

Genes signal late-stage laryngeal cancer, poorer outcome

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Researchers at Henry Ford Hospital have identified tumor-suppressing genes that may provide a more accurate diagnosis of disease stage and survival for laryngeal cancer patients than current standards.

The study finds genetic abnormalities of the ESR1 ([estrogen](#) specific receptor 1) gene and the HIC1 (hypermethylated in cancer 1) gene are predictors of late-stage laryngeal cancer and shorter survival, respectively, for patients with the disease.

Study results will be presented Wednesday, Oct. 7 at the American Academy of Otolaryngology-Head & Neck Surgery Foundation Annual Meeting & OTO EXPO.

"These two [genes](#) provide some insight into the biology of the tumor," says study senior author Maria J. Worsham, Ph.D., director of research in the Department of Otolaryngology at Henry Ford Hospital. "Loss of gene function as a result of abnormal methylation of promoter regions of tumor suppressor genes can be reversed by drugs that can restore normal gene function, opening the door to other treatment options for patients with laryngeal cancer."

Similar to previous studies on laryngeal cancer, the Henry Ford study also shows that African Americans are more likely to be diagnosed with late-stage laryngeal cancer.

This year alone, the American Cancer Society estimates 12,290 new cases of laryngeal cancer - cancers that start in the voice box - will be diagnosed.

Following diagnosis, the cancer stage is currently assessed based on tumor size and how far it's spread within the voice box, and whether the cancer has spread to lymph nodes or other organs. The stage (0-4) of the cancer helps health care

providers make a prognosis for survival and determine a possible course for treatment.

For the study, Henry Ford researcher and lead author Josena Stephen, M.D., and Dr. Worsham looked at 80 patients with laryngeal squamous cell cancer who were diagnosed between 1996 and 2008. Forty percent of the study group was African American.

Using tissue DNA samples the researchers examined the methylation status of 24 tumor suppressor genes and tested for the presence of the human papilloma virus (HPV). DNA methylation - a type of chemical modification of DNA where a methyl group (CH₃) can be added (hypermethylation) or removed (hypomethylation) - allows the researchers to look for genetic abnormalities within tumor samples.

The study found:

- Abnormal DNA methylation of ESR1 predicted late stage disease.
- African Americans are more likely to have advanced stage disease than their Caucasian counterparts, a finding consistent with previous research.
- Abnormal DNA methylation of HIC1, late stage disease, and vascular invasion were predictors of shorter survival.
- The median survival for patients in the study group was 4.2 years.
- HPV was much higher in this group of patients (37 percent), supporting the role of HPV in laryngeal cancer.
- The majority of patients were either current or past smokers and alcohol users, again

confirming the role these factors play in laryngeal cancer.

"When this research crosses from the lab to clinical care, the contribution of specific gene changes will assist in improving the accuracy of cancer staging and length of survival for laryngeal cancer patients," explains Dr. Worsham.

"So if a patient comes in with stage 1, based on current standards, and then we find methylation of ESR1, the patient may have underpinnings of a more aggressive tumor with characteristics that are more in line with a stage 3 or stage 4 diagnosis, refining treatment options."

Source: Henry Ford Health System ([news](#) : [web](#))

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