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RESEARCH PAPER

Deletion of galectin-3 in the host attenuates metastasis of murine melanoma by modulating tumor adhesion and NK cell activity

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Abstract Galectin-3, a β galactoside–binding lectin, plays an important role in the processes relevant to tumorigenesis such as malignant cell transformation, invasion and metastasis. We have investigated whether deletion of Galectin-3 in the host affects the metastasis of B16F1 malignant melanoma. Galectin-3-deficient (Gal-$3^{-/-}$) mice are more resistant to metastatic malignant melanoma as evaluated by number and size of metastatic colonies in the lung. In vitro assays showed lower number of attached malignant cells in the tissue section derived from Gal-$3^{-/-}$ mice. Furthermore, lack of Galectin-3 correlates with higher serum levels of IFN-γ and IL-17 in tumor bearing hosts. Interestingly, spleens of Gal-$3^{-/-}$ mice have lower number of $Foxp3^{+}$ T cells after injection of B16F1 melanoma cells. Finally, we found that while $CD8^{+}$ T cell and adherent cell cytotoxicity were similar, there was greater cytotoxic activity of splenic NK cells of Gal-$3^{-/-}$ mice compared with "wild-type" (Gal-$3^{+/+}$) mice. Despite the reduction in total number of $CD3\varepsilon^{-}NK1.1^{+}$, Gal-$3^{-/-}$ mice constitutively have a significantly higher percentage of effective cytotoxic $CD27^{high}CD11b^{high}$ NK cells as well as the percentage of immature $CD27^{high}CD11b^{low}$ NK cells. In contrast, $CD27^{low}CD11b^{high}$ less functionally exhausted NK cells and NK cells bearing inhibitory KLRG1 receptor were more numerous in Gal-$3^{+/+}$ mice. It appears that lack of Galectin-3 affects tumor metastasis by at least two independent mechanisms: by a decrease in binding of melanoma cells onto target tissue and by enhanced NK-mediated anti-tumor response suggesting that Galectin-3 may be considered as therapeutic target.

Keywords B16F1 · Galectin-3 · Malignant melanoma · Metastasis · NK cells

Abbreviations

B16F1	Murine skin melanoma cell line
Gal-3	Galectin-3
IFN-γ	Interferon-gamma
IL-17	Interleukin-17
IL-4	Interleukin-4
KLRG1	Killer cell lectin-like receptor G1
NK cells	Natural killer cells
TNF-α	Tumor necrosis-alpha

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Introduction

Galectin-3 is one of the 16 known members of the galectin family, which selectively binds β-galactoside. Depending on cell types and proliferative status, this molecule can be found in the cytoplasm, on the cell surface, within the nucleus, and in the extracellular compartment [1–3]. Galectin-3 binds and interacts with a numerous ligands in the intra- and extra-cellular environment and regulates many biological processes and signaling pathways in

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