Interleukin-10 promotes NK cell killing of autologous macrophages by stimulating expression of NKG2D ligands.

Abstract:
Under inflammatory conditions, the pleiotropic cytokine interleukin-10 (IL-10) is released in many tissues. It mediates anti-inflammatory effects in particular by inhibiting the release of T helper type 1 (Th1) cytokines. In contrast, we show here that NK cell cytotoxicity against autologous macrophages is elevated if both cell types are cultured with IL-10. The expression of most activatory NK receptors is increased after culture in the presence of IL-10. On the other hand, macrophages cultured in the presence of IL-10 show elevated expression of the NKG2D ligands major histocompatibility complex (MHC) class 1-like molecules (MIC) - A and - B, as well as UL-16 binding proteins (ULBP) - ULBP-1, ULBP-2 and ULBP-3. By masking the interaction of NK cells with macrophages through interruption of the NKG2D receptor with its ligands, we could reverse the IL-10-induced lysis of macrophages. Our data therefore reveal that IL-10 may exert a novel immunomodulatory role by stimulating NKG2D ligand expression on macrophages, thereby rendering them susceptible to NK cell elimination. This suggests that NK cells would delete macrophages and potentially other immature antigen-presenting cells (APC) or their precursors under inflammatory conditions as a feedback mechanism to shut off uncontrolled immune responses.