Publication Spotlight | Bio X Cell BE0101 in Action: IL-16 Remodels the Tumor Immune Microenvironment and Boosts Immunotherapy Efficacy

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Quick Overview

Title:
Interleukin-16 enhances anti-tumor immune responses by establishing a Th1 cell–macrophage crosstalk through reprogramming glutamine metabolism in mice

Journal: *Nature Communications* (IF 17.7)
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Antibody Used: Bio X Cell BE0101 (anti-PD-L1)

Read the full paper https://www.nature.com/articles/s41467-025-57603-1

Background

Immune checkpoint blockade (ICB) has revolutionized cancer therapy, yet many patients fail to respond due to an immunosuppressive tumor microenvironment (TME). While Th1 cells and anti-tumor macrophages (M1-type TAMs) are essential for effective immune responses, strategies to jointly activate both populations remain unclear.

Interleukin-16 (IL-16), a less-explored cytokine, has unclear roles in cancer immunology. This study systematically investigates IL-16 and uncovers its ability to reprogram glutamine metabolism, enhance Th1-TAM interactions, and synergize with anti-PD-L1 therapy to improve outcomes.

Key Findings

IL-16 Suppresses Tumor Growth and Correlates with Better Prognosis

- IL-16 levels are reduced in cancer patients and correlate with poor survival.
- IL-16 administration in E0771 breast cancer, LLC lung cancer, and MMTV-PyMT models significantly inhibited tumor progression.

IL-16 Drives Th1-Dominant Immunity

- Promotes Th1 polarization in CD4+ T cells, increasing IFN-γ and T-bet expression.

- Enhances CD8+ T cell cytotoxicity (GZMB, Perforin).
- Suppresses glutaminase (GLS), reducing glutaminolysis and shifting metabolism to support Th1 differentiation.

IL-16 Reprograms Macrophages via IFN-γ

- **Enhances Th1 immunity to indirectly shift TAMs toward an M1 phenotype.**
- **Upregulates CXCL9/CXCL10, promoting CXCR3+ T cell infiltration and anti-tumor function.**

IL-16 and BE0101 (anti-PD-L1) Work Synergistically

- BE0101 alone had limited efficacy; IL-16 plus BE0101 markedly slowed tumor growth.
- IL-16 enhanced IFN-γ, Prf1, and Gzmb expression post-ICB.
- Blocking CXCR3 or depleting macrophages abolished the synergy.

Clinical Correlation: IL-16 as a Predictive Biomarker

- Higher serum IL-16 levels predicted better responses to PD-1 therapy in lung cancer patients.
- ROC analysis yielded AUC of 0.895, suggesting high predictive accuracy.
- High IL-16 levels also correlated with longer progression-free survival.

Histamine–Mast Cell Axis Regulates IL-16

- Mast cell–derived histamine maintains IL-16 expression in TME.
- Histamine supplementation increased IL-16 levels and Th1 immunity.
- Disrupting histamine release (e.g., using DSCG) lowered IL-16 and impaired anti-tumor response.

🎯 Experimental Strategy and Summary

This multi-tiered study used mouse models, immunophenotyping, metabolomics, and patient data to build a mechanistic model of the IL-16–Th1–TAM axis:

- IL-16 inhibits GLS to reprogram glutamine metabolism in CD4+ T cells.
- Promotes Th1 cell differentiation and IFN-γ production.

- IFN-γ reprograms TAMs toward M1-like phenotype.
- M1 macrophages upregulate CXCL9/10, enhancing CD8+ T cell activity.
- IL-16 synergizes with anti-PD-L1 (BE0101) to improve ICB efficacy.
- Histamine sustains IL-16 expression—mast cells are upstream regulators.

💉 Methods At a Glance

- In Vivo Models: E0771, LLC, MMTV-PyMT spontaneous tumor mice
- Treatments: IL-16 (1μg/mouse), BE0101 (150μg), histamine, CXCR3 inhibitor, IFN-γ/IL-16 neutralization
- Techniques: Flow cytometry, QPCR, ELISA, metabolomics, single-cell RNA-seq
- Clinical Data: Lung cancer patient serum IL-16 levels pre–anti-PD-1 therapy (AUC = 0.895)

💉 Bio X Cell BE0101: A Key Enabler

The study successfully used Bio X Cell BE0101, an anti-PD-L1 monoclonal antibody, in combination therapy experiments to demonstrate IL-16's synergy with ICB. This validated BE0101’s role in driving functional immune checkpoint blockade in vivo.

Key Features of BE0101:

- Ultra-pure and endotoxin-free
- Animal-free formulation
- Optimized for in vivo functional blockade studies

💉 Bio X Cell — Empowering Every Scientific Breakthrough.

Product	Cat. No.	Clone	Application
InVivoMAb anti-mouse PD-L1 (B7-H1)	BE0101	10F.9G2™	Blocking

Bio X Cell—Empowering every scientific breakthrough.