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NKp46 Receptor-Mediated Interferon- γ Production by Natural Killer Cells Increases Fibronectin 1 to Alter Tumor Architecture and Control Metastasis.

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ABSTRACT

Natural killer (NK) cells are innate lymphoid cells, and their presence within human tumors correlates with better prognosis. However, the mechanisms by which NK cells control tumors in vivo are unclear. Here, we used reflectance confocal microscopy (RCM) imaging in humans and in mice to visualize tumor architecture in vivo. We demonstrated that signaling via the NK cell receptor NKp46 (human) and Ncr1 (mouse) induced interferon- γ (IFN- γ) secretion from intratumoral NK cells. NKp46- and Ncr1-mediated IFN- γ production led to the increased expression of the extracellular matrix protein fibronectin 1 (FN1) in the tumors, which altered primary tumor architecture and resulted in decreased metastases formation. Injection of IFN- γ into tumor-bearing mice or transgenic overexpression of Ncr1 in NK cells in mice resulted in decreased metastasis formation. Thus, we have defined a mechanism of NK cell-mediated control of metastases in vivo that may help develop NK cell-dependent cancer therapies.

KEYWORDS:FN1; IFN- γ ; NKp46; Ncr1; RCM imaging; tumor metastases

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