Endocrinol Nutr. 2016;63(Espec Cong):77

Endocrinología y Nutrición

P-030. - THE DIABETES-LINKED FACTOR HMG20A IS EXPRESSED IN ASTROCYTES AND MODULATES GLUCOSE-DERIVED LACTATE SECRETION

E. Fuente-Martín[a], J.M. Mellado-Gil[a], F.J. Bermúdez-Silva[b], J.C. Reyes[a]and B. Gauthier[a]

[a]CABIMER, Sevilla. [b]IBIMA, Málaga.

Resumen

Introduction and objectives: Polymorphisms in HMG20A have been linked to type 2 diabetes mellitus and potentially with obesity in multiple ethnic populations. This gene encodes a factor involved in central nervous system (CNS) development underlying a potential link between HMG20A deregulation and CNS-mediated glucose homeostasis. Fundamental to this process are astrocytes that generate lactate in response to glucose thereby increasing energy availability to neighboring neurons. Failure in this cross-talk results in metabolic diseases. Herein we aimed to establish whether HMG20A is expressed in mature astrocytes and whether it is implicated in the regulation of glucose derived lactate secretion important for neuronal function.

Material and methods: Immunohistochemistry for HMG20A and GFAP (astrocyte marker) or Tuj-1 (neuronal marker) was performed in mouse brain sections. The astrocytes C6 glioblastoma cell line was exposed to low (6 mM) or high (25 mM) glucose concentrations for 1, 24 or 48 hours and HMG20A expression levels were evaluated by Quantitative PCR. siRNA-mediated repression of HMG20A in C6 cells was employed to evaluate the function of HMG20A on astrocytes.

Results: High expression levels of HMG20A were detected in mouse brain as compared to other organ such as adipose tissue or muscle. Co-immunohistochemistry analysis confirmed the expression of this protein in both neurons and astrocytes. High glucose concentrations decreased HMG20A transcript levels at 24 and 48 hours while increasing the constitutive release lactate. Interestingly, siRNA-mediated repression of HMG20A in C6 cells caused a 60% decrease in transcript levels with a concomitant induction of lactate release at basal glucose concentrations. Expression levels of the glucose transporters, GLUT1 and GLUT2 as well as the receptors for leptin and insulin were increased by HMG20A repression indicative of more active astrocytes. Consequently, cell death was increased by 20% after HMG20A repression.

Conclusions: Glucose-targeted HMG20A expression potentiates astrocytes metabolic activity that may be important for the control of glucose homeostasis by neurons.

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