

**P059** Induction by glucose of beta-cell genes involved in glucose sensing requires Sterol regulatory element binding protein1 (SREBP1)

**F. Diraison<sup>1</sup>, M.A. Ravier<sup>2</sup>, H. Shimano<sup>3</sup>  
and G.A. Rutter<sup>4</sup>**

<sup>1</sup>University of Bristol, U.K., <sup>2</sup>University of Louvain, Belgium,  
<sup>3</sup> University of Tsukuba, Japan, <sup>4</sup>Imperial College, London.  
U.K.

**Aims:** Culture at elevated glucose concentrations potentiates glucose-induced insulin secretion from mouse islets. We found recently that the transcription factor SREBP1, a “master” controller of lipogenesis, was required for this response. Here, we have examined in mouse islets the effect of chronic hyperglycaemic culture and the impact of SREBP1 deletion in the expression of beta-cell specific genes. **Methods:** SREBP1<sup>-/-</sup> or wild-type mice islets were isolated and cultured for 96h at 8 or 30 mmol/l glucose. SREBP1c, fatty acid synthetase (FAS), acetyl-CoA carboxylase-1 (ACC1), glucose transporter-2 (SLC2A2), glucokinase (GCK), sulfonylurea receptor-1 (ABCC8), potassium inward rectifier 6.2 (KCNJ11), pancreatic-duodenal homeobox factor-1 (Pdx1) mRNA levels were determined after RNA extraction and quantitative real-time RT-PCR. **Results:** When chronically exposed to 30 *versus* 8 mmol/l glucose, SREBP1c, FAS, ACC1, SLC2A2, GCK, Pdx1, ABCC8, and KCNJ11 gene expression were increased in islets from wild-type mice, and this effect was abolished in SREBP1 deleted mice islets. **Conclusion:** These results demonstrate a requirement for SREBP1 in the induction by glucose of lipogenic genes, but also, for genes involved in the control of the beta-cell transcriptome (Pdx1) and glucose sensing (SLC2A2, GCK, KCNJ11, ABCC8).