Evaluation of bioinformatics characteristics of NPC1 protein (Niemann-Pick C1)

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Abstract: Niemann–Pick C1 protein (NPC1) is a late-lysosomal membrane protein involved in trafficking of cholesterol [1]. Defects in NPC1 activity leads to development of NPC disease, an autosomal recessive, neurodegenerative disorder characterized by the massive accumulation of cholesterol in lysosomal compartments [2]. In this study, bioinformatics properties of NPC1 were evaluated by NCBI, Expasy, Geneatlas and Protparam databases. Human NPC1 cDNA sequence predicts a protein of 1,278 amino acids with an estimated molecular weight of 142 kDa. Genatlas databases showed that NPC1 protein sequence including N terminal signal peptide (22 AAs), N-terminal domain (232 AAs), 13 membrane-spanning helices and sterol sensing domains (SSD), TM3 to TM7 and a dileucine motif LLNF in the C terminal region. N-terminal domain containing eight cysteine residues critical for the mobilization of cholesterol from lysosomes. Map Viewer was used to find a gene locus on a chromosome, and data showed that the NPC1 gene is located on chromosome 18q11.2. By PDB, Secondary structures of NPC1 is shown that major part of NPC1 was hydrophilic and the alpha-helix (38%; 348 AAs) was dominant secondary structure in the NPC1 protein. SMART program predicted NPC1 protein have 13 transmembrane domains, a phosphorylation region, 5 ubiquitination region, and 10 N-glycogenation regions. Amino acids composition of NPC1 was determined by Protparam tool and fount that Leucine and valine (10.5 and 8.2% respectively) are the most abundant amino acids in NPC1. Isoelectric point of NPC1 is 5.5 and its half-life is 30 hours in mammalian cells. Reactome database predicted that the only role of human NPC1 protein is exports free cholesterol from lysosomes into the cytosol. By Uniprot databases, alignment between the NPC1 and NPC2 proteins were analyzed and observed 43 amino acids repeated in both proteins and 46 amino acids were similar. 221 organisms have orthologs with human gene NPC1. According to the biogps databases, NPC1 is expressed extensively in adrenal gland, bronchial epithelial cells, retina and hypothalamus. Second structure prediction by phyre2 software shown that second structural was correct in some of parts and not in others. The results of these studies can be used to studies the binding NPC1 to cholesterol and other sterols.

Keywords: NPC1 protein, bioinformatics, Niemann–Pick C1 disease.

References

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