

**P055** Regulation of the Aryl Hydrocarbon Receptor Nuclear Translocator (ARNT) gene expression by the Carbohydrate-Responsive Element Binding Protein (ChREBP)  
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Background: Carbohydrate-Responsive Element-Binding Protein (ChREBP) is a recently-described transcription factor which has been shown to regulate carbohydrate metabolism in the liver and pancreatic  $\beta$  cells. Only four target genes for ChREBP have been identified so far. We have performed genome-wide analysis of ChREBP transcriptome using chromatin immunoprecipitation and high density oligonucleotide tiling arrays (ChIP-chip). Methods: ChIP-chip assay (Agilent technologies) was performed using MIN6 pancreatic  $\beta$  cell extracts. Luciferase reporter gene plasmids and RNAi duplexes were introduced using Lipofectamine and TransIT-TKO™ (Mirus Corp) respectively. mRNA was quantitated by Quantitative real-time PCR (TaqMan; ABI Prism) Results: Applying a threshold of  $p < 0.001$ , 160 genes were considered positive for ChREBP binding, representing less than 1% of the genome. Six of these genes are potentially linked to glucose-sensing or insulin secretion including the transcription factor ARNT/HIF1 $\beta$  implicated in altered gene expression and pancreatic-islet dysfunction in type 2 diabetes. Confirming a role for ChREBP in ARNT gene regulation, over-expression of ChREBP repressed ARNT promoter activity and ChREBP silencing increased ARNT mRNA levels. Conclusion: These results demonstrate that ChREBP acts as a repressor of the ARNT gene and is likely to be involved in the pathogenesis of type 2 diabetes.