



Superfund Research Program

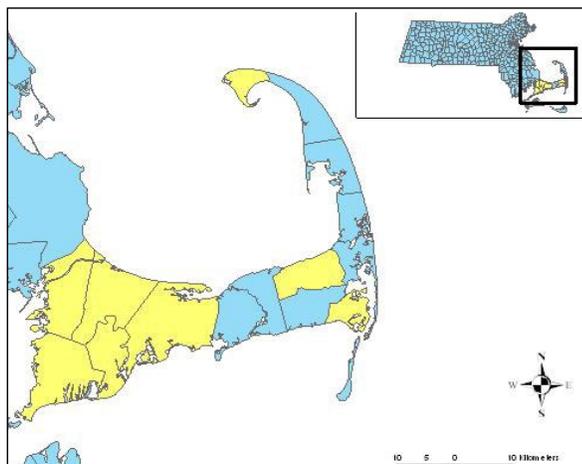
The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Boston University Superfund Research Center (BU SRC), to advance this work across the nation.

Research Highlights

Linking perchloroethylene and health effects

BU SRC researchers, led by Ann Aschengrau, Sc.D., determined that exposure to perchloroethylene (PCE), a commonly used commercial solvent, is linked to a variety of long-term health effects. They studied a group of people from the Cape Cod region of Massachusetts who were exposed from 1968 to 1980 when PCE leached into drinking water from the lining of distribution pipes.

The researchers found links between PCE exposure and an increased risk of breast cancer in women,¹ increased risk for birth defects,² and increases in reproductive issues, such as stillbirth, in pregnant women.³ Additional research revealed that prenatal and early-life exposure to PCE was associated with decreased performance on learning and memory tests,⁴ as well as elevated risk of mental illness, including post-traumatic stress disorder and bipolar disorder.⁵ These findings continue to provide a sound scientific basis for future risk assessments of PCE and related chemical contaminants.



Eight Cape Cod areas, highlighted in yellow, were in Aschengrau's study. (Figure courtesy of BU SRC)

A new approach to determine cancer risk from chemicals

Researchers at BU SRC, led by Stefano Monti, Ph.D., have shown that computational models of short-term exposure to a chemical can predict long-term cancer risk.⁶ The study is a step toward simpler and cheaper tests to screen chemicals.

Current approaches for testing chemicals for cancer risk can cost \$2 million to \$4 million per chemical to complete. As a result, less than two percent of the approximately 84,000 chemicals in commercial use have gone through standard testing.⁶ Work by Monti's group confirms that it is possible to predict the long-term health risks from exposure to a chemical, using computational models. By further developing this model, researchers will be able to better predict what chemicals may cause cancer and understand the biological processes that lead to cancer development.

BOSTON
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BU SRC researchers seek to understand the effects of exposures to hazardous chemicals on reproduction and development in humans and wildlife. They share their research tools and results to help inform decision-making by communities and government agencies, and to better protect human and ecological reproductive health and development.

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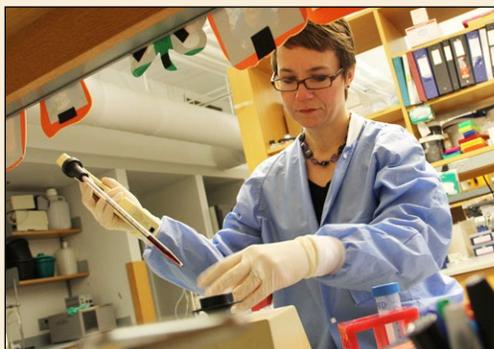
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Assessing bone health risks from flame retardant exposure

BU SRC researchers found that a component of a flame retardant, triphenyl phosphate (TPP), may stimulate growth of fat cells in bone marrow. This effect may suppress formation of bone cells and accelerate osteoporosis.⁷ Their work suggests that TPP, used in products such as furniture cushions, interacts with a protein that regulates fat cells. Jennifer Schlezinger, Ph.D., BU SRC project leader, noted that TPP is often present in our indoor environment, and the finding that it is biologically active is significant and warrants further investigation. The researchers are continuing to study how environmental toxicants, such as TPP, contribute to obesity and loss of bone health.



Schlezinger is studying how environmental contaminants affect bone health. (Photo courtesy of BU SRC)

Research overview

- Studying risk of birth defects in a population exposed to PCE in drinking water. (Ann Aschengrau, Ph.D., aaschen@bu.edu)
- Developing improved methods for mapping geographic patterns of exposure with health outcomes. (Veronica Vieira, D.Sc., vvieira@uci.edu)
- Determining molecular mechanisms by which complex mixtures of environmental contaminants impair immune system development and accelerate bone aging. (Jennifer Schlezinger, Ph.D., jschlezi@bu.edu)
- Understanding the effects of polychlorinated biphenyls (PCBs) on fish development. (Jared Goldstone, Ph.D., jgoldstone@whoi.edu)
- Unraveling how fish living in waters contaminated with PCBs can thrive. (Mark Hahn, Ph.D., mhahn@whoi.edu)

Sharing results

- BU SRC partners with community advocacy and environmental justice organizations, as well as local boards of health, to educate people on strategies to reduce hazardous substance exposures and prevent adverse health outcomes, and implement training on hazardous material regulations and solid waste reduction resources. (Madeleine Scammell, D.Sc., mls@bu.edu)
- BU SRC offers soil lead testing and educational material to community gardeners in the Boston area, and provides educational activities through the Museum of Science in Boston, and the Collaborative on Health and the Environment. (Wendy Heiger-Bernays, Ph.D., whb@bu.edu)

Other contributions to advance science

- The BU SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Sandor Vajda, Ph.D., vajda@bu.edu)
- The BU SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Michael McClean, Sc.D., mmcclean@bu.edu)

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the Boston University Superfund Research Center, visit www.busrp.org.

¹ Gallagher LG, Vieira VM, Ozonoff D, Webster TF, Aschengrau A. 2011. Risk of breast cancer following exposure to tetrachloroethylene-contaminated drinking water in Cape Cod, Massachusetts: reanalysis of a case-control study using a modified exposure assessment. *Environ Health* 10:47.

² Aschengrau A, Weinberg JM, Janulewicz PA, Gallagher LG, Winter MR, Vieira VM, Webster TF, Ozonoff DM. 2009. Prenatal exposure to tetrachloroethylene-contaminated drinking water and the risk of congenital anomalies: a retrospective cohort study. *Environ Health* 8:44.

³ Carwile JL, Mahalingaiah S, Winter MR, Aschengrau A. 2014. Prenatal drinking-water exposure to tetrachloroethylene and ischemic placental disease: a retrospective cohort study. *Environ Health* 13:72.

⁴ Janulewicz PA, White RF, Martin BM, Winter MR, Weinberg JM, Vieira V, Aschengrau A. 2012. Adult neuropsychological performance following prenatal and early postnatal exposure to tetrachloroethylene (PCE)-contaminated drinking water. *Neurotoxicol Teratol* 34(3):350-359.

⁵ Aschengrau A, Weinberg JM, Janulewicz PA, Romano ME, Gallagher LG, Winter MR, Martin BR, Vieira VM, Webster TF, White RF, Ozonoff DM. 2012. Occurrence of mental illness following prenatal and early childhood exposure to tetrachloroethylene (PCE)-contaminated drinking water: a retrospective cohort study. *Environ Health* 11:2.

⁶ Gusenleitner D, Auerbach SS, Melia T, Gomez HF, Sherr DH, Monti S. 2014. Genomic models of short-term exposure accurately predict long-term chemical carcinogenicity and identify putative mechanisms of action. *PLoS One* 9(7):e102579.

⁷ Pillai HK, Fang M, Beglov D, Kozakov D, Vajda S, Stapleton HM, Webster TF, Schlezinger JJ. 2014. Ligand binding and activation of PPARgamma by Firemaster 550: effects on adipogenesis and osteogenesis in vitro. *Environ Health Perspect* 122(11):1225-1232.



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Columbia University Superfund Research Center (Columbia SRC), to advance this work across the nation.

Research Highlights

Understanding and preventing arsenic toxicity



A child pumps low-arsenic water at a newly installed deep well in Bangladesh. (Photo courtesy of Columbia SRC)

A study in Maine by Columbia SRC researchers was the first in the U.S. to show an association between arsenic in drinking water and decreased intellectual function. Columbia SRC researchers found that children with higher levels of arsenic in their water scored lower on intelligence tests, as compared to children with lower levels of arsenic.¹ About 45 million people in the U.S. rely on private wells for drinking water.² This study builds upon 15 years of Columbia SRC arsenic research in the U.S. and abroad.

In Bangladesh, researchers are studying more than 24,000 people exposed to arsenic in drinking water. Columbia SRC researchers have documented associations between arsenic exposure and skin lesions, cardiovascular and lung diseases, and lower IQ scores.^{3,4}

Exploring ways to minimize health effects, Mary Gamble, Ph.D., demonstrated that folic acid supplements may help lower blood arsenic concentrations, and potentially help prevent arsenic toxicity.⁵ Her team is also exploring the possibility that other supplements or nutrients may have similar effects.

Enhanced cleanup methods for groundwater arsenic at U.S. Superfund sites

Benjamin Bostick, Ph.D., and Steven Chillrud, Ph.D., are finding ways to improve the cleanup of arsenic from contaminated aquifers at Superfund sites. Their studies suggest that a single injection of safe, inexpensive compounds into groundwater could form a barrier to trap dissolved arsenic for 10-20 years, greatly reducing the threat of groundwater contamination.⁶ Columbia SRC continues to use lab and field experiments to increase the efficiency of their strategy to immobilize arsenic in aquifers and to better understand its long-term use. This approach is one of several in the U.S. and overseas that focus on reducing exposures by lowering arsenic concentrations at the source.



Columbia SRC hypothesizes that magnetite (the black mineral) formed in aquifer sediments could immobilize dissolved arsenic in contaminated aquifers. (Photo courtesy of Columbia SRC)

COLUMBIA
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Columbia SRC forms interdisciplinary teams of biomedical and geoscience researchers to pinpoint exposure sources, exposure routes, and changes in populations that contribute to arsenic and manganese exposure risks. They are developing and implementing strategies to minimize exposures and reduce health risks using cost-effective approaches to solve environmental health problems.

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Encouraging use of low-arsenic wells to reduce exposure

Alexander van Geen, Ph.D., and his Columbia SRC team reported that a large proportion of wells in Bangladesh with high levels of arsenic that were labeled unsafe are still being used for drinking and cooking. Out of more than 10,000 wells, 19 percent were labeled as having high arsenic concentrations, and two out of three of those wells were still being used by villagers. The status of half of the wells was not known.⁷ Van Geen and colleagues are working to find ways to build and test more wells, and implement programs to label wells more effectively. They are also developing educational programs to persuade people to use wells known to be safe.

The importance of studying arsenic and manganese contamination

- Arsenic and manganese contamination in groundwater and soil leads to major public health, cleanup, and environmental policy problems in the U.S. and abroad.
- Nearly 200 million people in the world are chronically exposed to arsenic in drinking water and diet. Arsenic is associated with several types of cancer, as well as cardiovascular, lung, and other diseases.⁸

Research overview

- Studying chronic health effects of low-level arsenic exposure over time. (Habibul Ahsan, M.D., habib@uchicago.edu)
- Investigating how children's health is affected by exposure to arsenic and manganese in drinking water. (Joseph Graziano, Ph.D., jp24@columbia.edu)
- Determining how nutrition can change or prevent the effects of arsenic in the body. (Mary Gamble, Ph.D., mvg7@columbia.edu)
- Understanding the processes that threaten the quality of groundwater in aquifers, and ways to lower exposure to arsenic from aquifers. (Alexander van Geen, Ph.D., avangeen@ldeo.columbia.edu)
- Investigating how arsenic, manganese, iron, and sulfur move through groundwater and sediment. (Benjamin Bostick, Ph.D., bostick@ldeo.columbia.edu)
- Identifying and testing new ways to increase the speed and efficiency of treatments used to remove arsenic from groundwater. (Steven Chillrud, Ph.D., chilli@ldeo.columbia.edu)

Sharing results

- Columbia SRC promotes arsenic testing and treatment to reduce health risks in people that rely on wells for drinking water. (Yan Zheng, Ph.D., yzheng@ldeo.columbia.edu)
- Columbia SRC created an interactive geographical information system map that allows users to visualize critical data about environmental contaminants and other information about areas near Superfund sites.⁹ (Steven Chillrud, Ph.D., chilli@ldeo.columbia.edu)

Other contributions to advance science

The Columbia SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Alexander van Geen, Ph.D., avangeen@ldeo.columbia.edu; Diane Levy, Ph.D., dl2015@columbia.edu; Joseph Graziano, Ph.D., jp24@columbia.edu; Peter Schlosser, Ph.D., schlosser@ldeo.columbia.edu)

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For more information on the Columbia University Superfund Research Center, visit <http://superfund.ciesin.columbia.edu>.

¹ Wasserman G, Liu X, Loiacono N, Kline J, Factor-Litvak P, van Geen A, Mey J, Levy D, Abramson R, Schwartz A, Graziano J. 2014. A cross-sectional study of well water arsenic and child IQ in Maine schoolchildren. *Environ Health* 13(1):23.

² USGS (U.S. Geological Survey). 2014. USGS Water Science School: Domestic Water Use. Available: <http://water.usgs.gov/edu/wudo.html> [accessed 1 June 2015].

³ Chen Y, Parvez F, Gamble M, Islam T, Ahmed A, Argos M, Graziano J, Ahsan H. 2009. Arsenic exposure at low-to-moderate levels and skin lesions, arsenic metabolism, neurological functions, and biomarkers for respiratory and cardiovascular diseases: review of recent findings from the Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh. *Toxicol Appl Pharmacol* 239(2):184-192.

⁴ Wasserman G, Liu X, Parvez F, Ahsan H, Factor-Litvak P, van Geen A, Slavkovich V, Loiacono N, Cheng Z, Hussain I, Momotaj H, Graziano J. 2004. Water arsenic exposure and children's intellectual function in Araihaazar, Bangladesh. *Environ Health Perspect* 112(13):1329-1333.

