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SCOOP

THE NEWSLETTER OF THE UNC SUPERFUND BASIC RESEARCH PROGRAM

When hazardous chemicals meet skin

At UNC-Chapel Hill, an SBRP researcher is finding new ways to measure skin exposure and understand what happens when people come in contact with toxic materials.

The UNC SBRP 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.

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IF YOU WORK AROUND JET FUEL, it's inevitable that you'll get fuel on your skin and breathe in vapors. The same goes for auto mechanics or Superfund clean-up workers — it's nearly impossible to avoid contact with hazardous chemicals. Even those of us who don't work in high-risk areas will likely come in touch with toxic chemicals — whether pumping gas into our cars, putting mothballs in closets, or filling the lawnmower with fuel.

Principal Investigator Leena Nylander-French leads a research team at the University of North Carolina-Chapel Hill Superfund Basic Research Program (SBRP) studying what happens when people's skin comes in contact with, or they breathe in, hazardous materials like those found at Superfund sites. Her team has developed methods to effectively measure dermal and inhalation exposure, to track that exposure's impact within the body, and to explore how individual susceptibility may affect that impact.

Nylander-French's research focuses on polycyclic aromatic hydrocarbons (PAHs), a contaminant frequently found at Superfund sites as well as in daily life, in particular a common PAH called naphthalene.

"Naphthalene is usually present in PAH mixtures such as fuels, and research has shown it is a very good 'marker' for PAH exposure," she explains. "That means naphthalene is generally found in high enough concentrations that it's easy to measure on the surface of the skin and in its sub-layers, in inhaled air, and as it enters the blood stream and moves through the body."

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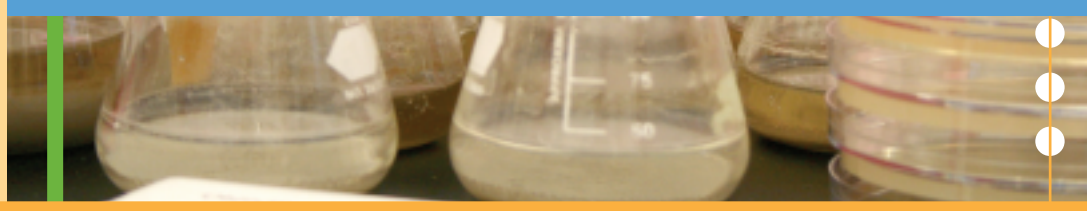


Making the science more complex is the fact that two people exposed to the same level of a contaminant may react differently, based on their genes.

As part of a collaborative U.S. Air Force Study of individuals who work around jet fuel, Nylander-French's team developed a noninvasive method called "tape stripping" to pull off the top layers of dead skin cells from the study subjects. By tape stripping the same spot multiple times, they could measure PAH exposure both in the top layer of skin and in successive skin layers, proving that PAHs gradually penetrate the skin and can enter the circulatory system.

This SBRP team also developed a technique to find protein adducts formed in the skin due to naphthalene exposure. These adducts, which form when a foreign substance combines chemically with proteins in the body, reflect exposure levels and may cause some type of adverse health effect. They are considered good biomarkers of skin exposure — proof that a person has been exposed to this compound through dermal contact, and that the toxin has begun to move through the body. Nylander-French's group has also used mathematical modeling to understand how this compound gets absorbed into the body and to estimate both dermal and inhalation exposure and the relative contribution of each to an individual's total exposure.

The team is now working to correlate adducts to specific adverse health effects, a breakthrough that should make it possible to determine the amount of dermal exposure an individual could have to PAHs while remaining safe from health consequences.

Making the science more complex is the fact that two people exposed to the same level of a contaminant may react differently, based on their genes. So Nylander-French is collaborating with scientists at the Centers for Disease Control and Prevention and Texas Tech University to study the DNA of Air Force study subjects to determine whether certain genes might affect the way the skin metabolizes naphthalene and other PAHs, the level of adducts in the skin, and potential individual susceptibility to adverse health effects.

In North Carolina, 25 out of 32 Superfund sites are contaminated with PAHs — including several military bases where jet fuel is abundant. Understanding the potential health effects of dermal and inhalation exposure to PAHs can help better protect people who work with jet fuel or remove hazardous materials from these sites.

