Genes linked to 50% of colorectal cancers, researchers say

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By Sue Miller
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An inherited susceptibility to polyps and cancer of the colon and rectum occurs in about a third of white Americans and contributes to more than 50 percent of all cases of such cancers, a new study shows.

In a report published today in the New England Journal of Medicine, University of Utah Medical Center scientists say they believe they have discovered the existence of one or perhaps more genes that put people at higher than normal risk of developing these cancers.

Until recent times, researchers have believed that colon and rectal cancer and benign growths known as polyps that can become cancerous were the product of the environment and primarily a dietary problem.

Now, the evidence emphasizes that the cancers of the lowest portion of the digestive tract arise from a combination of genetic and environmental factors.

The study, which was done in Utah where the population is primarily white and descended from British and Northern European immigrants, was based on colon exams of 670 people in 34 families with histories of colon and rectalcancer and polyps.

Dr. Lisa A. Cannon-Albright, who led the study, said that at least 53 percent of colorectal cancer had a hereditary susceptibility to the disease.

Colorectal cancer, a leading form of malignant disease in humans, strikes an esimated 147,000 Americans annuall, claiming the lives of about 60,00. As many as two out of three patients could be saved if these cancers were found earlier and treated promptly, according to the American Cancer Society.

The Cannon-Albright researchers said their findings reinforce suggestions that relatives of patients with colorectal cancer should be screened in doctors' offices for growths.

The ACS recommends that people older than 50 should have stool tests annually for signs of cancer and they should have proctosignoidoscopy — examination of the colon with a lighted tube — every three to five years.

In the light of the new findings, some specialists are urging exams as early as age 40 in people who have relatives with colon or rectal cancer.

The Cannon-Albright study concluded that 32 percent of all white Americans inherit one or two copies of a dominant gene that makes them susceptible to polyps. There is a 63 percent chance that people with the gene will get polyps by age 80.

The researchers did not estimate the chance that people who carry the gene will actually get colon or rectal cancer.

"We are not saying that genes are the only thing responsible for this, but only particular individuals who have inherited the susceptibility are at increased risk," Cannon-Albright said.

"Then, other factors, such as diet, act upon those people to transform polyps into colorectal cancer."

Too much fat and too little fiber traditionally have been blamed as the diet culprits that lead to colorectal cancer.

In a separate NEJM report, a team of researchers from the Johns Hopkins Oncology Center and from the University of Utah School of Medicine and the University of Leiden in the Netherlands said they have identified four specific genetic alterations they believe are in part responsible for colon and rectal cancer.

One alteration occurs in a tiny segment of an oncogene called "ras," associated with the growth of a small polyp into a larger and more dangerous one. Oncogenes are genes that have the potential to transform normal cells into cancerous cells.

"Ras" oncogenes, when altered in this way, can dramatically affect the growth of cells. The other alterations involve the loss of tumor suppressor genes that normally are present in cells and are thought to inhibit abnormal growth. In cancer cells, these genes are sometimes missing, resulting in an uncontrolled multiplication of cells.

Dr. Burt Vogelstein, an associate professor of oncology at Hopkins, who headed the research team, believes that one of these genes is lost early in tumor development while the other two are usually lost at later stages, possibly resulting in the conversion of a large polyp into a full-blown cancer.

"There's no doubt that these alterations are important in the development of cancer," Vogelstein said, "because when they occur, they are present in every cell on the tumor."

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