Superfund
fall 2009 • Issue #9
SCOOP
THE NEWSLETTER OF THE UNC SUPERFUND RESEARCH PROGRAM

Study provides valuable new insight into links between formaldehyde exposure and cancer

FORMALDEHYDE IS A UBIQUITOUS environmental pollutant that can enter the body through exposure to vehicle emissions, building materials, food, tobacco smoke, and most recently, the air inside Federal Emergency Management Agency (FEMA) trailers used to house people after disasters such as Hurricane Katrina. Formaldehyde is listed on the Superfund priority chemical list and is a known human and animal carcinogen: it causes nose and throat cancer in humans and nasal cancer in rats. Several recent studies have also suggested a possible link between inhaled formaldehyde and leukemia; however, this association is controversial.

Because exposure to formaldehyde is so widespread in our daily lives, and this chemical is known for its toxicity and links to cancer, there has been increased public concern over its safety. In the coming months, the U.S. Environmental Protection Agency, the International Agency for Research on Cancer, and the National Toxicology Program's Report on Carcinogens all plan to review the risks associated with formaldehyde.

A team at the UNC Superfund Research Program, led by SRP Director James Swenberg, has just completed a study that provides new data important for understanding the public health consequences of exposure to formaldehyde from occupational and environmental sources. This research examines the hypothesis that inhaled formaldehyde travels to distant parts of the body and is capable of causing leukemia.

The team includes SRP scientists investigating the role of oxidative stress in toxicity and carcinogenicity and the SRP's Chemistry and Analytical Core. The study was supported by grants from National Institute of Environmental Health Sciences for UNC's SRP and the Center for Environmental Health and Susceptibility and a grant from the Formaldehyde Council.

Using ultrasensitive, highly precise mass spectrometry technology, Swenberg and team measured the presence of DNA adducts — a chemical bonded to the molecular structure of DNA, the formation of which is the first step in the development of cancer — in the nasal lining of rats, as well as in their lungs, livers, spleens, thymuses and bone marrow, to determine if, and how much, formaldehyde was present at each of these sites.

One of the challenges they faced is that, in addition to coming from external (exogenous) sources, formaldehyde is also an essential (endogenous) component of all living cells and is produced within the cells. Therefore, the scientists had to figure out how to measure both sources of formaldehyde separately.

continued>>


Photo by Infrogmation of New Orleans, via Wikimedia Commons

Formaldehyde was found in the air inside Federal Emergency Management Agency (FEMA) trailers that housed people after Hurricane Katrina.

The UNC SRP brings together a diverse group of more than 70 biomedical researchers, engineers, chemists, statisticians, experts in conventional and bioremediation, environmental modelers and students. Together, we are achieving the program's goal to advance society's understanding of the human health and environmental risks associated with hazardous waste and to develop new environmental strategies and technologies for the cleanup of Superfund sites, thereby minimizing human and environmental risk.

New web address: **www.uncsrp.org**

formaldehyde, *from page 1>>*

In this study, laboratory rats inhaled a kind of formaldehyde that could be traced ([13CD2]-formaldehyde) for six hours a day, either for one day or five days. SRP scientists then used mass spectrometry to measure both endogenous and exogenous formaldehyde DNA adducts in nasal, lung, liver, spleen, thymus and bone marrow tissue.

SRP Director James Swenberg

"We found DNA adducts caused by the exogenous formaldehyde in the rats' noses, but these adducts did not form in the more distant tissues, even for the rats who inhaled formaldehyde for five days," Swenberg reports. "We also found that the number of DNA adducts from the exogenous formaldehyde was significantly greater in the noses of rats exposed for five days than in those exposed for just one day."

As expected, adducts from endogenous formaldehyde were present in tissues at all sites. However, Swenberg notes, the total amount of endogenous formaldehyde adducts in the rats' noses was greater than the amount of exogenous adducts.

"That raises the question, 'How can we have this many naturally occurring endogenous adducts present in the nose as well as the other tissues, and yet have cancer be so rare?' What we think is happening is that the inhaled formaldehyde is very toxic, primarily in the nose. Exposure to high concentrations of this chemical is causing many cells in the lining of the nose to die, and then they are replaced by newly dividing cells. It is this cell division, where the DNA copies itself, that is necessary to convert both endogenous and exogenous adducts to mutations. The process of converting an adduct to a mutation is the first of several steps toward the development of cancer."

This SRP study provides strong evidence for the cancer-causing impact of inhaled formaldehyde in the tissue of the nose. It also has powerful implications in the debate over the hypothesized link between inhaled formaldehyde and leukemia.

"This study is a wonderful example of how the SRP fosters high level interdisciplinary research and supports state-of-the-art analytical chemistry."

"Several previous epidemiological studies had drawn conflicting findings about the link between inhaled formaldehyde and leukemia. However, our research demonstrates that inhaled formaldehyde only induced DNA lesions at the site of contact (the nose), but not in DNA of distant organs. That clearly does not support the biological plausibility that inhaled formaldehyde causes leukemia," Swenberg states.

