but vertical is good for, say, a road next to a steel refinery next to a river where salmon spawn.”

All of these fixes may one day solve what at present seems like an intractable problem. Once everyone has a better idea of the contaminants in stormwater, people can start to recommend changes in a policy sphere. Source control is always better than treatment after the fact, as Kathy Peter points out. “You don’t want to be managing a problem like this in perpetuity,” she says.

Eric Wagner writes about science and the environment from his home in Seattle, where he lives with his wife and daughter. His writing has appeared in Smithsonian, Orion, and High Country News, among other places, and he is the co-author, with photographer Tom Reese, of the recently published book Once and Future River: Reclaiming the Duwamish. He is currently at work on a book about penguins.

**References**

Du, Bowen & M Lofton, Jonathan & T Peter, Katherine & Gipe, Alex & Andrew James, Christopher & K. Environ. Sci.: Processes Impacts, 2017,19, 1185-1196.

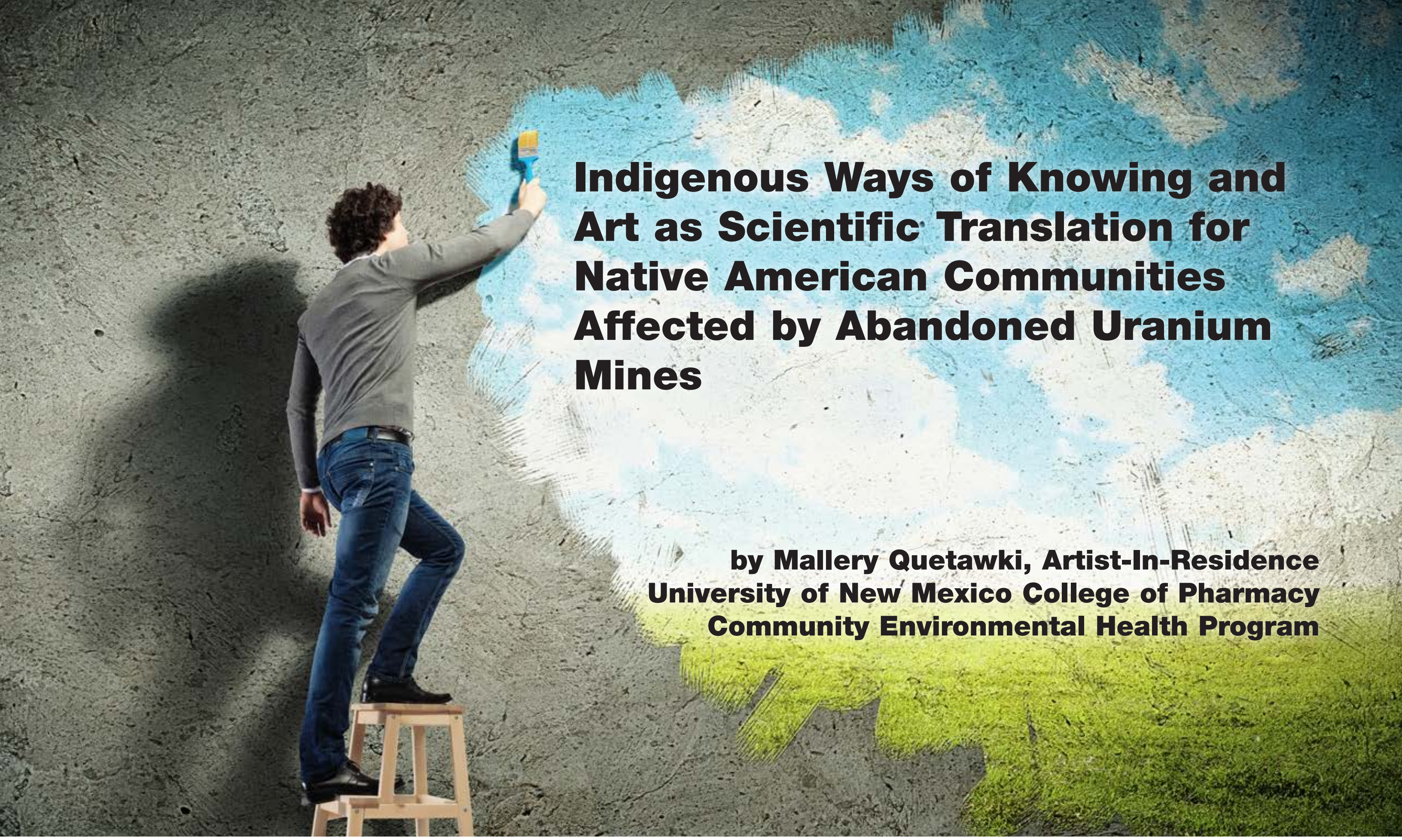
McIntyre, Jenifer & Scholz, Nathaniel & Baker, Joel & Kolodziej, Edward. (2017). Development of Suspect and Non-Target Screening Methods for Detection of Organic Contaminants in Highway Runoff and Fish Tissue with High-Resolution Time-of-Flight Mass Spectrometry. Environ. Sci.: Processes Impacts. 19. 10.1039/C7EM00243B.

Using High-Resolution Mass Spectrometry to Identify Organic Contaminants Linked to Urban Stormwater Mortality Syndrome in Coho Salmon. Katherine T. Peter, Zhenyu Tian, Christopher Wu, Peter Lin, Sarah White, Bowen Du, Jenifer K. McIntyre, Nathaniel L. Scholz, and Edward P. Kolodziej, Environmental Science & Technology 2018 52 (18), 10317-10327. DOI: 10.1021/acs.est.8b03287

T. Peter, Katherine & Herzog, Skuyler & Tian, Zhenyu & Wu, Christopher & Mccray, John & Lynch, Katherine & Kolodziej, Edward. (2018). Evaluating Emerging Organic Contaminant Removal in an Engineered Hyporheic Zone using High Resolution Mass Spectrometry. Water Research. 150. 10.1016/j.watres.2018.11.050.

Feist, Blake & R. Buhle, Eric & H. Baldwin, David & Spromberg, Julann & E. Damm, Steven & Davis, Jay & Scholz, Nathaniel. (2017). Roads to ruin: Conservation threats to a sentinel species across an urban gradient. Ecological Applications. 27. 10.1002/eap.1615.

