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Pan-Cancer Analysis of Magnesium-Sensitive-ITGAL and Its Immunopositive Effects in Head and Neck Squamous Cell Carcinoma

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Abstract
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Yang Hanxuan [1] , Zongwei Huang [2] , Ying Li [2] , Qiu Sufang [1]

1. Radiotherapy, Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fuzhou, CHN 2. Radiation Oncology, Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fujian, CHN

Corresponding author: Yang Hanxuan, yanghanxuaneklsl@163.com

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Abstract

Objectives:

Recent studies have proposed that Integrin subunit alpha L (ITGAL) is crucial to activate CD8+ T cells by participating in magnesium-mediated immune synapse formation and specific cytotoxicity. However, the functional roles and regulated mechanisms of ITGAL in multiple cancers' immune microenvironment are largely unknown.This study aims to analyze the relationship between ITGAL expression and Pan-cancer prognosis and immune microenvironment, and to provide a targeted antitumor strategy for ITGAL by influencing tumor immune microenvironment to treat head and neck cancer.

Methods:

ITGAL expression in pan-cancer and the association with prognosis and immune microenvironment were identified by analyzing gene expression profiles from "TCGA" and "GEO" database with bioinformatics tools and methods.

Results:

ITGAL was generally expressed in 27 pan-cancer tissues, and closely related to tumor prognosis. Analysis of "TCGA" and "GEO" databases by "Biomarker Exploration of Solid Tumors(BEST)" showed that high expression of ITGAL was associated with good prognosis in CESC, LUAD, SARC, HNSC and SKCM, Among of these cancers, we used 2 algorithms for the functional enrichment and found ITGAL participated in immune regulation-related pathways, especially in leukocyte-mediated cytotoxicity, lymphocyte-mediated immunity, adaptive immune response, cytokine signaling in the immune system, antigen processing and presentation. Then, we used 4 algorithms for immune infiltration analysis, and found ITGAL was positively correlated with infiltration of B cells, CD8+ T cells, CD4+ T cells, M1 macrophages in tumor tissues. In order to further analyze the relationship between ITGAL and immune infiltration of HNSC, "IOBR" was used to showed that ITGAL was related to CD8+T cell infiltration, T cell inflamed GEP and T cell inflamed. And it was validated with two immunotherapy cohorts. We divided the HNSC immune microenvironment into four types: immune-depleted(D), fibrotic(F), immune-enriched(IE), non-fibrotic and immune - enriched/fibrotic(IE/F), the results showed that ITGAL was closely related to IE which is related to good prognosis. Single-cell analysis of HNSC showed ITGAL expression was the highest in CD8+T cells. Finally, we found that, in HNSC, patients with high ITGAL expression were more likely to respond to Anti-PD-1/PD-L1 and Anti-PD-1 monotherapy.

Conclusion(s):

ITGAL is significantly associated with CD8+T cells and plays an important role in the tumor immune microenvironment of pan-cancer. Furthermore, our findings may provide a targeted antitumor strategy for ITGAL by influencing tumor immune microenvironment to treat head and neck cancer.