GRANT TO OPEN CENTER FOR ENVIRONMENTAL HEALTH AND SUSCEPTIBILITY AWARDED IN APRIL 2001

How do variations in people’s genes affect their susceptibility to environmental factors such as chemicals and radiation?

How does susceptibility differ according to age, particularly in early development?

How do toxins move through the body, and why does environmental exposure impact some people differently than others?

These are the types of questions that a diverse group of researchers at the new Center for Environmental Health and Susceptibility (CEHS) at the UNC-Chapel Hill School of Public Health are investigating through state-of-the-art environmental health research. In April 2001, UNC-CH was selected as the newest site for one of 22 such centers funded by the National Institute of Environmental Health Sciences (NIEHS). This exciting resource for North Carolina aims to help reduce the burden of environmentally related disease, enhance knowledge about how toxic chemicals affect humans, and improve our understanding of the environmental and genetic determinants of disease in different populations.

THREE AREAS OF RESEARCH FOCUS

The CEHS, led by Dr. James Swenberg, brings together UNC-CH scientists in environmental epidemiology, environmental health, and toxicology to concentrate on research in three core areas that can affect the likelihood of a person developing disease from exposure to hazardous materials:

1. Genetic susceptibility, or how variation in people’s genes changes their susceptibility to environmental exposure.
factors such as chemicals or radiation, and lifestyle choices like diet and smoking. In this core, researchers focus on molecular epidemiology, DNA damage and repair, and gene-environment interaction, to address possible health effects such as cancer, reproduction and developmental problems, and neurologic and cardiovascular disease.

2. **Developmental susceptibility**, or increased vulnerability to toxic agents during early stages of life. This core focuses on the health effects of environmental exposure from the time of conception through childhood and examines health impacts such as pregnancy loss, birth defects, developmental deficits and childhood cancer. Laboratory researchers and epidemiologists are also looking at paternal and maternal influences on susceptibility to environmental exposure.

3. **Toxicokinetic susceptibility**, which focuses on understanding how chemicals move through and are processed by the human body, and why some people react differently to these toxins than others. The CEHS researchers are looking at differences among individuals and across species to determine the effects of chemicals on human health and give us more accurate assessments of health risks.

The Center’s research in each of these areas is supported by four Facility Cores led by UNC-CH faculty who specialize in high-throughput genotyping, biostatistics and epidemiological methods, biomarkers, and nutrient assessment — expertise that is essential to this type of cutting-edge investigation. The CEHS also includes a community outreach and education program and pilot projects that encourage promising new collaborative research.

**CONNECTING THE CENTER’S WORK TO THE COMMUNITY**

A key component of the UNC-CH CEHS is the Community Outreach and Education Program (COEP). The COEP designs and implements programs to:

- Communicate the Center’s research findings to a broad audience so this knowledge can be used to improve public health programs and policy,
- Educate the public about how individual and group susceptibilities interact with environmental and occupational factors to cause disease, and
- Foster collaboration between Center scientists and community groups in order to involve community members in the research process to the maximum extent possible.

The COEP, which benefits from the community outreach and education expertise of UNC-CH’s Environmental Resource Program (ERP), sponsors a range of activities to ensure that the Center’s research taking place is widely understood by North Carolina community organizations, teachers, students, public health officials and businesses. The COEP’s activities include:

- Collaboration with community groups, state government officials, and Center scientists to guide the
CEHS’s efforts to share its research findings with the public and build community-academic partnerships to facilitate community involvement in research opportunities.

- A community-focused undergraduate internship program to give Carolina students hands-on experience in the field of environmental health and susceptibility.
- Professional development programs for North Carolina K–12 educators to enhance their ability to teach students about susceptibilities and the environmental and occupational aspects of health.
- A new website and this Sentinel newsletter to share the Center’s important work and its research findings with a broad audience.

The COEP has already engaged UNC-CH scientists and North Carolina citizens in focus groups to examine incentives and barriers to working together to achieve the CEHS’s goals, and surveyed NC teachers to determine topics of interest for professional development programs that draw on the CEHS’s research strengths. In addition, the Center has collaborated with a low-income community to collect data on local air pollution.

As highlighted in the following article, the COEP has also begun a project to develop, pilot and disseminate educational materials for lay audiences to examine the ethical, legal, and social issues involved in research on gene-environment interactions.

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**CEHS Wins Two New Research Grants**

**WITHIN JUST A FEW months of its creation, the UNC-CH CEHS was awarded the following two research grants from the National Institutes of Health.**

**UNDERSTANDING THE GENETICS OF TOXIN-INDUCED CANCER**

The first is a five-year, $7 million-plus grant to help define how individual genes influence a person’s risk of developing cancer as a result of exposure to toxins in the environment. CEHS researchers with expertise in toxicology, genomics and DNA repair are using powerful gene-focused technology to examine the reaction of 10,000 to 20,000 different genes in humans and mice when they are exposed to environmental toxic agents.

Dr. William K. Kaufmann, Director of the Center’s Genetic Susceptibility Research Core and Professor of Pathology and Laboratory Medicine in the School of Medicine, is the principal investigator for the UNC-CH team. “Lots of things that people are exposed to in everyday life contain mixtures of toxins, including car exhaust, cigarette smoke, air pollution and contaminated water,” he explains. “While some of these environmental toxins might influence a person’s risk of developing cancer, others might not. Furthermore, two people can be exposed to the same...”

