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Regulation of Fas and Fas-ligand expression in NK cells by cytokines and the involvement of Fas-ligand in NK/LAK cell-mediated cytotoxicity.

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This study demonstrates cytokine-mediated regulation of Fas and Fas-ligand (Fas-L) expression in human NK cells and the involvement of the Fas-L pathway in NK/LAK cytotoxicity. Freshly isolated, high purified human CD56+CD3- NK cells were found to express Fas and Fas-L. Cytokines further increased the Fas expression in the CD56+CD3- NK cells, with interleukin (IL)-2 being the most potent stimulus followed by IL-12, while IL-7 had no effect. IL-2 and IL-7 equally enhanced the Fas expression in the CD56+CD3+ population, while IL-12 had a less pronounced effect. Incubation of the CD56+CD3- NK cells with IL-2, but not with IL-12 and IL-7, led to an upregulation at the Fas-L expression, whereas neither of the cytokines affected the Fas-L expression in the CD56+CD3+ cells. Antagonistic Fas mAb M3 and Fas-IgG1 fusion protein significantly inhibited NK cytotoxicity towards Fas-expressing Jurkat cells, while non-antagonistic Fas mAb M31 and irrelevant CD14-IgG1 fusion protein had no effect. IL-2-generated LAK cells were much more potent than NK cells in exerting the cytotoxic effect on Jurkat cells, which was also partially inhibited to M3 and Fas-IgG1. Thus, human NK and LAK cells express Fas and Fas-L, utilize the Fas-L cytotoxic pathway and enhance the expression of these molecules in response to cytokines.

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