

Plasmacytoid Dendritic Cell-Specific Receptor ILT7/FcεRIγ Inhibits Toll-Like Receptor-Induced Interferon Production

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Immunoglobulin-like transcripts are a family of inhibitory and stimulatory cell surface immune receptors. Transcripts for one member of this family, ILT7, are selectively expressed in human plasmacytoid dendritic cells (pDCs). We demonstrate that ILT7 protein associates with the signal adapter protein FcεRIγ to form a receptor complex. Using an anti-ILT7 monoclonal antibody, we show that ILT7 is expressed specifically on human pDCs, but not on myeloid dendritic cells or other peripheral blood leukocytes. Crosslinking of ILT7 resulted in phosphorylation of Src family kinases and Syk kinase and induced a calcium influx in freshly isolated pDCs, which was blocked by Src family and Syk kinases inhibitors, thus indicating the activation of an immunoreceptor-based tyrosine activation motif (ITAM)-mediated signaling pathway. ILT7 crosslinking on CpG or influenza virus-stimulated primary pDCs inhibited the transcription and secretion of type I interferon and other cytokines. Therefore, the ILT7/FcεRIγ receptor complex negatively regulates the innate immune functions of human pDCs.