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*Dr. William Kaufmann (left), Director of the Center’s Genetic Susceptibility Research Core, consults with Charles Perou, Assistant Director of the Toxicogenomics Program.*
researchers are examining the mechanisms that control the division of cells to learn how that process is altered by damage to genes. This knowledge will be applied to determine whether people with breast cancer display defects in the normal pattern of response that increases their risk of developing additional mutations.

"Through this research project, we hope to determine why some known gene mutations enhance a person’s risk of developing cancer when exposed to environmental carcinogens, to discover new gene mutations that enhance risk, and to determine if genetic differences can help explain why some people seem predisposed toward cancer development after low-level toxin exposure while many others are not.” To understand how environmental toxic agents cause cancer and produce adverse effects on human health, researchers use inbred and genetically engineered mice as animal models.

This grant is part of a larger $37 million effort that includes four other academic research organizations and is headed by the NIEHS. The UNC-CH team is a collaboration between the CEHS and the Lineberger Comprehensive Cancer Center.

FURTHERING ENVIRONMENTAL EDUCATION AND RESEARCH

A $150,000 GRANT FROM the NIEHS is funding two programs at the Center. The first component of the grant is to educate the public on ethical, legal and social issues related to environmental genomics. Funding will allow the Center to develop educational modules on gene-environment risk factors for breast cancer and on the risks from gene-toxin interactions in the workplace. The Center’s COEP will develop and pilot these modules with two community partners, the North Carolina Breast Cancer Coalition and the North Carolina Occupational Safety and Health Project, and will ultimately disseminate these materials nationally. In Fall 2001, an interdisciplinary Scientific Advisory Board met to help develop these educational materials. UNC-CH is also collaborating with the COEP at the University of Cincinnati on this project.

The second component of the grant, led by Bill Kaufmann, is for an interdisciplinary research project to determine how the risk of developing breast cancer is affected by the body’s ability to repair DNA damage caused by environmental factors. CEHS researchers are examining the mechanisms that control the division of cells to learn how that process is altered by damage to genes. This knowledge will be applied to determine whether people with breast cancer display defects in the normal pattern of response that increases their risk of developing additional mutations.

UNC-CH senior Lindsay Kim (far right) analyzed federal data about air quality in Moncure, NC, and presented her findings to the community. Also pictured are (left to right) Valencia Deans, an NC State University senior, Ellen Pietroski of NC Waste Awareness and Reduction Network, and Harold Taylor, a lifelong resident and community activist.
Behind the Scenes: A Glance into the Research of Epidemiologist Andrew Olshan

DR. ANDREW OLSHAN
Professor of Epidemiology, directs the Center’s Developmental Susceptibility Research Core, which focuses on the effect of environmental exposures from conception through childhood. He also is a member of the Genetic Susceptibility Research Core. Here are research projects he is working on through the CEHS.

ENVIRONMENTAL AND GENETIC RISK FACTORS FOR CHILDHOOD CANCER

On the heels of a national study of neuroblastoma, a childhood nervous system tumor, Olshan is now conducting a five-year study of Wilms tumor, a rare childhood kidney tumor. Working through a national clinical trials network, he plans to identify about 800 cases of Wilms across the country. As in the first study, he will interview the parents of these children, and a control group of parents whose children don’t have cancer, about their exposures to chemicals at home and in the workplace, lifestyle factors and medical history. In collaboration with the Center’s Genetic Susceptibility Research Core, he also hopes to collect DNA samples from the parents and children to explore genetic factors that may impact the risk of developing childhood cancers when paired with certain toxic exposures.

“The fact that these particular cancers are diagnosed within the first four years of life points to a relatively small critical window of exposure. This gives us an excellent situation to study how cancer develops in these children, including exploring the parents’ exposures to environmental risk factors around the time of conception and the mother’s exposures during pregnancy.”

THE EFFECT OF DRINKING WATER ON MALE REPRODUCTIVE HEALTH

Building on a national study by fellow CEHS researcher Dr. David Savitz of possible links between the byproducts of drinking water disinfection and the risk of miscarriage, Olshan is partnering with the Environmental Protection Agency (EPA) to investigate the impact of these byproducts on male reproductive health. He is working with EPA reproductive toxicologist Dr. Sally Darney, an affiliate member of the Center’s Developmental Susceptibility Core, to interview and collect semen samples from the male partners of the women in Savitz’s study. “There is evidence in animals that these...”

“The Center has opened up new opportunities to learn about what other researchers are doing and has facilitated collaboration that may not have existed before.”

— Epidemiologist Andrew Olshan
byproducts in drinking water have a stronger effect on reproduction in males than in females, resulting in lower sperm count and higher prevalence of sperm abnormalities, for example. Adding on to Savitz’s national study gives us a unique and efficient opportunity to explore these issues in men.”

GENETIC LINKS TO HEAD AND NECK CANCER

Olshan’s biggest study crosses boundaries among the Center’s research cores, creating opportunities for collaboration with scientists specializing in genetic susceptibility, genotyping and DNA damage and repair. He has received funding from the National Cancer Institute for a five-year study to understand how a person’s genetic make-up interacts with the risk factors for head and neck cancer — smoking and alcohol consumption — to determine whether this type of cancer develops or not. Olshan plans to study about 1,500 cases of head and neck cancer in North Carolina. This is the largest study of its kind in the country. “Why can some people drink or smoke all their lives and not get cancer, while others do? We want to know the genetic factors that modify their risk. Head and neck cancer is an excellent model because we know what the risky behaviors are, so we can look at genetic factors that may be involved in metabolizing tobacco and alcohol and repairing the damage to DNA caused by smoking or drinking.”

SENTINEL
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