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Effect on breast tumors of DNA alternations in 3 genes described

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Cancer epidemiologists at the University at Buffalo have identified specific genes that are most likely to become cancer promoters when exposed to a process called DNA promoter hypermethylation.

Hypermethylation is a process that causes genes that promote normal cell growth to produce proteins that cause malignant behavior, or unregulated cell growth. Until now, data has been very limited regarding the mechanism and causes of hypermethylation, especially for hypermethylation in breast cancer. The purpose of the current study was to determine how DNA hypermethylation relates to other characteristics of breast tumors.

"It is well known that mutation in genes -- alterations in their sequence -- is one of the characteristics of tumors responsible for some of their disease properties," said Menghua Tao, Ph.D., research assistant professor of social and preventive medicine in the UB School of Public Health and Health Professions and first author on the study.

"In addition, it is now becoming clear that other changes in the DNA may also contribute to the development of cancer."

The researchers analyzed methylation status in three genes, known as E-cadherin, p16 and retinoic acid B2 receptor (RAR-B2), using tissue samples from 887 breast cancers. The samples were taken from women 35-79 years old who participated in the Western New York Exposures and Breast Cancer Study (WEB study). Extensive in-person interviews

were used to collect information on potential breast-cancer risk factors and confounding factors.

Results of the research were presented at the American Association of Cancer Research meeting held in Los Angeles in April.

"We found that hypermethylation of E-cadherin, but not of the other genes, was more likely to occur in estrogen receptor (ER)-negative than in ER-positive tumors," said Tao. ER-positive tumors are those that express receptors for the hormone estrogen. Such tumors respond to treatments that block these receptors.

"Similarly, hypermethylation of E-cadherin was more frequent among progestin receptor (PR)-negative cases," said Tao. "Compared to tumors that were both ER- and PR-positive, tumors that were both ER- and PR-negative were more likely to be E-cadherin hypermethylated.

"However, hypermethylation of E-cadherin, p16 and RAR-â2 was not associated with other clinicopathological features of breast cancer, such as tumor size, histological grade or nuclear grade.

"Our data suggested that promoter hypermethylation is common in breast cancer," Tao added. "Because promoter hypermethylation is potentially reversible, identifying cancers with different hypermethylation may have important consequences for breast-cancer treatment."

Source: University at Buffalo