

**P002** Glucose-dependent changes in GABA<sub>A</sub> receptor gene expression in pancreatic alpha cells

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In response to high glucose concentrations,  $\gamma$ -amino butyric acid (GABA) is released from pancreatic islet beta cells and activates GABA<sub>A</sub> receptor (GABA<sub>A</sub>R) chloride channels in alpha cells. This hyperpolarizing action of GABA may then inhibit the secretion of glucagon, implicating GABA as an important component of the intra-islet control of hormone release. At present, very little is known about the composition or regulation of GABA<sub>A</sub>Rs in pancreatic alpha cells. Here we have examined the expression of GABA<sub>A</sub>R subunit mRNAs in mouse islets and in the glucagon-releasing alpha-TC1-9 cell line. In addition, we have tested whether the expression of GABA<sub>A</sub>Rs is regulated by glucose. In both pancreatic islets and in alpha-TC1-9 cells, one-step RT-PCR revealed that only a subset of GABA<sub>A</sub>R subunit genes are expressed:  $\alpha$ 4,  $\beta$ 3 and  $\gamma$ 2 subunits. We used quantitative real-time RT-PCR to examine the effects on GABA<sub>A</sub>R gene expression of culturing cells at different concentrations of glucose (mM: 0.5, 1.0, 3.0, 10, 16) for up to 48 h. Glucose dose-dependently increased the expression of all subunits, with the expression of  $\alpha$ 4,  $\beta$ 3 and  $\gamma$ 2 subunits at 16mM glucose being 2-3fold above that at 1mM. This suggests that the local cellular environment in the pancreatic islet could be an important determinant of alpha cell GABA<sub>A</sub>R expression and glucagon release.