

P015 Arachidonic acid induces changes in gene expression and insulin secretion in the BRIN BD11 clonal rat pancreatic β -cell line

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Previous studies in our lab have shown that polyunsaturated fatty acids led to increased β -cell proliferation and increased L-alanine stimulated insulin secretion. In the present study, the effects of chronic exposure (24 hr) to the polyunsaturated fatty acid arachidonic acid (AA) on cell viability, insulin secretory function and gene expression was evaluated using clonal BRIN BD11 beta cells. The impact of AA derived metabolites via the cyclooxygenase (COX) and lipoxygenase (LOX) pathways was evaluated via specific inhibition of these crucial pathways. The effect of inhibition of AA liberating phospholipase A₂ (PLA₂) with respect to insulin secretion was also determined. Expression profiling of BRIN BD11 cells chronically exposed to 100 μ M AA was performed using oligonucleotide microarray analysis. Two genes were found to be significantly upregulated and two genes were shown to be significantly downregulated in response to 100 μ M AA. Addition of AA, with concurrent inhibition of the COX-1 isoform (using 100 μ M acetaminophen) significantly reduced ($p < 0.01$) nutrient induced insulin secretion. On the other hand addition of AA with concurrent inhibition of the COX-2 isoform (using 100 μ M NS-398) led to a significant increase ($p < 0.05$) in nutrient induced insulin secretion. Specific inhibition of PLA₂ resulted in a significant reduction ($p < 0.001$) in nutrient induced insulin secretion thus confirming that endogenously derived AA is critical for nutrient induced insulin secretion from BRIN BD11 cells. We conclude that AA and its metabolites generated via COX-1 are beneficial to β -cell gene expression, metabolism and insulin secretion dependent on stimulus-secretion coupling.