

P035 COUP-TFII is negatively regulated by insulin and glucose via the Foxo1 and ChREBP controlled pathways
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The transcription factor Chicken Ovalbumin Upstream Promoter-Transcription Factor II (also called NR2F2) is an orphan member of the steroid/thyroid hormone receptor superfamily. We reported that heterozygous pancreatic beta-cell deletion of COUP-TFII in mice led to abnormal insulin secretion with hyperinsulinemia in fasted and fed states and impaired glucose tolerance. Recently, we set out to elucidate the molecular function of COUP-TFII in pancreas and liver. COUP-TFII expression is inhibited in the pancreas and liver of mice refed with carbohydrate and in *ob/ob* mice. In pancreatic beta-cells, COUP-TFII gene expression is repressed by secreted insulin in response to glucose through Foxo1 signaling. *Ex vivo* functional analysis revealed that COUP-TFII reduced insulin production and secretion. Our results suggest that beta-cell insulin secretion is under the control of an autocrine positive feedback loop by alleviating COUP-TFII repression. In hepatocytes, both insulin and high glucose concentrations repressed COUP-TFII expression. Finally, we demonstrate that this negative glucose effect implicated ChREBP expression. We propose that COUP-TFII is a novel player in coordinately controlling insulin and glucose production.