Scientists report major advance in search for genes associated with colon cancer

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A 10-year study involving thousands of Israeli Jews and Arabs, led by researchers from American and Israeli institutions, has yielded important new information in the search for the genes that make a person more likely to develop colon cancer.

In a paper to be published in the July issue of *Cancer Biology and Therapy*, the international research team reports finding a significant link between genetic variation in a single region of human chromosome 8 and the risk of colorectal cancer.

The link was found by detailed comparisons of genetic material from thousands of colon cancer patients and non-patients, and by evaluating the incidence of colon cancer among the immediate family members of colon cancer patients.

In all, people who carry the specific genetic variation, called a marker, were found to be 23 percent more likely to have colon cancer than individuals without the marker. The researchers estimate that this single genetic variation might account for 14 percent of colorectal cancer cases in Israel, where colon cancer is the leading cause of cancer deaths. The specific marker is called the C allele of rs10505477.

Three other research teams are reporting similar findings today in the journal Nature Genetics, having simultaneously found their way to the same small area of chromosome 8, called 8q24, in the search for colon cancer genetic links. The fact that these studies were performed among

other populations around the world suggests that this one genetic marker is highly influential across ethnic groups.

The new Cancer Biology and Therapy paper is by an international group of scientists from the University of Michigan Medical School and U-M School of Public Health, the Catalan Institute of Oncology in Spain, the CHS National Israeli Cancer Control Center and Technion - the Israel Institute of Technology.

It's the product of an ongoing Michigan-Israel collaboration, the Molecular Epidemiology of Colorectal Cancer project, which for 10 years has searched for clues to colon cancer's genetic roots using samples from large numbers of people in Israel with known ancestral heritage. The project is funded by the National Cancer Institute, with additional funding from the Irving Weinstein Foundation.

The researchers compared the genetic makeup and family history of more than 1,800 colorectal cancer patients with that of 1,900 healthy people with the same breakdown of age, gender and ethnicity - either Ashkenazi Jew, Sephardic Jew or Arab/non-Jew. Samples of tumor tissue from many cancer patients were also tested. The genetic link between the marker and colon cancer was especially strong among patients diagnosed with colon cancer at a young age, under 50 years.

Stephen Gruber, M.D., Ph.D., the co-leader of the Michigan-Israeli team and first author of the new paper, says that the new finding is particularly interesting when considered alongside recent discoveries in the genetics of prostate and breast cancer.

"The same genetic region that predisposes to colon cancer has also recently been shown to be an important region predisposing to breast cancer and prostate cancer," he says. "The specific genetic cause for this joint susceptibility to three different cancers has not yet been

discovered, but several groups are working to close in on the mechanism that might cause these cancers."

Gruber is an associate professor of internal medicine and of human genetics in the U-M Medical School, and of epidemiology in the U-M School of Public Health. He directs the Cancer Genetics program in the U-M Comprehensive Cancer Center, which focuses on inherited cancer risks.

Genetic discovery in Israel through MECC has already proven highly informative. Senior author Gad Rennert M.D., Ph.D., of the Carmel Medical Center and the B. Rappaport Faculty of Medicine at Technion in Haifa, Israel, says "The study of populations in Israel has been shown to be exceptionally fruitful in contributing to knowledge about the genetics of leading cancers. This is due to the unique characteristics of the population and our ability to study it in a representative manner."

Unraveling the mysteries of the susceptibility to disease is moving rapidly since the publication of the complete sequence of the human genome in 2003. Says Gruber, "The mystery of the relationship between our genetic code and disease is now starting to become clear, and many scientists are turning to the same chapter to find important clues to colorectal cancer." He and his colleagues plan to continue their effort to zero in on the genetic variations involved in cancer.

While there is not yet a screening test for the genetic variation that was pinpointed in the study, Gruber and his co-authors emphasize that genetic testing is available for other known genetic variations linked to colorectal cancer. People with a strong family history of colon cancer, especially cases that began when relatives were younger than age 50, should get genetic counseling and have colonoscopies or other screening tests starting earlier in life than age 50.

“Colon cancer is one of the most common cancers in the United States, and the good news is that it’s largely preventable with early screening,” says Gruber. The American Cancer Society estimates that some 150,000 new cases of colon cancer will be diagnosed in 2007, and more than 50,000 deaths from colorectal cancer will occur.

Although most cancers are not "inherited," some families are particularly susceptible to cancer and may benefit from early detection or other risk reduction strategies. People concerned about a family history of cancer, or those who have been diagnosed with colon cancer before age 50 or after having two or more relatives diagnosed with the disease, should talk to their doctor about the possible benefits of genetic counseling, Gruber says. Counseling can be done for both patients and family members.

Source: University of Michigan