**Differential Usage of NF-κB Activating Signals by IL-1β and TNF-α in Pancreatic Beta Cells**

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**Background/Aims:** The cytokines interleukin (IL)-1β and tumor necrosis factor (TNF)-α induce β-cell death in type 1 diabetes via NF-κB activation. Although both IL-1β and TNF-α activate NF-κB in β-cells, NF-κB activation by IL-1β is stronger, leading to higher expression of NF-κB target genes putatively involved in β-cell dysfunction and death. We presently studied the specific characteristics of NF-κB activation in β-cells that may contribute for its pro-apoptotic effects following exposure to cytokines.

**Methods:** Rat insulin-producing INS-1E cells were exposed to either IL-1β or TNF-α. NF-κB activation was analyzed by NF-κB nuclear immunostaining. Regulation of kinases involved in NF-κB activation was evaluated by Western blot and kinase assay. Expression of IKKα, IKKβ, IKKγ, TAK1 and TRAF6 was silenced by specific siRNAs. Specific chemical inhibitors for JNK, IKK and proteosomal activity were used.

**Results:** IL-1β induces degradation of IKKβ via the proteasome, leading to a preferential use of IKK complexes containing only the IKKα subunit. This degradation is dependent, at least in part, on the presence of the IKKα subunit and activation of the TRAF6 signalling pathway. Activation of JNK via TAK1 is also important for IL-1β-induced IKKβ degradation, suggesting a new effect of this kinase, previously shown to contribute for cytokine-induced β-cell apoptosis.

**Conclusion:** We presently identified a differential usage of IKK complexes following β-cell exposure to IL-1β or TNF-α. This may affect the downstream signalling of NF-κB and help to explain the context-dependent regulation of apoptosis provided by this transcription factor.

**Word Keys: type 1 Diabetes, pancreatic β-cells, cytokines, NF-κB, IKK complex**

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