Researchers Produce First Comprehensive Genomic Map of Head and Neck Cancers

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A team that includes scores of researchers from across the country representing dozens of universities and medical institutions has produced the most comprehensive integrative analysis yet of head and neck squamous cell carcinomas (HNSCCs), a particularly malignant and deadly type of tumor that accounts for roughly 3 percent of all cancers in the United States.

The study, published in today's issue of *Nature*, is the product of The Cancer Genome Atlas (TCGA), a federally funded project to identify and catalog errors in DNA that cause cells to grow uncontrollably, resulting in at least 200 forms of cancer and many more subtypes.

Scott M. Lippman, MD, director of the UC San Diego Moores Cancer Center, and Ezra Cohen, MD, professor and associate director for translational science at Moores Cancer Center, are members of the network.

The vast majority of head and neck cancers begin in the squamous cells that line the moist surfaces of the mouth, throat, larynx (voicebox), nasal cavities and salivary glands. Symptoms include lumps that do not disappear, a persistent sore throat, difficulty swallowing or a change in voice.

Men are more than twice as likely to develop a HNSCC as women. An estimated 52,000 Americans are diagnosed each year. Worldwide, HNSCCs affect more than 600,000 patients per year. Alcohol and tobacco use are considered the two most important risk factors. Smoking is implicated in the rise of HNSCCs in developing countries; the role of human papillomavirus (HPV) has emerged as an important risk factor affecting non-smokers.

HNSCCs are deadly. Despite surgery, radiation and chemotherapy, roughly half of all patients die of the disease, usually within two years of initial diagnosis. Except for HPV status, investigations of various molecular and clinical risk factors have produced limited clinical benefit.

Past genome-wide profiling of HNSCC cases has been limited in scope and detail. Researchers with TCGA sought to create a much more comprehensive picture of molecular alterations

associated with the disease, one that could help direct future treatments.

"Treatment at a comprehensive cancer center would offer potential advantages, including the ability to detect molecular alteration with accuracy and availability of novel therapies in clinical trials that can be personalized to a person's cancer but not yet approved," said Cohen.

The scientists profiled 279 patients with HNSCCs (with the ultimate goal of characterizing 500 patients with tumors). They found that HPV-associated tumors were dominated by specific mutations and molecular alterations that differed from those linked to smoking-related HNSCCs. Other subgroups of tumors were connected to other specific mutations or losses of cellular function.

The findings have clinical import. In most of the HNSCCs studied, the researchers identified therapeutic candidate alterations. That is, by correcting targeted mutations, they said it might be possible to improve treatments of diverse HNSCCs or possibly prevent them altogether.

"The next steps are to understand more comprehensively which molecular alterations affect prognosis," said Cohen, "and more importantly, how to best treat patients whose tumors harbor these mutations. These are challenges currently being addressed at Moores Cancer Center."

Co-authors are all members or affiliates of The Cancer Genome Atlas.

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Care at UC San Diego Health System

Head and Neck Cancers

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