How do genetic variations among individuals lead to different responses when people are exposed to toxic chemicals in the environment?

According to UNC Geneticist David Threadgill, PhD, mice can help answer this question.

Threadgill, a UNC associate professor of genetics and a member of the Center for Environmental Health and Susceptibility (CEHS) at the University of North Carolina at Chapel Hill, has an entire laboratory devoted to creating experimental mouse strains that model the genetic diversity present in the human population.

“By creating experimental mouse models of complex and highly variable human populations in the lab, we can learn about the molecular and cellular changes that occur when individuals are influenced by their environment,” he explains. “We can also study how those changes differ among individuals, which can lead to much higher incidences of common diseases in some people, from cancer or cardiovascular disease to reproductive problems or asthma.”

In September, Threadgill and several colleagues at UNC were awarded a five-year grant from the National Cancer Institute to establish the Systems Genetics Research Consortium. The consortium’s goal is to develop a large experimental mouse population, called the “Collaborative Cross,” that genetically mimics the diverse genetic backgrounds found in the human population. Starting with eight genetically diverse mouse strains, the Collaborative Cross will ultimately capture almost 90 percent of the known variation present in laboratory mice and will provide a genetic reference population for modeling human disease.

“With the sequencing of the human genome and all of the
Michele La Merrill looked at these two facts and wondered: Does obesity increase one’s susceptibility to exposure to these chemicals?

La Merrill, a recent graduate of the Toxicology Program, uses mouse models to explore how exposure to environmental chemicals might pose a different risk for the obese population, particularly for breast cancer.

“Researchers have found a window of time early in life when exposure to chemicals can strong-
I’ve looked at how early life exposure to dioxin (a contaminant found in herbicides and industrial incineration processes) interacts with obesity to modify the way that the mouse breast eventually goes through puberty.”

La Merrill exposed lean and obese mice to dioxin both in utero and through their mothers’ milk. She found that, like humans, overweight mice go through breast development faster than lean mice. She also found that the lean mice were not responsive to dioxin exposure in terms of breast development — they went through puberty normally. However, in the obese mice, mammary gland development was delayed by this early exposure.

This year, the CEHS expanded the Pilot Projects Program to provide two awards of $40,000 specifically to physician-scientists, to stimulate the interaction of physician-scientists with population (epidemiology) and basic scientists in a translational research approach that will enhance understanding of human diseases.

- **TERRY L. NOAH, MD**, associate professor and division chief, UNC Pediatric Pulmonology, is using this funding to study the effects of diesel exhaust particles on influenza-induced nasal inflammation in allergic rhinitics. This work could help identify novel antioxidant strategies for reducing the impact of inhaled oxidant pollutants on virus-induced asthma exacerbations.

- **JOANNE M. JORDAN, MD, MPH**, associate professor, Medicine and Orthopedics and adjunct associate professor, Epidemiology, is using the grant to study metals and biomarkers of joint metabolism in a community-based cohort, the Johnston County Osteoarthritis Project. The study's primary objective is to understand how exposure to toxic metals such as lead and mercury affects osteoarthritis.

For more information on the research taking place at the UNC-Chapel Hill CEHS, or to view current publications, visit [cehs.sph.unc.edu](http://cehs.sph.unc.edu)
The CEHS Community Education and Outreach Core (COEC) is partnering with local health departments to provide breast cancer awareness workshops, primarily to African American women and people in rural and underserved communities.

In conjunction with National Breast Cancer Awareness Month, the COEC partnered with the Chatham County Health Department to co-sponsor evening workshops at churches in Bear Creek and Moncure, two of the more rural communities in the county. Two additional workshops were hosted at churches in Pittsboro and Siler City. Breast Cancer, Genes and the Environment shares the latest CEHS research and includes activities that encourage participants to reduce their risk of breast cancer by eating healthfully, exercising, quitting smoking, maintaining a healthy weight, and avoiding other risk factors. At these workshops, a health department representative also spoke about the county’s federally funded breast and cervical cancer screening program.

Currently, the COEC is focusing on outreach to churches as an effective way to reach minority populations. “Studies show that African American women are dying from breast cancer at higher rates than Caucasian women,” notes Neasha Graves, COEC Project Coordinator, who presents the workshops. “Many health departments actually have federally funded mandates to provide breast and cervical cancer screenings for women and to assure that they are receiving diagnostic and follow-up care. These workshops have been a great way for us to educate this at-risk population while also helping the health departments reach out and encourage women to take advantage of this valuable resource.”

Eighty men and women participated in the first four workshops in Chatham County. In their evaluations, participants reported increased knowledge of genetic and environmental risk factors and expressed strong interest in seeing the program spread to other churches in the area. The COEC anticipates co-sponsoring workshops in Lee, Harnett and Sampson Counties later this year.

For more information about the Breast Cancer, Genes and the Environment workshop, contact Neasha Graves at (919) 966-3746 or at neasha_graves@unc.edu.

The COEC partnered with local ABC television affiliate WTVD-11 last summer to produce and air two public service announcements on sun safety and skin cancer prevention. The 30-second spots, which were broadcast from May through August, featured CEHS member and skin cancer expert Bill Kaufmann, PhD.