"This study is a wonderful example of how the SRP fosters high level interdisciplinary research and supports state-of-the-art analytical chemistry," Swenberg adds. "The close collaboration between the Chemistry and Analytical Core and Project 1 scientists played a critical role in making this important research possible."

research highlights

Artificial skin expands opportunities to study chemical exposure

WHEN YOU'RE TRYING TO DETERMINE WHAT HAPPENS when auto and airplane mechanics get hazardous chemicals on their skin, there's only so much testing you can do on people. So UNC SRP Principal Investigator Leena Nylander-French and her team are developing synthetic "skin" that they can use in laboratory studies to assess what happens, and which health risks arise, when people come in contact with naphthalene, a dangerous contaminant often found in fuels.

Leena Nylander-French

"We can't use animal models because their skin is very different from humans — pigs, for instance, don't have the same immunological function in their skin as we do. We can't use human skin tissue because we'd need significant skin biopsies, and of course injecting chemicals into human subjects wouldn't be ethical," Nylander-French explains. "By creating an artificial skin built from human epithelial cells grown in the lab and incorporating donor cells from different human subjects, we can safely and effectively conduct studies that shed light on the individual differences in susceptibility to chemical exposure."

Nylander-French's lab is continuing its studies on Air Force workers exposed to naphthalene from jet fuel. Having determined the genotype of each subject, the UNC scientists are now working to understand what role the genomic structure plays in exposure risk. Since no one has done a similarly complex study, Nylander-French's team is still trying to determine the best statistical methods to analyze the data and incorporate it into exposure models.

Photo courtesy Dobbins Air Reserve Base

Once the synthetic skin model is complete, the SRP team will use genotype information from the Air Force workers to add a genetic component to that skin so they can investigate the metabolic processes in skin samples with different genetic make-ups. This will yield valuable insight into how and why individuals differ in their susceptibility to toxic chemicals. The team is also planning to conduct similar studies using artificial lung tissue to simulate the exposure workers face when they inhale these chemicals.

"Using this innovative approach, we'll be able to compare the skin and lung tissue to see how they differ in penetration and in activation of the metabolic pathways. It's a new and exciting way to test; one that's more relevant to humans."

In collaboration with Dr. Meenhard Herlyn at the Wistar Institute in Philadelphia, Nylander-French received a challenge grant from the National Institute of Environmental Health Sciences (1RC1ES018210-01) to develop an artificial skin tissue that can quickly screen for toxic compounds.

New models predict underground movement of contaminants with greater precision

TO MAKE SENSE OUT OF THE data collected at Superfund sites and in the Superfund Research Program labs, researchers need complex, accurate deterministic models. SRP Researchers Casey Miller and Bill Gray are developing and improving models that can help predict what will happen to contaminants at Superfund sites as they move underground, and to test the potential impact of different approaches to cleaning up the sites.

Casey Miller

These are very complex chemicals and very complicated processes, Gray cautions, so he and Miller are constantly working with other researchers and computation experts to fine-tune these models to mimic more accurately what SRP researchers are actually seeing in the lab.

Miller and Gray have developed a new approach called Thermodynamically Constrained Averaging Theory (TCAT), a modeling method that takes into account processes occurring at both the most intricate levels and at larger scales. For instance, while measuring the movement of substances between individual grains of sand at Superfund sites would be impossible, TCAT can help tie together information taken at the individual-grain scale with data from entire columns of soil or from the field in a way that allows researchers to draw appropriate conclusions.

As Gray explains, "Modeling not only helps us understand how these contaminants move in the subsurface; they can also tell us what we *don't* know about the way the material behaves, which gives us insight into what experiments we still need to do."

SRP wins three supplemental grants

UNC SRP INVESTIGATORS HAVE BEEN AWARDED SUPPLEMENTAL GRANTS under the American Recovery and Reinvestment Act of 2009 to support these important projects:

- A collaboration between the SRP at UNC and the SBRC at Duke to investigate mechanisms which seem to give a population of killifish (Fundulus heteroclitus) **resistance to liver cancer** caused by exposure to polycyclic aromatic hydrocarbons (PAHs). UNC scientists will analyze killifish taken from pristine waters and those contaminated by PAHs to look for DNA damage, metabolism of PAHs, and differences in physiology. This work will provide new insights into mechanisms contributing to cancer and cancer resistance, and further enhance the development of this species of fish as a model for human and environmental health research.