McIntyre, Jenifer & Lundin, Jessica & R Cameron, James & I Chow, Michelle & Davis, Jay & Incardona, John & Scholz, Nathaniel. (2018). Interspecies variation in the susceptibility of adult Pacific salmon to toxic urban stormwater runoff. Environmental pollution (Barking, Essex : 1987). 238. 196-203. 10.1016/j.envpol.2018.03.012.



# Indigenous Ways of Knowing and Art as Scientific Translation for Native American Communities Affected by Abandoned Uranium Mines

by Mallery Quetawki, Artist-In-Residence
University of New Mexico College of Pharmacy
Community Environmental Health Program

Uranium and other heavy metals have the potential to disrupt physiologic function inside the human body whether through DNA damage or other types of cellular disruptions. There are many complex mechanisms that occur starting from the route of transmission to the actual physiological impacts of long term exposure. These concepts are challenging to understand so we have to be creative on how we translate science to a non-scientific audience because effective communication and transparency are key when working with research participants and patients in health care. With several Native American communities located within close proximity to abandoned uranium mines (AUMs), how do we communicate these findings to the unique groups of people who have their own languages, cultural identities and traditional ancestral knowledge that may be in conflict with Western thoughts and ideas? How do we strive for transparency and yet remain respectful to the cultural sensitivities of the Native American communities and individuals involved in our research?

## Art as Translation

Part of the answer came in 2016 during a sheep roast in Tachee/Blue Gap, a community on the Navajo Reservation in Arizona. This annual meeting of partners involved in our P50 Native Environmental Health Research Equity Center, our external advisors, and partner community members produced a recommendation for assisting in translation of the science behind the research. The community, although grateful of the research and the sharing of its progress, expressed that they did not really understand what was being presented to them. It is here that they suggested that the center should simplify the science for the community using some sort of visual aid, such as art, and not just language interpretation or the scientific graphics currently used alone as there are many scientific terms that cannot be translated into the local indigenous languages. From a previous observation of culturally related artwork depicting human anatomy on display in the lobby of the Zuni Comprehensive Community Health Center in Zuni Pueblo, Dr. Johnnye Lewis invited me to her office and pitched the idea of using art as a tool for translation. The previous series of anatomy paintings had gained a positive reception from Zuni tribal members and health care providers alike, so this venture presented me an opportunity to branch out into a research focused direction, knowing its importance and positive outcomes within my own community.

Using art as a method of translation has promoted effective communication between scientists, practitioners and indigenous communities which has resulted in greater understanding. It has also provided a welcoming atmosphere for all involved within our centers and programs. Native-themed design, symbolism and iconology, familiar to our partner tribes, was used to create community engagement material such as posters, pamphlets, and health study roadmaps and timelines. To date there are nine acrylic paintings that have been created along with several culturally related images that use computer-generated graphic art. Each visual is created by conducting research on the design through direct interviews with researchers, community members, and tribal keepers of traditional knowledge, along with literature research on the scientific or health related concept. It almost requires a person to be a scientist, a member of the local tribe(s), and fluent-speaker of the Native language packaged into one to even begin describing basic scientific terminology for the grandmothers and grandfathers back home. I alone cannot create art without help from our multidisciplinary team here at the center.

### CEHP Overview

The University of New Mexico's Community Environmental Health Program (UNM CEHP), led by Dr. Lewis, is a multi-center program that is currently working on understanding toxicity in multiple generations within indigenous communities associated with chronic exposures to metal mixtures in abandoned mine waste. Our partnerships are not only with other academic institutions and tribal governments but community members themselves. We also have a strong partnership with the Southwest Research & Information Center(SRIC), located here in Albuquerque, that provides us with immense support on community outreach and engagement activities. Our multidisciplinary teams work cohesively across the following programs and centers:

- The Center for Native Environmental Health Research Equity (Native EH Equity) (NIEHS P50 ES026102/USEPA 83615701): This center addresses environmental health disparities through biomedical and environmental research and Native-focused community engagement methods. The Center's three core tribal partner communities are from Navajo, Crow, and Cheyenne River Sioux. The Center not only examines toxicities of metal mixtures but strives to build research capacity and improve the understanding and interpretation of data across tribal communities. The Center seeks to develop a framework that characterizes the unique exposure pathways and defines health from a perspective that is not only reflective of tribal perceptions, but is also ultimately useful in informing regulatory decision making.

- The Navajo Birth Cohort Study/Environmental influences on Child Health Outcomes (NBCS/ECHO) pediatric cohort (NIH-OD UG3OD023344): The national ECHO study evaluating the role of environment, broadly defined to include behavioral, physical, and social risk factors as well as environmental chemical contaminants, on child development in the US. The NBCS cohort was originally focused on the association between exposure to uranium mine waste and child development on Navajo Nation. As an ECHO site, the scope is broadened and will allow risks and protective factors to be assessed in the context of other tribal and nontribal communities.

- The University of New Mexico's Metal Exposure and Toxicity Assessment on Tribal Lands of the Southwest (UNM METALS) Superfund Research Program Center (NIEHS P42ES024079): METALS studies exposure and toxicity of mixed metals in uranium mine waste on tribal communities in the Southwest in order to develop and implement risk reduction strategies. The Center uses multi-directional Community Engagement and Research Translation Cores to develop and implement transgenerational approaches to risk communication and risk avoidance that integrate indigenous learning models (e.g., tribal ecological knowledge) and Western science. This program's core tribal partner communities are Tachee/Blue Gap-Navajo Nation, Red Water Pond Road Community-Navajo Nation, and Laguna Pueblo.

### Abandoned Uranium Mines (AUM)

There are about 160,000 abandoned hard rock mine sites in proximity to tribal lands in the Western US. About 1,000 of the AUMs or waste sites occur on the Navajo Reservation in New Mexico and Arizona (Lewis, Hoover and MacKenzie, 2017). In 77% of those AUMs, USEPA site screening shows gamma radiation more than 2x background. In addition, these sites all represent sources of exposure to multiple metals in the waste. Communities have lived in proximity to these underground, surface, and open-pit mines and their associated abandoned waste sites for more than 70 years. Native communities have a potential for increased exposure and higher sensitivity to toxicity due to reliance on local resources and understudied genetic and epigenetic metabolic distribution differences. Most of the AUMs and waste piles remain unmarked, having no proper signage to warn people of potential hazards. Indigenous communities often rely heavily on local resources such as local wells for water, and on surface water for traditional harvesting of vegetation and minerals for food, paint, and medicinal purposes. EPAs estimate that >40% of surface water headwaters in the West are contaminated by mine waste further adds to the potential risk to these communities.

