NIEHS
National Institute of Environmental Health Sciences

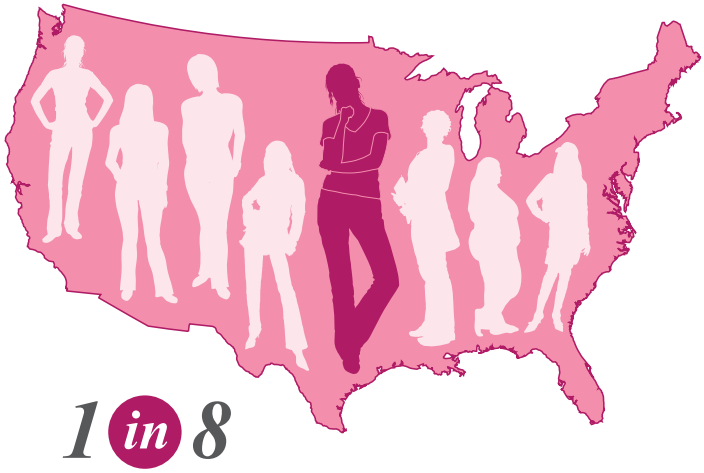
Breast Cancer Risk and Environmental Factors

For millions of women whose lives have been affected by breast cancer, the 1994 discovery of the first breast cancer gene by researchers from the National Institute of Environmental Health Sciences (NIEHS) and their collaborators, was a welcome sign of progress in the fight against this disease. While this discovery and others like it are certainly encouraging, statistics tell us that breast cancer is still a major health concern for women everywhere. According to the American Cancer Society, breast cancer is the most common cancer among women in the United States, other than skin cancer.

Gene-Environment Interactions

For years, NIEHS has played a leadership role in funding and conducting studies on the ways in which environmental exposures increase breast cancer risk. This research includes animal studies to understand the role of environmental agents in the initiation and progression of cancer, as well as research on chemical risk factors and genetic susceptibility in human populations.

Sisters of breast cancer patients, who share many of the same genes, are more likely to develop the disease themselves, and are likely to have been exposed to the same environmental risk factors during early childhood.



The chance of a woman in the U.S. having invasive breast cancer sometime during her life (ACS, 2012)

Although scientists have identified many risk factors that increase a woman's chance of developing breast cancer, they do not yet know how these risk factors work together to cause normal cells to become cancerous. Most experts agree that breast cancer is caused by a combination of genetic, hormonal, and environmental factors.

The Sister Study

As new research continues to unravel the mysteries surrounding the causes of breast cancer, NIEHS scientists have recruited more than 50,000 women to participate in a landmark study looking at the possible interplay between genetics and the environment in the development of this disease. The Sister Study includes diverse sisters of women diagnosed with breast cancer from across the country.

The researchers are comparing the genetic profiles and environmental exposures of sisters who don't develop breast cancer with those who do become cancer patients, in order to uncover clues that will help us better understand why some women develop cancer and others do not.

