

**P008** Differential regulation of the ER stress response in pancreatic beta-cells exposed to long chain saturated and mono-unsaturated fatty acids

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Type 2 diabetes is characterized by a long-term reduction in beta-cell mass which may be mediated, in part, by elevated free fatty acids (FA). A mechanism associated with endoplasmic reticulum (ER) stress could be involved in  $\beta$ -cell loss since morphological alterations to the ER have been reported in FA-treated cells. The present work has investigated the effects of FA on ER stress responses in BRIN-BD11 pancreatic  $\beta$ -cells.

Palmitate (C16:0; 0.05-0.25mM) reduced beta-cell viability in a time-dependent manner (6-24h) and caused dramatic alterations to the cell morphology, including marked distension of ER membranes. Palmitoleate (C16:1) antagonized the cytotoxicity of palmitate completely such that the cells remained viable and could proliferate but it only partially alleviated the morphological changes seen in the ER. The PERK signalling pathway of ER stress was activated dose-dependently (0.025–0.15mM) in palmitate-treated cells as indicated by increased phosphorylation of the initiation factor eIF2 $\alpha$ , expression of the transcription factor ATF4 and induction of the pro-apoptotic factor CHOP-10/GADD153. Palmitoleate inhibited the expression of these markers caused by palmitate.

Palmitoleate inhibits the induction of markers of ER-stress in beta-cells indicating that it may exert its protective actions on cell viability, at least in part, by reducing the pro-apoptotic response associated with ER stress