

12th European Diabetes Congress

September 15-17, 2016 Berlin, Germany

Unfolding the novel role of *SLC35b4* in glucose production and diabetes: Localization, expression, protein profiling and pathway analysis in HepG2 cells

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Type II diabetes is one of the most common endocrine disorders. The cumulative action of genetic variants account for 10% of heritability. *SLC35b4*, a solute receptor associated with obesity, insulin resistance and gluconeogenesis, transports UDP-N-acetylglucosamine and UDP-Xylose. The correlation between expression and functionality and the mechanism of action have not been elucidated. This study aimed to investigate the regulation of protein expression and localization of *SLC35b4*. We also aimed at comparing differentially expressed proteins between a knockdown of *SLC35b4* and controls in HepG2 cells in order to decode its implication in macromolecules glycosylation and sugar production. Responsiveness was assayed using western blot analysis and immunostaining. To identify the cytoplasmic compartment harboring *SLC35b4*, double immunofluorescence (*SLC35b4*-Golgi apparatus and endoplasmic reticulum) studies were performed. The subcellular localization was confirmed using a PLA technique (duo-link). 2D gel electrophoresis and MALDI_TOF were used to identify differentially expressed proteins. Pathway analysis was performed to understand the downstream effect of the gene knock-out. Results revealed *SLC35b4* is increased up to 60% upon glucose stimulation. *SLC35b4* localized with Golgi apparatus and to a lesser extent with the endoplasmic reticulum. The presence of *SLC35b4* in the Golgi apparatus confirms its involvement in the biosynthesis of glycoconjugates proteins. Four proteins were under-expressed when *SLC35b4* gene was knocked out (HSPD, HSPA8, TUBA1A, and ENO1), all of which are involved in pathways affecting glucose and insulin homeostasis. We suggest that *SLC35b4* activation alters the glycosylation pattern inside the cells causing an improvement of the insulin ability to inhibit endogenous glucose production.

Biography

Soha N Yazbek is an Assistant Professor of Genetics at the Medical Laboratory Sciences Program, AUB. She is trained in Basic Genetics and focuses on researching the genetic basis of complex multifactorial diseases (diabetes and non-communicable diseases). She also works to identify the research gap in non-communicable diseases in selected countries of the region. Recently, her research has focused on the genetic disease status and the genetic service response in Lebanon. She holds a PhD in Genetics from Case Western Reserve University, and MS in Molecular Biology from the Lebanese American University and a BS in Medical Laboratory Sciences at AUB.

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