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# Study examines biomarkers in HPV negative squamous-cell carcinomas of the head and neck

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A quartet of proteins that play critical roles in cell replication, cell death, and DNA repair could lead to better targets for therapy against treatment-resistant head-and-neck squamous cell cancers.

In a study to be presented at the AACR Annual Meeting 2014 on Tuesday, April 8, Ranee Mehra, MD, a medical oncologist who specializes in head and neck cancers at Fox Chase Cancer Center, and colleagues, showed a correlation between the expression levels of these proteins in head-and-neck cancers negative for human papilloma virus (HPV). These tumors have a poorer prognosis than HPV-positive head-and-neck cancers.

The cancers arise in the cells that line moist surfaces in the mouth, including the lips, tongue, and gums, as well as the throat, larynx, and sinuses. The National Cancer Institute reports that some 75 percent of these cancers are caused by tobacco and alcohol use—and that use of the two together are a greater risk than use of either separately.

Mehra's research could help determine potential treatments for head and neck cancers. "The ultimate goal would be to better understand a tumor's protein signature and underlying biology so that, in the future, we can better understand treatments are more likely to be beneficial to our patients with head and neck cancer."

She and colleagues looked at protein expression levels in samples from 101 cases of head-and-neck cancer banked from 1990 to 2002 in the Fox Chase tissue repository. One advantage of using this tissue, Mehra says, is that samples are cross-reference with patient treatment and survival data. Using tissue microarrays, which allow researchers to examine at a large number of samples at one time, the team looked for expression of ERCC-1, a DNA repair protein; survivin, a protein that inhibits programmed cell death or apoptosis; and two proteins active during cell division, Aurora A and phospho-Aurora A.

The research showed positive associations between expression of the repair protein ERCC1 and each cell-division protein, AuroraA (P

A review of a publically available database examining mRNA expression levels for the four proteins showed a highly significant correlation between Aurora A and survivin (P = .002), confirming the protein microarray findings.

Survivin expression may prove a marker for improved survival, especially in patients who were treated with surgery plus radiation, Mehra said. She found that tumors with less than a median level of survivin expression were associated with improved patient survival compared to tumors with more than a median level of survivin (P = .03).

ERCC1 is already a potential prognostic biomarker for survival among patients treated with radiation after surgery. In a study published in Clinical Cancer Research last year, Mehra and colleagues found lower levels of ERCC1 predicted improved survival among patients treated with radiation.

"We hope to understand how these various pathways and mechanisms interrelate with each others. Understanding those pathways would help guide future research," Mehra said.

Provided by Fox Chase Cancer Center