

EFFECTS OF VITAMIN E AND PROINSULIN C-PEPTIDE ON HYDROGEN PEROXIDE-INDUCED CYTOTOXICITY IN RINm5F INSULINOMA CELLS AND RAT PANCREATIC ISLETS

Mares-Guia, T.R.; Mariani, D.B.; Santos, E.O.; Campos, A.C.V.; Grazioli, G.; Sogayar, M.C.

Biochemistry Department, Chemistry Institute, University of São Paulo, São Paulo, SP, Brazil.

Death of pancreatic  $\beta$ -cells is the fundamental cause of type 1 diabetes mellitus and it is also associated to whole pancreas and islet transplantation failure. Oxidative stress plays a crucial role in  $\beta$ -cell death, therefore, we investigated whether vitamin E (vitE) and proinsulin C-peptide, a cytoprotective hormone, could protect rat insulinoma (RINm5F) cells and isolated rat pancreatic islets from oxidative damage caused by hydrogen peroxide ( $H_2O_2$ ). RINm5F cells ( $5 \times 10^4$ /well) or rat pancreatic islets (10/well) were cultured for 24h in RPMI-1640 medium supplemented with 10% fetal calf serum and antibiotics. Cultures were pretreated with varying concentrations of C-peptide for 1 and 24h and with vitE for 30min. Cells and islets were incubated, respectively, with  $100\mu M$  and  $500\mu M$   $H_2O_2$  for 2h and cell viability was determined by the C,N-diphenyl-N-4,5-dimethyl thiazol-2-yl tetrazolium bromide (MTT) colorimetric assay. Exposure to  $H_2O_2$  reduced the amount of viable cells to  $33 \pm 3.4\%$ . VitE ( $50\mu M$ ) and C-peptide ( $10nM$ ) were both cytoprotective, significantly increasing the amount of viable cells to  $92 \pm 15.9\%$  and  $45 \pm 3.1\%$ , respectively. Other combinations of  $H_2O_2$ , vitE and C-peptide as well as different periods of incubation are currently being tested. In conclusion, a proper dose of vitE and C-peptide could provide an effective means to protect  $\beta$ -cells from oxidative damage.

FINEP, FAPESP, CNPq, Biommm S.A.