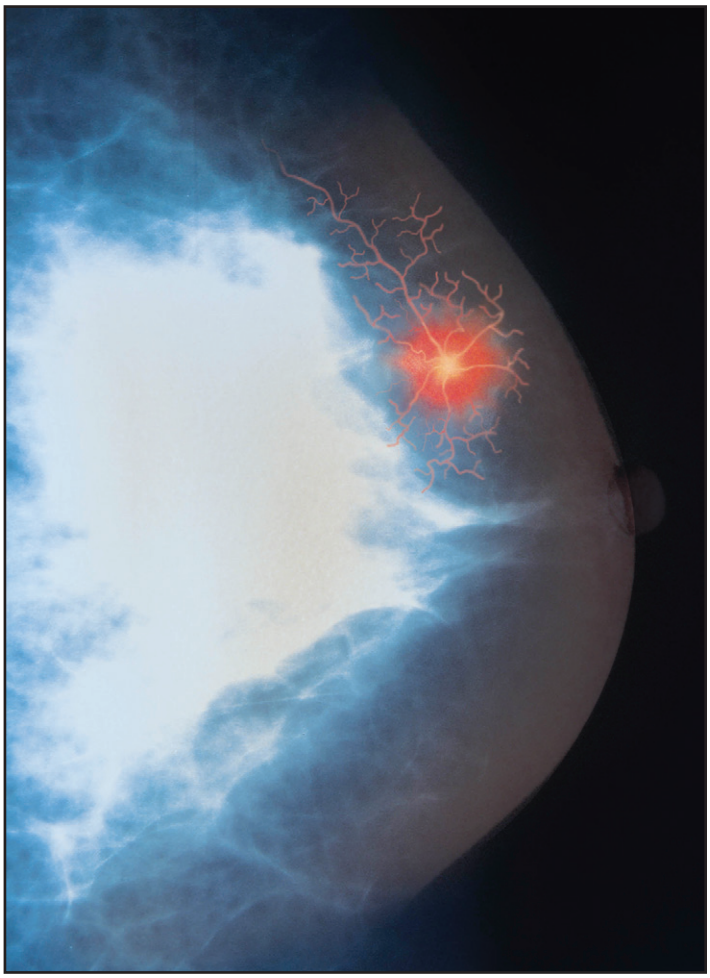
PO BOX 12233 • Research Triangle Park, NC 27709
Phone: 919.541.3345 • http://www.niehs.nih.gov

Printed on recycled paper.
October 2012

NIH...Turning Discovery Into Health®

Study volunteers provide samples of their blood, urine, toenail clippings, and household dust, which may be analyzed for pesticides, heavy metals, and other environmental chemicals that may be linked to breast cancer development. The researchers will also look for specific gene variations that may predispose a woman to the effects of cancer-causing agents. Women enrolled in the study also complete detailed questionnaires about their health history, past environmental exposures, and lifestyle. The participants then complete yearly follow-up questionnaires to account for changes in their health status or environmental exposures.

Additionally, with funding support from the Susan G. Komen for the Cure foundation, NIEHS was able to successfully enroll 1,500 families into the Two Sister Study. Sister Study participants, whose sister had breast cancer under age 50, and their available biological parents were invited to participate in this family-based study. The study aims to investigate the genetic and environmental factors that influence young-onset breast cancer.



Discovery of the BRCA1 Gene

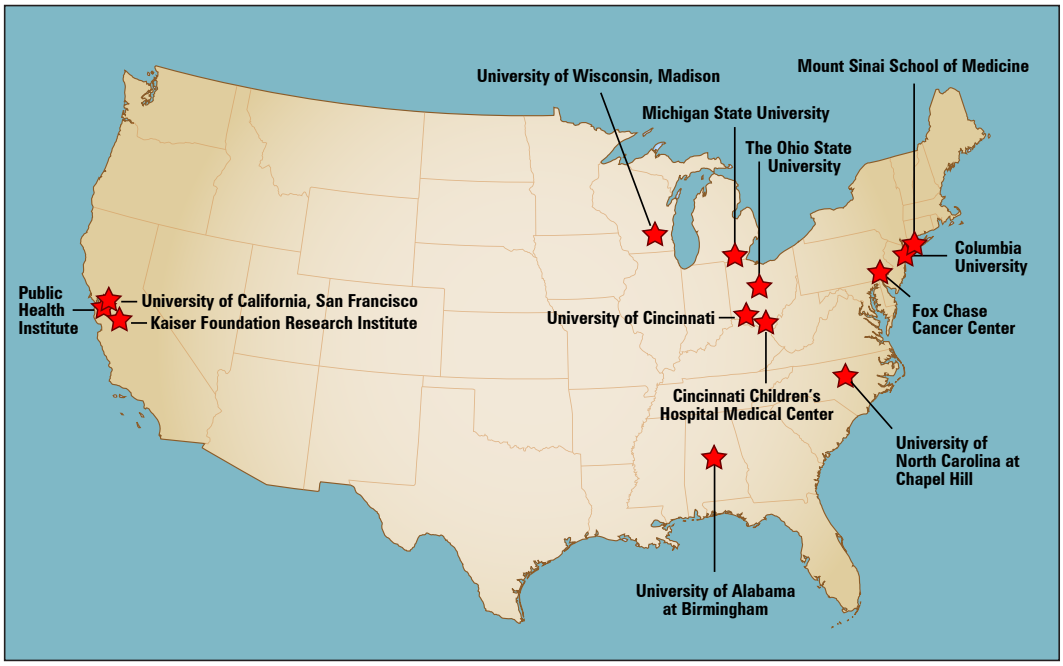
The impact of family history on breast cancer risk suggests that genetic factors play an important role in breast cancer susceptibility. Researchers are just beginning to understand how changes in certain genes can impair the gene's ability to control cell growth and division, causing normal breast cells to become cancerous. In 1994, NIEHS scientists collaborated with researchers from the University of Utah Medical Center to identify a gene called BRCA1 that, when defective, can predispose a woman to hereditary breast and ovarian cancer.[1] Diagnostic tests can now identify women who have inherited defective copies of the gene and are more likely to develop breast cancer.

