Monoclonal microbial EDP1503 induces antitumor responses via gut-mediated activation of both innate and adaptive immunity

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INTRODUCTION

inflammatory microbe prior to culture with CFSE measured by flow cytometry.

transferred to wells containing CFSE lead to the strong induction of CXCL10 compared to other strains of

EDP1503 is a human commensal strain of Bifidobacterium animalis lactis with potent antitumor activity. Treatment with EDP1503 in vitro promotes the production of type 1 effector molecules by cells of the innate immune system, including the transactivation of human NK cells. Oral delivery of EDP1503 microtherapy leads to tumor control comparable to checkpoint inhibition in multiple subcutaneous syngeneic tumor models. This treatment promotes the immunogenic remodeling of the tumor microenvironment to favor the infiltration of protective effector cells (2). In the CT-26 colon carcinoma model, this protection is dependent on both NK and CD8+ T cells; however, NK cells are insufficient to mediate protection in the absence of CD8+ T lymphocytes (3). Our data suggests a model where EDP1503 stimulates NK cell transactivation which potentiates cross-priming of tumor-specific CTL by XCR1+ DC1 to limit tumor growth (6).

RESULTS

EDP1503 Stimulates Type I Immune Responses

EDP1503 transactivates human NK cell cytotoxic activity

Conclusions

• Oral delivery of EDP1503 is effective in multiple tumor models (CT26, B16-F10, and MC38).
• EDP1503 induces a proinflammatory gene signature (CICL10, II12p70, IFNγ, IL-1β, TNFα, and IL-12). EDP1503 transduced monocyte-conditioned supernatants induce NK cell cytolytic activity.
• CD44+ effector lymphocyte populations (NK, NKT, CD4+, CD8+) upregulate CD25 and IFNγ upon stimulation with EDP1503.
• EDP1503 induces a proinflammatory chemotactic signature within the TME.
• NK and CD8+ T cells display an activated phenotype post-EDP1503 treatment. Both NK and CD8+ T cells are required for a productive anti-tumor response induced by EDP1503. Moreover, NK cells are insufficient to mediate protection in the absence of CD8+ T lymphocytes.

Selected References