

P048 Proteomic analysis of cytokine-induced dysfunction and death in insulin producing INS-1E cells: new insights into the pathways involved

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Cytokines released by islet-infiltrating immune cells play a crucial role in β -cell dysfunction and apoptotic cell death in type 1 diabetes. The aim of this study was to analyze protein changes in INS-1E cells exposed to inflammatory cytokines *in vitro* using 2-dimensional difference gel electrophoresis (pH4-7 and pH6-9). After 24h of incubation, 158 proteins (out of a total of 3855 protein spots) showed altered expression by the combination of IL-1 β and IFN- γ , whereas only 42 and 23 proteins were altered by IL-1 β or IFN- γ alone, respectively ($n=4$, $p \leq 0.01$). Identification of 141 of these spots revealed proteins playing a role in insulin processing, cytoskeleton organization, protein and RNA metabolism, as well as proteins associated with endoplasmic reticulum- and oxidative stress/defense. Network analysis indicated that 42 of the proteins from the IL-1 β + IFN- γ , -treated cells interact with each other ($p < 1.27e-05$), suggesting the presence of a protein-interactome. The present findings unveil novel mechanisms for cytokine-induced β -cell dysfunction and apoptosis.