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Immune-Related Gene IGSF9 Can Predict the Prognosis of Nasopharyngeal Carcinoma

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Abstract
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Abstract

Objectives:

The application value of immunotherapy in nasopharyngeal carcinoma (NPC) has been widely studied. However, how to effectively screen out the benefit groups of immunotherapy is the hot and difficult point of current research. Therefore, it is of great significance to explore the molecular markers of immune-related therapeutic targets and therapeutic effects for NPC.

Methods:

In this study, 188 pre-treatment tumor samples and 19 normal nasopharyngeal mucosa samples diagnosed with NPC in Fujian Cancer Hospital from 2015 to 2017 were analyzed by RNA sequencing (FJCH cohort). Transcriptomic data from three NPC cohorts from the Integrated Gene Expression Database (GEO) were downloaded for validation. The R package "limma" was used to screen for differential genes. Progression-free survival (PFS) was the primary endpoint, and Kaplan-Meier analysis was used for prognostic analysis. The immune score of NPC samples was evaluated by the "ESTIMATE" algorithm. Weighted gene co-expression network analysis (WGCNA) was performed to screen for modules significantly associated with immune scores and identify key genes. The R package "clusterProfiler" was used for Gene Ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG) for modular gene functional enrichment analysis. Univariate and multivariate Cox regression analyses were performed to evaluate the prognostic value of key genes. The diagnostic and prognostic value of key genes was evaluated by receiver operating characteristic (ROC) curves.

Results:

The WGCNA package was used to construct the weighted co-expression network of FJCH cohort transcriptome data, and it was concluded that the Brown module was closely related to the immunity of NPC. GO functional annotation analysis and KEGG enrichment analysis were performed on the genes in the above module, and the results showed that the module was closely related to the activation of immune response. Then, the above module genes were intersected with the differential genes of cancer and para-cancer in FJCH, GSE12452 and GSE53819 coorporates and the prognostic genes of PFS in FJCH and GSE102349 chorts, and then a key gene IGSF9 was selected. The area under ROC curve of IGSF9 in FJCH, GSE12452 and GSE53819 were 0.907, 0.848 and 0.975, respectively, suggesting the excellent diagnostic value of IGSF9 in NPC. Prognostic analysis showed that patients with high IGSF9 expression had worse PFS (FJCH cohort: P=0.032; GSE102349 cohort: P=0.033). Univariate and multivariate Cox regression analysis showed that IGSF9 was an independent prognostic factor for NPC (univariate: HR=1.006, 95%CI: 1.003-1.009, P< 0.001; Multivariate: HR=1.005, 95%CI: 1.001-1.008, P=0.007). IGSF9 had certain predictive performance in predicting NPC survival (FJCH cohort: AUC for predicting PFS at 1, 3 and 5 years were 0.623, 0.598 and 0.638, respectively; GSE102349 cohort: AUC for predicted 1 - and 3-year PFS was 0.612 and 0.664, respectively).

Conclusion(s):

Our study identified a new diagnostic and prognostic biomarker for NPC, IGSF9, and revealed that it may be associated with NPC immunity. These findings have inspired the study of molecular mechanisms of NPC tumor immunomodulation.