

P048 IFN- α regulates Toll-like receptor-mediated IL-27 gene expression in human macrophages

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Interleukin 27 (IL-27) is a new member of the IL-12 family of cytokines. Biologically active IL-27 is a heterodimer composed of EBI3 and p28 proteins. IL-27 controls the intensity and duration of adaptive immune responses. It induces the early differentiation of Th1 cells and suppresses the development of IL-17-producing Th cells. We report that Toll-like receptor (TLR) -dependent expression of IL-27 in human macrophages is regulated by IFN- α via transactivation of p28 gene. We identified an IFN-stimulated response element (ISRE) in the IL-27 p28 gene promoter and show that stimulation of macrophages with IFN- α results in the binding of interferon regulatory factor 1 (IRF-1) to the ISRE p28 site. Contribution of IFN- α explains the difference that we see in the IL-27 expression of macrophages, which are stimulated with TLR agonists. Agonists for TLR3, TLR4 or TLR7/8 induce the expression of both IL-27 genes. TLR2 agonist, in contrast, fails to activate p28 although it enhances the expression of EBI3. This is due to the inability of TLR2 agonist to switch on the expression of IFN- α . The data establishes a molecular basis for the regulation of IL-27 expression and underscores the role of IFN- α in the TLR-mediated immune responses.