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Researchers identify genetic markers for aggressive head and neck cancer

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Scientists at Albert Einstein College of Medicine of Yeshiva University have identified genetic markers that signal poor outcomes for patients with head and neck cancer. These findings could one day lead to a genetic test that could help select or predict successful treatment options for patients with this type of cancer. The results were published in the *American Journal of Pathology*.

Head and neck cancer refers to tumors in the mouth, throat or larynx (voice box). Each year, about 40,000 men and women in the U.S. develop head and neck cancer, making it the sixth most common cancer in the U.S. Surgery, chemotherapy and/or radiation are the main treatment options but cause serious side effects: surgery may involve removing large areas of the tongue, throat, or neck and can affect appearance, and any type of therapy can cause swallowing or speech problems that can significantly affect quality of life. Despite curative treatment attempts, on average only about half of patients survive beyond five years after treatment. This is greatly affected by the size and location of the tumor.

The Einstein study focuses on microRNAs, a recently identified class of short RNA molecules that play key roles in regulating gene expression. Abnormal microRNA levels have been associated with all types of cancer yet examined.

In previous research, the Einstein scientists and other groups reported that approximately 50 specific microRNAs were expressed at higher or

lower levels in head and neck tumor cell lines compared with normal cells. In this study, the Einstein researchers, for the first time, have linked levels of specific microRNAs with tumor recurrence and poorer survival in head and neck cancer.

The Einstein team analyzed samples from 104 head and neck cancer patients from Montefiore Medical Center, The University Hospital and Academic Medical Center for Einstein. The patients were treated and followed over five years. At the time of cancer diagnosis and before any therapy, researchers removed samples tumor tissue from patients, as well as normal tissue adjacent to their tumor, and measured microRNA levels in the two types of tissue.

Patients who fared worst had the lowest levels of two particular microRNAs—miR-205 and let-7d—in their tumor tissue. Specifically, these patients were four times more likely to have an earlier metastasis or local-regional recurrence of their cancer than patients with higher levels of miR-205 and let-7d in tumor tissue.

These findings may eventually be put to practical use, allowing physicians to identify potentially aggressive head and neck cancers and choose the most appropriate treatment. "A biologic marker identifying aggressive tumors would allow us to direct therapy more appropriately, minimizing over or under-treatment," explained Richard Smith, M.D., the lead clinician on the paper. Dr. Smith is associate professor of clinical otorhinolaryngology-head & neck surgery and associate professor of surgery at Einstein, and vice-chair of otorhinolaryngology-head & neck surgery at Einstein and Montefiore.

"In addition, these molecules, or modified forms of these molecules, can potentially be used in treatment because their small size allows them to be reintroduced into cells with the possibility of altering the behavior of a tumor," says Geoffrey Childs, Ph.D., professor of pathology at

Einstein and corresponding author of the article.

"Our next steps are to confirm these results in a new patient population and to find additional markers that would allow us to develop a reproducible and accurate prognostic test," explained Nicolas Schlecht, Ph.D., assistant professor of epidemiology and population health, and of medicine at Einstein. Dr. Schlecht is also the Miriam Mandel faculty scholar in cancer research and a senior author of the paper.

More information: The paper titled "Low-Level Expression of MicroRNAs let-7d and miR-205 are Prognostic Markers of Head and Neck Squamos Cell Carcinoma" appeared in the March 2009 issue of the American Journal of Pathology and can be found at: ajp.amjpathol.org/

Source: Albert Einstein College of Medicine