

Large study uncovers molecular alterations in head and neck cancers

January 28 2015



TCGA researchers have uncovered new details about the potential role of the human papillomavirus in head and neck cancers. HPV-related head and neck cancers have been growing in number. Credit: Ernesto del Aguila, NHGRI

Investigators with The Cancer Genome Atlas (TCGA) Research Network have discovered genomic differences - with potentially important clinical implications - in head and neck cancers caused by

infection with the human papillomavirus (HPV). HPV is the most common sexually transmitted virus in the United States, and the number of HPV-related head and neck cancers has been growing. Almost every sexually active person will acquire HPV at some point in their lives, according to the Centers for Disease Control and Prevention.

The researchers also uncovered new smoking-related cancer subtypes and potential new drug targets, and found numerous genomic similarities with other cancer types. Taken together, this study's findings may provide more detailed explanations of how HPV infection and smoking play roles in head and [neck cancer](#) risk and disease development, and offer potential novel diagnostic and treatment directions.

The study is the most comprehensive examination to date of genomic alterations in head and neck cancers. The results were published online Jan. 28, 2015 in the journal *Nature*. TCGA is jointly supported and managed by the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI), both parts of the National Institutes of Health.

The U.S. Food and Drug Administration-approved HPV vaccines should be able to prevent the cancers caused by HPV infection in head and neck cancers and elsewhere, including anal cancer, whose incidence has also been increasing. However, these vaccines work by preventing new infections, and the long interval between infection and cancer development make it important to understand the molecular changes that bring about these HPV-positive head and neck cancers - as well as those that lead to the HPV-negative cancers - and to develop new approaches for treating them.

"The rapid increase in HPV-related head and neck cancers, noticeably in oropharyngeal tumors, has created an even greater sense of urgency in the field," said D. Neil Hayes, M.D., M.P.H, senior author of the study

report and associate professor of medicine at the University of North Carolina (UNC) and the UNC Lineberger Cancer Center at Chapel Hill. Oropharyngeal cancer starts in the oropharynx, which is the part of the throat just behind the mouth. "We're uncovering differences between tumors with and without HPV infection, and these new data are allowing us to rethink how we approach head and neck cancers."

In the study, researchers performed genomic analyses on 279 tumors - head and neck squamous cell carcinomas (HNSCC) - from untreated patients. Approximately 80 percent of tumor samples were from individuals who smoked. The majority of samples were oral cavity cancers (61 percent) and larynx cancers (26 percent).

While only about 25 percent of head and neck cancers are linked to HPV infection, TCGA researchers confirmed that many patients with HPV-associated tumors have specific alterations of the gene FGFR3 and mutations in the PIK3CA gene, which are also found in a much broader set of mutations in smoking-related tumors. In contrast, while the EGFR (epidermal growth factor receptor) gene is frequently altered in HPV-negative tumors in smokers, it is rarely abnormal in HPV-positive tumors. Such insights may help in developing potential therapies and biomarkers, noted Dr. Hayes.

Head and neck cancers comprise a constellation of tumors of the mouth, throat, larynx, nasal cavity, salivary gland and elsewhere that have frequently been attributed to tobacco and alcohol use in most patients. Some 90 percent are [squamous cell carcinomas](#), which occur in the surface layers of cells in the body. An estimated 55,000 people developed head and neck cancer in the United States in 2014. Approximately 12,000 Americans die from the diseases each year. Head and neck cancers are common worldwide, with more than 600,000 cases diagnosed each year.

"The rising worldwide incidence of head and neck cancers makes these types of large integrated genomic analyses by TCGA vital to establish a more detailed understanding of disease causes and behavior, and for the development of new treatment approaches," said NIH Director Francis S. Collins, M.D., Ph.D.

Scientists found that more than 70 percent of head and neck cancers had alterations in genes for growth factor receptors (EGFR, FGFR, IGFR, MET, ERBB2, DDR2), signaling molecules (PIK3CA, HRAS) and cell division regulation (CCND1). These genes may play roles in pathways that control cell growth and proliferation, and for which therapies are either available or in development.

The investigators also discovered new clues about drug resistance in head and neck cancers. They found that genes affecting about 40 percent of such cancers form key parts of a pathway that helps determine cell survival and drug resistance. They showed that extra copies of the genes FADD and BIRC2, or mutations in or the absence of the CASP8 gene in smoking-related cancers - all which affect the process of programmed cell death - may underlie the resistance of cancer cells to current treatments. Similarly, the absence of the TRAF3 gene, or extra copies of a gene for the growth-promoting E2F1 protein in HPV-related cancers, may also increase resistance.

The findings showed similarities between [head and neck cancer](#) genomes and other cancers, including squamous cell lung and cervical, indicating possible common paths of cancer development, and potential treatment opportunities. "It is surprising to see that head and neck tumor genomes are remarkably similar to cervical and squamous lung cancer genomes. They are from very different organs, but they show similar losses and gains of genetic material across tumors," Dr. Hayes noted. These common genetic abnormalities belong to a pathway that protects cells from damage and stress.

"These novel findings help establish a genomic map of various head and neck cancers, provide new insights into other similar cancers and may further our understanding of how viruses can impact disease," said NHGRI Director Eric D. Green, M.D., Ph.D.

"While many head and neck cancers are preventable, they are increasingly common throughout the world, and often challenging to effectively treat over the long term," said NCI Director Harold Varmus, M.D. "This type of broad analysis provides important new clues for future research and treatment directions."

More information: The Cancer Genome Atlas Research Network. Comprehensive genomic characterization of head and neck squamous cell carcinomas. *Nature*. Online January 28, 2015. [DOI: 10.1038/nature14129](https://doi.org/10.1038/nature14129)

Provided by NIH/National Human Genome Research Institute

Citation: Large study uncovers molecular alterations in head and neck cancers (2015, January 28) retrieved 10 April 2024 from <https://medicalxpress.com/news/2015-01-large-uncovers-molecular-neck-cancers.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--