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Autor(en) des Beitrags:             Wiethe, C; Schiemann, M; Busch, D; Haeberle, L; Kopf, M; Schuler, G; Lutz, MB

Titel des Beitrags:                Interdependency of MHC class II/self-peptide and CD1d/self-glycolipid presentation by TNF-matured dendritic cells for protection from autoimmunity.

Abstract:                        Dendritic cells (DC) are key regulators of T cell immunity and tolerance. NKT cells are well-known enhancers of Th differentiation and regulatory T cell function. However, the nature of the DC directing T and NKT cell activation and polarization as well as the role of the respective CD1d Ags presented is still unclear. In this study, we show that peptide-specific CD4(+)IL-10(+) T cell-mediated full experimental autoimmune encephalomyelitis (EAE) protection by TNF-treated semimatured DCs was dependent on NKT cells recognizing an endogenous CD1d ligand. NKT cell activation by TNF-matured DCs induced high serum levels of IL-4 and IL-13 which are absent in NKT cell-deficient mice, whereas LPS plus anti-CD40-treated fully mature DCs induce serum IFN-gamma. In the absence of IL-4Ralpha chain signaling or NKT cells, no complete EAE protection was achieved by TNF-DCs, whereas transfer of NKT cells into Jalpha281(-/-) mice restored it. However, activation of NKT cells alone was not sufficient for EAE protection and early serum Th2 deviation. Simultaneous activation of NKT cells and CD4(+) T cells by the same DC was required for EAE protection. Blocking experiments demonstrated that NKT cells recognize an endogenous glycolipid presented on CD1d on the injected DC. Together, this indicates that concomitant and interdependent presentation of MHC
II/self-peptide and CD1d/self-isoglobotrihexosylceramide to T and NKT cells by the same partially or fully matured DC determines protective and nonprotective immune responses in EAE.