Although genetics is an important contributor to breast cancer development, twin studies conducted by scientists in Scandinavia showed that inherited factors accounted for only 27 percent of breast cancer risk.[2] Another study shows that the breast cancer rates of descendants of Japanese women, who migrate to the United States, become similar to the higher breast cancer rates of Western women within one or two generations.[3] These findings point to the significant role played by environmental factors in determining breast cancer susceptibility.

Breast Cancer and the Environment Research Program

During early childhood and adolescence, the breast tissue is developing and maturing, and recent studies suggest that environmental exposures, such as certain chemicals, diet, and social factors, during these critical stages of development, may affect breast cancer risk later in life.

In an effort to uncover the links between early environmental exposures and cancer risk throughout the course of life, NIEHS is partnering with the National Cancer Institute to support the Breast Cancer and the Environment Research Program (BCERP). The BCERP supports transdisciplinary research on the interaction of chemical, physical, biological, and social environmental factors with genetic factors during specific developmental windows of susceptibility. The program's network of scientists, clinicians, and community partners are working in close collaboration on two different approaches — one focusing on puberty in young girls and the other examining other critical windows of susceptibility.



Breast Cancer and the Environment Research Program

The Puberty Studies are investigating and identifying predictors of early-onset puberty, by studying 1,200 young girls, aged 6 to 8 at the time of enrollment. The girls have periodic visits to assess hallmarks of pubertal development and changes in exposures of interest. The underlying rationale for this study is that early sexual maturation is associated with increased risk of breast cancer, and this may represent a critical period in establishing long-term breast cancer risk. Researchers are focusing on environmental exposures, including chemicals in personal and household products that may be hormonally active; lifestyle factors, such as food intake and physical activity; body size and development; and psychosocial factors.

Another component of the program, called the Windows of Susceptibility Studies, is exploring other developmental periods throughout the life span, including *in utero* and menopause. These investigations could be informative, especially in light of novel findings of the effects of diet, hormone replacement therapy, and long-term exposure to agents, such as endocrine disruptors, in adults, as well as children. Using basic science techniques in laboratory animals, cell cultures, and epidemiological and population studies, researchers are looking how the environment interacts with a person's genes to affect breast cancer risk. There are also studies looking at how multiple generations can be affected through an individual's exposure, for example, how the mother's exposure may affect her child's susceptibility to breast cancer.

Throughout the BCERP, researchers are collaborating with breast cancer advocates and others to build and promote partnerships with community members, public health practitioners, policymakers, and other stakeholders. Across the board, the research findings are being developed into public health messages designed to educate young girls and women about the roles of the environment in breast cancer development, and the importance of reducing their exposures.

Chemical Exposures in Human Populations

In some regions of the country where there is an unusually high incidence of breast cancer, environmental factors have been targeted as a possible cause for this increase. During the 1990s, NIEHS and the National Cancer Institute cofunded the Long Island Breast Cancer Study Project, one of the largest and most comprehensive studies ever conducted on the environmental causes of breast cancer, to investigate the high rate of breast cancer in Long Island, New York.