⁵ Gamble M, Liu X, Slavkovich V, Pilsner R, Ilievski V, Factor-Litvak P, Levy D, Alam S, Islam M, Parvez F, Ahsan H, Graziano J. 2007. Folic acid supplementation lowers blood arsenic. *Am J Clin Nutr* 86:1202-1209.

⁶ Jing S, Chillrud S, Mailloux BJ, Bostick B. 2014. Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Available: http://superfund.ciesin.columbia.edu/sfund_files/documents/events/SRP2013_JingSunFirstPlacePoster.pdf [accessed 1 June 2015].

⁷ Van Geen A, Ahmed EB, Pitcher L, Mey JL, Ahsan H, Graziano JH, Ahmed KM. 2014. Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km sq. area of Bangladesh. *Sci Total Environ* 488-489:484-492.

⁸ Naujokas M, Anderson B, Ahsan H, Aposhian H, Graziano J, Thompson C, Suk W. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.

⁹ Columbia University Superfund Research Program Online Mapping Project — NPL Superfund Footprint: Site, Population, and Environmental Characteristics. http://superfund.ciesin.columbia.edu/sfmapper/map_intro.htm [accessed 1 June, 2015].



Superfund Research Program

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Research Highlights

Studying the adverse health effects of arsenic



Dartmouth SRC researchers Mary Lou Guerinot, Ph.D., and Brian Jackson, Ph.D., led a team that measured arsenic in a previously underrecognized source — common foods. Arsenic exposure is associated with a diverse range of health effects, including several types of cancer, cardiovascular disease, and lung disease.¹ Researchers detected significant concentrations of arsenic in organic brown rice syrup, used as an alternative to high fructose corn syrup in many foods, including toddler formulas.² Their research

inspired further studies of arsenic in the diet, and they are continuing to identify and quantify dietary sources of arsenic to better reduce exposures.

In other work, Bruce Stanton, Ph.D., and his team are identifying cellular changes in lung cells that occur with arsenic exposure.³ Their results may explain why arsenic reduces the ability of the immune system to fight lung infections.⁴ They found that when human epithelial cells, which normally line the inside of airways, were exposed to arsenic, they had decreased amounts of a protein that is important for producing mucous.³ With less mucous, bacteria and viruses are more likely to linger and cause infections.

Public health and mercury contamination in fish

Celia Chen, Ph.D., and the Dartmouth SRC Research Translation Core brought together an international group of scientists and policy stakeholders in 2010 to establish the Coastal and Marine Mercury Ecosystem Research Collaborative (C-MERC). Their goal was to review current knowledge — and knowledge gaps — relating to mercury contamination of the world's marine fish, a global environmental health problem. In 2012, C-MERC authors published a series of 11 scientific papers related to their findings, including sources of mercury, how marine fish absorb mercury, effects on human health, and policy implications. They also produced a companion report, *Sources to Seafood: Mercury Pollution in the Marine Environment*, summarizing the C-MERC findings.⁵



Chen, far right, collects samples near the Callahan Mine Superfund site in Brooksville, Maine. (Photo courtesy of Dartmouth SRC)

Dartmouth



(Photo courtesy of Dartmouth SRC)

Dartmouth SRC researchers seek to understand ways in which arsenic and mercury in the environment affect ecosystems and human health. Their work focuses on reducing exposures and understanding pathways that contribute to disease. They communicate their results to communities, grass-roots organizations, and state and federal agencies.

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Videos to inform the public about mercury

To explain research findings on arsenic in well water and mercury in seafood, Dartmouth SRC produced two 10-minute videos.

The video, *In Small Doses: Arsenic*, targets residents relying on wells for their drinking water. It explains how naturally occurring arsenic moves into groundwater, what can be done to remove it, and current science surrounding the question of how much is too much. The video also stresses the importance of testing water from private wells.⁶

The video, *Mercury: From Source to Seafood*, explains how mercury accumulates in seafood and the potential health effects from mercury exposure. It also describes health benefits of eating fish with lower concentrations of mercury, and the need to keep mercury from entering the environment.⁷



Dartmouth SRC also reaches out to the community through science festivals. Michael Paul, left, explains how arsenic can get into drinking water, to fourth grade students at a New Hampshire water festival. (Photo courtesy of Dartmouth SRC)

Research overview

- Studying arsenic in food, and factors that control arsenic absorption by grains, especially rice. (Mary Lou Guerinot, Ph.D., mary.lou.guerinot@dartmouth.edu)
- Studying how arsenic affects the immune system, and causes or worsens bacterial infections in the lung. (Bruce Stanton, Ph.D., bruce.a.stanton@dartmouth.edu)
- Determining whether arsenic affects glucose and blood pressure during pregnancy. (Margaret Karagas, Ph.D., margaret.karagas@dartmouth.edu)
- Using field studies and laboratory experiments to learn how changes in the environment, such as temperature and salt content in water, might affect accumulation of mercury in various organisms in estuaries. (Celia Chen, Ph.D., celia.y.chen@dartmouth.edu)

Sharing results

- Dartmouth SRC builds partnerships with target communities in northern New England to enhance their ability to understand and address the health risks posed by toxic metals in the environment. These communities include owners of private wells, consumers of food products of concern, and parent groups. (Mark Borsuk, Ph.D., mark.borsuk@dartmouth.edu)
- Dartmouth SRC facilitates the understanding and application of research by partnering with government agencies, hosting collaborative workshops, collecting community feedback on risk perceptions, engaging in Web-based communication, and providing media training. (Celia Chen, Ph.D., celia.y.chen@dartmouth.edu)

Other contributions to advance science

- The Dartmouth SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Brian Jackson, Ph.D., brian.jackson@dartmouth.edu)
- The Dartmouth SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Bruce Stanton, Ph.D., bruce.a.stanton@dartmouth.edu)

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¹ Naujokas M, Anderson B, Ahsan H, Aposhian H, Graziano J, Thompson C, Suk W. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.

² Jackson BP, Taylor VF, Karagas MR, Punshon T, Cottingham KL. 2012. Arsenic, organic foods, and brown rice syrup. *Environ Health Perspect* 120(5):623-626.

³ Bomberger JM, Coutermarsh BA, Barnaby RL, Stanton BA. 2012. Arsenic promotes ubiquitylation and lysosomal degradation of cystic fibrosis transmembrane conductance regulator (CFTR) chloride channels in human airway epithelial cells. *J Biol Chem* 287(21):17130-17139.

⁴ Kozul CD, Ely KH, Enelow RI, Hamilton JW. 2009. Low-dose arsenic compromises the immune response to influenza A infection in vivo. *Environ Health Perspect* 117(9):1441-1447.

⁵ Dartmouth College Superfund Research Center. 2012. Sources to Seafood: Mercury Pollution in the Marine Environment. Available: www.dartmouth.edu/~toxmetal/assets/pdf/sources_to_seafood_report.pdf [accessed 1 June 2015].

⁶ Dartmouth College Superfund Research Center. 2011. *In Small Doses: Arsenic*. Available: www.dartmouth.edu/~toxmetal/InSmallDoses [accessed 1 June 2015].

⁷ Dartmouth College Superfund Research Center. 2012. *Mercury: From Source to Seafood*. Available: www.dartmouth.edu/~toxmetal/mercury-source-to-seafood [accessed 1 June 2015].



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Duke University Superfund Research Center (Duke SRC), to advance this work across the nation.

Research Highlights

Developmental sensitivity to insecticides



Infants and children exposed to environmental contaminants early in life can have health effects that last into adulthood.

been stopped at infancy.¹ These data suggest that children exposed to dexamethasone prenatally or as infants may be especially sensitive to the toxic effects of environmental contaminants. The results add to the growing evidence that environmental exposures during childhood can have lasting effects, even into adulthood.

Duke SRC researchers found that a drug used to prevent premature delivery and help protect premature infants' lungs may make them more likely to develop neurobehavioral problems when also exposed to insecticides, and that these effects may continue later in life.¹ The drug dexamethasone, a type of steroid, is given to approximately 400,000 infants each year, and to pregnant women at risk of delivering prematurely.²

Theodore Slotkin, Ph.D., and his team exposed rats to dexamethasone during pregnancy, and then exposed their offspring to the insecticide chlorpyrifos, which is used on agricultural crops in nearly 100 countries and the U.S. The offspring had worsened neurobehavioral outcomes than rats exposed to either the steroid or the insecticide alone. The neurobehavioral effects were observed in adolescent and adult rats, even though exposure had

Studying how fish thrive in polluted waters

Duke SRC researchers determined that embryos from fish living in contaminated waters are resistant to the toxic effects of chemicals that typically cause developmental defects in fish.³ Richard Di Giulio, Ph.D., leads a team that is studying killifish living in the area of the Elizabeth River that is part of the Atlantic Wood Industries Superfund site in Portsmouth, Virginia.⁴ The site is heavily contaminated with polycyclic aromatic hydrocarbons (PAHs), which are known to cause cancer and birth defects in animals.⁵ When treated with different developmental toxicants, embryos from fish in more highly contaminated waters had fewer heart malformations than fish from less contaminated waters.³ Researchers are striving to understand how these fish have adapted to the contaminated waters, in order to explore ways to prevent toxicity in animals and humans.



Duke SRC graduate students Daniel Brown and Audrey Bone collect killifish at the Atlantic Wood Industries Superfund site for further research. (Photo courtesy of Duke SRC)



Duke SRC collaborative researchers seek to understand how early-life exposures to toxic chemicals may alter development and lead to health issues later in life. They study how pesticides, PAHs, and flame retardants impact brain development, thyroid function, and more. They are also developing new strategies to clean up hazardous waste sites.

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Using nanoparticles and bacteria to clean up contaminated water

Duke SRC researchers found that iron nanoparticles can help bacteria clean up a wide variety of toxic chemicals in water at contaminated sites. Mark Wiesner, Ph.D.; Claudia Gunsch, Ph.D.; and Heileen Hsu-Kim, Ph.D., reported that iron-containing nanoparticles increased the breakdown of toxic chemicals when added to a water treatment system. This system relies on bacteria to help break down the chemicals, and the nanoparticles make the process more efficient.⁶

The importance of studying developmental toxicants

- Pesticides, like chlorpyrifos, are widely used in agriculture worldwide. Early-life exposure has been associated with neurobehavioral and other health effects.⁷
- PAHs are highly toxic chemical mixtures that are created when products like oil, coal, and garbage are burned. PAHs are found in air, soil, and foods, especially grilled or charred foods.⁶

Research overview

- Studying how exposures to pesticides, PAHs, flame retardants, and other chemicals interfere with normal brain development and metabolism. (Theodore Slotkin, Ph.D., t.slotkin@duke.edu)
- Identifying ways that embryos from fish living in highly contaminated water resist the toxic effects of PAHs. (Richard Di Giulio, Ph.D., richd@duke.edu)
- Developing strategies to use nanomaterials and bacteria to treat contaminated sediments and water. (Mark Wiesner, Ph.D., wiesner@duke.edu)
- Measuring exposures to flame retardants and identifying health effects. (Heather Stapleton, Ph.D., heather.stapleton@duke.edu)

Sharing results

Duke SRC connects with government agencies, industry professionals, community organizations, K-12 teachers, and other partners to bring information and research results about environmental health and toxic exposures to the public. Underserved communities are a particular focus. (Charlotte Clark, Ph.D., cclark@duke.edu)

Other contributions to advance science

- The Duke SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Heather Stapleton, Ph.D., heather.stapleton@duke.edu; Edward Levin, Ph.D., edlevin@duke.edu)
- The Duke SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Edward Levin, Ph.D., edlevin@duke.edu)

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¹ Levin ED, Cauley M, Johnson JE, Cooper EM, Stapleton HM, Ferguson PL, Seidler FJ, Slotkin TA. 2014. Prenatal dexamethasone augments the neurobehavioral teratology of chlorpyrifos: significance for maternal stress and preterm labor. *Neurotoxicol Teratol* 41:35–42.

² Matthews SG, Owen D, Banjanin S, Andrews MH. 2002. Glucocorticoids, hypothalamo-pituitary-adrenal (HPA) development, and life after birth. *Endocr Res* 28(4):709-718.

³ NIEHS (National Institute of Environmental Health Sciences). 2014. Duke University: Nanoparticle Based Strategies for Remediation of Contaminated Sediments: Implications, Synergies, and Antagonistic Effects With Associated Nano-Bioremediation. Available: <http://go.usa.gov/3BPWh> [accessed 1 June 2015].

⁴ Clark BW, Cooper EM, Stapleton HM, Di Giulio RT. 2013. Compound- and mixture-specific differences in resistance to PAHs and PCB-126 among *Fundulus heteroclitus* subpopulations throughout the Elizabeth River estuary (Virginia, USA). *Environ Sci Technol* 47(18):10556-10566.

⁵ EPA (U.S. Environmental Protection Agency). 2014. Superfund Information Systems: Cleanup Activities at Atlantic Wood Industries, Inc. Available: <http://cumulis.epa.gov/supercpad/SiteProfiles/index.cfm?fuseaction=second.CleanupActs&id=0302836> [accessed 1 June 2015].

⁶ EPA (U.S. Environmental Protection Agency). 2008. Polycyclic Aromatic Hydrocarbons (PAHs). Available: <http://www.epa.gov/osw/hazard/wastemin/minimize/factshts/pahs.pdf> [accessed 1 June 2015].

⁷ Gonzalez-Alzaga B, Lacasana M, Aguilar-Garduno C, Rodriguez-Barranco M, Ballester F, Rebagliato M, Hernandez AF. 2014. A systematic review of neurodevelopmental effects of prenatal and postnatal organophosphate pesticide exposure. *Toxicol Lett* 230(2):104-121.



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Louisiana State University Superfund Research Center (LSU SRC), to advance this work across the nation.

