

P074 Suppression of TRAF2 expression by siRNA reduces cytokine-mediated apoptosis in insulin-secreting INS-1E cells

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Type 1 diabetes is characterized by complete destruction of the insulin-producing pancreatic β -cells in an immune-mediated process in which the pro-inflammatory cytokines interleukin (IL)-1 β and interferon (IFN)- γ are thought to play an important role. Recent findings suggest that cytokines cause endoplasmic reticulum (ER) stress which leads to β -cell apoptosis. In other cells, ER stress activates a TRAF2-ASK1-JNK stress pathway leading to cell death. Further, micro array analyses have shown upregulation of TRAF2 mRNA expression following cytokine exposure in both primary and clonal β -cells. In this study, we investigated if the TRAF2-ASK1-JNK pathway is functional in cytokine-induced, ER stress-mediated β -cell apoptosis. This was examined by determining the impact of cytokines on TRAF2 protein expression and the consequence of blocking TRAF2 expression by siRNA for cytokine-induced apoptosis in rat INS-1E cells. We found that a 24-h exposure to a combination of IL-1 β and IFN γ upregulated the expression of TRAF2 by ~2-fold. Transient transfection of cells with siRNA directed against TRAF2 suppressed TRAF2 expression by ~75%. TRAF2 siRNA caused a reduction in apoptotic cell death induced by cytokines. In conclusion, our results point towards a pro-apoptotic role of TRAF2 in mediating cytokine-induced, ER stress-dependent apoptosis in INS-1E cells.