### Ancestral Knowledge and Indigenous Ways of Knowing

In order to adequately conduct research and translate results, it is a core practice for UNM CEHP and its centers to include community member insight and local indigenous knowledge. It is extremely important to CEHP and its partners that we continue to include community members in the process of collection, translation and policy mitigations so that our dialogue among stakeholders, policy makers, trustees, communities and researchers remains open and transparent. Our community partners from the Southwest, which include Navajo and Laguna, have their own languages (Diné and Keres respectively) and cultures. We also collaborate with the communities of the Northern Plains which also retain their languages and culture. The Cheyenne River Sioux speak Lakota and the Crow or Apsáalooke speak the Crow language. There are many differences between each of the four core tribes we partner with yet there are key similarities that bring these groups together. These similarities we harness into our translation methods to remain inclusive of everyone involved.

It is a difficult idea to fully appreciate if one has not associated themselves with Native American sense of self and the world. This holistic approach in ways of life has been passed down since time in memorial, from our ancestors who created civilizations on unforgiving land and in the most trying of times. This idea of survival and our connectedness to land and other forms of life have been coined as indigenous ways of knowing. It is the idea that we recognize the cycle that exists between life on the planet, the planet itself and a spiritual world. All co-exist and all remain in balance. The ceremonies of tribal communities focus on restoring and protecting this balance. There are a lot of similar aspects that coincide with Western science and this type of ancestral knowledge, which continues to be practiced by Indigenous people. This area of similarity is where we have been able to create a dialogue familiar to us all, regardless of race, culture, language and education level. This respect for cultural values has created an atmosphere within which findings and ideas can be shared between research and community partners in a way that replaces previous tension and unclear understanding on both sides.

**Fig.1: DNA Repair- Mallery Quetawki (Zuni Pueblo). 2017. 16 x 20 in. Acrylic on Watercolor Paper. DNA has the ability to repair itself through complex mechanisms and pathways when damage occurs. Its intricacy of repair can be compared to the creation of beaded items in Native Culture. The design used is from the Crow Nation. The use of the flower design symbolizes the idea of regrowth.**

## Zinc Intervention: A Case Study

The Thinking Zinc study is an example of using indigenous knowledge, language, art and western science while remaining respectful to cultural beliefs. This study being conducted by the METALS program is looking at supplementing zinc, at the daily recommended level, to understand if beneficial effects seen in cell systems and animal models where toxicity of metals can be reduced or reversed by zinc can also benefit communities living among AUMs. Our community liaisons and other indigenous staff members along with our PIs and involved researchers have melded all the above mentioned methods of communication to explain this study to community partners and work together on the protocol. Our Navajo Nation liaisons along with others who are fluent speakers of Diné have found words, much like the Code Talkers did in World War II, to describe Zinc as Beesh Dootł'izh (metal + blue, the one that is). The Diné word for zinc was actually found in a memoir by the Navajo Code Talker Chester Nez (Nez and Avila, 2011). By introducing the intent of researchers using Diné, they follow up with presenting the study in the Native perspective by using art to describe the science. To place the study in a traditional context, our liaisons have also included examples and samples of traditional foods that contain natural zinc. This not only clarified the intent to supplement but has also initiated a sense of revitalization of traditional foods in the community. Our NBCS video collection has had increasing views on how to make blue corn mush, an ancestral food high in zinc. Together, we have been able to successfully present ideas that

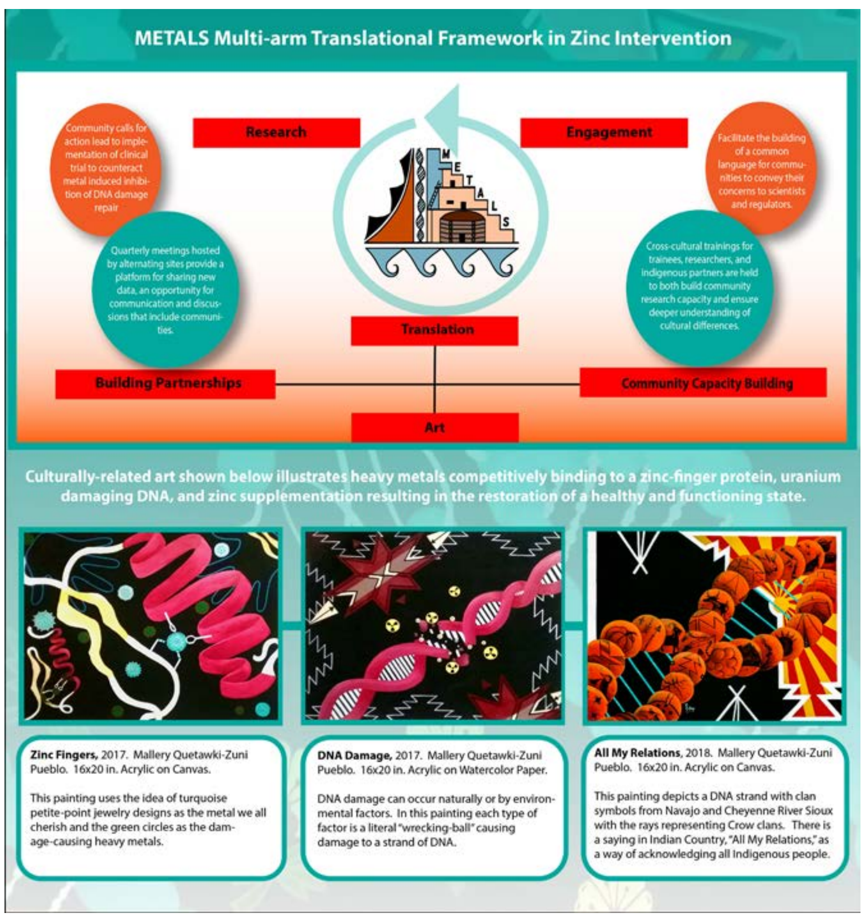



**Fig. 2: A summary of images used to describe DNA and Zinc Proteins to Indigenous Communities.**

were once too complex for words and too broad to simplify with basic graphics.