Research Highlights

Understanding air pollutants containing free radicals



LSU SRC trainee Phillip Potter works with Dellinger to investigate the formation and reaction of EPFRs in thermal processing of Superfund waste. (Photo courtesy of LSU SRC)

LSU SRC researchers measured how fast certain small toxic particles, found in air and soil at Superfund sites and elsewhere, break down in the environment.¹ The particles, called environmentally persistent free radicals (EPFRs), are created when solid waste and fuel burn, and contain unstable chemical components that can damage cells in humans and animals.² Because EPFRs may pose risks for lung and cardiovascular diseases,^{3,4} understanding where they can be found and how long they last is important.

William Gehling, Ph.D., and Barry Dellinger, Ph.D., identified three different rates of EPFR decay — fast (21 days or less), slow (21-5,028 days), and no decay.¹ The researchers are now working to understand why some EPFRs remain in the environment longer than others, posing greater risk to human health. LSU SRC researchers are also studying whether EPFRs are formed during certain types of cleanup processes at Superfund sites that involve burning toxic wastes.⁵

EPFR exposure and asthma in children

Stephania Cormier, Ph.D., and her research team reported airway cells exposed to EPFRs may increase the likelihood for developing asthma later in life. In a mouse study, the researchers saw an increased allergic immune response after exposure to EPFRs, but other types of immune responses were decreased.³ These decreases may reduce the ability to fight infections.

In other studies, Kurt Varner, Ph.D., and his team demonstrated that EPFR exposure reduces heart function and increases the heart's sensitivity to ischemia, a reduction in blood supply to tissues.⁴ This study suggests that EPFRs may pose an increased risk to people with cardiovascular disease.



EPFRs form in combustion and thermal processes, including hazardous waste incineration and diesel combustion.

LOUISIANA STATE UNIVERSITY



LSU SRC is studying EPFRs, a pollutant found in air, soil, and sediment. Researchers are studying how EPFRs are formed, how to reduce exposures, and how they may affect our health. They share their research findings to help inform environmental health decisions and put science to work.

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The importance of studying EPFRs

- Infants and children may be especially sensitive to the toxic effects of EPFRs and other air pollutant particles, and early life exposure may be linked to long-term, persistent lung disease.⁶
- Ongoing efforts to reduce air pollutants have economic merit. For example, the U.S. could save \$15 million annually from fewer hospitalizations of urban infants with the lung disease bronchiolitis, if air pollution standards were cut by 7 percent.⁷

Research overview

- **Uncovering toxicity pathways from inhalation exposure to EPFRs that may lead to lung disease and asthma.** (Stephania Cormier, Ph.D., University of Tennessee Health Science Center, scormier@uthsc.edu)
- **Understanding how exposure to EPFRs alters lung and cardiac functions, and blood flow.** (Kurt Varner, Ph.D., kvarne@lsuhsc.edu)
- **Identifying what components in soils, contaminated with the wood preservative pentachlorophenol, are responsible for EPFR formation.** (Robert Cook, Ph.D., rlcook@lsu.edu)
- **Understanding how airborne EPFRs are formed during cleanup processes at Superfund sites.** (Slawomir Lomnicki, Ph.D., slomni1@lsu.edu)
- **Identifying pathways that link EPFR exposures to biological responses and toxicity.** (Wayne Backes, Ph.D., wbacke@lsuhsc.edu)
- **Determining structural and chemical interactions that occur at Superfund sites that lead to EPFR formation.** (Erwin Poliakoff, Ph.D., epoliak@lsu.edu)

Sharing results

- LSU SRC researchers engage people in communities close to Superfund sites to learn about community concerns and communicate research findings. They also work with the Louisiana Environmental Action Network, a community organization with more than 100 affiliated groups. (Margaret Reams, Ph.D., mreams@lsu.edu)
- LSU SRC partners with health and environmental professionals, as well as the U.S. Environmental Protection Agency, to communicate the importance of their research on EPFRs. They serve as a resource for business and technology leaders who, in turn, help LSU SRC scientists develop and market intellectual property. (Maud Walsh, Ph.D., evwals@lsu.edu)

Other contributions to advance science

- The LSU SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Randall Hall, Ph.D., rhall@lsu.edu; Slawomir Lomnicki, Ph.D., slomni1@lsu.edu; Tammy Dugas, Ph.D., tdugas@lsuhsc.edu)
- The LSU SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Robin McCarley, Ph.D., tunnel@lsu.edu)

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Legislative Authority:

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the Louisiana State University Superfund Research Center, visit www.srp.lsu.edu.

¹ Gehling W, Dellinger B. 2013. Environmentally persistent free radicals and their lifetimes in PM2.5. *Environ Sci Technol* 47(15): 8172-8178.

² Louisiana State University Superfund Research Center. 2014. EPFRs: Environmentally Persistent Free Radicals. Available: www.srp.lsu.edu/files/item24088.pdf [accessed 1 June 2015].

³ Saravia J, You D, Thevenot P, Lee GI, Shrestha B, Lomnicki B, Cormier SA. 2014. Early-life exposure to combustion-derived particulate matter causes pulmonary immunosuppression. *Mucosal Immunol* 7:694-704.

⁴ Burn BR, Varner KJ. 2015. Environmentally persistent free radicals (EPFRs) compromise left ventricular function during ischemia/reperfusion injury. *Am J Physiol Heart Circul Physiol* 308(9):H998-H1006.

⁵ Dela Cruz AL, Cook RL, Lomnicki SM, Dellinger B. 2012. Effect of low temperature thermal treatment on soils contaminated with pentachlorophenol and environmentally persistent free radicals. *Environ Sci Technol* 46(11):5971-5978.

⁶ Saravia J, Lee GI, Lomnicki S, Dellinger B, Cormier SA. 2013. Particulate matter containing environmentally persistent free radicals and adverse infant respiratory health effects: a review. *J Biochem Mol Toxicol* 27(1):56-68.

⁷ Sheffield P, Roy A, Wong K, Trasande L. 2011. Fine particulate matter pollution linked to respiratory illness in infants and increased hospital costs. *Health Aff (Millwood)* 30(5):871-878.



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Michigan State University Superfund Research Center (MSU SRC), to advance this work across the nation.

Research Highlights

Using clay to immobilize dioxins in soils

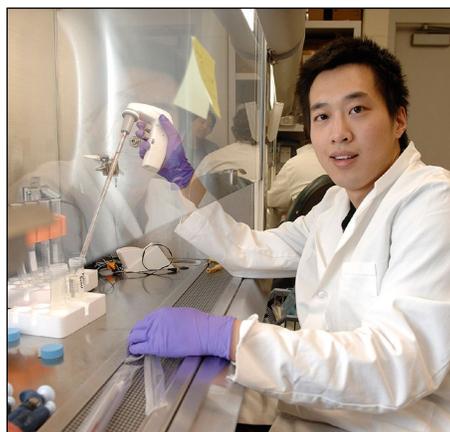


Boyd uses state-of-the-art technology to chemically analyze organoclays and soils to improve cleanup of dioxins and other contaminants in soils. (Photo courtesy of MSU SRC)

Stephen Boyd, Ph.D., and his research team at MSU SRC improved the ability of a type of clay, called organoclay, to bind dioxins and dioxin-like compounds in soils, preventing them from moving into water, plants, and animals.¹ Dioxins and dioxin-like compounds are byproducts of various industrial processes. They are also produced during improper incineration, such as burning municipal waste, and natural events, such as forest fires and volcanoes. People are primarily exposed through food and air.² Dioxin-like compounds are toxic and can cause severe skin rashes, altered immune responses, hormonal disruption, and cancer.³ Boyd's team compared their organoclay to other soil additives, such as granular activated carbon, and found that the organoclay performed better. They are currently studying several other soil additives to find the ones that work best, to help reduce human exposures to dioxins.

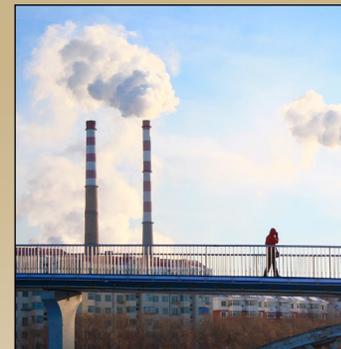
New models help determine toxicity levels of contaminants

As part of efforts to reduce the need for animal testing, Norbert Kaminski, Ph.D., and his colleagues used sophisticated mathematical models to help understand the potential toxicity of environmental contaminants in the body.⁴ Traditionally, animals have been used to test contaminants, but more alternatives to animal testing are now becoming available. Using in vitro testing data combined with mathematical models, Kaminski and his team identified patterns of biological responses to help quantify health risks at different doses. This data may help inform government regulatory agencies about safe levels of contaminants in the environment.



MSU SRC scientists, including Haitian Lu, do laboratory testing, as well as computer modeling, to find new approaches to reduce animal testing. (Photo courtesy of MSU SRC)

MICHIGAN STATE UNIVERSITY



Research at MSU SRC focuses on reducing exposures and human health risks related to dioxins and dioxin-like compounds, which are considered highly toxic. They use a state-of-the-art systems approach that integrates computer modeling and computational approaches with biomedical research to understand how dioxins affect complex biological systems.

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Engaging communities and government agencies

MSU SRC members facilitate dialogue with stakeholders by partnering with U.S. Environmental Protection Agency Region 5, Michigan Department of Agriculture and Rural Development, Michigan Department of Environmental Quality, local governments, and industry groups. They are also building community-university partnerships through meetings, community fairs, and educational experiences in the schools and community.



To enhance communication, MSU SRC is conducting social science research to understand how factors such as trust, social networks, and math literacy, can affect local residents' understanding of dioxin contamination and cleanup in their community.

Research overview

- Uncovering relationships between genetic differences in a population and their response to different amounts of dioxins, to better predict health risks. (John LaPres, Ph.D., lapres@msu.edu)
- Studying additives to soils that can immobilize dioxins, to prevent exposures. (Stephen Boyd, Ph.D., boyds@msu.edu)
- Understanding the role of microbes in the gut, how they affect the biological response to dioxin exposure, and how they might protect the body from dioxin toxicity. (Syed Hashsham, Ph.D., hashsham@egr.msu.edu)
- Studying bacteria that can degrade dioxins to help clean up contaminated sites. (Gerben Zylstra, Ph.D., zylstra@aesop.rutgers.edu)
- Determining ways that dioxins alter immune responses and susceptibility to disease. (Norbert Kaminski, Ph.D., kamins11@msu.edu)
- Finding connections between dioxin exposure, and development of metabolic syndrome and diabetes. (Timothy Zacharewski, Ph.D., tzachare@msu.edu)

Sharing results

- MSU SRC facilitates dialogue with stakeholders by organizing conferences and workshops, and partnering with federal and local government agencies. (Brad Upham, Ph.D., upham@msu.edu)
- MSU SRC has developed a strong partnership with communities in the Michigan Tri-Cities area (Saginaw, Midland, and Bay City) to engage community members in issues related to dioxin contamination. (James Dearing, Ph.D., dearjim@msu.edu)

Other contributions to advance science

- The MSU SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (James Tiedje, Ph.D., tiedje@msu.edu; Rory Conolly, Sc.D., conolly.rory@epa.gov)
- The MSU SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Jay Goodman, Ph.D., goodman3@msu.edu)

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the Michigan State University Superfund Research Center, visit <http://cit.msu.edu/superfund2013>.

¹ Johnston CT, Khan B, Barth EF, Chattopadhyay S, Boyd SA. 2012. Nature of the interlayer environment in an organoclay optimized for the sequestration of dibenzo-p-dioxin. *Environ Sci Technol* 46(17):9584-9591.

² ATSDR (Agency for Toxic Substances and Disease Registry). 2011. ToxFAQs for Chlorinated Dibenzo-p-dioxins (CDDs). Available: www.atsdr.cdc.gov/toxfaqs/tf.asp?id=363&tid=63 [accessed 1 June 2015].

³ NIEHS (National Institute of Environmental Health Sciences). 2012. Dioxins Fact Sheet. Available: www.niehs.nih.gov/health/materials/dioxins_new_508.pdf [accessed 1 June 2015].

⁴ Zhang Q, Bhattacharya S, Conolly RB, Clewell HJ, Kaminski NE, Andersen ME. 2014. Molecular signaling network motifs provide a mechanistic basis for cellular threshold responses. *Environ Health Perspect* 122(12):1261-1270.

Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Northeastern University Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) Superfund Research Center (SRC), to advance this work across the nation. PROTECT is a multi-project, multi-institution collaboration that involves Northeastern University, University of Puerto Rico Medical Sciences Campus, University of Puerto Rico at Mayaguez, and University of Michigan.

Research Highlights

Phthalate activation of oxidative stress in placental tissues

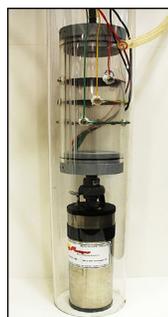
Looking at human placental cells, PROTECT researchers discovered that exposure to di-2-ethylhexyl phthalate (DEHP), a type of phthalate used as a softener in some plastics, triggered an oxidative stress response that may be linked to preterm birth.¹ Oxidative stress is a process in cells that can result in cell and tissue damage and other problems. Rita Loch-Carusio, Ph.D., at the University of Michigan, and her PROTECT team are identifying possible biological explanations to understand how exposure to environmental pollutants, such as phthalates, can lead to early labor and preterm birth.¹



Iman Hassan, Ph.D., analyzes human placental cells exposed to phthalates. (Photo courtesy of Northeastern University)

Using solar power to clean up contaminants

Akram Alshawabkeh, Ph.D., at Northeastern University, leads a PROTECT team that is developing a sustainable, solar-powered system for removing trichloroethylene (TCE) and other contaminants from groundwater.^{2,3} TCE, an industrial solvent and degreaser, is one of the most common soil and groundwater contaminants in the U.S., and is linked to cancer.⁴ The solar panels produce electric currents that trigger chemical reactions in groundwater, changing TCE into a less toxic form.³ The researchers have applied for a patent on this device, and are currently testing whether it can be used to clean up other contaminants.