Nylander-French has collaborated with other UNC SBRP investigators to compare the impact on those Air Force workers from inhaling the PAH fumes versus skin contact, and to evaluate dermal exposure to PAH-contaminated soil. The SBRP's Chemistry Core has played an important role in this work, particularly in the development of the techniques to detect skin protein adducts.

Nylander-French was drawn to dermal research because so little is known about how the skin reacts to exposure to foreign, potentially dangerous compounds. "In the past, we considered inhalation as the most important route of exposure, largely ignoring the skin, which we considered a protective organ — just a layer of dead cells. But now we know the skin is a very important immunologic organ that reflects the health of the individual: it efficiently metabolizes many of these foreign substances, yet some can penetrate into the skin and gain access to systemic circulation and effect health. It is an exciting area to study."

POLYCYCLIC AROMATIC HYDROCARBONS (PAHs) are a group of more than 100 different chemicals found in over 600 Superfund sites. Although some PAHs are manufactured, most are formed during the incomplete burning of certain substances. PAHs primarily enter the environment through volcanic eruptions, forest fires and exhaust from cars, but are also found in jet fuel, tobacco smoke and cooked foods, especially charcoal-broiled foods. PAHs are found in the air, soil and water. They can also be encountered in some medicines, pesticides, dyes, asphalt and plastic. Certain PAHs may cause cancer of the lung, skin and bladder in humans.

Computer model extrapolates limited data to map PAH exposures

Ben Allshouse

BY APPLYING A SOPHISTICATED environmental model developed within the UNC SBRP, researchers can take measurements of toxin levels from just a few sites and use that information to project exposure levels over an entire area.

Ben Allshouse, a PhD student who works with SBRP Investigator Marc Serre, has helped use this model to map New Yorkers' exposure levels to the PAHs released when the Twin Towers fell on 9/11.

Even before 9/11, New York had an extensive network of monitors around the city to continuously measure particulate matter released into the air. PAHs are in the particulate matter, but it would be much too expensive and time-consuming to individually process samples from every monitor to determine the amount of PAHs in each. Instead, the UNC team measured the levels of nine different PAHs in particulate matter collected from three locations along the fence line of Ground Zero, and another location about a mile uptown. They then created a model to apply those ratios to measurements at the other monitored sites around the city to estimate the amount of each PAH present at each location.

Using the model, Allshouse and Serre have created maps of lower Manhattan and Brooklyn, where they believe the highest levels of PAH exposure occurred. "Some researchers have hypothesized that PAH exposure may be associated with lower birth rates, pre-term births and other health effects that have occurred in the area beyond Ground Zero, but no one had collected PAH data beyond the immediate site," Allshouse notes. "Those researchers can use our maps to see if there is, in fact, an association between what they've found on birth outcomes and our estimates of PAH exposures."

The UNC researchers plan to use this model in a larger context to estimate PAH levels in particulate matter monitoring devices set up around the country. Again, individually measuring PAH levels in these devices would be time- and cost-prohibitive, so they will use a similar approach to extrapolate measurements taken at just a few sites.

"Obviously there are some disadvantages to taking data from a small area and extrapolating it over a larger area," Allshouse acknowledges, "but in the absence of other ways to get this beneficial information, modeling provides the best option out there, and so far we've gotten good results."

The relationship between TCE metabolism, genes and susceptibility

TRICHLOROETHYLENE (TCE) IS A chemical that was once used in everything from dry cleaning solutions to nail polish remover to engine degreasers. It is found in the soil at many Superfund sites and can lead to a range of health problems. The problem for human health is likely not TCE itself, but the products it forms (metabolites) once it enters the body and is broken down.

Michelle DeSimone, a first-year doctoral student in toxicology at UNC-Chapel Hill, is working in the laboratory of SBRP Investigator Ivan Rusyn to understand the relationships between different TCE metabolites, the impact of these metabolites on the body, and the reasons why individuals react differently to TCE exposure.

Michelle DeSimone

DeSimone and Rusyn are using 16 different strains of mice to simulate the genetic variation seen in humans. Within each strain, the mice are genetically identical, but between strains the genes are distinct — just like in people. In the first stage of the project, the researchers exposed each strain to TCE for up to 24 hours, then collected blood, urine and tissue samples. Now DeSimone is working with the SBRP's Chemistry and Analytical Core, using state-of-the-art instruments to develop a profile of the seven metabolites found in each strain.