*DNA Repair* (fig. 1) was used as the cover art for the zinc supplement study. This piece depicts a strand of beads (DNA) that have come undone. The needle at the end of a string is beginning to repair the beading. Taboo discussions were avoided by working around the words and adding positive ideas instead. Comparing the re-stringing of a strand of beads to DNA repair instead of focusing on the negative impacts that a damaged DNA can cause is a more effective way of communicating this particular concept with our audience. It is better to mention ways to correct or intervene than it is to talk of illnesses and ailments that may result from metal exposures. When the people are able to conceptualize what is happening on the land and in their bodies, then can we introduce more in-depth health concerns and effectively demonstrate the relationships between metals, DNA damage and repair and the role of zinc in restoring balance. With community input and research on bead working, I was able to incorporate a Crow design into the painting and use a floral motif as a symbol for regrowth and healing. In regards to this zinc study, there are three more paintings depicting zinc proteins, DNA damage and a complete DNA model as seen through the Native lens (fig. 2).

The zinc intervention will also be looking at immune function. *Immune Response* (fig. 3) and *Autoimmunity* (fig. 4) are examples of this mechanism that cannot be seen with the naked eye but can be visualized using art. Both immunological pathways and our spiritual beliefs are sets of complex ideas that work together for the protection of the health of an individual. Just like the varieties of leukocytes and antibodies of the immune system, our spirit animals of strength are ever present to defend us from potentially harmful invaders. Our totems and belief in the supernatural power of spirits are our guides in life that we feel keep an individual healthy in terms of mind, body and soul. In the *Immune Response* painting, I introduce the buffalo, bear and war pony as those animal totems we seek for strength, including other methods of spiritual protection such as turquoise, arrowheads and sweat lodges. In the *Autoimmunity* painting these animals are attacking one another just like the processes involved in an autoimmune disorder. This dichotomy of ideas, when presented visually as an intertwined whole, brings the "ah ha!" moment to both sides of our collaborations and creates a similar language for easier communication.

Native culture and belief systems, although esoteric, can be appreciated by a mixture of audiences if all interests are represented. In the case of the paintings created for this multi-center program, it has been able to reach both cohorts and scientists in ways that form an understanding for both sides. These sides work together as one and have provided our indigenous communities a sense of ownership of the research being done on their lands. As Native peoples, I can attest to the idea that we want to be informed, we appreciate consent with full disclosure and due diligence. Our livelihoods and spirituality is deeply connected to the lands in which we live. What hurts the land hurts us. In order for our hearts to be aligned with the work done by non-Native researchers and academics, we need a common understanding

**Fig.3: Immune Response- Mallery Quetawki (Zuni Pueblo). 2017. 16 x 20 in. Acrylic on Canvas. Just like our totems and animals of strength we use in spiritual protection, there are different types of cells involved in keeping our body safe from attack. The bear, war pony, buffalo, arrowheads and sweat lodges can be compared to the different types of leukocytes ready to attack in a moment's notice.**

**Fig.4: Autoimmunity- Mallery Quetawki (Zuni Pueblo). 2018. 16x20 in. Acrylic on Canvas. Autoimmunity is translated to Native symbology by showing the animals of strength and protection attacking one another. These strength totems are what protect the mind, body and spirit. Just like the process of an autoimmune disorder, these protectors are "attacking self."**

both in necessity of the research and the respectful approach to the people of the area of concern. Indigenous knowledge, art and Western science can create this cohesive movement toward a common goal. To continue the harmonies in the cycle of life, this oath to the planet and its protection begin at birth for indigenous persons, but can be adopted by researchers to integrate this dimension into their work.

*Research reported here was supported by the National Institute of Environmental Health Sciences of the National Institutes of Health under Award Numbers P42ES025589, and P50ES026102; and by the Office of the Director of the National Institutes of Health under cooperative agreement UG3OD023344. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.*

*This material was also developed in part under Assistance Agreement No. 83615701 awarded by the U.S. Environmental Protection Agency to the University of New Mexico Health Sciences Center. It has not been formally reviewed by EPA. The views expressed are solely those of the speakers and do not necessarily reflect those of the Agency. EPA does not endorse any products or commercial services mentioned in this publication.*

*We would also like to acknowledge the support of Ms. Quetawki's work by the University of New Mexico NCI-designated Comprehensive Cancer Center and the University of New Mexico College of Pharmacy for institutional support that aided development of the Artist-in-Residence program.*

Mallery Quetawki is from the rural Pueblo of Zuni in western New Mexico. She is the mother of two and shares residence in both Albuquerque and Zuni Pueblo. She received her B.S. in Biology with a minor in Art studio in the summer of 2009 from UNM-ABQ. She is currently the Artist-in-Residence with the Community Environmental Health Program at the University of New Mexico College of Pharmacy. Her work with this program is on display in the Stanford House conference room at 1000 Stanford Dr. NE, Albuquerque, NM. Mallery has used art to translate scientific ideas, health impacts and research on uranium mines that are currently undergoing study in several Indigenous communities.

Mallery has two self-published coloring books entitled *Zuni Pottery Designs to Color* and *Sunfaces*. She has a large-scale mural on permanent display at the Indian Pueblo Cultural Center that depicts the history of the Zuni People from Creation to modern times. She also has an oil painting symbolizing the ties between the Grand Canyon and Zuni culture as part of a traveling collaboration called the *Zuni Map Art Project*. It is hosted by A:shiwi A:wan Museum and Heritage Center. The collaborative set of art has been displayed at the American Museum of Natural History in New York City, NY. The Map Art was featured in a documentary by National Geographic on an episode of Wild Chronicles. The map art is also accompanied by the book entitled *A:shiwi A:wan Ulohnanne - The Zuni World* by Jennifer McLerran & Jim Enote. Other noted works include a 12-piece pastel and ink set entitled *What Makes a Zuni?* on permanent display at the Zuni IHS in Blackrock, NM and a mural painted at the Ho'n A:wan Park in Zuni Pueblo.

## References

Lewis, J., Hoover, J. & MacKenzie, D. (2017). Mining and Environmental Health Disparities in Native American Communities. Current Environmental Health Report, 4: 130.

Navajo Birth Cohort Study Part XVII: Blue Corn Mush. (March, 2015). Retrieved March 28, 2019 from, https://www.youtube.com/watch?v=krsGLVY9qFM&t=138s

Navajo Nation: Cleaning Up Abandoned Uranium Mines. Abandoned Uranium Mines Site Screen Reports. (2008-2011). Retrieved March 15, 2019 from, https://www.epa.gov/navajo-nation-uranium-cleanup/abandoned-uranium-mines-site-screen-reports

Nez, C. & Avila, J. (2011). Code Talker: The First and Only Memoir By One of the Original Navajo Code Talkers of WWII.





