MedicalXpress

Rating HPV biomarkers in head, neck cancers: Combinations work better than viral DNA in tumors alone

September 18 2012

Not all head and neck cancers are created equal. Those started by infection with the human papillomavirus are less often fatal than those with other causes, such as smoking. Detection of a reliable fingerprint for HPV could help patients avoid unnecessarily harsh treatment. A new study finds that while one popular biomarker for HPV is not a reliable predictor of mortality from the cancers alone, combinations of some biomarkers showed much more promise.

"Everybody who has studied it has shown that people with virally associated disease do better," said Karl Kelsey, aprofessor of epidemiology and pathology and laboratory medicine at Brown University, and corresponding author of the study in *Cancer Research*. "There are now clinical trials underway to determine if they should be treated differently. The problem is that you need to appropriately diagnose virally related disease, and our data suggests that people need to take a close look at that."

In the study, Kelsey and his multi-institutional team of co-authors measured the ability of a variety of biomarkers to predict mortality from head and neck squamous cell carcinoma (HNSCC). Their data came from hundreds of adult head and neck cancer patients in the Boston area that they have been tracking since late 1999. As part of that data set, they were able to look at blood serology and tumor tissue samples, and they interviewed participants about risk behaviors such as smoking and

drinking.

DNA alone not reliable

One of the most important findings of the study, Kelsey said, is that extracting and amplifying the DNA of HPV in tumors, a popular notion among doctors given its success in confirming HPV's role in cervical cancers, is not particularly helpful in predicting eventual mortality from head and neck cancer.

For example, among 94 patients for whom the researchers could assess the predictive value of all the biomarkers in the study, HPV DNA was present in tumors of 59 patients and absent in 35. Among the 59 who had the DNA, 23 of them, or 39 percent, had died. Among the 35 without the DNA, 13 of them, or 37 percent had died.

"You can't just do PCR [a DNA amplification technique] of the virus in the tumor and assume it means much," Kelsey said.

More promising combinations

Among several other potential HPV biomarkers in patients, the most reliable predictors of mortality turned out to be certain combinations of them, particularly antibodies to the E6 and E7 proteins that are expressed by the virus and have the effect of turning off cells' ability to suppress tumors.

Kelsey and his colleagues found that measuring blood serum levels of antibodies that respond to E6 and E7 helped to assign meaning to measures of HPV DNA in tumors. Among people who had both HPV DNA and E6/E7 measurements, those with HPV DNA in tumors who were E6/E7 negative died in 30 of 56 cases, while those with HPV DNA

in tumors who were E6/E7 positive died in only eight of 55 cases.

Levels of E6 and E7 antibodies in blood also proved telling in combination with staining tumors to detect the p16 protein, which indicates that tumor-suppression has been inactivated. Among patients in whom both those tests were both run, those with p16 overexpression who were E6/E7 negative had a much higher rate of death (11 in 17 cases) than people who did not overexpress p16 and were E6/E7 positive (3 in 9 cases) or those who overexpressed p16 and who were also E6/E7 positive (6 in 37 cases).

"Our study strongly suggests that the combination of detection of HPV 16 DNA in HNSCC tumors or p16 immunostaining with E6/E7 antibodies represents the most clinically valuable surrogate markers for the identification of patients with HNSCC who have a better prognosis," Kelsey and his co-authors concluded.

In a companion paper published simultaneously in Cancer Research another team found that measuring viral load and patterns of viral gene expression were also useful markers.

Provided by Brown University