A pilot-scale setup of a solar-powered reactor for on-site transformation of contaminants in groundwater is currently being tested. (Photo courtesy of Northeastern University)

Developing detection and exposure assessment tools

Roger Giese, Ph.D., at Northeastern University, and his PROTECT team invented a convenient tool, the Porous Extraction Paddle (PEP), to extract contaminants from a large volume of urine or water at a remote location for later testing in the lab.⁵ The PEP device will greatly reduce researcher efforts and costs by simplifying field collection of samples, which can number in the thousands.



The PEP device, which resembles a tea bag, extracts chemicals from urine or water in the field so the samples are conveniently-sized for shipment to a lab for analysis. (Photo courtesy of Northeastern University)

Northeastern University



The Northeastern University PROTECT SRC is studying exposure to environmental contaminants and their contribution to preterm birth, or births occurring before 37 weeks of gestation, in the United States, and U.S. territory of Puerto Rico. They also seek to better understand movement of hazardous chemicals in groundwater systems, and develop green cleanup strategies to reduce exposures.

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Transport and exposure pathways in groundwater systems

Ingrid Padilla, Ph.D., and her team at the University of Puerto Rico at Mayaguez identified flow patterns of contaminants in a specific type of groundwater system, called karst aquifers, that supply drinking water in Puerto Rico, as well as several U.S. states and much of the developing world.^{6,7} The karst aquifers contain cave systems that are vulnerable to contamination from toxic chemicals, such as DEHP and TCE, which are believed to contribute to Puerto Rico's high preterm birth rate.⁸ So far, their data supports the hypothesis that the aquifers have a large capacity to store and slowly release contaminants.⁹



Hydrogeologist Padilla, left, and students examine well equipment installed through the Monte Encantado aquifer cave in Puerto Rico. (Photo courtesy of Northeastern University)

The importance of studying Superfund contaminants

- In Puerto Rico, the preterm birth rate is nearly 20 percent of live births,⁸ and evidence suggests that exposures to Superfund and related contaminants are contributing factors.
- The racial, ethnic, and socioeconomic status of the community, along with the high risk of exposure to contaminants, highlight the relevance of PROTECT to environmental justice.

Research overview

- Identifying chemicals that contribute to preterm birth. (Roger Giese, Ph.D., Northeastern University, r.giese@neu.edu)
- Understanding how contaminants move into and through aquifers, and the impact on exposure risks. (Ingrid Padilla, Ph.D., University of Puerto Rico at Mayaguez, ingrid.padilla@upr.edu)
- Applying state-of-the-art methods to study biological mechanisms involved in preterm birth related to environmental factors. (John Meeker, Sc.D., University of Michigan, meekerj@umich.edu)
- Creating solar-powered systems to clean up Superfund chemicals from aquifers. (Akram Alshawabkeh, Ph.D., Northeastern University, aalsha@neu.edu)
- Studying biological pathways that link exposures to contaminants to preterm birth. (Rita Loch-Caruso, Ph.D., University of Michigan, rlc@umich.edu)

Sharing results

- PROTECT serves as a bridge between researchers, communities, government agencies, and stakeholders to foster effective communication and application of research findings and technologies. (Phil Brown, Ph.D., Northeastern University, p.brown@neu.edu)

Other contributions to advance science

- The PROTECT SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Jose Cordero, M.D., University of Puerto Rico, jose.cordero6@upr.edu; David Kaeli, Ph.D., Northeastern University, kaeli@ece.neu.edu)
- The PROTECT SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Thomas Sheahan, Ph.D., Northeastern University, t.sheahan@neu.edu)

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Section 311(a) of the Superfund Amendments and Reauthorization Act (SARA) of 1986

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the Northeastern University Superfund Research Center, visit www.northeastern.edu/protect.

¹ Tetz, LM, Cheng AA, Korte CS, Giese RW, Wang P, Harris C, Meeker JD, Loch-Caruso R. 2013. Mono-2-ethylhexyl phthalate induces oxidative stress responses in human placental cells in vitro. *Toxicol Appl Pharmacol* 268(1):47-54.

² Yuan S, Liao P, Alshawabkeh AN. 2014. Electrolytic manipulation of persulfate reactivity by iron electrodes for trichloroethylene degradation in groundwater. *Environ Sci Technol* 48(1):656-663.

³ PROTECT (Puerto Rico Testsite for Exploring Contamination Threats). 2014. Project 5: Green Remediation by Solar Energy Conversion Into Electrolysis in Groundwater. Available: www.northeastern.edu/protect/research/p5 [accessed 1 June 2015].

⁴ ATSDR (Agency for Toxic Substances and Disease Registry). 2014. ToxFAQs for Trichloroethylene (TCE). Available: www.atsdr.cdc.gov/toxfaqs/faq.asp?id=172&tid=30 [accessed 1 June 2015].

⁵ PROTECT (Puerto Rico Testsite for Exploring Contamination Threats). Project 3: Discovery of Xenobiotics Associated with Preterm Birth. Available: www.northeastern.edu/protect/research/p3 [accessed 1 June 2015].

⁶ Anaya AA, Padilla I, Macchiavelli R, Vesper D, Meeker JD, Alshawabkeh AN. 2014. Estimating preferential flow in karstic aquifers using statistical mixed models. *Groundwater* 52(4):584-596.

⁷ USGS (U.S. Geological Survey). 2012. Karst and the USGS. Available: <http://water.usgs.gov/ogw/karst/index> [accessed 1 June 2015].

⁸ Martin JA, Hamilton BE, Ventura SJ, Osteman MJK, Wilson EC, Mathews TJ. 2012. Births: Final Data for 2010. *Natl Vital Stat Rep* 61(1):1-72.

⁹ Padilla I, Irizarry C, Steele K. 2011. Historical contamination of groundwater resources in the North Coast Karst Aquifers of Puerto Rico. *Rev Dimens* 3:7-12.

Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the Oregon State University Superfund Research Center (OSU SRC), to advance this work across the nation.

Research Highlights

Measuring tribal exposures that may raise cancer risk



Tipis are used for smoking salmon by the Confederated Tribes of the Umatilla Indian Reservation. (Photo courtesy of OSU SRC)

An OSU SRC study reported that exposure to polycyclic aromatic hydrocarbons (PAHs) from salmon smoked by traditional tribal methods, if consumed at high levels over many years, may increase cancer risks.¹ PAHs, which are associated with increased risk of certain cancers and other diseases, are byproducts of combustion, such as burning fuels, forest fires, and grilled foods, and are present in air, water, soil, and foods.² Collaborating with the Confederated Tribes of the Umatilla Indian Reservation, Anna Harding, Ph.D., Barbara Harper, Ph.D., and their teams measured PAHs and other exposures specific to tribal lifestyles.³ The researchers also identified tribal-specific factors that may affect environmental exposures.⁴ This information may help decision-makers at contaminated sites that directly affect tribal lands and resources.

Identifying genes involved in developmental toxicity

Using state-of-the-art technology, Robert Tanguay, Ph.D., and his team identified over a thousand genes in developing zebrafish that are affected by PAH exposure.⁵ Zebrafish are a proven model for human development and disease. The team screened for changes in gene activity for the entire zebrafish genome, estimated to contain more than 26,000 genes.⁶ Researchers are now working to understand how those changes may lead to adverse health effects in people.



Tanguay assesses the health of adult zebrafish. (Photo courtesy of OSU SRC)

Identifying novel compounds associated with PAHs

Researchers led by Staci Simonich, Ph.D., have discovered previously unknown types of nitrated PAHs that may be highly toxic.⁷ The scientists identified chemical reactions that lead to formation of these newly identified chemicals, and found that they caused genetic damage in lab tests, suggesting the potential for causing cancer. OSU SRC researchers are measuring these and other PAHs at Superfund sites to find ways to reduce the amounts of these contaminants in the environment.



An OSU SRC multidisciplinary team uses state-of-the-art techniques to better understand PAHs found in air, soil, water, and diet. They are studying how to measure exposure accurately, how PAHs affect development, and how to test for and clean up PAHs in the environment.

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Sampling devices help predict exposure

Kim Anderson, Ph.D., and other OSU SRC researchers developed a new cost-effective method for estimating how much of the contaminants in water may be absorbed by crayfish and other aquatic organisms.⁸ These contaminants can transfer to humans who eat seafood. The researchers conducted sample collections near the Portland Harbor Superfund Mega-site in Oregon. Combining sample measurements with mathematical modeling, the researchers were able to predict how much of the contaminants could potentially build up in aquatic organisms. This information may help scientists estimate human exposure and health risks based on measurements of contaminants in water.



Graduate students from Anderson's lab collect samples in the Portland Harbor. (Photo courtesy of OSU SRC)

Research overview

- Developing devices to measure the amount of contaminants that can be absorbed by living organisms, as well as the toxicity of PAH mixtures, to predict health risks. (Kim Anderson, Ph.D., kim.anderson@oregonstate.edu)
- Applying modeling techniques to understand human responses to different levels of individual contaminants, as well as mixtures. (Richard Corley, Ph.D., rick.corley@pnnl.gov)
- Identifying PAH breakdown products formed during cleanup processes in contaminated soils and sediments. (Staci Simonich, Ph.D., staci.simonich@oregonstate.edu)
- Understanding absorption and elimination of the PAH benzo(a)pyrene in humans, identifying susceptible individuals, and assessing health risks. (David Williams, Ph.D., david.williams@oregonstate.edu)
- Identifying neurodevelopmental and cardiovascular health effects of embryonic exposure to PAHs. (Robert Tanguay, Ph.D., robert.tanguay@oregonstate.edu)

Sharing results

- OSU SRC is translating scientific findings into effective and appropriate risk assessment strategies, to reduce environmental disparities and improve the health of Pacific Northwest tribes. (Anna Harding, Ph.D., anna.harding@oregonstate.edu)
- OSU SRC is facilitating the understanding and application of their research, by partnering with government agencies, and using Web technologies and social media to increase community and tribal awareness of Superfund sites and other issues related to hazardous waste contamination. (Justin Teegarden, Ph.D., Pacific Northwest National Laboratory, justin.teegarden@pnl.gov)

Other contributions to advance science

- The OSU SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Kim Anderson, Ph.D., kim.anderson@oregonstate.edu; Katrina Waters, Ph.D., Pacific Northwest National Laboratory, katrina.waters@pnl.gov)
- The OSU SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Craig Marcus, Ph.D., craig.marcus@oregonstate.edu)

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the Oregon State University Superfund Research Center, visit <http://superfund.oregonstate.edu>.

¹ Forsberg ND, Stone D, Harding A, Harper B, Harris S, Matzke MM, Cardenas A, Waters KM, Anderson KA. 2012. Effect of Native American fish smoking methods on dietary exposure to polycyclic aromatic hydrocarbons and possible risks to human health. *J Agric Food Chem* 60(27):6899-6906.

² EPA (U.S. Environmental Protection Agency). 2008. Polycyclic Aromatic Hydrocarbons (PAHs). Available: <http://www.epa.gov/osw/hazard/wastemin/minimize/factsheets/pahs.pdf> [accessed 1 June 2015].

³ Harding A, Harper B, Stone D, O'Neill C, Berger P, Harris S, Donatuto J. 2012. Conducting research with tribal communities: sovereignty, ethics, and data-sharing issues. *Environ Health Perspect* 120(1):6-10.

⁴ Harper B, Harding A, Harris S, Berger P. 2012. Subsistence exposure scenarios for tribal applications. *Hum Ecol Risk Assess* 18(4):810-831.

⁵ Goodale BC, Tilton SC, Corvi MM, Wilson GR, Janszen DB, Anderson KA, Waters KM, Tanguay RL. 2013. Structurally distinct polycyclic aromatic hydrocarbons induce differential transcriptional responses in developing zebrafish. *Toxicol Appl Pharmacol* 272(3):656-670.

⁶ Howe K, Clark MD, Torroja CF, Torrance J, Berthelot C, Muffato M, et al. 2013. The zebrafish reference genome sequence and its relationship to the human genome. *Nature* 496(7446):498-503.

⁷ Jariyasopit N, McIntosh M, Zimmermann K, Arey J, Atkinson R, Cheong PH, Carter RG, Yu TW, Dashwood RH, Massey Simonich SL. 2014. Novel nitro-PAH formation from heterogeneous reactions of PAHs with NO₂, NO₃/N₂O₅, and OH radicals: prediction, laboratory studies, and mutagenicity. *Environ Sci Technol* 48(1):412-419.

⁸ Forsberg ND, Smith BW, Sower GJ, Anderson KA. 2014. Predicting polycyclic aromatic hydrocarbon concentrations in resident aquatic organisms using passive samplers and partial least-squares calibration. *Environ Sci Technol* 48(11):6291-6299.



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of Arizona Superfund Research Center (UA SRC), to advance this work across the nation.

Research Highlights

Using plants to stop the spread of mine waste

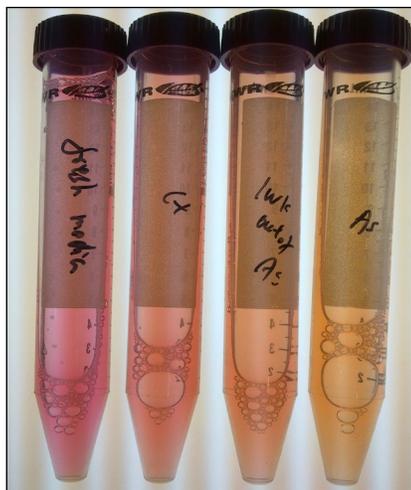


Specific types of plants and soil conditions are being investigated for their ability to stabilize areas contaminated with mine tailings. (Photo courtesy of UA SRC)

Work by UA SRC suggests that certain native plants significantly reduce dust from mine tailing sites.¹ Mine tailings, materials left over after removing the valuable portion of ore, cover thousands of acres in the western United States. This finely crushed waste is often acidic, contains harmful metals like arsenic, and lacks vegetation. Raina Maier, Ph.D., and her colleagues are developing a strategy for long-term management of mine waste by growing native plants of the desert southwest on these sites. Working with U.S. Environmental Protection Agency Region 9 and the site owner, the researchers started a field trial at the Iron King Mine and Humboldt Smelter Superfund site in Arizona in 2010, and are currently in phase 3 of the trial. The positive results have led to partnerships with four mining companies, who are now working with Maier's group to apply the method at their active and inactive mining sites.