# Healthful Living: A Prevention Paradigm to Reduce Vulnerability to Environmental Pollutant Toxicity

**by Bernhard Hennig, Ph.D., R.D., Kelly Pennell, Ph.D., P.E., and Dawn Brewer, University of Kentucky Superfund Research Center**

**Eat fruits and vegetables and exercise to help protect the body from environmental pollution**

The University of Kentucky Superfund Research Center (UK-SRC) investigates how both nutrition and physical activity can reduce our vulnerability to toxic environments, thereby preventing disease. Our research findings suggest that healthful nutrition and physical activity may be a sensible way to prevent diseases associated with many environmental toxic insults. Because reducing disease risks associated with exposures to environmental pollutants requires multi-level and interdisciplinary strategies, our Center includes both biomedical and environmental science-based projects whose purpose is to reduce exposure to pollution. In addition, our engineering and environmental sciences researchers consider ways in which green engineering technologies can be used to identify and reduce environmental exposures.

**Prominent environmental pollutants in Kentucky: polychlorinated biphenyls (PCBs) and trichloroethylene (TCE)**

Our primary focus has been on chlorinated organic compounds, especially polychlorinated biphenyls (PCBs) and trichloroethylene (TCE). PCBs and TCE are prevalent at Superfund sites across the nation and are among those of greatest concern in terms of adverse health effects and difficulty of remediation. TCE is used as a degreasing solvent at many industrial, and military sites, and was formerly widely used in the dry cleaning industry. PCBs were officially banned in the late 1970s, but had many industrial applications and were widely used in transformers. Despite decades of cleanup efforts, these pollutants are a national concern due to their high toxicity, persistence, and widespread occurrence in the environment. They are detected at Superfund (and other hazardous waste) sites located across the Commonwealth in both rural and urban areas.

**Title Images: Participants of the Tanglewood 2 Table walking and farmer's market program spend time with their family and friends each week as they walk the Tanglewood Trail to the farmer's market to redeem their $10 voucher on fruits and vegetables.**

**A University of Kentucky graduate student picks blackberries from the bushes planted by the Community Engagement Core at the Boyle County Senior Center for older adults attending the Center to enjoy.**

UK-SRC has collaborated for many years with governmental, industry and community stakeholders at Kentucky's largest Superfund site, the 700-acre Paducah Gaseous Diffusion Plant, to provide context for our laboratory research, technology transfer efforts, and our methods for engaging with communities. The knowledge gained by working at this site has influenced our research, resulted in cutting-edge laboratory discoveries, and full-scale engineering technologies. It also has taught us how community members make sense of information related to toxics and their health.

**Healthy lifestyles decrease pollution-derived inflammation linked to chronic disease development**

Nutrition can lessen the toxicity of environmental pollutants by reducing inflammation and oxidation, which are responsible for the development of non-communicable diseases. A major focus is on links between nutrition, environmental pollution, and heart disease. Although we are invested in determining novel mechanisms of toxicity of individual and pollutant mixtures, our

**Following a recipe demonstration, a Family and Consumer Science Extension Agent plates up a salad for community members to enjoy following a nutrition and environmental pollution- focused education lesson.**

long-term goal is to determine how to protect against pollutant-induced inflammation and cardiovascular disease. We have demonstrated that diets high in bioactive nutrients may prevent the pro-inflammatory effects of PCBs. In a recently published study, we fed mice a diet supplemented with polyphenols found in green tea, and found that mice fed this anti-inflammatory diet were protected from PCB toxicity. In fact, these green-tea fed mice exhibited stronger internal antioxidant defenses, which may help explain why they were protected from a subsequent exposure to PCBs. Since we know that many environmental stressors exert their toxicity by inducing chronic inflammation, it makes sense that diets high in anti-inflammatory compounds may buffer the body against toxic insults.

In another study, we discovered that PCBs can increase levels of an enzyme in the liver that generates a metabolite in the

**A University of Kentucky undergraduate researcher provides a recipe sample and recipe card to community members participating in the Tanglewood 2 Table walking and farmer's market voucher program.**

blood, called trimethylamine N-oxide (TMAO). TMAO is also associated with meat and dairy products. Several other studies in humans have shown that circulating levels of TMAO are a powerful risk factor for heart disease. Our research shows that healthy diets might be particularly beneficial for people who are exposed to PCBs and have elevated TMAO levels.

**Translating the basic science of the UK-SRC to communities: promoting increased fruit and vegetable consumption and physical activity**

Our research has been influenced by the significant health issues that Kentucky faces. While obesity, diabetes, cardiovascular disease, hypertension and cancer are national challenges, Kentucky ranks high, as compared to other states. When we couple the health issues facing Kentucky with environmental exposures, we are keenly aware of the health burdens that our community faces. The Appalachian Region in particular is afflicted not only by high incidences of chronic diseases, poverty, and poor nutrition, but increased exposure to environmental pollution as well.

As a land-grant institution, the University of Kentucky is committed to improving people's lives through excellence in education, research, and service. To this end, UK-SRC works with various community partners to help address and alleviate these adverse conditions. We do this by intervening at multiple levels of the social ecological model of health behavior change, including the individual, community and organizational levels. This allows us to implement education into existing community programs that reach populations throughout Kentucky. In Southwestern Kentucky, Dayhoit, home to the National Electric Coil Company/ Cooper Industries National Priority List Superfund site, we partner with the Cooperative Extension Service Family and Consumer Science (FCS) agent to deliver nutrition lessons and cooking demonstrations. In Eastern Kentucky, we support a community-initiated farmer's market voucher and walking program in Whitesburg, Kentucky. In Central Kentucky, we partner with the Boyle County Senior Center, FCS and Horticulture Extension agents to deliver BerryCare: a Blackberry Club for Older Adults. This program provides a sustainable, affordable and accessible source of blackberries for community members to consume as well as providing an opportunity to be physically active through gardening. The program provides blackberry bushes and a lesson series that highlights the health benefits of berries and how they can help protect against the harmful effect of environmental pollution. Blackberries are the focus because, as the State Fruit of Kentucky, they grow well throughout Kentucky, and the UKSRC biomedical research projects have investigated the effects of certain anti-inflammatory properties bioactive nutrients found in blackberries.

