EVALUATION OF VARIANTS IN DNAJB6 AS A MODIFIER OF DISEASE EXPRESSION IN PATIENTS WITH NIEMANN-PICK TYPE C.

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The NPC1 gene codes for a transmembrane protein that is responsible for the transport of low-density lipoproteins to late endosomal/lysosomal compartments. Mutations in this gene are associated to Niemann-Pick type C (NP-C) disease, an autosomal recessive disorder characterized by lysosomal storage of unesterified cholesterol that leads to progressive neurodegeneration and hepatosplenomegaly. Different chaperones have been associated with NPC1 gene expression, including both luminal as well as cytosolic proteins. DNAJB6 belongs to Hsp40 family, a cytosolic group of chaperons. The aim of this study was to investigate whether specific polymorphisms in DNAJB6 gene can be associated to phenotypic expression of NP-C patients. DNA samples from 43 unrelated NP-C patients and 50 healthy individual were included in this study. Patient’s group was subdivided according to mutation severity. Five intronic tag SNPs (rs4716704, rs9647660, rs12668448, rs4716707, and rs6459770) in the DNAJB6 gene were selected from HapMap and genotyped using validated TaqMan® assay. Allelic and genotypic frequencies were established and compared, and haplotypes were defined using PHASE software. Statistical analyses were performed using SPSS software. We have observed a higher frequency of C allele (rs4716704) in patients when compared to controls. Genotypic distribution was similar between patients and controls. We have also found higher frequency of ACCAG, GCCAG, and GCTGA haplotypes in patients. No additional statistically significant differences were observed between groups. Findings presented here are being further analyzed in order to understand the significance of this variation in patients with NP-C. This work together with other previous studies are providing additional knowledge into the role of chaperones in NP-C disease.

Key-words: Niemann-Pick type C, NPC1 gene, DNAJB6 chaperone.

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