A new understanding of arsenic toxicity

A research team led by Walt Klimecki, D.V.M., Ph.D., and Bernard Futscher, Ph.D., found that chronic, low-dose arsenic exposure causes human cells to change their metabolism, specifically how they metabolize sugar for energy, through a process normally reserved for conditions of oxygen starvation.² The study suggests that arsenic tricks the cells by triggering their sensors for low oxygen conditions, even when the cells have an abundance of oxygen. This may have important consequences for arsenic-associated disease because a similar shift in sugar metabolism has been observed in diseases such as diabetes and cancer. Arsenic is thought to contribute to a diverse range of diseases, including cancer, heart disease, and diabetes.³ This new information about metabolism changes helps researchers understand how arsenic causes health problems, and may ultimately help prevent and treat them.



Exposure to arsenic causes changes in cellular metabolism, visualized in the laboratory as color changes in the medium. (Photo courtesy of UA SRC)



UA SRC is studying the human and environmental risks associated with hardrock mining of metal in arid environments and developing innovative cleanup technologies to limit these risks. The arid climate of the southwestern U.S. and U.S.-Mexico border brings unique challenges when it comes to contaminants in the environment.

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Community engagement along the border

The 2,000-mile border between the U.S. and Mexico is a unique arid region, and people residing along the border are at risk for exposure to a variety of environmental contaminants. As one of their outreach projects, UA SRC worked with Hispanic community health advocates, promotoras de salud, on environmental issues relevant to the border of Arizona and Sonora, Mexico. Together, UA SRC Community Engagement Coordinator Denise Moreno Ramírez, UA SRC researchers, and promotoras developed training materials in English and Spanish on topics including arsenic and risk assessment. The modules have been used in the U.S. and Mexico, and are publicly available.⁴ Currently, UA SRC is drawing on this model to develop educational materials for tribal community colleges, focusing on mining and its environmental and social impacts on tribal lands.



Promotoras from the Regional Center for Border Health Inc. and Sunset Community Health Center participate in a hands-on activity that helps them visualize dispersion of a contaminant. UA SRC has partnered with promotoras, who provide environmental health information in primarily Spanish-speaking neighborhoods. (Photo courtesy of UA SRC)

Research overview

- Identifying how plants, such as buffalo grass, can help reduce human exposure to mining waste at active and inactive mining sites. (Raina Maier, Ph.D., rmaier@ag.arizona.edu)
- Examining energy metabolism during arsenic-induced tumor cell formation in lung cancer. (Walter Klimecki, D.V.M., Ph.D., klimecki@pharmacy.arizona.edu)
- Identifying contaminants in dust from mining operations and predicting its movement in the environment. (Eric Betterton, Ph.D., betterton@atmo.arizona.edu)
- Determining if inhalation of arsenic-containing dust during critical stages of development leads to changes in lung function as an adult. (R. Clark Lantz, Ph.D., lantz@email.arizona.edu)
- Understanding what factors determine the amount of toxic metals in mining waste that can be absorbed by living organisms. (Jon Chorover, Ph.D., chorover@cals.arizona.edu)
- Identifying contaminants in acid rock drainage and groundwater at hardrock mining sites, and developing cleanup strategies. (Mark Brusseau, Ph.D., brusseau@ag.arizona.edu)
- Examining how arsenic induces changes in epigenetic gene regulation during human cancer formation. (Bernard Futscher, Ph.D., bfutscher@azcc.arizona.edu)

Sharing results

- UA SRC is strengthening the ability of stakeholders in the U.S., Mexico, and tribal nations to address hazardous waste problems by providing culturally-relevant training, education, and teaching tools. (Sarah Wilkinson, Ph.D., wilkinso@pharmacy.arizona.edu; Karletta Chief, Ph.D., kchief@email.arizona.edu)
- UA SRC is partnering with international stakeholders to form the Latin American Hub for Environmentally Sustainable Mining. (Jim Field, Ph.D., jimfield@email.arizona.edu)
- UA SRC, in partnership with the UA Lowell Institute for Mineral Resources, is building a network of mining expertise that will serve as a global resource to solve environmental health problems related to hardrock mining. (Raina Maier, Ph.D., rmaier@ag.arizona.edu)

Other contributions to advance science

- The UA SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Jon Chorover, Ph.D., chorover@cals.arizona.edu)
- The UA SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Raina Maier, Ph.D., rmaier@ag.arizona.edu)

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of Arizona Superfund Research Center, visit <http://superfund.pharmacy.arizona.edu>.

¹ Solis-Dominguez FA, White SA, Hutter TB, Amistandi MK, Root RA, Chorover J, Maier RM. 2012. Response of key soil parameters during compost-assisted phytostabilization in extremely acidic tailings: effect of plant species. *Environ Sci Technol* 46(2):1019-1027.

² Zhao F, Severson P, Pacheco S, Futscher BW, Klimecki WT. 2013. Arsenic exposure induces the Warburg effect in cultured human cells. *Toxicol Appl Pharmacol* 271(1):72-77.

³ Naujokas MF, Anderson B, Ahsan H, Aposhian HV, Graziano JH, Thompson C, Suk WA. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.

⁴ The University of Arizona Superfund Research Program. 2015. Promotor Modules. Available: <http://superfund.pharmacy.arizona.edu/learning-modules/promotor-modules> [accessed 1 June 2015].



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of California, Berkeley Superfund Research Center (UC Berkeley SRC), to advance this work across the nation.

Research Highlights

Identifying biomarkers of benzene and arsenic exposure



UC Berkeley SRC scientist Tom Burton analyzes samples to improve methods to clean up groundwater. (Photo courtesy of UC Berkeley SRC)

Martyn Smith, Ph.D., and his team identified changes in specific genes that may be biomarkers of benzene exposure.¹ Benzene is an industrial chemical that has been shown to cause leukemia.² Using sophisticated mathematical methods, the researchers revealed a relationship between benzene dose and response of the genes, which is present even at very low levels. These biomarkers hold great promise for helping to better measure benzene exposure and assess health risks.

Allan Smith, M.D., Ph.D., and Craig Steinmaus, M.D., identified biomarkers in urine that may provide clues about why some individuals are more sensitive to arsenic's toxic effects.³ Arsenic exposure is associated with cancer and other health effects.⁴ In this study, the UC Berkeley SRC team found that people who have more

of a certain type of arsenic breakdown product in their urine were more likely to have lung or bladder cancer.³ Researchers are now working to determine why individuals metabolize arsenic differently to help better understand sensitivities to arsenic. UC Berkeley SRC researchers were among the first to document that early life exposures result in health effects during adulthood.⁵

New device for convenient on-site well water treatment

David Sedlak, Ph.D., and colleagues obtained a provisional patent in 2015 for a new compact and inexpensive system to remove a wide variety of environmental contaminants at well heads.⁶ The system is energy-efficient, convenient to use, and removes contaminants from water without creating toxic byproducts. Research is now focused on testing the long-term performance of the system, improving the technology, and reducing the cost of manufacturing the parts.



The patented device developed by Sedlak and his team uses a combination of electrical current and ultraviolet light treatments to remove contaminants from groundwater and other water sources. (Photo courtesy of UC Berkeley SRC)



Researchers at UC Berkeley SRC are working to improve their understanding of the relationship between exposures and disease. Chemicals being studied include arsenic, benzene, mercury, and polycyclic aromatic hydrocarbons. Their research aims to provide better risk assessments, reduce cleanup costs, and develop prevention strategies to improve and protect public health, ecosystems, and the environment.

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Sensors for detecting mercury in the environment

UC Berkeley SRC researchers led by Catherine Koshland, Ph.D., developed a new portable sensor that uses a film of gold nanoparticles to detect extremely low amounts of mercury in water.⁷ Mercury exposure is associated with neurological problems, such as poor memory and attention, particularly when one is exposed during early development.⁸ The technology replaces current methods requiring costly laboratory instruments to measure mercury.

Former UC Berkeley SRC trainees Jay James, Ph.D., and Jeffrey Crosby, Ph.D., worked on this project with Koshland and moved the technology out of the lab after completing their doctoral degrees. James and Crosby patented the technology and founded the company Picoyune to provide cost-effective and reliable mercury monitoring for industrial and environmental applications.⁹

The importance of studying biomarkers of arsenic and benzene

- Arsenic and benzene are known to cause cancer, and exposure is associated with lung, liver, and other health problems.^{2,4,10}
- Some people, including children, have higher risk for health problems after exposure to hazardous chemicals. Understanding why will help find ways to protect their health.¹¹

Research overview

- Identifying biomarkers of arsenic exposure, susceptibility, and disease over the lifespan, and how arsenic causes disease. (Allan Smith, M.D., Ph.D., ahsmith@berkeley.edu)
- Improving efficiency of environmental contaminant cleanup by using bacteria that can break down chemicals. (Lisa Alvarez-Cohen, Ph.D., alvarez@ce.berkeley.edu)
- Identifying biological markers and pathways that link benzene exposure to diseases, including leukemia. (Martyn Smith, Ph.D., martynts@berkeley.edu)
- Developing cost-effective technologies and approaches to clean up hazardous chemicals in groundwater. (David Sedlak, Ph.D., sedlak@ce.berkeley.edu)
- Identifying genetic factors that make some individuals more susceptible to health problems after exposure to pollutants. (Luoping Zhang, Ph.D., luoping@berkeley.edu)

Sharing results

UC Berkeley SRC shares research findings and scientific knowledge with communities, government agencies, business leaders, and others involved in the cleanup of Superfund sites. Researchers have also obtained patents for new technologies for chemical testing and cleanup that can be put to use to solve real problems. (Amy Kyle, Ph.D., adkyle@berkeley.edu)

Other contributions to advance science

The UC Berkeley SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Daniel Nomura, Ph.D., nomura@berkeley.edu; Mark van der Laan, Ph.D., laan@stat.berkeley.edu)

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Legislative Authority:

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of California, Berkeley Superfund Research Center, visit <http://superfund.berkeley.edu>.

¹ Thomas R, Hubbard AE, McHale CM, Zhang L, Rappaport SM, Lan Q, Rothman N, Vermeulen N, Guyton KZ, Jinot J, Sonawane BR, Smith, MT. 2014. Characterization of changes in gene expression and biochemical pathways at low levels of benzene exposure. *PLoS One* 9(5):e91828.

² Khalade A, Jaakkola MS, Pukkala E, Jaakkola JJ. 2010. Exposure to benzene at work and the risk of leukemia: a systematic review and meta-analysis. *Environ Health* 9:31.

³ Melak D, Ferreccio C, Kalman D, Parra R, Acevedo J, Perez L, Cortes S, Smith AH, Yuan Y, Liaw J, Steinmaus C. 2014. Arsenic methylation and lung and bladder cancer in a case-control study in northern Chile. *Toxicol Appl Pharmacol* 274(2):225-231.

⁴ Naujokas MF, Anderson B, Ahsan H, Aposhian, HV, Graziano JH, Thompson C, Suk WA. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.

⁵ Smith AH, Marshall G, Yuan Y, Ferreccio C, Liaw J, von Ehrenstein O, Steinmaus C, Bates MC, Selvin S. 2006. Increased mortality from lung cancer and bronchiectasis in young adults after exposure to arsenic in utero and in early childhood. *Environ Health Persp* 114(8):1293-1296.

⁶ University of California, Berkeley Office of Intellectual Property and Industry Research Alliances. 2015. System for Efficient, Environmentally Friendly Water Treatment. Available: <http://techtransfer.universityofcalifornia.edu/NCD/NCDPDF.aspx?ncid=24449> [accessed 1 June 2015].

⁷ Crosby JS, James JZ, Lucas D, Koshland CP. 2014. Determination of total mercury concentration in aqueous samples with gold nanoparticles. *Anal Methods* 6(4):1254-1260.

⁸ EPA (U.S. Environmental Protection Agency). 2014. Mercury: Health Effects. Available: <http://www.epa.gov/mercury/effects.htm> [accessed 1 June 2015].

⁹ NIEHS (National Institute of Environmental Health Sciences). 2014. Translating research into products to improve public health. Available: <http://www.niehs.nih.gov/news/newsletter/2014/6/science-translating> [accessed 1 June 2015].

¹⁰ EPA (U.S. Environmental Protection Agency). 2008. Polycyclic Aromatic Hydrocarbons (PAHs). Available: <http://www.epa.gov/wastes/hazard/wastemin/minimize/factshts/pahs.pdf> [accessed 1 June 2015].

¹¹ Environmental Health Perspectives. 2013. Children's Health Collection 2013. Available: <http://ehp.niehs.nih.gov/chc-2013> [accessed 1 June 2015].

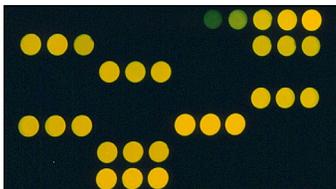


Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of California, Davis Superfund Research Center (UC Davis SRC), to advance this work across the nation.

Research Highlights

Powerful new tools for detecting chemical contaminants



In a CALUX assay, wells that contain dioxins light up with a green color, and the color gains intensity with increasing amounts of dioxins. (Photo courtesy of UC Davis SRC)

UC Davis SRC researchers are blazing new trails by developing highly sensitive, specific, cost-effective, and portable methods to detect contaminants in biological samples and the environment. Michael Denison, Ph.D., developed the Chemical-Activated Luciferase Gene Expression (CALUX) assay for large-scale testing of dioxin-like compounds.¹ The CALUX assay is widely used for contaminant testing, such as monitoring industrial wastewaters.² Dioxin-like compounds are found in air, water, foods, and soils, and exposure can lead to skin disease, cancer, and developmental problems.³

Using a different approach, Bruce Hammock, Ph.D., and Shirley Gee discovered that proteins called antibodies can be used as tools to identify pesticides and dioxins in a highly specific manner. These antibodies allowed them to develop new cost-effective assays that rapidly detect a variety of contaminants in very large numbers of biological and environmental samples at a low cost.^{4,5,6} UC Davis SRC researchers also created a new portable device that detects flame retardants, and results can be read using a smart phone camera.⁷ The device allows researchers to test samples outside of the lab.

