

NKG2D-mediated immune responses

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NKG2D is an activating receptor expressed on NK cells, CD8+ T cells, and gd- TcR+ T cells that has been implicated in innate and adaptive immunity, providing host defense against tumors and viruses. In addition, recent studies suggest it also contributes to autoimmune disorders, including type I diabetes and rheumatoid arthritis. NKG2D signals by its association with DAP10 in human cells and with DAP10 and DAP12 in mouse cells. In humans and mice, at least six genes have been identified that encode high affinity ligands for NKG2D. These include mouse RAE-1a, b, g, d, and e, H60 and MULT-1. An interesting feature of NKG2D is its regulation by ligand. When NKG2D binds ligand, the receptor is rapidly modulated and internalized. In recent studies, we have investigated the consequences of chronic exposure of NK cells to NKG2D ligands and have demonstrated that this results in inactivation of NKG2D-mediated tumor immunity. These findings are relevant to recent observations documenting a potential tumor escape mechanism involving the secretion of soluble forms of NKG2D ligands in cancer patients.

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