"Our hypothesis is that the differences in metabolism of TCE are genetically controlled," DeSimone explains, "so this multi-strain approach can help us identify the genetic basis of susceptibility and understand how toxicity works."

Once the metabolite profiles are complete, the scientists can determine whether the level of a particular metabolite corresponds to a

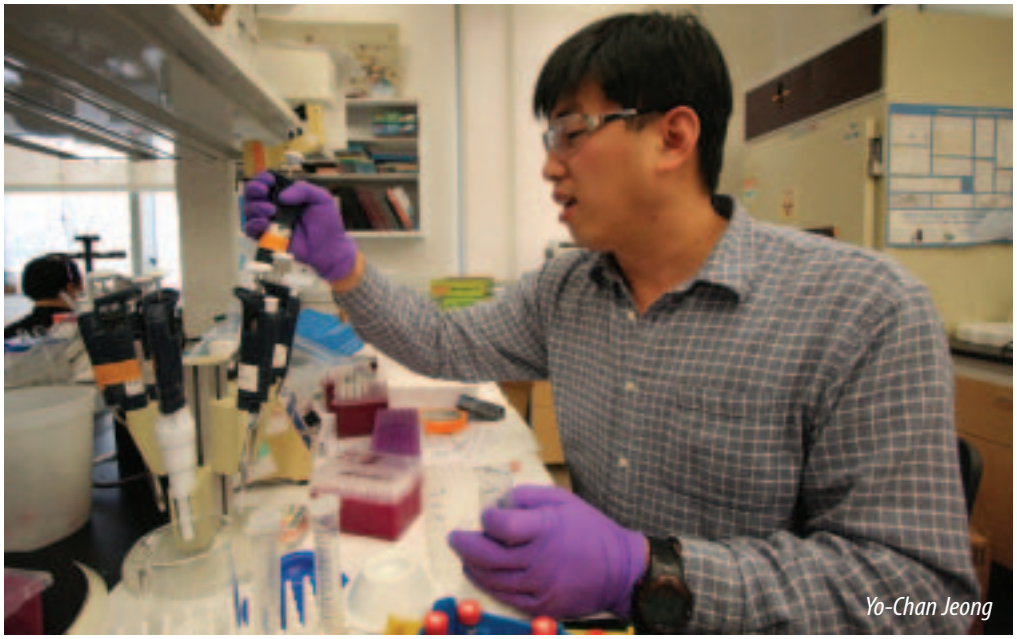
Exploring the links between toxic chemicals, DNA damage and disease

SOME TOXIC CHEMICALS, including many found at Superfund sites, can cause damage to an exposed person's DNA. The chemicals can produce substances called reactive oxygen species (ROS), which can attack DNA and cause changes to its structure. As the damaged DNA duplicates, it can create genetic mutations, the first stage in developing cancer, premature aging and other health problems.

Post-doctoral Fellow Yo-Chan Jeong is working with UNC SBRP Director James Swenberg to investigate the role of this oxidative DNA damage from exposure to hazardous chemicals in the development of cancer and other diseases at the molecular level. Jeong is focusing on Polychlorinated Biphenyls (PCBs) and dioxins, chemical compounds commonly found at Superfund sites.

Among the things that Jeong and Swenberg have discovered in their research is that, while there are both toxic and nontoxic forms of PCBs, some nontoxic PCBs can actually amplify the toxicity of other chemicals.

"In the environment, there is always a mixture of chemicals, but in the past the impact of the nontoxic PCBs hadn't been calculated when evaluating toxicity from contaminants," Jeong notes. "Our findings, combined with results from the National Toxicology Program, showed that these nontoxic PCBs should be factored in."

