

**P007** Role of Sterol Regulatory Element Binding Protein1 (SREBP1) in the potentiation of glucose stimulated insulin secretion by chronic hyperglycemia

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**Aims:** Chronic hyperglycaemia potentiates glucose-induced insulin secretion from mouse islets. Up-regulation of SREBP1, a transcription factor implicated in the control of lipogenesis, may be involved in mediating these effects. Here, we investigated the impact of SREBP1 deletion in mice on glucose homeostasis *in vivo* and on the response of islets to chronic hyperglycaemia *in vitro*. **Methods:** Intraperitoneal glucose tolerance tests were performed after intraperitoneal injection of 2g/kg glucose. For hyperglycaemic culture, islets isolated by collagenase digestion were incubated for 96 h at 8 or 30 mM glucose. Glucose-stimulated insulin secretion (GSIS) was measured by radioimmunoassay. **Results:** Although SREBP1(-/-) mice displayed impaired glucose tolerance, GSIS was identical in islets freshly isolated from SREBP1(-/-) and wild-type mice. After culture under conditions of chronic hyperglycaemia insulin release stimulated acutely by 17.0 vs 3 mM glucose was significantly impaired in SREBP1(-/-) islets compared with islets from normal mice. **Conclusions:** SREBP1 expression is not required for the normal stimulation of insulin secretion by glucose but is required for the potentiation of GSIS provoked by hyperglycaemia in mice. The present data thus implicate a role for  $\beta$ -cell lipid synthesis in this adaptation to hyperglycemia.