



RESEARCH

IFN- α / β /IFN- γ /IL-15 pathways identify GBP1-expressing tumors with an immune-responsive phenotype

Lei Wang¹ · Yuoxuan Wei¹ · Zheng Jin^{2,3} · Fangfang Liu¹ · Xuchang Li¹ · Xiao Zhang⁴ · Xiumei Bai⁴ · Qingzhu Jia^{5,6} · Bo Zhu^{5,6} · Qian Chu¹

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Abstract

Immunotherapy is widely used in cancer treatment; however, only a subset of patients responds well to it. Significant efforts have been made to identify patients who will benefit from immunotherapy. Successful anti-tumor immunity depends on an intact cancer-immunity cycle, especially long-lasting CD8⁺ T-cell responses. Interferon (IFN)- α / β /IFN- γ /interleukin (IL)-15 pathways have been reported to be involved in the development of CD8⁺ T cells. And these pathways may predict responses to immunotherapy. Herein, we aimed to analyze multiple public databases to investigate whether IFN- α / β /IFN- γ /IL-15 pathways could be used to predict the response to immunotherapy. Results showed that IFN- α / β /IFN- γ /IL-15 pathways could efficiently predict immunotherapy response, and guanylate-binding protein 1 (*GBP1*) could represent the IFN- α / β /IFN- γ /IL-15 pathways. In public and private cohorts, we further demonstrated that *GBP1* could efficiently predict the response to immunotherapy. Functionally, *GBP1* was mainly expressed in macrophages and strongly correlated with chemokines involved in T-cell migration. Therefore, our study comprehensively investigated the potential role of GBP1 in immunotherapy, which could serve as a novel biomarker for immunotherapy and a target for drug development.

Keywords GBP1 · Tumor microenvironment · Immunotherapy · Biomarker

Lei Wang, Yuoxuan Wei, and Zheng Jin have contributed equally to this study.

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Abbreviations

AUC	Area under the receiver operating characteristic curve
DEGs	Differentially expressed genes
DAB	Diaminobenzidine
GBP1	Guanylate-binding protein 1
GEO	Gene Expression Omnibus
GEPs	Gene expression profiles
ICI	Immune checkpoint inhibitor
ICB	Immune checkpoint blockade
IHC	Immunohistochemistry
MDSCs	Myeloid-derived suppressor cells
NSCLC	Non-small cell lung cancer
ORR	Objective response rate
OS	Overall survival
TAMs	Tumor-associated macrophages
TCGA	The Cancer Genome Atlas
TMB	Tumor mutational burden
TME	Tumor microenvironment
UMAP	Uniform Manifold Approximation and Projection

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