Fundulus heteroclitus mummichog, Taken at St. Michaels, Chesapeake Bay 2006 Brian Gratwicke

- A collaboration between researchers at UNC and the University of Arizona to use state-of-the-science technology and methods to observe the **dissolution of dense non-aqueous phase liquids** (DNAPLs), the most common cause of subsurface contamination at Superfund sites and a major risk to human health. These observations will be used to verify and improve an analytical model that will enable more cost-effective decisions on how to remediate these underground contaminants and more accurate estimates of short- and long-term risks to human health.
- A partnership between the UNC SRP's Research Translation Core (RTC) and the Medical Evaluation and Risk Assessment program of the North Carolina Department of Health and Human Services (NCDHHS) to develop NCDHHS's capacity to identify populations at greatest **risk from well water contamination** and provide public health strategies to reduce such exposure. The RTC will develop a database to identify patterns of concern related to well water contamination from 25 substances, and will create maps to illustrate these patterns to enable NCDHHS to identify and track well water contamination trends and to communicate this information to local governments in potentially impacted communities. The UNC team will also provide training for NCDHHS, other state agencies and local health departments in the use of these tools for their use in future risk analysis.

WE'RE NOW THE SRP

Effective immediately, programs throughout the country have dropped the "basic" in Superfund Basic Research Program and are now simply the Superfund Research Program (SRP). This title more accurately conveys the broad range of science taking place at UNC and around the country. In light of this, our web address has changed to:

www.uncsrp.org

PLEASE TAKE A MOMENT TO UPDATE YOUR BOOKMARKS.

Helping government agencies use Superfund science

IN JULY 2009, THE UNC SUPERFUND RESEARCH PROGRAM'S Research Translation Core (RTC) hosted a meeting at UNC-Chapel Hill between RTC leaders from 15 SRPs and representatives from the U.S. Environmental Protection Agency (EPA), the U.S. Agency for Toxic Substances and Disease Registry (ATSDR), the National Institute of Environmental Health Sciences and the NC Department of Health and Human Services. In all, over 40 environmental health leaders came together to discuss ways to work together to improve the use of scientific findings emanating from the SRP. The meeting increased participants' understanding of the work practices within EPA and ATSDR and their science and science communication needs as they relate to the Superfund cleanup program. This dialogue continued with EPA and ATSDR representatives participating in the 2009 SRP Annual Meeting.

For presentations and discussion summaries, visit srpcollaborations.wordpress.com/7-28-09/

SRP Video opens Neuse RiverKeeper Foundation meeting

AN EIGHT-MINUTE DOCUMENTARY PRODUCED BY THE RTC, on the contamination of local waterways and cleanup of the local Ward Transformer NPL Site, was used by the Neuse Riverkeeper Foundation to open a community meeting in February 2009. The video, "Protecting Our Water: PCB Contamination at Ward Transformer," is one of two produced by the RTC to complement our educational efforts. The meeting included a panel discussion, featuring RTC Director Fred Pfaender as one of the panelists. You can view this video at www.uncsrp.org or vimeo.com/user1260496/videos.

Teaching N.C. educators about water quality

FOR THE THIRD STRAIGHT SUMMER, THE UNC SRP and the Albemarle-Pamlico National Estuary Program (APNEP) co-sponsored a teacher professional development institute, "Environment & Health: Making Connections through Water Quality Investigations," for NC middle and high school science teachers. NCDENR's Office of Environmental Education hosted the week-long workshop in Salter Path, NC.

> **"I feel like I just audited six graduate classes and left with materials developmentally appropriate for my middle school science students. So many of these activities and labs will provide wonderful opportunities for students to analyze, evaluate and synthesize crucial scientific information."**
> ***Sarah Lancaster, middle school science teacher***

Twenty-three science teachers and non-formal environmental educators learned about water quality in our state and its implications for environmental health. SRP K-12 Science Education Manager **Dana Haine** led hands-on activities with teachers that addressed chemicals in the environment, toxicology, point and non-point source pollution, hazardous waste, environmental health, and the EPA's Superfund Program. The research taking place within UNC SRP, such as remediation of DNAPL contamination, was also highlighted. Research Translation Core Director **Fred Pfaender**, an environmental microbiologist, joined participants during a field trip to Sturgeon City, a former wastewater treatment plant and now the headquarters of the City of Jacksonville's Water Quality Initiative, to give a presentation about bioremediation. Participants also completed exercises that enabled them to investigate hazardous waste sites in their local communities, viewed the *Frontline* documentary "Poisoned Waters," and discussed the role of scientific information in empowering communities to address issues of environmental justice.

Participating teachers have consistently been able to apply the knowledge and activities from the institute to enhance their curricula, giving their students interesting, hands-on ways to learn about local and regional water quality issues while also incorporating Superfund-related topics.

Superfund Research Program

SUPERFUND SCOOP

This newsletter is published annually by the UNC-Chapel Hill Superfund Research Program, with funding from grant number P42-ES005948 from the National Institute of Environmental Health Sciences, NIH.

JAMES A. SWENBERG
Program Director
919.966.6139
james_swenberg@unc.edu

FREDERIC PFAENDER
Research Translation Director
919.966.3842
fred_pfaender@unc.edu

KATHLEEN GRAY
Research Translation Co-Director
919.966.9799
kathleen_gray@unc.edu

SUPERFUND SCOOP
LAURA ERTEL, *Writer*
REGINA MCCOY, *Design*

UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH