



University of Cincinnati Press Release
Lung Cancer

A national research consortium led by a University of Cincinnati (UC) Medical Center scientist has found evidence of a genetic cause for lung cancer.

This is the first suggestion that lung cancer, long tied to cigarette smoking and other external causes, might also be an inherited disease.

With over 160,000 deaths expected in 2004, lung cancer is by far the leading cause of cancer death in the United States, and the survival rate after five years is only 15 percent.

The findings are reported in the August 22 issue of *American Journal of Human Genetics* by a multi-institution team known as the Genetic Epidemiology of Lung Cancer Consortium (GELCC), headed by Marshall Anderson, PhD, of UC Medical Center's Department of Environmental Health. UC's Susan Pinney, PhD, collaborated with Dr. Anderson in this research, which was funded by the National Cancer Institute (NCI).

Although a specific lung cancer gene has yet to be identified, the researchers say they have found a major lung cancer "susceptibility locus" on chromosome 6, and evidence of a susceptibility region on three other chromosomes.

"This is a very important first step in identifying the actual gene or genes that predispose a person or a whole family to lung cancer," Dr. Anderson says. "Identifying these genetic regions has exciting potential for patient care."

"The discovery of genes for other types of cancer has led to better understanding of those diseases, which in turn can lead to better strategies for treatment and prevention. We hope that uncovering a gene or genes responsible for lung cancer will do the same for this devastating disease."

In terms of cancer prevention, Dr. Anderson says, "We'll be able to determine whether a family has a bad gene, then tell those who carry it to avoid any form of smoking, and possibly even environmental smoke."

"In this case," adds Dr. Pinney, "unlike genetically linked breast cancer, for which there is no known cause that is a modifiable health behavior, family members actually will be able to do something to reduce their risk for the disease."

Genes, which are located in fixed positions on the cell's chromosomes, carry the DNA code that determines inherited characteristics, including a risk of certain diseases.

The region of the chromosome where the lung cancer markers were found contains about 50 genes, whose activity in several types of cancer cells appears to be decreased. The researchers also found several genes in this area that are believed to be involved in tumor suppression and cell growth, which could cause the decreased genetic activity.

The research team studied 52 families, including 12 from Cincinnati, that had at least three immediate family members affected by lung, throat or laryngeal cancer. Of these families, 23 had five or more affected members in at least two generations.

Most of the Cincinnati families were referred by the Oncology Hematology Care Inc. medical practice. Others were referred by Greater Cincinnati hospitals and by ALCASE, a national organization for lung cancer education, support and advocacy.

The researchers used 392 already identified genetic markers to compare gene profiles of affected and non-affected family members. They found strong evidence that the development of lung cancer was inherited with a marker on chromosome 6. Markers on chromosomes 12, 14 and 20 also indicated a possible connection to lung cancer susceptibility, but the evidence was not as strong.

“The importance of these findings,” says Dr. Anderson “is that they clearly demonstrate certain families are at high risk for lung cancer, comparable to the family link for breast, prostate, and colon cancer, and we have identified the susceptibility locus.”

The data show that family members who carry this marker, and by inference a gene, are much more likely to develop lung cancer from cigarette smoking than non-carriers.

In non-carriers who smoke, says Dr. Anderson, the risk of lung cancer increases with the number of cigarettes they smoke and the length of time they have been smoking.

“Carriers, however, appear to be at very high risk from even small amounts of cigarette smoke or even environmental smoke,” says Dr. Anderson, “and that’s a very important public health issue.”

Although only 18 percent of heavy smokers get lung cancer, which indicates a degree of variability in susceptibility to lung cancer, Dr. Anderson adds, “We have identified a sub group that’s at very high risk.”

The next step, says Dr. Anderson, is to examine the chromosome 6 segments more closely in order to locate the exact gene or genes that cause lung cancer. Only after a gene is identified will the scientists be able to determine the percentage of high-risk lung cancer families that carry the gene on chromosome 6.

“We’re confident the gene is there,” Dr. Anderson says. “We’ve seen evidence with every analytical model we’ve used. We’ll find it.”

The GELCC researchers include Susan Pinney, PhD, University of Cincinnati, Jonathon Wiest, PhD, and Daniela Seminara, PhD, NCI; Joan Bailey-Wilson, PhD, NHGRI; Christopher Amos, PhD, M.D. Anderson Cancer Center; Gloria Petersen, PhD, and Mariza de Andrade, PhD, Mayo Clinic; Pamela Fain, PhD, University of Colorado; Ann Schwartz, PhD, Karmanos Cancer Institute; Ming You, PhD, Washington University, St. Louis; John Minna, MD, and Adi Gazdar, MD, University of Texas Southwestern Medical Center; Henry Rothschild, MD, Louisiana State University Health Sciences Center; and Teresa Coons, PhD, Saccomanno Research Institute.

Dr. Pinney emphasizes that the researchers continue to search for families at high risk for lung cancer. “We’re especially looking for people with three relatives, living or deceased, who have had lung cancer among their parents, grandparents, aunts and uncles, or their own brothers and sisters,” she says.

To participate in the Genetic Epidemiology of Lung Cancer Consortium study, log on to the GELCC Web site at www.eh.uc.edu/gelcc, or phone 513-558-3120, 513-558-4028 or 513-558-0559. For further information see the ALCASE Web site at www.alcase.org