In the study, scientists focused their investigation on three widespread pollutants to which many of the Long Island residents had been exposed — organochlorine pesticides, including DDT and its metabolite DDE; polychlorinated biphenyls, toxic compounds used in electrical transformers; and polycyclic aromatic hydrocarbons (PAHs), a primary component of urban air pollution. Although there was some evidence of a modest increase in the risk of breast cancer from PAH exposure, the researchers did not identify any environmental factors that could be responsible for the high incidence of breast cancer in the Long Island area.[4] In a separate study conducted on Long Island women, researchers at Stony Brook University found no association between exposure to electromagnetic fields from residential power use and breast cancer risk.[5]

Cancer-causing Substances

Scientists are particularly interested in whether exposure to naturally occurring and synthetic chemicals may influence breast cancer risk. This includes exposure to chemicals in the air we breathe, the food and beverages we consume, and the chemicals that come in contact with our skin.

The National Toxicology Program, an interagency program headquartered at NIEHS that evaluates agents of public health concern, has listed six substances in its Report on Carcinogens (RoC) that cause or may cause breast cancer in humans.[6] These include diethylstilbestrol, a synthetic form of estrogen that was used to prevent miscarriages; steroidal estrogens used for menopausal therapy; X-ray and gamma radiation; alcoholic beverages; tobacco smoking; and the sterilizing agent, ethylene oxide.

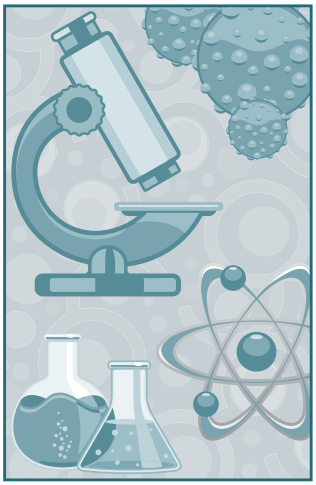
The RoC also lists over 60 substances that have been shown to cause mammary gland cancer in laboratory animals, including food additives or contaminants, such as byproducts from cooking meats at high temperatures; pharmaceuticals; consumer or manufacturing products, such as flame retardants, chemical solvents, and dyes; industrial chemicals used to make rubber; vinyl and polyurethane foams; pesticides; and environmental pollutants formed largely from burning fuels. Most of these substances also caused tumors at many other tissue sites besides the mammary gland. Few studies in humans have evaluated whether these substances are risk factors for breast cancer, and designing these studies in humans can be challenging.

Additionally, NIEHS in-house researchers are finding that early life exposures to some chemicals can alter rodent mammary gland development, disrupt lactation, and may increase susceptibility to breast cancer. The timing of exposures appears to be a critical element in development of adverse outcomes. Knowing that mammary gland development and tumor types are similar between rodents and humans, the researchers are working to develop and encourage the use of mammary gland assessments in developmental research studies, chemical test guidelines, and risk assessments.[7]

More research is needed to pinpoint the environmental and genetic factors that determine breast cancer susceptibility. Once scientists can identify the elements that are associated with cancer risk, appropriate interventions and precautions can be designed for those who are most likely to develop the disease.

Human Studies

Animal Studies



Laboratory Studies

[1] Miki et al. 1994. A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science 266(5182):66-71.

[2] Lichtenstein et al. 2000. Environmental and heritable factors in the causation of cancer: analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med 343(2):78-85.

[3] Shimizu et al. 1991. Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. Br J Cancer 63(6):963-966.

[4] Gammon et al. 2002. Environmental toxins and breast cancer on Long Island. I. polycyclic aromatic hydrocarbon DNA adducts. Cancer Epidemiol Biomarkers Prev 11(8):677-685.

[5] Schoenfeld et. al. 2003. Electromagnetic fields and breast cancer on Long Island: a case-control study. Am J Epidemiol 158(1):47-58.

[6] HHS (U.S. Department of Health and Human Services). 2011. Report on Carcinogens, Twelfth Edition. Washington, D.C.: U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program. Available: http://ntp.niehs.nih.gov/go/roc12 [accessed 2 October 2012].

[7] Rudel et al. 2011. Environmental exposures and mammary gland development: state of the science, public health implications, and research recommendations. Environ Health Perspect 119(8):1053-1061.