

## **In Silico Analysis of Deleterious nsSNPs (Missense) of Dihydrolipoamide Branched-Chain Transacylase E2 Gene Associated with Maple Syrup Urine Disease Type II**

**Authors :** Zainab S. Ahmed, Mohammed S. Ali, Nadia A. Elshiekh, Sami Adam Ibrahim, Ghada M. El-Tayeb, Ahmed H. Elsadig, Rihab A. Omer, Sofia B. Mohamed

**Abstract :** Maple syrup urine (MSUD) is an autosomal recessive disease that causes a deficiency in the enzyme branched-chain alpha-keto acid (BCKA) dehydrogenase. The development of disease has been associated with SNPs in the DBT gene. Despite that, the computational analysis of SNPs in coding and noncoding and their functional impacts on protein level still remains unknown. Hence, in this study, we carried out a comprehensive in silico analysis of missense that was predicted to have a harmful influence on DBT structure and function. In this study, eight different in silico prediction algorithms; SIFT, PROVEAN, MutPred, SNP&GO, PhD-SNP, PANTHER, I-Mutant 2.0 and MUPO were used for screening nsSNPs in DBT including. Additionally, to understand the effect of mutations in the strength of the interactions that bind protein together the ELASPIC servers were used. Finally, the 3D structure of DBT was formed using Mutation3D and Chimera servers respectively. Our result showed that a total of 15 nsSNPs confirmed by 4 software (R301C, R376H, W84R, S268F, W84C, F276C, H452R, R178H, I355T, V191G, M444T, T174A, I200T, R113H, and R178C) were found damaging and can lead to a shift in DBT gene structure. Moreover, we found 7 nsSNPs located on the 2-oxoacid\_dh catalytic domain, 5 nsSNPs on the E\_3 binding domain and 3 nsSNPs on the Biotin Domain. So these nsSNPs may alter the putative structure of DBT's domain. Furthermore, we detected all these nsSNPs are on the core residues of the protein and have the ability to change the stability of the protein. Additionally, we found W84R, S268F, and M444T have high significance, and they affected Leucine, Isoleucine, and Valine, which reduces or disrupt the function of BCKD complex, E2-subunit which the DBT gene encodes. In conclusion, based on our extensive in-silico analysis, we report 15 nsSNPs that have possible association with protein deteriorating and disease-causing abilities. These candidate SNPs can aid in future studies on Maple Syrup Urine Disease type II base in the genetic level.

**Keywords :** DBT gene, ELASPIC, in silico analysis, UCSF chimera

**Conference Title :** ICBBCB 2018 : International Conference on Bioinformatics, Biomedicine, Biotechnology and Computational Biology

**Conference Location :** Montreal, Canada

**Conference Dates :** May 24-25, 2018