

P071 Molecular mechanisms involved in IL-1 β and TNF- α -induced pancreatic beta-cell-death
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The cytokines IL-1 β and TNF- α induce the transcription factor NF- κ B which contributes to β -cell death. Recent observations suggest that NF- κ B blocking is more effective in preventing IL-1 β +IFN- α - than TNF- α +IFN- γ -induced β -cell apoptosis. We presently examined the reasons behind these different effects of cytokines in insulin-producing INS-1E cells and FACS-purified primary rat β -cells.

Blocking NF- κ B activation by the use of an adenoviral construct protected β -cells from both IL-1 β +IFN γ - or TNF α +IFN γ -induced apoptosis ($P \leq 0.05$ vs non-infected cells; $n=8-12$). Microarray analysis (using our "home-made" APOCHIP) of INS-1E cells treated with IL-1 β or TNF- α for 2h, 4h, 8h, 12h and 24h showed similar patterns of gene expression. IL-1 β , however, induced a higher expression of NF- κ B target genes that are putatively involved in β -cell dysfunction and death as compared to TNF- α . Furthermore, IL-1 β induced an earlier translocation of NF- κ B to the nucleus as compared to TNF- α , which was paralleled by an earlier and stronger activation of the IKK complex.

In conclusion, the present observations suggest that the differences between IL-1 β - and TNF α -induced β -cell death are at least in part explained by differential intensity of NF- κ B activation, reflected in a differential transcription of key target genes.