

**P054** Effects of dexamethasone on IGF-1 signalling in insulin secreting cells

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The proper functioning of insulin secreting cells depends on IGF-1 signalling. Thus, overexpression of IRS-2 prevents, while reduced IRS-2 phosphorylation favours the development of diabetes mellitus. Previously we described that dexamethasone (dex) increases apoptosis in insulin secreting cells. The aim of the present study was to examine the interactions of dex with IGF-1 signalling. Insulin secreting INS-1 cells were cultured under standard conditions (11 mM Glucose and 10% FCS) and test substances added for 1-4 d. Apoptosis was quantified by DAPI-stained condensed nuclei and by TUNEL assay. Proliferation was measured by BrdU-staining. The amount and phosphorylation of proteins was quantified by Western blotting. Glucose (increased from 5 to 11 mM)- and IGF-1 (50 ng/ml)-induced cell proliferation was completely inhibited by LY294002, an inhibitor of PI3 kinase, and by dex (100 nM, 1-4 d). In parallel, dex inhibited IRS-2 and PKB phosphorylations, an effect partially restored by IGF-1. In the presence of IGF-1, dex-induced cell death was reduced by 54 %. Surprisingly, when LY294002 was added to inhibit IGF-1 activation of PI3 kinase, dex-mediated apoptosis was inhibited by 75 %, while PKB was dephosphorylated. The addition of p42/p44 MAP kinase inhibitor PD98059 antagonized the protection of apoptosis by IGF-1. These data suggest that IGF-1-stimulated proliferation via PI3-kinase is inhibited by dex, while IGF-1 protection against cell death occurs in the absence of PKB phosphorylation, probably through activation of MAP-kinase pathways and counteracts dex-mediated apoptosis.