In summary, and based on our research findings and the mission statement and strategic plan of NIEHS/NIH, we recommend that future directions in environmental health research should explore this healthful lifestyle paradigm that incorporates a consideration of the relationships between nutrition and physical activity, exposure to environmental toxicants, and disease. In fact, healthful nutrition and physical activity interventions may provide the most sensible means to develop primary prevention strategies of diseases associated with many environmental toxic insults.

# Sensing Change: New Technology Could Make Heavy Metals Testing More Accessible to Researchers, Clinicians, and Communities

**by Erin N. Haynes, Dr.P.H.**
**Professor and Chair of Epidemiology,**
**University of Kentucky College of Public Health**
**and**
**Allison Elliott-Shannon, M.A.**
**Director of Communication,**
**University of Kentucky College of Public Health**

**The sensor that can detect levels of toxic metals in human blood samples or water is about the size of a USB flash drive.** *(Courtesy University of Cincinnati)*

What if measuring heavy metal exposure in humans required no clinic visit, no medical training, and virtually no wait time? What if it could be accomplished with minimal staff training, at low cost, and via portable technology? And what if that technology could double as a tool to empower members of vulnerable communities to monitor their own drinking water?

Thanks to a portable, point-of-care sensor developed by Erin Haynes, Dr.P.H., of the University of Kentucky College of Public Health, and Ian Papautsky, Ph.D., of the University of Illinois College of Medicine, testing for toxic metals in blood could soon be faster, easier, and less expensive than ever.

The idea for the sensor – which specifically targets manganese and lead levels in the blood – grew out of research conducted by Haynes in Marietta, a rural southern Ohio community that is home to a manganese refinery.

"Parents would bring their children to our research clinic wanting to know if their child had been exposed to dangerous levels of toxicants, like lead or manganese; however, because it was a research study and we had to send samples in batches, it would take several months before the blood metal concentration levels were made available," Haynes said. "This presented a real issue, because if we did find elevated levels, vital public health interventions had already been delayed."

Traditional heavy metals testing requires multiple blood draws over time, taken by a phlebotomist via venipuncture – not easy for small children to endure. Requiring only a few drops of blood – obtained via finger-stick – the disposable sensor eases the testing process for children and families.

"Getting a single drop of blood from a child is a lot easier," Papautsky said.

Even with a smaller blood sample, the sensor is very sensitive. According to Papautsky, the sensor can report a range of manganese levels in the low parts per billion (ppb) range, and between 5 ppb to 50 ppb for lead.

"The Environmental Protection Agency's action level for lead in drinking water is 15 ppb, so our device can detect lead levels at least three times below the EPA guideline," Papautsky said.

The sensor can also be used to test manganese and lead levels in water, again requiring only a few drops of liquid. With its dual utility, the technology could serve multiple roles in environmental health investigations and interventions.

"For example, the sensor could detect contamination in public drinking water supplies," said Haynes. "Once high levels are detected in water, the sensor technology could then be used to quickly detect elevated blood lead levels in children – greatly expediting public health interventions."

The ability of the sensor to detect metals in blood will be determined during an upcoming field study in Southeast Side Chicago—where manganese dust frequently circulates through residential areas from nearby industrial sites. Haynes and her team will be recruiting 150 children to participate in a research study aimed at identifying if children are exposed to manganese at levels that cause harm. The team will also compare the results of blood tests analyzed by the sensor and by a traditional laboratory. Soon, Haynes hopes to see the technology providing real-time results in multiple settings—including on job sites, in clinics, and in research studies.

The investigators expect that the sensors will ultimately cost about ten dollars each, not including one-time costs for software and hardware.

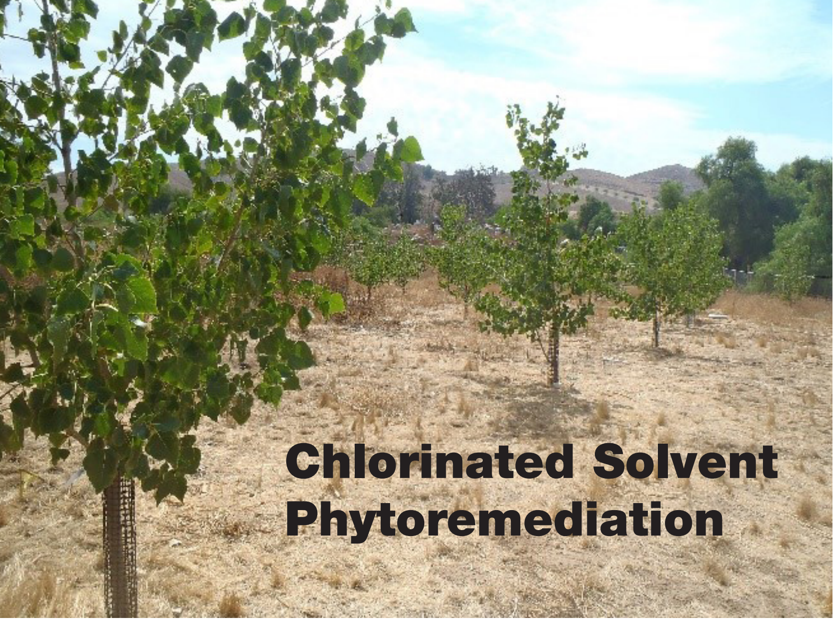

**Erin N. Haynes, Dr.P.H. (left), and Ian Papautsky, Ph.D. (right), holding prototypes of the sensor.** *(Courtesy University of Cincinnati)*

By putting this tool into the hands of local stakeholders, the researchers hope to empower community members and health care professionals to collect quality exposure data, and to encourage them to use and communicate the data in a way that's understandable and action-oriented.

"We envision that the sensor will also be used in point-of-care devices that provide needed feedback on heavy-metal levels, and will have the potential for large-scale use in clinical, occupational, and research settings, said Haynes. "We would also like to expand the sensor's capacity to measure other toxic heavy metals in blood, including arsenic, mercury, copper, and cadmium."

Grant funding information:

NIH/NIEHS R21/R33ES024717-02 Papautsky/Haynes (MPI), 03/01/2015 – 02/28/2020, "*Validation and Demonstration of point-of-care sensor for multi-metal exposure assessment*."