The series also included two 15-minute segments on WTVD’s Sunday “Heart of Carolina Perspectives” program, broadcast in July and September. In these segments, Dr. Kaufmann and UNC cancer genetics expert Norman “Ned” Sharpless, MD explained how melanoma develops, the increasing incidence, warning signs and preventive measures, and the relationship between genes and the environment as it relates to skin cancer. They also discussed the Center’s participation in the international Genes, Environment and Melanoma (GEM) study, which aims to improve understanding of the causes of malignant melanomas. Skin cancer survivors Jon Peterson and Catherine Andrews also appeared on the shows to share their personal experiences battling melanoma and to advocate for sun safety.

“...This was a wonderful opportunity for us to reach a wide audience in the region, so we could inform people about the importance of sun safety in reducing their risk of developing skin cancer,” says Neasha Graves, COEC Project Coordinator.
Getting the (word on) lead out

The COEC is partnering with the North Carolina Department of Environment and Natural Resources (DENR) Children’s Environmental Health Branch to staff and coordinate the federally funded North Carolina Childhood Lead Poisoning Prevention Program (CLPPP). Environmental Health Educator Amy MacDonald, who joined the COEC staff in September 2007 to coordinate CLPPP, works with DENR staff, environmental health specialists and local health departments throughout the state to provide outreach and education on lead poisoning and prevention to parents, childcare centers and schools. Lead exposure, which is particularly prevalent in children exposed to lead-based paint, can cause impaired growth and learning disabilities. Children under the age of six are most at risk.

MacDonald and COEC Project Coordinator Neasha Graves conduct educational workshops, hand out information at health fairs, field media requests and develop materials on topics such as pregnancy and lead poisoning that health departments can use as educational tools. MacDonald also answers calls to the Childhood Lead Poisoning Prevention Hotline (1-888-774-0071). During the holiday season, she presented to 70 environmental health specialists from across the NC Piedmont region on the recent federal lead-related toy recalls, and was interviewed on UNC-TV about lead and toys.

MacDonald recently completed risk assessor and lead inspector training, enabling her to go into the homes of poisoned children to determine the source of the lead poisoning. She plans to enhance other DENR-funded initiatives in the coming year, some of which include teaming up with local health departments to offer training on lead abatement and lead-safe work practices.

MacDonald, who before joining the COEC was a climate policy educator for Environmental Defense and the Southern Alliance for Clean Energy, also works on environmental health aspects of climate change. As one of 1,000 people in the United States trained to present Al Gore’s slide show from “An Inconvenient Truth,” she has done several presentations in North Carolina on the health impacts of climate change and is working with the town of Chapel Hill on its carbon reduction efforts.

For more information on lead poisoning prevention outreach and the environmental health aspects of climate change, contact Amy MacDonald at (919) 966-2463 or at amyjmac@email.unc.edu.

Lead is invisible to the naked eye and has no smell. Washing children’s hands often, especially before they eat and after playing outside, can reduce exposure.

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advances in technology that have come out of biomedical science over the last 10 years, we now have the ability to, in much greater detail, understand the complexities of human biology by using appropriate experimental populations,” Threadgill notes.

Successfully developing the Collaborative Cross will enable Threadgill and other researchers to perform detailed laboratory studies to explore the links between genetic variation and environmental influences. One study already underway, an obesity-related collaboration with two other UNC investigators, puts the mice into a model of the human built environment to see how that environment influences the development of obesity and other diseases, based on the differing genetics of the mouse strains. Fellow CEHS member and Nutrition Professor Daniel Pomp actually designed a mini-environment for the mice that allows the investigators to observe whether the mice want to exercise (Do they act like “couch potatoes,” or choose to go to the mouse “health club”?), how much they exercise, their metabolism level, and how those factors interact with their genetic makeup to alter the health of the individual.

This experimental mouse population will also be used in studies such as those being performed now by two of Threadgill’s graduate students, Michele La Merrill and Michelle DeSimone, to understand how genetics plays a role in an individual’s susceptibility to exposure to dioxin and trichloroethylene and the possible links to cancer. (See articles in this newsletter.)

A geneticist by training, Threadgill credits the existence of Carolina’s CEHS for drawing him into the field of environmental health research. “After coming to UNC in 2000 and becoming active in the CEHS, it really provided me with a much broader perspective on the importance of the interaction between genetics and environmental factors.”

Threadgill sees many benefits for North Carolinians that can ultimately come out of this research. “In North Carolina, obesity rates are rising fast; cancer rates are high.

We want to identify genetic signatures or types of individuals that are more susceptible to the influences of modern society. Such influences could include the built environment, diet and exercise, or exposure to certain chemicals. Once we can make those identifications, then we might be able to find ways to prevent the higher levels of these and other common diseases from developing in those individuals.

“If we can understand what is potentially increasing someone’s risk for developing a disease, we can hopefully mitigate it in some way.”

*Building a Better Mouse Model, from page 1*

Do they act like “couch potatoes,” or choose to go to the mouse “health club”?

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