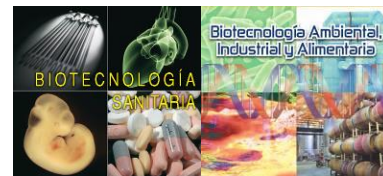


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Poster

## Characterization of the "diabesity" gene HMG20A in pancreatic islets



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### ABSTRACT

**Motivation:** Type 2 Diabetes (T2D) accounts for 90-95% of diagnosed diabetic patients, which tendency in the next years is also expected to increase. Recent genomic wide association studies showed a correlation of an allelic variation of HMG20A with T2D in some ethnic groups. Up to date, there is no scientific evidence of the role of this gene in pancreatic tissue. But, in central nervous system, HMG20A regulates the expression of NeuroD, common in pancreas and nervous system morphogenesis. Here, our group makes an approach to characterize HMG20A in pancreatic islets, focusing on its involvement in glucose-stimulated insulin secretion (GSIS) and pancreatic islets development. We want to demonstrate that: 1) HMG20A is expressed in endocrine pancreas 2) HMG20A modifies expression of genes involved in pancreas development 3) silencing HMG20A affects expression levels of insulin secretion related genes and functionality.

**Methods:** Qualitative expression of HMG20A is tested out in slides of pancreatic sections obtained from control mice. Co-localization with  $\alpha$  or  $\beta$  cells is analyzed by immunofluorescence using anti-HMG20A, anti-insulin/glucagon antibodies and Dapi for nuclei. INS-1E cells are cultured and treated with a specific siRNA against HMG20A or a non-specific siRNA control during 72h. Genes involved in insulin secretion and endocrine pancreas development are assayed via qRT-PCR in INS1-E cells after siRNA treatment. Pdx1, Pax4, MafA and HMG20A expression levels are assessed following 2- $\Delta\Delta$ Ct method. Finally, HMG20A silenced mouse islets and INS-1E are cultured at low glucose (2.8 mM) and high glucose medium (22 mM) following quantification of insulin secretion by ELISA.

**Results:** Immunofluorescence confirmed co-localization of HMG20A with insulin ( $\beta$ -cell) and with glucagon ( $\alpha$ -cells) producing cells in mouse pancreas. HMG20A expression diminished a 60% after treating INS1-E cells with a specific siRNA for HMG20A. Insulin secretion regulator gene, MafA, is downregulated significantly (50-60%) after HMG20A silencing. Pax4 expression significantly increased meanwhile Pdx1 showed a tendency to decrease. A 40% drop in insulin secretion is obtained in siHMG20A treated mouse islets compared to control.

**Conclusions:** This data confirms HMG20A expression in pancreatic islets and impairment of insulin secretion when it is knocked down. Hence, concluding that HMG20A plays an important role in physiological GSIS and regulating pancreatic development related genes.

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