# Chlorinated Solvent Phytoremediation

**by John L. Freeman III, Ph.D.**
**Chief Science Officer - Principal Investigator**
**Intrinsyx Environmental - NASA Ames Research Park**
**and**
**Christopher M. Cohu, Ph.D.**
**CEO and Cofounder**
**Phytoremediation and Phytomining Consultants United**

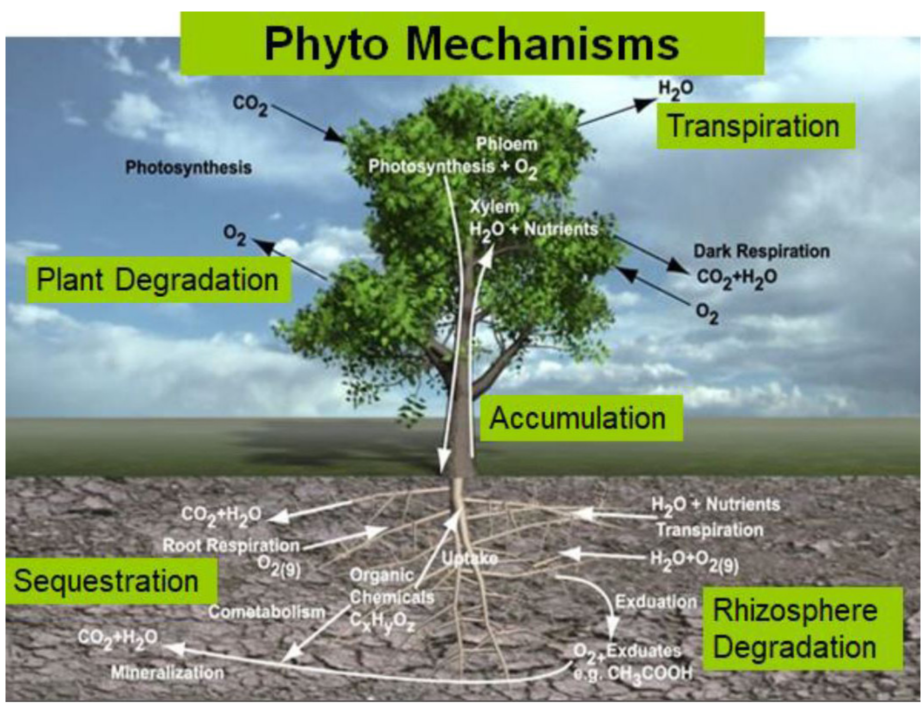
## Background

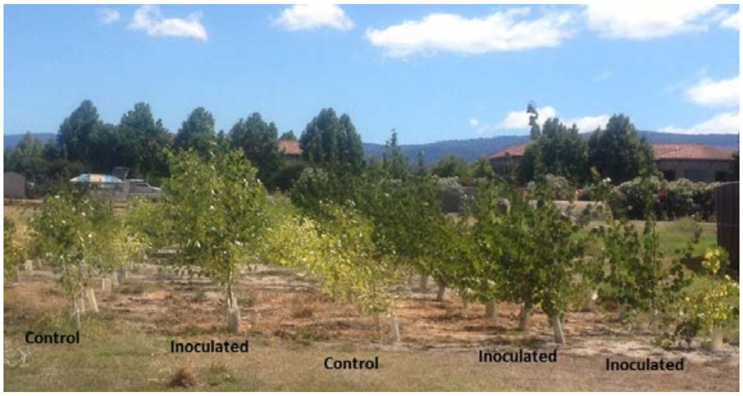
**Phytoremediation** is the use of plants to extract a wide range of heavy metals and organic pollutants from the soil. Phytoremediation removes metals and volatile organic compounds from soils through strategic installation of plants. These plants uptake pollutants into their biomass to store or degrade them. [3]

Chlorinated compounds as environmental contaminants occur in many forms, from solvents to industrial chemicals to pesticides. Many of our phytoremediation installation sites contain shallow aquifer groundwater contamination 25 feet below ground surface (bgs) or deeper using pump and onsite subsurface irrigation for treatment. Most exhibit high concentrations of chlorinated contaminants in soil at source locations, and many can exhibit elevated salts and metals. At Intrinsyx and PPCU we are pioneering the next generation of chlorinated contaminant phytoremediation, and the presence of high contaminant concentrations, high salts, and challenging environments are no longer an issue. Our endophyte-assisted phytoremediation (EAP) approach combines naturally occurring bacterial endophytes with native plant species to enhance the degradation of chlorinated contaminants (some cases even fluorinated). All our bacterial endophytes are capable of living within plants and are beneficial to the plants. One of our bacterial endophytes (PDN3) actively degrades chlorinated compounds like perchloroethylene (PCE), trichloroethylene (TCE), and the many degradation products like vinyl chloride (VC) (Kang et al. 2012; Doty et al. 2017); and have the added benefit of conferring increased plant tolerance to the contaminant. We are also in the process of testing the PDN3 endophyte on other chlorinated industrial chemicals, pesticides and even Perfluorinated compounds (PFC). Enhanced degradation of organic contaminants, along with increased plant tolerance to those contaminants, has allowed us to install phytoremediation systems that outperform other phytoremediation installations.

Chlorinated solvents e.g. PCE, TCE and VC contamination in soil and groundwater pose considerable hazards to plants, animals and human health; and are often very challenging to effectively remediate while also being cost-effective. Our newly developed technologies that combine TCE-degrading bacterial endophytes and hybrid poplar trees to remediate these chlorinated solvents has been successfully deployed at several sites and has thus far demonstrated to be the best long-term solution while also being the cheapest.

Hybrid poplar trees have been deployed for several decades to help address chlorinated solvent contamination in soil and groundwater in a process known as phytoremediation (remediation using plants). These hybrid poplars are ideal because they transpire vast amounts of water up through their roots and out their leaves into the atmosphere. One mature hybrid poplar tree is capable of transpiring more than 3,000 gallons per year. As water moves into the hybrid poplars the chlorinated solvents are also drawn up.






In addition, the tree roots help to promote aeration and natural degradation of chlorinated solvents. However, in many cases the chlorinated solvents begin to accumulate in the trees and if accumulation in plant tissues becomes great enough it will reduce growth rates and phytoremediation effectiveness, and can even kill the trees. In fact, one of the greatest barriers to using hybrid poplar trees, or any plants, in the remediation of chlorinated solvents, especially at high concentrations, is the phyto-toxicity of the contaminant and also salts in soil or water (irrigation or ground) onsite.