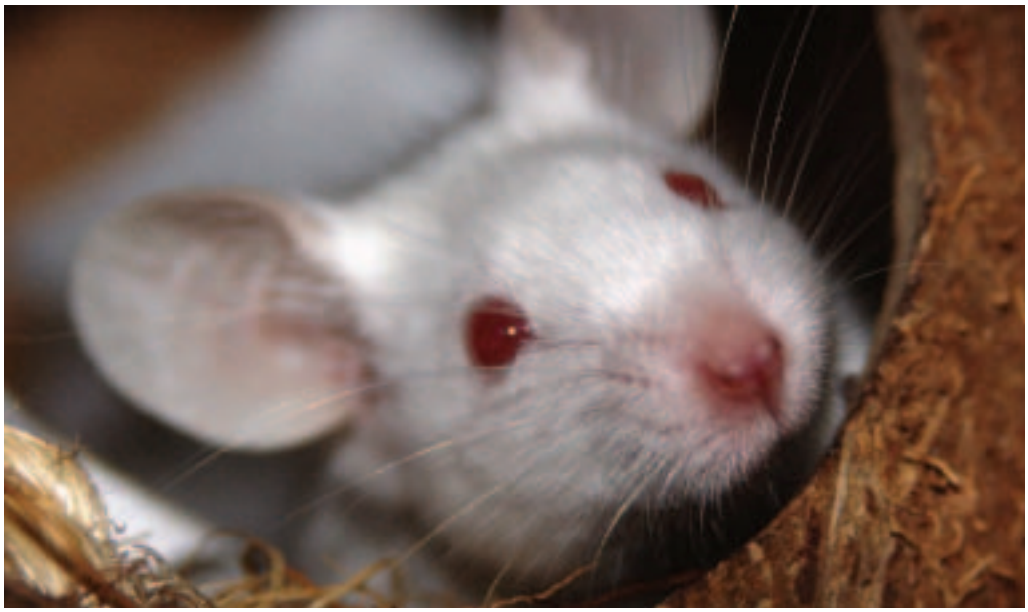

Yo-Chan Jeong

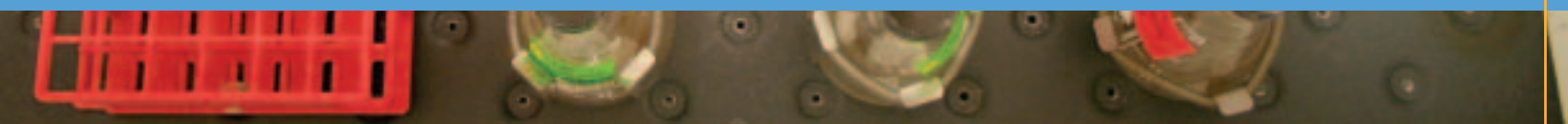
The UNC researchers are now studying the impact of chemical exposure in laboratory animals, which experience oxidative DNA damage similarly to humans. They are also applying what they've learned about dioxins and PCBs to other chemicals, and are collecting samples of fish from Superfund sites to try to understand the distribution of chemicals and toxicities so they can extrapolate that data to humans living near Superfund sites.

"The knowledge gained should serve as a foundation for more effective biomonitoring programs for people who have been exposed to these toxic chemicals, as well as more effective remediation programs for these pollutants."

specific adverse health effect, such as liver or kidney disease, and select representative strains for in-depth, long-term studies. This approach will tell them whether differences in TCE metabolism control toxicity or if there are other genes involved in determining susceptibility to liver and kidney injury.

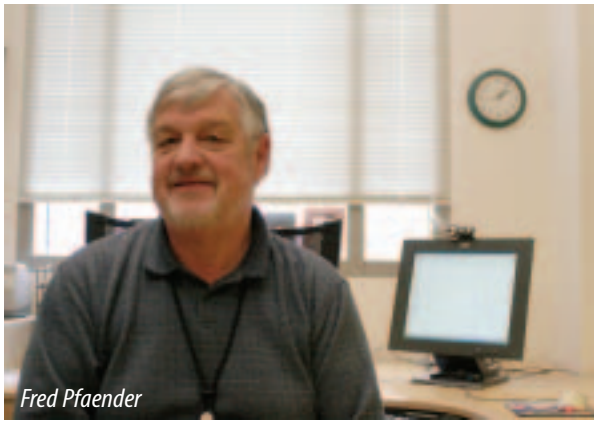
Ultimately, DeSimone says, the investigators will determine how what they've learned in mice applies to human susceptibility to TCE toxicity. "If we can identify specific genes associated with susceptibility to TCE, the same genes may put certain human populations at risk for health problems due to TCE exposure. This is a cutting-edge approach, and its goal is to help regulators properly set TCE exposure limits in the environment, which would serve to protect human health."