Education through an entrepreneurship academy

UC Davis SRC sponsors an annual entrepreneurship academy for commercializing science and engineering innovations. The intensive three-day program acts as a springboard to move research out of the lab, by educating students and researchers about potential business opportunities. It also teaches them how to communicate ideas and research results effectively. Venture capitalists, entrepreneurs, university faculty, and industry executives serve as mentors, providing participants with knowledge and networks to commercialize their research. UC Davis SRC also encourages trainees from other SRCs around the country to participate in the academy and provides travel funds to promote this interdisciplinary opportunity. Through the academy, UC Davis SRC shares its expertise in putting science to work to solve problems.



Students learn about bringing research to market by participating in an activity at the entrepreneurship academy. (Photo courtesy of UC Davis SRC)



UC Davis SRC seeks to understand how hazardous substances cause disease, and how to clean up those substances in the environment. They are also developing innovative sensors and portable devices for measuring contaminants in biological samples and the environment that are highly innovative, rapid, sensitive, and cost-effective.

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Bioremediation provides solution to groundwater contamination

Kate Scow, Ph.D., and her team developed a new bioremediation approach using bacteria to break down and treat methyl tertiary-butyl ether (MTBE) in wastewater at water treatment plants.⁸ Bioremediation is a treatment that uses naturally occurring organisms to break down hazardous substances into less toxic or nontoxic substances. MTBE is used as a fuel additive. Its use has declined in the U.S. in recent years. MTBE is linked to cancer and neurological effects when inhaled or ingested.⁹ This new bioremediation technology successfully lowered MTBE levels at a very rapid rate when it was used to treat groundwater in North Hollywood, California aquifers.⁸

The importance of studying hazardous waste sites

Hazardous waste sites contain complex chemical mixtures that can be difficult to study. UC Davis SRC is developing rapid and inexpensive ways to identify those mixtures using innovative detection systems.

Research overview

- Assessing effects of environmental hazards on reproductive health. (Bill Lasley, Ph.D., billasley@ucdavis.edu)
- Developing cost-effective systems to detect hazardous chemicals. (Michael Denison, Ph.D., msdenison@ucdavis.edu)
- Using nanomaterials to develop sensors to detect hazardous substances. (Ian Kennedy, Ph.D., imkenedy@ucdavis.edu)
- Developing field-portable detectors for human and environmental monitoring. (Shirley Gee, sjee@ucdavis.edu)
- Identifying health effects of nanoparticles in the environment. (Ian Kennedy, Ph.D., imkenedy@ucdavis.edu)
- Predicting movement of contaminants in groundwater systems. (Kate Scow, Ph.D., kmscow@ucdavis.edu)
- Developing biological indicators to assess how the Superfund chemical naphthalene contributes to lung injury. (Alan Buckpitt, Ph.D., arbuckpitt@ucdavis.edu)

Sharing results

UC Davis SRC shares research results to improve understanding of how Superfund chemicals harm human health, and how to reduce exposures to those chemicals, to help government officials and the public make informed decisions about reducing risk. (Candace Bever, Ph.D., crspier@ucdavis.edu)

Other contributions to advance science

- The UC Davis SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Bruce Hammock, Ph.D., bdhammock@ucdavis.edu; Dietmar Kuelz, Ph.D., dkuelz@ucdavis.edu)
- The UC Davis SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Pamela Lein, Ph.D., pjlein@ucdavis.edu)

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of California, Davis Superfund Research Center, visit www.superfund.ucdavis.edu.

¹ University of California, Davis Office of Research. 2010. Amplified recombinant cell bioassay for the detection of dioxin and related Ah receptor ligands. Available: techtransfer.universityofcalifornia.edu/NCD/21033.html?campus=DA [accessed 1 June 2015].

² Addeck A, Croes K, Van Langenhove K, Denison MS, Elhamalawy A, Elskens M, Baeyens W. 2014. Time-integrated monitoring of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/Fs) in urban and industrial wastewaters using a ceramic toximeter and the CALUX bioassay. *Chemosphere* 94:27-35.

³ NIEHS (National Institute of Environmental Health Sciences). 2012. Dioxins. Available: www.niehs.nih.gov/health/materials/dioxins_new_508.pdf [accessed 1 June 2015].

⁴ Hua X, Yin W, Shi H, Li M, Wang Y, Wang H, Ye Y, Kim HJ, Gee SJ, Wang M, Liu F, Hammock BD. 2014. Development of phage immuno-loop-mediated isothermal amplification assays for organophosphorus pesticides in agro-products. *Anal Chem* 86(16):8441-8447.

⁵ Bever C, Majkova Z, Radhakrishnan R, Suni I, McCoy MR, Wang Y, Dechant JE, Gee SJ, Hammock BD. 2014. Development and utilization of camelid VHH antibodies from alpaca for 2,2',4,4'-tetrabrominated diphenyl ether detection. *Analyt Chem* 86(15):7875-7882.

⁶ Han J, Kim HJ, Sudheendra L, Hass EA, Gee SJ, Hammock BD, Kennedy IM. 2013. Electrophoretic build-up of multi nanoparticle array for a highly sensitive immunoassay. *Biosens Bioelectron* 41:302-308.

⁷ Chen A, Wang R, Bever CR, Xing S, Hammock BD, Pan T. 2014. Smartphone-interfaced lab-on-a-chip devices for field-deployable ELISA. *Biomicrofluidics* 8(6):064101.

⁸ Hicks K, Schmidt R, Nickelsen MG, Boyle SL, Baker JM, Tornatore PM, Hristova KR, Scow KM. 2014. Successful treatment of an MTBE-impacted aquifer using a bioreactor self-colonized by native aquifer bacteria. *Biodegrad* 25(1):41-53.

⁹ Phillips S, Palmer RB, Brody A. 2008. Epidemiology, toxicokinetics, and health effects of methyl tert-butyl ether (MTBE). *J Med Toxicol* 4(2):115-126.

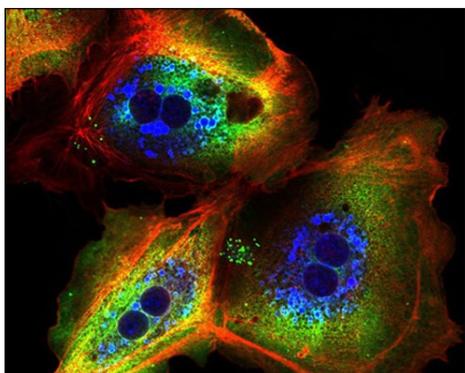


Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of California, San Diego Superfund Research Center (UCSD SRC), to advance this work across the nation.

Research Highlights

Linking exposures to liver disease and cancer

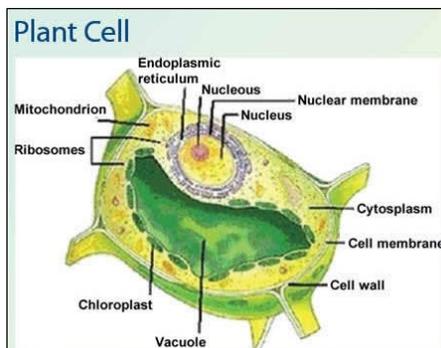


Karin's work shows how liver cells become cancerous after exposure to carcinogenic chemicals. (Photo courtesy of UCSD SRC)

The antibacterial chemical triclosan, which is added to many personal care products, such as hand soap, can promote liver tumor formation in mice, according to University of California, Davis and UCSD SRC research.¹ Michael Karin, Ph.D., and Robert Tukey, Ph.D., collaborated as part of their work to understand the effects of hazardous substances on liver function and cancer. They reported that triclosan exposure alone resulted in increased numbers of liver cells, increased liver damage, and decreased liver function. When mice were exposed to triclosan and the cancer-causing agent diethylnitrosamine (DEN) together, more mice had liver tumors and their tumors were larger compared to mice exposed to DEN alone.¹ Karin's UCSD SRC team also identified liver cells that were precancerous. They are using these cells to increase understanding of how normal cells become cancer cells, using genetic and biochemical approaches.²

Metal uptake in seeds and leaves of plants

The UCSD SRC team, led by Julian Schroeder, Ph.D., identified a gene that regulates how much of different metals accumulate in the seeds and leaves of plants.³ Some metals are important nutrients, like zinc and iron, but other metals, like cadmium, can be toxic to humans.⁴ This information may help scientists modify plants so they can absorb more metals from contaminated soil or water and be used as a tool for cleaning up Superfund sites. Researchers may also be able to reduce metal accumulation in plants to prevent exposures to metals that are present in certain foods, such as arsenic in rice.⁵



Schroeder's team is studying how metals accumulate in plant cells. (Photo courtesy of UCSD SRC)

UC San Diego



The UCSD SRC interdisciplinary team seeks to better understand molecular processes that cause health problems for people exposed to environmental contaminants, and works to improve contaminant detection, monitoring, and cleanup. They also work to solve problems that are unique to California's coastal environment and the densely populated U.S.-Mexico border region.

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A community garden as a living laboratory

Keith Pezzoli, Ph.D., and his team are working with the nonprofit Global Action Research Center to transform a vacant 20,000 square foot lot into a community garden and platform for environmental health education called the Ocean View Growing Grounds (OVGG).⁶ The lot in southeast San Diego is a brownfield site, which is previously-owned land that may contain hazardous substances. OVGG participants are working with UCSD SRC scientists and the city of San Diego to do environmental testing and develop strategies to clean up the site. The garden will transform one of San Diego's disadvantaged neighborhoods into a food forest and living laboratory to test soils and plants.



Pezzoli, right, is helping convert a brownfield into an urban garden in San Diego. (Photo courtesy of UCSD SRC)

The importance of studying environmental contaminants

- Liver cancer was the fifth most frequently diagnosed cancer in 2010, with an estimated 23,000 deaths in 2014.⁷
- Cadmium and arsenic exposures are associated with cancer, cardiovascular disease, lung disease, and other adverse health effects.^{4,8}

Research overview

- Understanding genetic susceptibilities to arsenic and cadmium toxicity. (Paul Russell, Ph.D., prussell@scripps.edu)
- Researching protective effects of natural antioxidants in arsenic-induced liver disease. (Robert Tukey, Ph.D., rtukey@ucsd.edu)
- Understanding how pre-existing liver disease affects sensitivity to toxicant exposures. (David Brenner, Ph.D., dbrenner@ucsd.edu)
- Understanding effects of toxicants on precancerous liver cells and liver cancer, and how normal cells become cancer cells. (Michael Karin, Ph.D., karinoffice@ucsd.edu)
- Developing field-portable devices to detect hormone-disrupting and cancer-causing chemicals. (William Trogler, Ph.D., wtrogler@ucsd.edu)
- Investigating heavy metal uptake and detoxification in plants used for cleanup. (Julian Schroeder, Ph.D., jischroeder@ucsd.edu)
- Studying how Superfund contaminants affect cellular functions, and how changes are linked to health problems. (Ronald Evans, Ph.D., evans@salk.edu)

Sharing results

- UCSD SRC works with the San Diego-Tijuana community, providing environmental health and scientific research information. In turn, researchers learn about community needs that may help guide future research. (Keith Pezzoli, Ph.D., kpezzoli@ucsd.edu)

Other contributions to advance science

- The UCSD SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Pamela Mellon, Ph.D., pmellon@ucsd.edu; Mark Ellisman, Ph.D., mellisman@ucsd.edu)
- The UCSD SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Pamela Mellon, Ph.D., pmellon@ucsd.edu)

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of California, San Diego Superfund Research Center, visit <http://superfund.ucsd.edu>.

¹ Yueh MF, Taniguchi K, Chen S, Evans RM, Hammock BD, Karin M, Tukey RH. 2014. The commonly used antimicrobial additive triclosan is a liver tumor promoter. *Proc Natl Acad Sci U S A* 111(48):17200-17205.

² He G, Dhar D, Nakagawa H, Font-Burgada J, Ogata H, Jiang Y, Shalpour S, Seki E, Yost S, Jepsen K, Frazer K, Harismendy O, Hatzia Apostolou M, Iliopoulos D, Suetsugu A, Hoffman RM, Tateishi R, Koike K, Karin M. 2013. Identification of liver cancer progenitors whose malignant progression depends on autocrine IL-6 signaling. *Cell* 155(2):384-396.

³ Mendoza-Cozatl DG, Xie Q, Akmakjian GZ, Jobe TO, Patel A, Stacey MG, Song L, Demoin DW, Jurisson SS, Stacey G, Schroeder JI. 2014. OPT3 is a component of the iron-signaling network between leaves and roots and misregulation of OPT3 leads to an over-accumulation of cadmium in seeds. *Molec Plant* 7(9):1455-1469.

⁴ ATSDR (Agency for Toxic Substances & Disease Registry). 2008. Cadmium Toxicity: What Diseases Are Associated With Chronic Exposure to Cadmium? Available: www.atsdr.cdc.gov/csem/csem.asp?csem=6&po=12 [accessed 1 June 2015].

⁵ Khan MA, Castro-Guerrero N, Mendoza-Cozatl DG. 2014. Moving toward a precise nutrition: preferential loading of seeds with essential nutrients over non-essential toxic elements. *Front Plant Sci* 5:51.

⁶ University of California, San Diego Superfund Research Center. 2014. New Plant Science Program for Urban Agriculture. Available: <http://superfund.ucsd.edu/news/plant-testing-program> [accessed 1 June 2015].

