Genetic variations in miRNA processing pathway and binding sites help predict ovarian cancer risk

April 19 2009

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Genetic variations in the micro-RNA (miRNA) processing pathway genes and miRNA binding sites predict a woman's risk for developing ovarian cancer and her prospects for survival, researchers from The University of Texas M. D. Anderson Cancer Center reported at the 100th annual meeting of the American Association for Cancer Research.

"We found a gene dosage effect, the more unfavorable variations a woman has, the greater her ovarian cancer risk and the shorter her survival time," said senior author Xifeng Wu, M.D., Ph.D., professor in M. D. Anderson's Department of Epidemiology. Median survival, for example, ranged from 151 months for women with fewest unfavorable variations to 24 months for those with the most.

Several variations also indicate likely response to platinum-based chemotherapy.

"Our findings have the potential clinical application of indicating a patient's prognosis and showing who will respond to different therapies by analyzing a single blood sample," Wu said. "We also will incorporate this genetic information with epidemiological information to build a comprehensive model to predict susceptibility to ovarian cancer."

The team chose the miRNA processing pathway because it is crucial to production of miRNAs, the small molecules that regulate between one third and half of all genes. The researchers also chose the binding sites on host genes where miRNAs exert their effects on gene expression.

They analyzed 219 potential functional single nucleotide polymorphisms (SNPs) - variations of a single DNA building block in a gene - in eight genes that process miRNA and at the miRNA binding sites of 129 cancer-relevant genes. The study examined genetic information from 417 cancer patients and 417 healthy controls. To minimize the possible confounding effects of ethnicity, 339 Caucasian cases and 349 controls were analyzed.

They discovered 12 SNPs to be significantly associated with ovarian cancer risk. Moreover, compared to women with five or fewer unfavorable genotypes, women with eight or more of these unfavorable genotypes were 4.5 times more likely to develop ovarian cancer and

women with six to eight unfavorable SNPs were at twice the risk.

The team also found 21 SNPs significantly associated with overall survival. Median survival was 151 months for women with six or fewer unfavorable variations; 42 months for those with seven to nine unfavorable variations; and 24 months for those with 10 or more. One of the outcome risk SNPs also was strongly associated with platinum-based chemotherapy response, with those having the SNP 3.4 times less likely to respond to chemotherapy.

Wu collaborated with Dong Liang, Ph.D, in the College of Pharmacy and Health Sciences, Texas Southern University, and Karen Lu, M.D., professor in M. D. Anderson's Department of Gynecologic Oncology, on this study.

The unique study was the first to examine the association of genetic variants related to miRNA with ovarian cancer risk, overall survival for ovarian cancer patients, and platinum-based chemotherapy response. Such a wide-ranging inquiry was made possible by M. D. Anderson's extensive clinical and genetic data sets, Wu said,

Source: University of Texas M. D. Anderson Cancer Center (news : web)