EFFECTS OF PROINSULIN C-PEPTIDE ON CYTOKINE-MEDIATED CYTOTOXICITY IN RINm5F INSULINOMA CELLS AND RAT PANCREATIC ISLETS

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Type 1 and late stages of Type 2 diabetes are characterized by pancreatic β-cell dysfunction and death. Inflammation is one of the key events that trigger β-cell death and proinflammatory cytokines are directly involved in the process. In the present study, we investigated whether proinsulin C-peptide, a cytoprotective hormone, could protect rat insulinoma (RINm5F) cells and isolated rat pancreatic islets from damage caused by IL-1β and TNF-α. RINm5F cells (10^4/well) or rat pancreatic islets (10/well) were cultured on 96-well plates for 24 h in RPMI-1640 medium supplemented with 10% fetal calf serum, L-glutamine and antibiotics at 37°C and 5% CO_2. Cultures were pretreated with varying concentrations of recombinant human C-peptide for 24h. Cell cultures and islets were incubated with varying cytokine concentrations for 24h and cell viability was determined by the C,N-diphenyl-N-4,5-dimethyl thiazol-2-yl tetrazolium bromide (MTT) colorimetric assay. Exposure to 5ng.mL^{-1} IL-1β and 50ng.mL^{-1} TNF-α reduced the amount of viable cells to 35±2.7% and viable pancreatic islets to 40±1.8%. Physiological concentrations of C-peptide failed to protect cells and islets from cytokine-mediated cytotoxicity, but a pharmacological dose (10nM) proved to be significantly protective. Incubation for different periods of times with human C-peptide as well as with rat C-peptide are currently being tested.

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