⁷ Siegel R, Ma J, Zou Z, Jemal A. 2014. Cancer statistics, 2014. *CA Cancer J Clin* 64(1):9-29.

⁸ Naujokas MF, Anderson B, Ahsan H, Aposhian HV, Graziano JH, Thompson C, Suk WA. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of Iowa Superfund Research Program (ISRP), to advance this work across the nation.

Research Highlights

Partnering to reduce PCB exposures

ISRP researchers have launched a partnership to clean up polychlorinated biphenyls (PCBs) using phytoremediation, a process in which plants are used to contain, degrade, or eliminate contaminants from soils and water.¹ Working with the town of Altavista, Virginia, and Ecolotree Inc., a small business focusing on phytoremediation, scientists are using poplar trees to reduce exposures from a PCB-contaminated lagoon. They are also studying the processes that influence PCB containment and detoxification by the poplar trees, with the goal of minimizing airborne exposures and reducing health risks to the community.² Craig Just, Ph.D., and David Osterberg are helping coordinate efforts to implement this plan as a low-cost and sustainable approach.



Poplar trees were planted on test plots next to a lagoon to reduce PCB contamination. (Photo courtesy of ISRP)

Finding ways plants can help clean contaminated soil and groundwater



Researchers have found that switchgrass may help safely remove PCBs from the environment.

Researchers led by Jerald Schnoor, Ph.D., have shown that a combination of specific types of bacteria and switchgrass plants growing together remove up to 47 percent of PCBs from contaminated soils.³ PCBs are a family of chemical compounds that had been widely used in industrial applications and still persist in the environment in air, water, soil, and foods. PCB exposure can lead to severe skin rashes, liver damage, cancer, and other adverse health effects.⁴ The combination of bacteria and plants, such as switchgrass and poplar trees, has potential to be a powerful solution for cleaning up PCB-contaminated soils and sediments, and holds promise as a sustainable, cost-effective method that may be less disruptive than traditional cleanup methods.



Researchers at ISRP are working to better understand how PCBs move through the environment via water, air, and other pathways, and how they affect human health. Their goal is to reduce exposures and prevent adverse health effects.

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Measuring airborne exposures to PCBs

Peter Thorne, Ph.D., and his research team found that schools in a research study area had much higher indoor PCB concentrations than students' homes, and accounted for the majority of the children's inhalation exposures.⁵ The analysis compared groups of children and their mothers living in urban East Chicago, Indiana, and in rural Columbus Junction, Iowa. The Indiana site has a history of industrial activity that created polluted canals that are currently undergoing dredging, which may release PCBs into the air. ISRP researchers are further studying the children's PCB exposures in more detail. For example, Thorne's team is measuring what proportion comes from air versus diet. They are also defining mathematical relationships between PCBs in air and levels in blood. Very few studies have examined airborne exposures, so work to examine this pathway is critical to understanding the health effects of PCBs.

The importance of studying PCBs

- People are exposed to PCBs through eating or drinking contaminated food, inhalation, and skin contact.⁴
- Although the manufacturing of PCBs was stopped in 1977, PCBs do not readily break down, and can remain in the environment for long periods of time. PCBs are also found in dyes and paints as byproducts of manufacturing.^{4,6}

Research overview

- Identifying sources and fate of airborne PCBs. (Keri Hornbuckle, Ph.D., keri-hornbuckle@uiowa.edu)
- Measuring exposure to airborne PCBs in mothers and their children. (Peter Thorne, Ph.D., peter-thorne@uiowa.edu)
- Investigating PCB-induced cell damage and ways to prevent cellular toxicity. (Prabhat Goswami, Ph.D., prabhat-goswami@uiowa.edu)
- Studying toxic effects of PCB metabolites. (Michael Duffel, Ph.D., michael-duffel@uiowa.edu)
- Determining how airborne PCBs lead to gene damage, cancer, and other health effects. (Larry Robertson, Ph.D., larry-robertson@uiowa.edu)
- Investigating how plants can be used to clean up PCBs at contaminated sites. (Jerald Schnoor, Ph.D., jerald-schnoor@uiowa.edu)

Sharing results

- ISRP brings together scientists and community advisory boards from Iowa, Illinois, and Indiana to address environmental concerns about PCBs, provide educational programs at schools, and share research findings with communities. (David Osterberg, david-osterberg@uiowa.edu)

Other contributions to advance science

- The ISRP research support facilities provide vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Keri Hornbuckle, Ph.D., keri-hornbuckle@uiowa.edu; Peter Thorne, Ph.D., peter-thorne@uiowa.edu; Hans-Joachim Lehmler, Ph.D., hans-joachim-lehmler@uiowa.edu)
- The ISRP integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Gabriele Ludewig, Ph.D., gabriele-ludewig@uiowa.edu)

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of Iowa Superfund Research Program, visit <http://iowasuperfund.uiowa.edu>.

¹ Just C, Osterberg D, Licht L. 2014. The Iowa Superfund Research Program, Ecolotree, and the Town of Altavista begin a new partnership. In: Partnerships for Research Translation and Community Engagement in the Superfund Research Program November 2014 Annual Meeting Abstracts for Posters. Available: www.srpannualmeeting.org/wp-content/uploads/2014/11/SRPRTC_CEC_PosterAbstracts.Final_adk_1.pdf [accessed 1 June 2015].

² Meggo RE, Schnoor JL, Hu D. 2013. Dechlorination of PCBs in the rhizosphere of switchgrass and poplar. *Environ Poll* 178:312-321.

³ Liang Y, Meggo R, Hu D, Schnoor JL, Mattes TE. 2014. Enhanced polychlorinated biphenyl removal in a switchgrass rhizosphere by bioaugmentation with *Burkholderia xenovorans* LB400. *Ecol Eng* 71:215-222.

⁴ ATSDR (Agency for Toxic Substances and Disease Registry). 2014. ToxFAQs for Polychlorinated Biphenyls (PCBs). Available: www.atsdr.cdc.gov/toxfaqs/tf.asp?id=140&tid=26 [accessed 1 June 2015].

⁵ Ampleman MD, Martinez A, DeWall J, Rawn DFK, Hornbuckle KC, Thorne PS. 2015. Inhalation and dietary exposure to PCBs in urban and rural cohorts via congener-specific measurements. *Environ Sci Technol* 49(1):1156-1164.

⁶ Hu D, Hornbuckle KC. 2009. Inadvertent polychlorinated biphenyls in commercial paint pigments. *Environ Sci Technol* 44(8):2822-2827.

Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of Kentucky Superfund Research Center (UK SRC), to advance this work across the nation.

Nutrition protects against toxicity

Even with the best cleanup efforts, it is nearly impossible to remove all harmful chemicals at a site. Other ways to lessen harmful effects are needed. To this end, Bernhard Hennig, Ph.D., leads a research program studying how diet affects the toxicity of environmental contaminants. His team discovered that some food components can interfere with cellular function, while others can protect against cell damage. They found that the type of fat in a diet, not just the amount, can reduce cell damage triggered by polychlorinated biphenyls (PCBs).¹ For example, Hennig found that a diet with a high ratio of omega-3 to omega-6 fatty acids, or diets supplemented with green tea, can reduce cell and tissue damage caused by PCBs and other pollutants.² They also found diets rich in polyphenols, which are antioxidants found in fruits, vegetables,

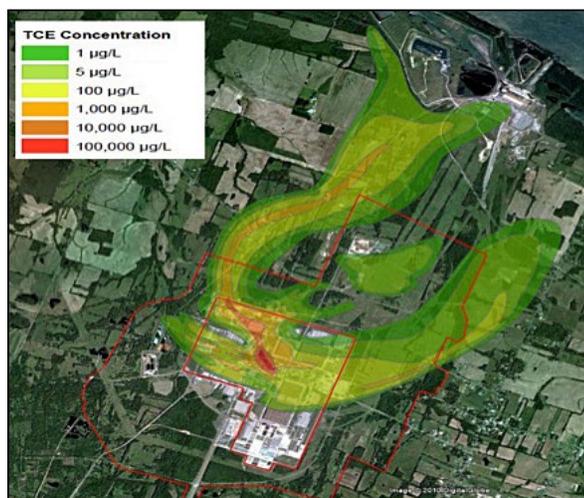


Salmon is a good source of omega-3 fatty acids.

and other plant foods, can protect against PCB-induced blood vessel, or vascular, inflammation and associated diseases.¹

Water purifier harnesses the use of nanomembranes

Given that water is the basis of life, Dibakar Bhattacharyya, Ph.D., and other scientists developed a system to improve drinking water quality by reducing the risk of contamination. Their system removes chlorinated organic contaminants, such as trichloroethylene (TCE), from groundwater.³ The functionalized, iron-based nanomembrane cleanup device may offer an inexpensive way to provide clean drinking water in areas of the world where chemical contamination is common. The technology may also remove toxic selenium, used in coal-burning power plants, from water.



TCE plumes at the Paducah Gaseous Diffusion Plant. (Photo courtesy of UK SRC)

Lindell Ormsbee, Ph.D., is working closely with Bhattacharyya to employ the nanomembrane technology at the Paducah Gaseous Diffusion Plant in Kentucky, the state's largest Superfund site. This technology can also be used to break down PCBs into harmless byproducts by using inexpensive oxidative processes.



Research efforts at UK SRC focus on reducing exposures to hazardous substances. They are working to understand how nutritional components, such as antioxidants and plant-derived polyphenols, can be used to counteract negative health effects in people exposed to harmful chemicals, such as chlorinated organic compounds. These chemicals include PCBs and TCE, which are common at Superfund sites in Kentucky and nationwide. They also work toward developing strategies to improve detection of, and reduce exposure to, these harmful chemicals.

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PCB exposure may contribute to obesity

PCB exposure, even at low levels, may contribute to the development of obesity and obesity-associated diseases, according to research led by Lisa Cassis, Ph.D. Her team found that exposure to PCBs can result in increased body fat and produce inflammation in fat cells, called adipocytes, increasing risk for diabetes and cardiovascular disease.⁴



Despite a production ban in 1979, and decades of cleanup efforts, the structural stability of PCBs allows them to remain a persistent environmental contaminant and accumulate in the food chain.⁵ Obesity is common, serious, and costly. More than one-third of U.S. adults (34.9 percent) are obese. The estimated annual medical cost of obesity in the U.S. was \$147 billion in 2008.⁶

Research overview

- Identifying plant-based bioactive food components with antioxidant and anti-inflammatory properties that may lessen the toxicity of PCBs to the layer of cells that line blood vessels. (Bernhard Hennig, Ph.D., bhennig@uky.edu)
- Collaborating with a membrane manufacturing company, ULTURA Inc. of Long Beach, California, to develop a full-scale, functionalized membrane filter for water cleanup applications, which also may have other uses, including disinfection and virus inactivation. (Dibakar Bhattacharyya, Ph.D., db@engr.uky.edu)
- Developing new pollutant sensing and capture systems that use nontoxic, biology-inspired, specialized nanocomposites for selective, sensitive, and inexpensive monitoring and removal of PCBs from contaminated sites. (J. Zach Hilt, Ph.D., zach.hilt@uky.edu)
- Identifying how PCBs affect body metabolic processes and increase risk for Type 2 diabetes, and whether resveratrol, an antioxidant found in certain plant foods, can be used to prevent or treat PCB-induced harm in fat cells. (Lisa Cassis, Ph.D., lcassis@uky.edu)
- Studying molecular mechanisms involved in postnatal complications following perinatal PCB exposure, and how diet and exercise can be used as health interventions. (Kevin Pearson, Ph.D., kevin.pearson@uky.edu)

Sharing results

- UK SRC shares nutrition research findings with the general public, including Superfund communities in Kentucky. (Lisa Gaetke, Ph.D., lgaetke@uky.edu)
- UK SRC communicates relevant findings to government officials and regulators, strengthens partnerships with other agencies and universities, and supports implementation of project technologies. (Lindell Ormsbee, Ph.D., lormsbee@engr.uky.edu)

Other contributions to advance science

- The UK SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Andrew Morris, Ph.D., a.j.morris@uky.edu)
- The UK SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Bernhard Hennig, Ph.D., bhennig@uky.edu)

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For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of Kentucky Superfund Research Center, visit www.uky.edu/research/superfund.

¹ Arsenescu V, Arsenescu RI, King V, Swanson H, Cassis LA. 2008. Polychlorinated biphenyl-77 induces adipocyte differentiation and proinflammatory adipokines and promotes obesity and atherosclerosis. *Environ Health Perspect* 116(6):761-768.

² Majkova Z, Layne J, Sunkara M, Morris AJ, Toborek M, Hennig B. 2011. Omega-3 fatty acid oxidation products prevent vascular endothelial cell activation by coplanar polychlorinated biphenyls. *Toxicol Appl Pharmacol* 251(1):41-49.

³ Gui M, Smuleac V, Ormsbee LE, Sedlak DL, Bhattacharyya D. 2012. Iron oxide nanoparticle synthesis in aqueous and membrane systems for oxidative degradation of trichloroethylene from water. *J Nanopart Res* 14:861.

⁴ Newsome BJ, Petriello MC, Han SG, Murphy MO, Eske KE, Sunkara M, Morris AJ, Hennig B. 2014. Green tea diet decreases PCB 126-induced oxidative stress in mice by up-regulating antioxidant enzymes. *J Nutr Biochem* 25(2):126-135.

⁵ EPA (U.S. Environmental Protection Agency). 2013. Basic Information: Polychlorinated Biphenyl (PCB). Available: www.epa.gov/epawaste/hazard/tsd/pcbs/about.htm [accessed 1 June 2015].

⁶ CDC (Centers for Disease Control and Prevention). 2014. Adult Obesity Facts. Available: www.cdc.gov/obesity/data/adult.html [accessed 1 June 2015].



Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of North Carolina at Chapel Hill Superfund Research Center (UNC SRC), to advance this work across the nation.

