The Use of NKG2D Signaling in NK Cell Immunotherapy

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Natural killer (NK) cells are an important subset of immune cells in anti-tumor immunity; however, much is still unknown about what mechanisms activate NK cells and make them more efficient at killing cancer cells. The purpose of this study was to determine whether NK cells could be induced to express NKG2D ligands and the subsequent effect of NKG2D signaling between healthy NK cells on NK cell tumor killing ability, as measured by cytotoxicity and cytokine secretion, using mouse NK cells as a model. NK cells where NKG2D was absent or present were isolated from mouse spleens and activated with cytokines; NKG2D ligand expression and cytokine concentration were measured for 5 days post activation. Additionally, cytotoxicity was measured via a killing assay performed on the fourth day after activation. Activation induced expression of NKG2D ligands beginning on day 2 post activation. NK cells deficient in NKG2D were found to be more effective in killing target cancer cells, and showed increased consumption of IL-12, a cytokine that activates anti-tumor immunity in NK cells, as well as increased secretion of MCP-1, a cytokine that can promote immune destruction of a malignancy or enhance tumor growth, depending on tumor type. The results of this study indicate that the NKG2D signaling pathway can be exploited to enhance immunotherapy treatments using NK cells, either by blocking or upregulating NKG2D.

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