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BLOCKADE OF HUMAN LILRB4/ILT3 INHIBITS THE FORMATION OF LUNG METASTASIS IN MELANOMA MODEL

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Background Targeting the immunosuppressive tumor microenvironment to enhance or recover anti-tumor functions is a promising strategy to favor tumor regression and response to checkpoint immunotherapy. LILRB4 is an inhibitory immune receptor, also named ILT3, that is primarily expressed in myeloid cells. We previously showed with *in vitro* assays that ILT3 is highly expressed in tumor-associated macrophages (TAMs) and binds fibronectin (Fn), which is ubiquitously expressed in the extracellular matrix and enriched in various primary tumor tissues and metastatic sites.¹ Therefore, targeting ILT3 can be a promising therapeutic strategy to reprogram TAMs and promote tumor control.

Methods Transgenic mice (LILR-T) that carry the human LILR cluster comprising the ILT3 gene were generated. A recombinant anti-human ILT3 monoclonal antibody (an NGM831 surrogate antibody) that blocks the interaction between ILT3 and Fn was produced. The anti-tumor efficacy and immune profile were investigated in the B16 lung metastasis model in LILR-T mice treated with anti-ILT3 antibody.

Results Analysis of ILT3 expression in the LILR-T mouse showed a consistent expression pattern with that in humans across different tissues. We found that ILT3 blockade has beneficial effects on anti-tumor immune responses in B16 lung metastasis *in vivo* and promotes metastasis control.

Conclusions These results suggest that ILT3 blockade could be an effective approach to reprogram tumor myeloid infiltrates and promote tumor control. Our study further elucidates the role of ILT3 in the tumor immune cell composition.

REFERENCE

1. Paavola KJ, *et al.* The Fibronectin-ILT3 interaction functions as a stromal checkpoint that suppresses myeloid cells. *Cancer Immunol. Res.* 2021;**9**, 1283–1297.

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