P026 Effects of prolonged exposure to high glucose on glucose metabolism and metabolomic profiles in pancreatic beta cells.

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Long term exposure to high levels of glucose has been shown to have detrimental effects on beta cell function. The current study investigated the effects of high glucose levels on metabolic pathways to enhance our understanding of the mechanisms of glucotoxicity.

BRIN-BD11 cells were cultured under the following conditions for 20 h: (1) 5 mM (2) 11.1 mM or (3) 25 mM glucose. Following this period the cells were further incubated for 2h with [U-^{13}C]glucose and extracts prepared. ^{1}H and ^{13}C NMR spectra were acquired and analyses were performed on both targeted metabolites and untargeted global metabolomic profiles.

Following prolonged exposure to 25 mM glucose the amount of ^{13}C label at glutamate C4 decreased significantly from 33.8 to 27.7 nmol/mg protein ($P<0.05$). These changes indicate changes in fluxes through pyruvate carboxylase(PC) and pyruvate dehyrdogenase(PDH) and further analyses are underway to determine the fluxes. To gain information on changes in metabolites that were not directly produced from glucose a metabolomic approach was used.

A novel approach of combining flux analysis and metabolomic profling was applied to probe the metabolic disturbances caused by prolonged exposure to high glucose. Results will be presented in the context of glucotoxicity.