Research Highlights

Understanding genetic susceptibility to environmental chemicals



Researchers led by Ivan Rusyn, M.D., Ph.D., identified genetic differences that can influence an individual's susceptibility to the toxic effects of trichloroethylene (TCE).¹ TCE, a common groundwater contaminant, is linked to liver cancer and other health problems.² Rusyn's team compared different strains of mice, similar to a diverse group of people, to see whether they break down TCE differently. They reported that a specific metabolic break-down product, called trichloroacetic acid, was associated with liver enlargement and other liver effects. This result suggests that people who produce more trichloroacetic acid may be more susceptible to TCE's effects, and sheds light on how TCE may cause liver cancer. The information is also important for assessing potential health risks for people exposed to TCE.

Understanding arsenic health effects in newborns

Using a large-scale, state-of-the-art screening approach, Rebecca Fry, Ph.D., and her research team reported that changes in proteins in newborn umbilical cord blood were linked to the amount of arsenic in the mother's urine.³ Arsenic exposure during development is associated with a wide range of health effects, including cancer, that can persist into adulthood.⁴

Fry's team reported both increases and decreases in 111 different proteins in cord blood of newborns exposed to arsenic in the womb. Almost half of these proteins are involved in immune responses and inflammation. When researchers compared the results for boys and girls, they found that boy infants with increased protein had early indicators of possible neurological effects later in life. These results provide insight into arsenic effects in children, and why some people are more susceptible to arsenic than others.



Fry, second from right, and her team study arsenic exposure during development. (Photo courtesy of UNC SRC)



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Researchers at UNC SRC seek to understand the human health and environmental risks associated with exposure to the highest priority chemicals regulated under the Superfund program. Priority chemicals include polycyclic aromatic hydrocarbons (PAHs), halogenated hydrocarbons, and heavy metals. They also develop strategies to more efficiently clean up hazardous waste sites.

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Identifying contaminants at hazardous waste sites

Damian Shea, Ph.D., UNC SRC researcher and professor at North Carolina State University, has developed a new sampling device for detecting multiple chemicals in water, soil, and sediments, and measuring how much of those chemicals can be absorbed by living organisms.⁵ The new device uses special plastics that act like sponges to soak up chemicals for later testing in the lab. The researchers have been using it to collect and test more than 200 top-priority chemicals at five Superfund sites in North Carolina and Virginia.⁶



The new sampling device developed by Shea's team helps researchers collect and transport samples more easily. (Photo courtesy of UNC SRC)

The importance of science-based risk assessment

- Risk assessment is the process used to identify the type and magnitude of health risks that exist in specific circumstances, such as near a Superfund site.⁷
- Government agencies, like the U.S. Environmental Protection Agency, use scientific data to make informed regulatory decisions about health risks.⁸ UNC SRC research helps inform those decisions.

Research overview

- Identifying biological markers of exposure to specific chemicals, to strengthen the scientific basis for risk assessment. (James Swenberg, Ph.D., james_swenberg@unc.edu)
- Understanding genetic differences in liver and kidney cancer susceptibility, and risk assessment for TCE. (Ivan Rusyn, Ph.D., irusyn@cvm.tamu.edu)
- Applying new analytical tools to understand critical pathways for toxicity related to metals, such as cadmium and arsenic. (Rebecca Fry, Ph.D., rfry@email.unc.edu)
- Evaluating complex microbial communities in bioremediation systems to break down chemicals, in particular PAHs. (Michael Aitken, Ph.D., aitken@email.unc.edu)
- Quantifying chronic exposure and bioavailability of toxic compounds in environmental systems. (Damian Shea, Ph.D., d_shea@ncsu.edu)

Sharing results

The UNC SRC Research Translation Core focuses on communicating the center's research findings, enabling government officials and the public to make informed decisions about reducing risk. They are also responding to research and outreach needs identified by government agencies and local health departments in communities with hazardous waste sites. (Kathleen Gray, kgray@unc.edu)

Other contributions to advance science

- The UNC SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Fred Wright, Ph.D., fred_wright@ncsu.edu; Avram Gold, Ph.D., avram_gold@unc.edu)

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For more information on the University of North Carolina at Chapel Hill, Superfund Research Center, visit <http://sph.unc.edu/srp>.

¹ Yoo HS, Bradford BU, Kosyk O, Shymonyak S, Uehara T, Collins LB, Bodnar WM, Ball LM, Gold A, Rusyn I. 2015. Comparative analysis of the relationship between trichloroethylene metabolism and tissue-specific toxicity among inbred mouse strains: liver effects. *J Toxicol Environ Health A* 78(1):15-31.

² ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Trichloroethylene – ToxFaqs. Available: www.atsdr.cdc.gov/toxfaqs/tfacts19.pdf [accessed 1 June 2015].

³ Bailey KA, Laine J, Rager JE, Sebastian E, Olshan A, Smeester L, Drobna Z, Styblo M, Rubio-Andrade M, Garcia-Vargas G, Fry RC. 2014. Prenatal arsenic exposure and shifts in the newborn proteome: interindividual differences in tumor necrosis factor (TNF)-responsive signaling. *Toxicol Sci* 139(2):328-337.

⁴ Naujokas M, Anderson B, Ahsan H, Aposhian H, Graziano J, Thompson C, Suk W. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.

⁵ University of North Carolina Gillings School of Global Public Health. 2014. Measuring Chronic Exposure to Bioavailability of Organic Chemicals and Their Metabolites. Available: <http://sph.unc.edu/superfund-pages/research-projects/measuring-chronic-exposure-to-bioavailability-of-organic-chemicals-and-their-metabolites> [accessed 1 June 2015].

⁶ NIEHS (National Institute of Environmental Health Sciences). 2014. University of North Carolina-Chapel Hill: Details – Superfund Research Program. Available: http://tools.niehs.nih.gov/srp/sites/index.cfm?Project_ID=P42ES59480109 [accessed 1 June 2015].

⁷ EPA (U.S. Environmental Protection Agency). 2012. Risk Assessment: Basic Information. Available: <http://epa.gov/riskassessment/basicinformation.htm#arisk> [accessed 1 June 2015].

⁸ EPA (U.S. Environmental Protection Agency). 2012. Human Health Risk Assessment. Available: <http://epa.gov/riskassessment/health-risk.htm> [accessed 1 June 2015].

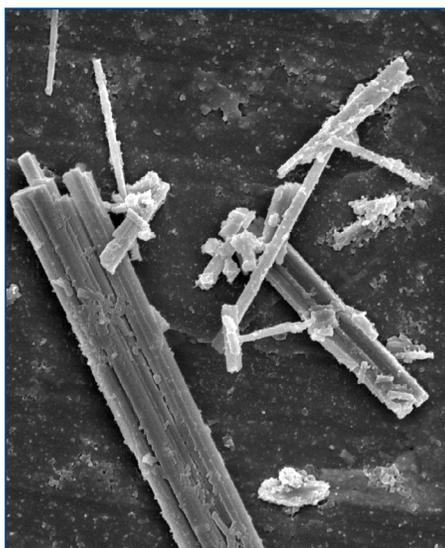


Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of Pennsylvania Superfund Research Center (Penn SRC), to advance this work across the nation.

Research Highlights

Identifying social determinants of susceptibility to mesothelioma



Inhaled asbestos fibers can remain in lungs for a long time, increasing risk for lung disease. (Photo courtesy of Penn SRC)

Frances Barg, Ph.D., and her research team are working with a community in Ambler, Pennsylvania, to study lifestyle patterns and circumstances of asbestos exposure for links to cancer development. Asbestos is a group of minerals that occur naturally in the environment as bundles of fibers that can be separated into thin, durable threads. It is used to make many products, such as insulation and roofing, and is associated with mesothelioma. Mesothelioma is a cancer of the cells lining the lungs, abdominal cavity, and cardiac cavity caused by exposure to asbestos. About 6,000 people in Ambler live within a half-mile of a former manufacturing plant that disposed of over 1.5 million cubic yards of asbestos-containing waste products on the now cleaned up Superfund site.¹ Barg's team has formed strong relationships with the community that will help them collect information about community, occupational, and social factors that may contribute to the development of mesothelioma.

Flaxseed oil and new cancer prevention approaches

Two researchers at Penn SRC have launched a new project to explore whether dietary flaxseed oil can help prevent mesothelioma. Melpo Christofidou-Solomidou, Ph.D., and her team study the role of inflammation and oxidative damage in lung injury and disease. Inflammation and oxidative damage are immune-related responses that play a role in tissue damage.² In previous mouse studies, Christofidou-Solomidou showed that flaxseed oil, a natural antioxidant and dietary supplement, could prevent lung damage from radiation exposure.³ In collaboration with Steven Albelda, M.D., and his lab, they are studying whether dietary flaxseed oil may reduce oxidative stress and prevent mesothelioma tumor formation. Harnessing Albelda's expertise in clinical testing of treatments for lung-related diseases,⁴ Penn SRC hopes to test preventive treatments in patients.



Penn SRC researchers are exploring the possibility of using dietary flaxseed oil to help prevent lung diseases associated with asbestos exposure.



Penn SRC fosters problem-based, solution-oriented research related to asbestos transport, exposure, cleanup, and adverse health effects, in particular, mesothelioma. Their approach is to use environmental and biomedical research to advance scientific understanding, and to address environmental health concerns of government agencies and affected communities.

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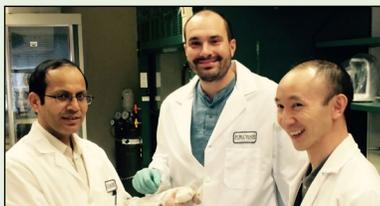
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Identifying the genetic basis of mesothelioma

Joseph Testa, Ph.D., and his team are combining genetic studies with mouse model research to better understand mesothelioma risk factors and prevention. The research has identified genetic mutations in a tumor suppressor gene associated with a high incidence of the disease.⁵ The mouse model they developed shows high similarity to human mesothelioma, including similarities in the types of tumor suppressor genes that are suggested to be important for tumor development.⁶ His team's findings were the first to link a genetic mutation to mesothelioma risk.



Penn SRC researchers, from left, Yuwaraj Kadariya, M.D., Ph.D.; Craig Menges, Ph.D.; and Mitchell Cheung, Ph.D., are working with Testa to better understand the role of genetics in mesothelioma. (Photo courtesy of Penn SRC)

The importance of studying asbestos

- Once asbestos particles are inhaled, they can remain there for a long time and cause lung scarring and inflammation.⁷
- Exposure to asbestos is associated with increased risk of lung cancer and mesothelioma.⁷

Research overview

- Understanding how tumors develop in mesothelioma. (Joseph Testa, Ph.D., joseph.testa@fcc.edu)
- Identifying biomarkers for asbestos exposure and mesothelioma. (Ian Blair, Ph.D., ianblair@mail.med.upenn.edu)
- Evaluating supplements that may lower risk of asbestos-induced mesothelioma. (Melpo Christofidou-Solomidou, Ph.D., melpo@mail.med.upenn.edu)
- Determining how asbestos moves in groundwater and identifying ways to prevent exposures. (Douglas Jerolmack, Ph.D., sediment@sas.upenn.edu)
- Finding new ways to clean up asbestos sites using plants and fungi. (Jane Willenbring, Ph.D., erosion@sas.upenn.edu)
- Identifying social determinants of risk in a community near an asbestos Superfund site. (Frances Barg, Ph.D., bargf@uphs.upenn.edu)

Sharing results

- Penn SRC translates knowledge and discoveries into actionable items by forging productive partnerships with the public and private sectors. (Richard Pepino, Ph.D., rpepino@sas.upenn.edu)
- Penn SRC fosters two-way exchange of knowledge among researchers and stakeholders in Ambler, Pennsylvania. (Edward Emmett, M.D., emmetted@mail.med.upenn.edu)

Other contributions to advance science

- The Penn SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Wei-Ting Hwang, Ph.D., whwang@mail.med.upenn.edu)
- The Penn SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Trevor Penning, Ph.D., penning@upenn.edu)

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of Pennsylvania Superfund Research Center, visit www.med.upenn.edu/asbestos.

¹ EPA (U.S. Environmental Protection Agency). 2015. Ambler Asbestos Piles Current Site Information. Available: www.epa.gov/reg3hscd/npl/PAD000436436.htm [accessed 1 June 2015].

² Nowsheen S, Aziz K, Kryston T, Ferguson N, Georgakilas A. 2012. The interplay between inflammation and oxidative stress in carcinogenesis. *Curr Molec Med* 12(6):672-680.

³ Pietrofesa RA, Solomides CC, Christofidou-Solomidou M. 2014. Flaxseed mitigates acute oxidative lung damage in a mouse model of repeated radiation and hyperoxia exposure associated with space exploration. *J Pulmon Respir Med* 4:215.

⁴ Stevenson JP, Kindler HL, Papasavvas E, Sun J, Jacobs-Small M, Hull J, Schwed D, Ranganathan A, Newick K, Heitjan DF, Langer CJ, McPherson JM, Montaner LJ, Albelda SM. 2013. Immunological effects of the TGFβ blocking antibody GC1008 in malignant pleural mesothelioma patients. *Oncimmunol* 2(8):e26218.

⁵ Testa JR, Cheung M, Pei J, Below JE, Tan Y, Sementino E, Cox NJ, Dogan AU, Pass HI, Trusa S, Hesdorffer M, Nasu M, Powers A, Rivera Z, Comertpay S, Tanji M, Gaudino G, Yang H, Carbone M. 2011. Germline BAP1 mutations predispose to malignant mesothelioma. *Nat Genet* 43(10):1022-1025.

⁶ Altomare DA, Vaslet CA, Skele KL, De Rienzo A, Devarajan K, Jhanwar SC, McClatchey AI, Kane AB, Testa JR. 2005. A mouse model recapitulating molecular features of human mesothelioma. *Cancer Res* 65(18):8090-8095.

⁷ NCI (National Cancer Institute). 2009. Asbestos exposure and cancer risk.

Available: www.cancer.gov/about-cancer/causes-prevention/risk/substances/asbestos/asbestos-fact-sheet [accessed 1 June 2015].