A newly developed system for the phytoremediation of chlorinated solvents removes the phyto-toxicity of the chlorinated solvents by using beneficial bacterial endophytes discovered by the University of Washington that live inside of the trees and actively degrade the chlorinated solvents into non-toxic forms. We discovered that 1 out of over 600 bacteria strains isolated from poplar and willow trees exhibited the capability to break down chlorinated solvents and releases chloride. Three years ago a pilot project to test this bacterial endophyte strain in different cultivars of hybrid poplar trees was initiated on an EPA Superfund site that contains a TCE plume. This study successfully demonstrated that inoculation of hybrid poplar trees with the chlorinated solvent degrading bacterial endophytes dramatically improved the degradation of TCE as well as improve overall tolerance to the TCE when compared to the uninoculated controls (see image below). Increased TCE degradation in hybrid poplar trees inoculated with the bacterial endophyte was demonstrated by analyzing tree cores for TCE, and the soil immediately adjunct to the trunk for chloride concentrations. When compared to the controls that are not inoculated within each hybrid poplar cultivar, all trees inoculated with the endophyte demonstrated very little to no TCE accumulation along with increased chloride levels in the soil. The control trees exhibited TCE accumulation as well as no indication of increased chloride in the soil. The findings from this study are published in the journal Environmental Science and Technology.

To date, Intrinsyx and PPCU have successfully planned and deployed seven sites for our clients (e.g. Ramboll) dealing with TCE and other chlorinated solvent contamination. Furthermore, we are also now using a unique set of salt and boron tolerant poplar together with these endophytes to tolerate both the TCE and often salty conditions on these sites. Please feel free to contact us to receive more information and a proposal on how we can help you tackle your chlorinated solvent contamination using the very latest techniques in phytoremediation.

**Case Study:**

<u>Site Location:</u> Former Industrial Facility in Southern California

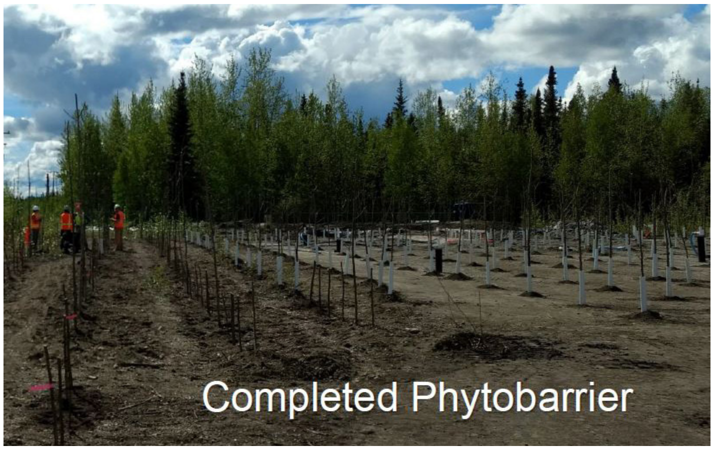
<u>Prime Contractor:</u> Ramboll

This case study was conducted in southern California at a former industrial facility with high levels of TCE (20 mg/l) on a groundwater plume between 3 and 25 feet below ground surface, and high concentrations of salts. In the spring of 2015 we installed over 300 trees, half of which consisted of our new variety of salt and boron tolerant poplar trees (RRR) for placement in zones with the highest salt concentrations (see image to right; also see our whitepaper on our salt and boron tolerant poplar and willow trees). All the trees were inoculated with our PDN3 endophyte upon installation, as well as a follow-up re-inoculation in the spring of 2018.

**Outcomes**

Trees are established (see image at right), and the 2017 tree tissue sampling and lab analyses indicate that trees are engaging the TCE plume, even in areas with a depth to groundwater contaminantion at 20 feet bgs. Groundwater monitoring wells indicate that downgradient TCE concentrations are stabilizing and decreasing while upgradient plume concentrations fluctutate and sometimes increase during wetter seasons. Overall, the trees are beginning to have a possitive impact on groundwater plume TCE concentrations and we expect the 2018 and 2019 seasons to really begin to accelerate the TCE degradation.

Based on the success of this site and others (e.g. see Doty et al. 2017) the market for the PDN3 endophyte is expanding rapidly. This endophyte has been used in our phytoremediation installations from the midwestern U.S. to the Pacific Coast and up to Alaska! Many of our clients include major environmental firms, oil and gas companies, and large IT technology companies headquartered in Silicon Valley.




**Intrinsyx Environmental** provides cutting edge solutions to complex environmental remediation challenges. Intrinsyx is a woman and minority owned small business with a proven track record in providing innovative solutions and strategies to meet the needs of our clients and partners. Our clients include the federal government and several Fortune 100 companies in the Energy and Technology sectors. Intrinsyx's environmental scientists are leaders in the field of Phytoremediation, which is the use of plants and their associated microbes to remediate contaminated soil and water. We use our novel collection of plants and microbes to design Integrated Biological Systems for remediating the most prolific environmental pollutants in soil, surface water, and groundwater.[1]

**Phytoremediation and Phytomining Consultants United**, LLC is a phytoremediation installation and consulting services group composed of experts in the field of phytoremediation and phytomining. PPCU specializes in providing biological solutions for soil and water remediation projects that accelerate degradation of organic contaminants such as Total petroleum hydrocarbons (TPH), the BTEX group of contaminants (benzene, ethylbenzene, toluene and xylene), and trichloroethylene (TCE).[2]

**References**


1. Intrinsyx Environmental, https://www.intrinsyxenvironmental.com/. Accessed on March 12, 2019
2. Peuke, A. D., & Rennenberg, H. (2005). Phytoremediation. *EMBO reports*, *6*(6), 497-501.
3. Phytoremediation and Phytomining Consultants United LLC, http://www.phytoconsultants.com/. Accessed March 12, 2019
4. Kang et al. 2012 Biodegradation of Trichloroethylene by an Endophyte of Hybrid Poplar. *Appl. Environ. Microbiol.* 78(9):3504
5. Doty et al. 2017 Enhanced Degradation of TCE on a Superfund Site Using Endophyte-Assisted Poplar Tree Phytoremediation. *Environ. Sci. Technol.* 51(17):10050

**Christina Lee Brown Envirome Institute**
University of Louisville School of Medicine
Division of Cardiovascular Medicine
580 S. Preston Street
Louisville, KY 40202