FPN: 758P

A comprehensive analysis of tumor-infiltrating immune cells in HPV-associated cancers

Hong Yang[1,2], Anqi Lin[1], Kaiying Wei[1], Jian Zhang[1], Peng Luo[1]

[1]Department of Oncology, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, China.
[2]The First Clinical Medical School, Southern Medical University, Guangzhou, Guangdong, China.

Introduction

• With 690,000 (31%) of the 2.2 million new infection-attributable cases of cancer diagnosed in 2018, human papillomavirus (HPV) is the second most important infectious cause of cancer worldwide.

• The specific tumor microenvironment (TME) after HPV infection could shape tumor progression and influence therapeutic response, yet underlying mechanisms are not fully understood.

Methods

Transcriptomic profiles from 7 datasets and corresponding clinical traits of patients with cervical, bladder, and head-and-neck cancers were downloaded from Gene Expression Omnibus (GEO) and The Cancer Genome Atlas (TCGA) database respectively: TCGA-CESC, TCGA-HNSC, TCGA-BLAC, GSE3292, GSE6791, GSE65858, GSE181805. Tumor-infiltrating immune cell composition was estimated by CIBERSORT, xCELL, and MCPcounter algorithms. After identifying differentially expressed genes, we performed Gene Set Enrichment Analysis (GSEA) and Single-Sample Gene Set Enrichment Analysis (ssGSEA) with collections from the Molecular Signatures Database (MSigDB) to evaluate pathway enrichment between HPV (+) and HPV (-) groups.

Conclusions

In HPV-associated cancers, HPV infection may stimulate the eventual growth and differentiation of tumor-infiltrating γδ T cells via upregulating the TCR signaling pathway and downregulating Wnt and Hedgehog signaling pathways.

Contact: Hong Yang, E-mail: smuyanghong@i.smu.edu.cn

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

南方医科大学珠江医院（第二临床医学院）
ZhuJiang Hospital of Southern Medical University (The Second Clinical Medical College)

Results

Infiltration of gamma-delta T cells (γδ T) upregulated in HPV-positive groups

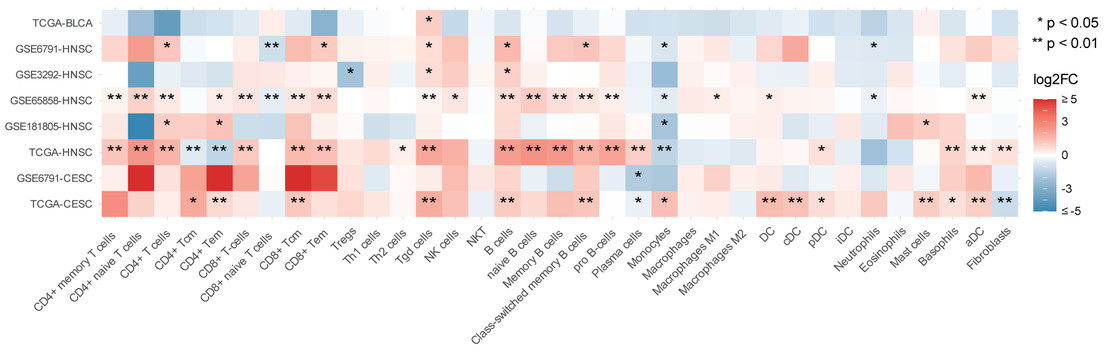

Figure 1. xCell results of tumor-infiltrating immune cells among HPV-associated cancers

• Among all 7 datasets, we observed higher levels of gamma-delta T (γδ T) cells in HPV (+) groups via the xCell algorithm, five of which showed statistical significance ($p < 0.05$, Fig.1).

• HPV (+) groups also presented the higher infiltration of B cells and lower infiltration of monocytes.

Hedgehog, Wnt, and TCR signaling pathway might modulate tumor-infiltrating γδ T

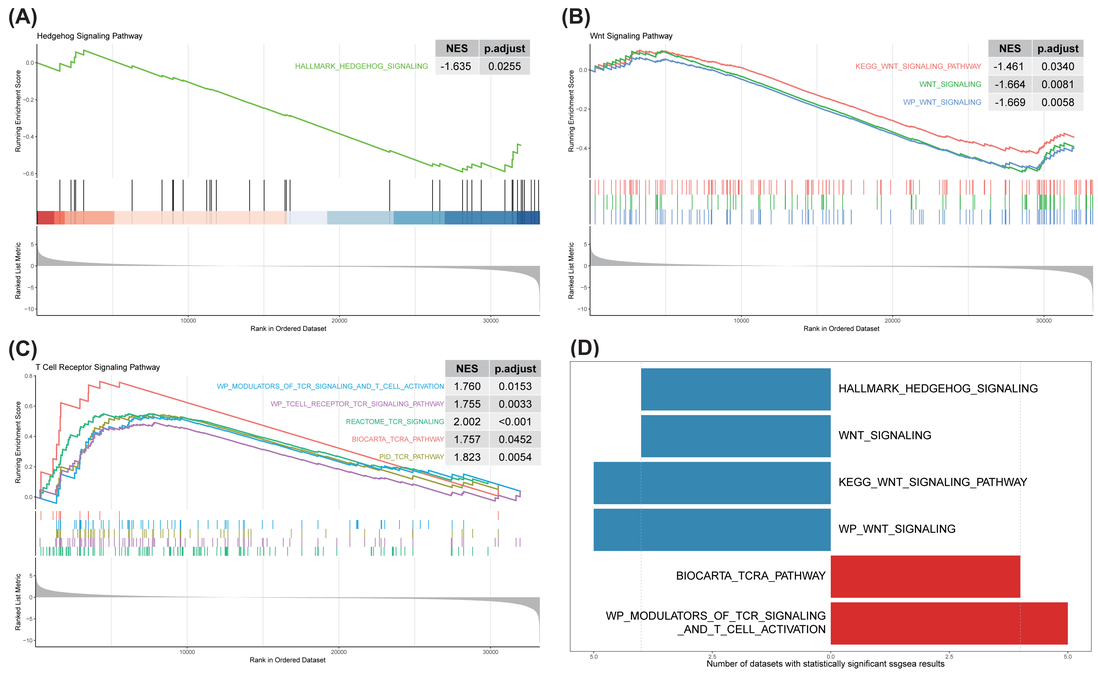

Figure 2. GSEA and ssGSEA results revealed differentially enriched pathways between HPV (+) and HPV (-) groups

• In the TCGA-CESC cohort, GSEA revealed that HPV infection activated the T-cell receptor (TCR) signaling pathway, while suppressed pathways promoting immune cells development, growth, and differentiation, such as the Wnt signaling pathway and Hedgehog signaling pathway (TCR: NES = 1.76, adj.p = 0.02; Wnt: NES = -1.67, adj.p = 0.01; Hedgehog: NES = -1.63, adj.p = 0.03; Fig.2A-C).

• Similar results were obtained for the remaining seven cohorts, except for bladder cancer whose mechanisms leading to infiltration differences need further discussion.

• Of note, ssGSEA results also proved that the enrichment scores for the TCR signaling pathway were significantly higher while Wnt and Hedgehog signaling pathways showed lower scores in HPV (+) groups ($p < 0.05$, Fig.2D).