

Know your biomarkers: How PRKD1 is linked to head and neck cancers (HNSCC)

COSMIC adds new oncogene that may be beneficial in diagnosing HNSCC

Head and neck cancers are a heterogeneous collection of malignancies of the tissues and organs of the head and neck. They affect the larynx, lips, mouth, nose, throat, and salivary glands. These cancers most commonly begin in the squamous cells that line the mucosal surfaces of the head and neck. Tobacco and alcohol use, which work synergistically, as well as HPV infections, are responsible for 70 –75% of cases.

Collectively these cancers are the seventh most common malignancy diagnosed worldwide. In the United States, head and neck cancers account for nearly 4% of all cancers.

However, their diverse phenotypic, etiological, and biological characteristics make treating them very challenging. The survival rates for many types of head and neck cancers have improved little over the past forty years.

The past decade has seen an unprecedented increase in our understanding of the biology and etiology of head and neck cancers, particularly, head and neck squamous cell carcinoma (HNSCC). Genome-wide sequencing projects have identified several recurrently mutated genes such as TP53, PIK3CA, NOTCH1, TP63 and CDKN2A.

Over the last decade, COSMIC has closely monitored—and manually and systematically curated— relevant head and neck cancer publications. COSMIC versions v48, v55-56 v64, v66, v83-84, v86-88, and v94 all had new, relevant head and neck cancer content.

The latest COSMIC release focuses on curating data on less common head and neck cancers, like those that develop in the salivary glands, sinuses, or muscle and bone in the head and neck. It adds curated variant and patient data from 56 publications, and it contains 129 new site-histology pairs accompanied by sequencing data.

With the volume of new studies and big data in COSMIC's centralized database, you now have access to the largest collection of head and neck cancers—and specific rarer cancer types within this class—based on curated mutations, individual and tumor features, and histopathology.

COSMIC's detailed content allows you to analyze synonymous vs. non-synonymous mutations, mutation rates, and base substitution frequencies. With it, you can also develop heatmaps of individual mutations present. Because COSMIC data contains structured sample and tumor characteristics, you can explore the changing mutational landscape if you overlay the mutation data with information about the curated patient population, such as risk factors like tobacco, alcohol and HPV. Frequency data across mutations and genes may reveal significantly mutated genes and relevant variants. In summary, the COSMIC centralized data allows users to define new potential head and neck cancer subtypes, unpick their etiologies, and understand the biological processes of specific cancer subtypes. Ultimately, you can define and optimize drug targets to improve the overall outcome of patients suffering from head and neck cancers.

The latest COSMIC release also comprehensively curates a new cancer gene, PRKD1, which was identified for defining a subset of head and neck cancers.

Protein kinase PRKD1

The Protein kinase D1 (14q12) gene has been added to the Cancer Gene Census as a Tier 2 gene for its role in fusions found in cribriform adenocarcinomas of the salivary gland. It is a serine/threonine protein kinase involved in several signalling pathways and many cellular processes including cell migration and differentiation, cell survival and regulation of cell shape and adhesion. COSMIC's head and neck cancer curation focus includes several papers reporting recurrent p.E710D mutations in the majority of polymorphous low-grade adenocarcinomas (PAC), the second most common malignant tumour of minor salivary glands (COSP [46408](#), [49877](#), [49498](#), [49500](#), [49502](#) & [PMID 3149293](#)). The p.E710D mutation is also found in a minority of cribriform adenocarcinomas of the salivary gland (CASG) (COSP [49877](#) & [PMID 3149293](#)), but not in more aggressive head and neck adenoid cystic carcinomas or pleomorphic adenomas (COSP [49498](#)), nor in other solid tumours and leukemias. A minority of PACs and a majority of CASGs carry fusions involving either PRKD1, 2 or 3. Other PRKD1 mutations are found at lower frequencies in a variety of other tumours including breast, leukaemia, lymphoma and gastric cancers.

References

1. PMID: 29607493.
2. 1. Ferlay J SJ, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.0. Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 2014. <http://globocan.iarc.fr/>.
3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. CA: A Cancer Journal for Clinicians 2021; **71** (1):7–33.
4. PMID: 19569190.
5. PMID: 21798893.