

P003 The effect of over- expression of the mitochondrial Aspartate- Glutamate carrier Aralar1 on insulin secretion and metabolism in the BRIN- BD11 cell line

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In the beta cell, mitochondrial NADH- shuttles are important for coupling glycolysis to mitochondrial energy metabolism. Aralar1, an Aspartate-Glutamate carrier in the Malate- Aspartate shuttle, has been found to play an important regulatory role in oxidative glucose metabolism and insulin secretion in rat derived INS- 1E cells as well as in the clonal BRIN- BD11 cell line. We have now over- expressed Aralar1 by the means of the recombinant Adenovirus AdCA- Aralar1 in clonal BRIN BD11 cells and have investigated the involvement of Aralar1 in stimulation of glucose and amino acid metabolism plus insulin secretion in the presence or absence of the aminotranferase inhibitor Aminooxyacetate. The following parameters were determined: Glucose, alanine, aspartate and glutamine consumption, lactate and glutamate generation, mitochondrial membrane potential, NADH and ATP levels, triglyceride and glycogen content and insulin secretion. Aralar1 over- expression in BRIN-BD11 cells resulted in enhanced glucose consumption ($p < 0.05$), mitochondrial membrane hyperpolarization ($p < 0.05$), NADH levels ($p < 0.05$) and insulin secretion ($p < 0.01$). Insulin secretion and glucose consumption were further enhanced by the presence of 10mM alanine (+30%, $p < 0.01$ and +25%, $p < 0.05$) whereas both were significantly reduced by the presence of 10mM L- aspartate ($p < 0.05$). Addition of L- glutamine did not significantly change any of these parameters. Alanine consumption was significantly increased in cells over- expressing Aralar1 ($p < 0.05$) whereas aspartate consumption at both basal and 16.7mM glucose levels showed no difference to control cells. The presence of 5mM aminooxyacetate did not inhibit insulin secretion or glucose consumption in Aralar1- over- expressing cells. In conclusion, the Aspartate- Glutamate exchanger Aralar 1 may be an important site for metabolic control and stimulus-secretion coupling in the pancreatic beta cell.