

# **Histamine Receptor 1 Expression is Increase in Head and Neck Cancer Tumors and is Associated with Poor Patient Outcomes**

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## **Introduction**

Histamine receptor 1 (HRH1) is a key mediator of histamine signaling in cells and influences several biological processes. While HRH1's role in normal physiology has been well explored, its role in cancer remains unclear. We focused on identifying the levels of HRH1 in head, neck, and throat cancers (HNSCC). In 2020, HNSCC was the 7th most common cancer globally with a 5-year survival rate of 68.5%.

## **Methods**

We examined transcriptomic data from HNSCC samples in the TCGA database, which harbors samples from a diverse cohort across sexes, ages, and ethnicities (n=520 tumor, n=44 normal). We also examined RNAseq from individuals with tongue cancer for whole tumors (n=26 tumor, n=12 normal) and single-cells.

## **Results**

We found that HRH1 was significantly upregulated in HNSCC tumors compared to normal tissues, with consistent findings across patients of all sexes, ages, and ethnicities. Interestingly, HRH1 was upregulated at all tumor stages. Methylation analysis revealed decreased levels of methylation in the HRH1 promoter, which correlated with the upregulated expression of the HRH1 gene. In addition, we found that several genes involved in histamine break-down were reduced in expression in tumors while the expression for histamine synthesis and transport was unchanged. We found that HRH1 expression was markedly elevated in tongue tumors specifically. Single-cell RNAseq data indicates that HRH1 was predominantly expressed in epithelial cells and fibroblasts in tongue tumors. Importantly, HRH1 expression levels were strongly correlated with oral cancer patient survival outcomes. Ninety percent of patients with low HRH1 expressing tumors survived, whereas only 50% of patients with high HRH1 levels survived past 72 months.

## **Conclusions**

These findings suggest that HRH1 upregulation is associated with poor prognosis in head, neck, and throat cancers, particularly in tongue cancer. HRH1 may serve as both a potential prognostic

biomarker and a therapeutic target in these malignancies, warranting further investigation into its role in cancer progression and response to treatment.