

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

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Received: 24 January 2024 / Accepted: 9 March 2024 © The Author(s) 2024

#### 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)- $\omega$ /p/IFN- $\gamma$ /interleakin (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- $\omega$ /p/IFN- $\gamma$ /IL-15 pathways could be used to predict the response to immunotherapy. Results showed that IFN- $\omega$ /p/IFN- $\gamma$ /IL-15 pathways could efficiently predict immunotherapy response, and guanylate-binding protein 1 (GBPI) could represent the IFN- $\omega$ /p/IFN- $\gamma$ /IL-15 pathways. In public and private cohorts, we further demonstrated that GBPI could efficiently predict the response to immunotherapy. Functionally, GBPI 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

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<b>Abbrevi</b>	ations
AUC	Area under the receiver operating characteristic
	curve
DEGs	Differentially expressed genes
DAB	Diaminobenzidine
GBPI	Guanylate-binding protein 1
GEO:	Gene Expression Omnibus
GEPs	Gene expression profiles
ICI	Immune checkpoint inhibitor
ICB	Immune checkpoint blockade
THIC	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
TIMUE	Tumor microenvironment
UMAP	Uniform Manifold Approximation and
	Projection

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#### **Table of Contents 15 Pathways To Succeb**

- 1. Understanding the eBook 15 Pathways To Succeb
  - The Rise of Digital Reading 15 Pathways To Succeb
  - $\circ\,$  Advantages of eBooks Over Traditional Books
- 2. Identifying 15 Pathways To Succeb
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
- 3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an 15 Pathways To Succeb
  - User-Friendly Interface
- 4. Exploring eBook Recommendations from 15 Pathways To Succeb
  - Personalized Recommendations
  - 15 Pathways To Succeb User Reviews and Ratings
  - o 15 Pathways To Succeb and Bestseller Lists
- 5. Accessing 15 Pathways To Succeb Free and Paid eBooks
  - 15 Pathways To Succeb Public Domain eBooks
  - 15 Pathways To Succeb eBook Subscription Services

- 15 Pathways To Succeb Budget-Friendly Options
- 6. Navigating 15 Pathways To Succeb eBook Formats
  - ∘ ePub, PDF, MOBI, and More
  - 15 Pathways To Succeb Compatibility with Devices
  - 15 Pathways To Succeb Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - o Adjustable Fonts and Text Sizes of 15 Pathways To Succeb
  - Highlighting and Note-Taking 15 Pathways To Succeb
  - Interactive Elements 15 Pathways To Succeb
- 8. Staying Engaged with 15 Pathways To Succeb
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers 15 Pathways To Succeb
- 9. Balancing eBooks and Physical Books 15 Pathways To Succeb
  - Benefits of a Digital Library
  - o Creating a Diverse Reading Collection 15 Pathways To Succeb
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine 15 Pathways To Succeb
  - Setting Reading Goals 15 Pathways To Succeb
  - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of 15 Pathways To Succeb
  - Fact-Checking eBook Content of 15 Pathways To Succeb
  - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks
- 14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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