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Gene variations alter risk of esophageal cancer

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Variations in a common gene pathway may affect esophageal cancer risk, a dangerous and rapidly increasing type of cancer, according to research by scientists at The University of Texas M. D. Anderson Cancer Center.

Results of the study, which is the first to look at the association between variations in genes related to microRNAs (miRNAs) and esophageal cancer, are published in the November issue of *Cancer Prevention Research*, a journal of the American Association of Cancer Research.

"Previous research has shown miRNAs control approximately one-third of human genes and may play a part in cancer risk," said the study's lead author, Xifeng Wu, M.D., Ph.D., a professor in the Department of Epidemiology at M. D. Anderson. "But whether genetic variants of miRNA-related genes influence esophageal cancer has largely remained unknown."

To examine the potential roles of these variations in esophageal cancer, researchers looked at the relationships among 41 single-nucleotide polymorphisms (SNPs) in 26 miRNA-related genes and risk of esophageal cancer. SNPs are places in the human genome that vary by a single DNA chemical building block or nucleotide.

Seven genotypes were significantly associated with esophageal cancer risk, and four more showed at least a borderline significance. The risk of esophageal cancer became higher in correlation to an increase in the

number of the unfavorable genotypes present.

"This research showed not only that a single gene contributes to the risk of esophageal cancer, but more importantly that the joint effect of several genetic elements can increase risk," said the study's first author, Yuanqing Ye, Ph.D., an instructor in the Department of Epidemiology at M. D. Anderson.

Esophageal cancer ranks sixth in cancer-related deaths worldwide, and it is becoming more common. According to the American Cancer Society, more than 16,000 people will be diagnosed and more than 14,000 people will die of the disease in the United States this year.

"Incidence of esophageal cancer has increased six-fold in the past three decades, and the survival rate is poor," Wu said. "MicroRNAs are exciting because they can modulate the expression of so many human genes."

Major risk factors for esophageal cancer include tobacco smoking, alcohol consumption and reflux disease. The high prevalence of these risk factors in the general population and rare occurrence of this disease provide a clue that genetic predisposition to the disease may play an important role.

Researchers recruited 346 people who were newly diagnosed with esophageal cancer at M. D. Anderson and matched them by age, gender and ethnicity to 346 people without cancer. Only results for Caucasians were reported because of the low numbers of other races that enrolled.

While patients tended to be current smokers and have higher body mass index (BMI), there was no difference between the two groups in alcohol consumption.

One of the most notable findings was a SNP in the mir423 region, which was associated with a significantly lower esophageal cancer risk. The protective effect was significant for smokers and nonsmokers 64 years old and younger, but not for older subjects.

Mir423 also is found in leukemia cells and is altered significantly in other diseases including heart disease and Alzheimer's disease.

Future large-scale, multi-center studies are necessary to confirm these findings, Wu said.

"Our ultimate goal is to construct a comprehensive risk prediction model that includes not only genetic factors, but epidemiological and clinical variables as well, in hopes of predicting the probability of developing esophageal cancer in general population," she said.

Source: University of Texas M. D. Anderson Cancer Center