

P006 Carbohydrate Response-Element Binding-Protein regulates lipogenic genes and *Pdx-1* expression in MIN6 β -cells.
G. da Silva Xavier, F. Diraison, Q. Qian, G.A. Rutter, and I. Leclerc.
University of Bristol, Department of Biochemistry.

Carbohydrate Response-Element Binding-Protein (ChREBP) is required for the expression of several hepatic glycolytic and lipogenic genes. We show here that ChREBP regulates the expression of the liver-type pyruvate kinase (L-PK), fatty acid synthase (FAS) and pancreatic duodenum homeobox-1 (*Pdx-1*) genes in MIN6 pancreatic β -cells. Chromatin immunoprecipitation assay revealed binding of ChREBP to the L-PK promoter and silencing of ChREBP expression by RNA interference or microinjection of α -ChREBP antibodies into single cells led to a 3.75 ± 0.0096 fold decrease in preproinsulin promoter activity at 30 mM glucose completely abolished activation of the L-PK promoter by 30 vs 3 mM glucose. Correspondingly, ChREBP silencing abolished the increase in endogenous L-PK mRNA induced by 30mM (vs 3mM) glucose and prevented the increase in triglyceride content at 30mM glucose. Whereas FAS gene expression was increased by ChREBP, expression of the *Pdx-1* gene was inhibited by this factor. The latter effect was apparently indirect with no direct binding of ChREBP to any of the ten potential E-boxes in the proximal (2 Kb) *Pdx-1* promoter. We conclude that glucose-induced increases in ChREBP expression may contribute to triglyceride accumulation in the β -cell in type II diabetes. Consequent changes in the expression of *Pdx-1* and other genes may eventually lead to the loss of normal glucose-induced insulin secretion.