From discovery to market

Boot camp teaches UNC researchers how to transfer discoveries in the lab into usable products and services in the marketplace


Fred Pfaender

MOST RESEARCHERS HAVE LITTLE experience taking the technological advances they've developed in the laboratory and making them available for a broad range of users — that is, commercializing their inventions so that more people can buy, use and benefit from them.

In October, to help UNC scientists better understand the discovery-to-market transition — and to make them aware of how the university can help them through this complex process — the UNC Superfund Basic Research Program, along with the UNC Office of Technology Development and the Department of Environmental Sciences and Engineering, co-sponsored a two-day Technology Development Boot Camp. Fifty-five faculty members, postdoctoral scholars, graduate students and staff attended the free workshop.

In keeping with the Boot Camp theme, participants figuratively went through intensive basic training as patent lawyers, business school professors, venture capitalists and veteran entrepreneurs educated them on the basics of intellectual property, patents and copyrights, licensing and starting a company. They learned how to secure early-stage funding, the basics of IPOs and acquisitions — even how to determine whether to start a new company or partner with an existing one. By the time the participants were dismissed, they were also familiar with university policies, procedures and resources.

The highly rated Boot Camp will be offered again in the fall.

"Superfund Basic Research Programs regularly produce technologies to aid clean-up of hazardous materials or to shed light on the links between hazardous waste and human health," notes SBRP Research Translation Core Director Fred Pfaender. "We want to educate our people about the potential of their technology, so they can make informed choices about how best to share their inventions with others. This is valuable information both for academic researchers and for those who go on to work in industry or government."

DENR partnership: From the university to the field

THE UNC SBRP'S RESEARCH Translation Core has developed a multi-faceted partnership with the N.C. Department of Environment and Natural Resources (DENR).

Twice a year, UNC SBRP researchers present science seminars at the Raleigh offices of DENR's Superfund Section. The seminars give SBRP scientists a chance to share their innovative research, emphasizing its potential implications for Superfund cleanup in our state. At the same time, the seminars inform the SBRP's research agenda by helping UNC faculty learn about the cleanup issues DENR professionals face at their sites.

At DENR's request, the SBRP is also part of an interagency group working on a statewide plan to address issues at the 180-plus formerly used defense sites (FUDS) in North Carolina, where various types of contamination were left behind by the military. The working group also includes representatives from DENR, the U.S. Army Corps of Engineers and the Environmental Protection Agency.

Art Shacter (left), a DENR Superfund Section staff member, discusses the cleanup of a formerly used defense site with a member of the Butner community.

This year, the UNC SBRP will launch an internship program to give graduate students an opportunity to learn about DENR's Superfund Section and the Environmental Protection Agency's Superfund program. Students will gain hands-on experience working on problems encountered by those managing Superfund programs and sites, and will see how the research being conducted by the UNC SBRP relates to the issues and problems occurring at real sites.

"The SBRP is in a unique position to link government agencies with the expertise and resources of the university," says SBRP Senior Research Associate Diana Tarrant. "Together with DENR, we have built a true partnership that has benefited both organizations as well as the citizens of North Carolina."

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Visit for details on our current research, enhanced search tools for publications, and valuable resources for communities and educators.

SUPERFUND SCOOP

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Educating the community about the impact of Superfund on local recreation site

LAST SPRING, THE UNC SBRP'S Research Translation Core (RTC) partnered with Lake Crabtree County Park in Wake County to sponsor a workshop for teachers on "The Science and Civics of Superfund at Lake Crabtree." Lake Crabtree, near Raleigh-Durham Airport, is a focus of attention and concern because of its proximity to the Ward Transformer Superfund Site, the offsite contamination found in the lake, and its corresponding potential environmental impact.

At the one-day workshop, middle and high school educators learned how to incorporate this local environmental issue into their classrooms using hands-on materials and activities. SBRP educators taught participants about environmental health risks and decision making at Superfund sites and led a discussion of whether environmental health is a basic human right. Deborah Robertson, assistant manager for Lake Crabtree County Park said, "Partnering with the UNC SBRP was very beneficial for us. UNC staff brought much needed expertise in Superfund to our workshop, and I could not have offered it without the knowledge, expertise and materials they provided."

Last fall, the RTC also offered hands-on activities for families at Lake Crabtree's *WaterFest*, a public celebration of water quality.

Parents and children learned about UNC SBRP research and water quality at Waterfest.

UNC SCHOOL OF PUBLIC HEALTH

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