

Functional characterization of DNAM-1 (CD226) interaction with its ligands PVR (CD155) and Nectin-2 (PRR-2/CD112)

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CD226 (DNAM-1) is an adhesion molecule involved in NK and T-cell-mediated cytotoxicity against certain tumors. Here we have identified the human poliovirus receptor related (PRR) family members CD155 (poliovirus receptor; PVR) and CD112 (nectin-2/PRR-2) as the ligands for human CD226. Ectopic expression of human CD155 and/or CD112 rendered mouse BW5147 T cells more susceptible to IL-2-activated T cell and NK cell-mediated cytotoxicity, and killing was specifically inhibited by anti-CD226 mAb or anti-CD155 or -CD112 mAbs, demonstrating functional interactions of CD226 with CD155 and CD112. Although the binding affinities between soluble CD226 and CD155 or CD112 were similar, CD226 seems to prefer CD155 to CD112 as a physiological ligand. The homophilic interaction of CD112 may adversely affect CD226 binding to CD112. We also demonstrate that ligation of CD226 and LFA-1 with their respective ligands cooperate in triggering cytotoxicity and cytokine secretion by T cells and NK cells.