Endocrinol Nutr. 2016;63(Espec Cong):11

Endocrinología y Nutrición

O-011. - THE DIABETES-LINKED FACTOR HMG20A TARGETS ISLET GENES INVOLVED IN INSULIN SECRETION

J.M. Mellado-Gil[a], E. Fuente-Martín[b], P.I. Lorenzo[b], J.C. Reyes[b], F.J. Bermúdez-Silva[c], M. Aguilar-Diosdado[d] and B. Gauthier[b]

[a]Hospital Universitario Puerta del Mar, Cádiz. CABIMER, Sevilla. [b]CABIMER, Sevilla. [c]IBIMA, Málaga. [d]Hospital Universitario Puerta del Mar, Cádiz.

Resumen

Introduction and objectives: Recent genome-wide association studies (GWAS) have identified *HMG20A* as a susceptibility locus for type 2 diabetes mellitus (T2DM). This gene encodes a factor that binds chromatin and exerts global genomic changes. Thus the role of HMG20A in the development and establishment of T2DM is far from evident. To assign a function to HMG20A in islet physiology, we aimed herein to: 1) Assess the expression levels of HMG20A in islets and whether acute or chronic exposure to glucose alters these levels and 2) determine the impact of HMG20A on glucose-stimulated insulin secretion (GSIS).

Material and methods: HMG20A transcript levels were assessed by quantitative PCR (QT-PCR) in various tissues under basal or high glucose concentrations. Protein levels were also assessed by immunohistochemistry in islets. To evaluate the effect of HMG20A on beta cell function, expression levels of potential targets involved in insulin biosynthesis and secretion such as NEUROD, SNAP25, SYTVII, PI3K, Glucokinase (GK), GLUT-1 and GLUT-2 were measured following 72 hours of siRNA-mediated repression of HMG20A in MIN-6 and INS-1 cells. Data mining for HMG20A expression levels in both Type 1 (T1DM) and T2DM patients was performed using the Nextbio database from Illumina (www.nextbio.com).

Results: High levels of HMG20A were detected in islets as compared to muscle and adipose tissue, whereas the transcript was more abundant in the liver. HMG20A protein was detected in mouse and human beta cells as well as in other islet cell types. Short-term exposure to glucose induced a transient increase in HMG20A transcript levels reaching a maximum of 2-fold at 72 hours in human islets with similar results in MIN-6 cells. However, expression of HMG20A was decreased in T2DM and T1DM patients as compared to non-diabetic subjects. siRNA-mediated repression of HMG20A in MIN-6 as well as in INS-1 cells resulted in decreased expression of NEUROD, INSULIN, and GK whereas PI3K and GLUT2 were increased. In parallel, GSIS was impaired following siRNA-mediated HMG20A repression in INS-1 cells.

Conclusions: HMG20A modulates GSIS through regulation of metabolism-secretion coupling genes.

Funding: This work is funded by the ISCIII (PI13/00593 to BG) and the Ministerio de Economía y Competitividad (JCI-2012-12491 to EFM).