

P047 The effects of SOCS-3 on cytokine-induced chemokine expression in pancreatic β -cells

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We have previously shown that Suppressor of Cytokine Signaling-3 (SOCS-3) can inhibit IL-1 β and IFN- γ induced NO-production and apoptosis in β -cells. In the present project we wish to investigate if SOCS-3 can influence cytokine-induced expression of chemokines in β -cells. Chemokines are important in establishing the inflammatory infiltrate in insulinitis as they recruit activated immune cells to sites of inflammation. Using a β -cell line with inducible SOCS-3 expression we showed, by real-time PCR, that IL-1 β (150 pg/ml) induced a time-dependent increase in MCP-1 and MIP-2 mRNA expression with a maximal 46-fold and 14-fold induction respectively after 6 hours of stimulation. This induction was inhibited by 80% when SOCS-3 was expressed in the cells ($p \leq 0,05$) for MCP-1 and by 22% for MIP-2 ($p \leq 0,05$). In dose-response experiments both chemokines were significantly inhibited by SOCS-3 with increasing amounts of IL-1 β . In a promoter study SOCS-3 significantly inhibited the IL-1 β induced activity of an MCP-1 promoter construct. These data indicate that SOCS-3 can inhibit cytokine-induced chemokine expression in β -cells.