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Homozygosity mapping in maple syrup urine disease patients from Iran: Identification of novel, recurrent mutations

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Introduction: Maple syrup urine disease (MSUD) is a rare inborn error of metabolism of branched-chain amino acid metabolism. The disease prevalence is higher in populations with the higher rate of consanguineous marriage like Iran (38.6%). Different mutations have been previously reported in *BCKDHA, BCKDHB, DBT* and *DLD* is known to be responsible for MSUD phenotype.

Materials & Methods: In this study, two sets of multiplex polymorphic STR (short tandem repeat) markers linked to the above-mentioned genes were used in homozygosity mapping in order to find probable pathogenic changes in 40 studied families. The families which showed homozygous haplotypes for *BCKDHA, BCKDHB* and *DBT* genes were subsequently sequenced.

Results: Our findings revealed that exon 2, 4 and 6 of *BCKDHA* gene contained most of the mutations which were novel. The changes include one reported point mutation (c.890G>A (p. R297H)), 7 nucleotide insertion (c.355-356 Ins 7nt (p. D355Dfs)) and a splice site mutation (c.288G>A). In *BCKDHB* gene we identified one reported (c.853 C>T (p. R285X)) and two novel point mutations [(c.599 C>T (p. P200L), c.484 A>G (p. N162D)]. In DBT gene we found novel homozygote deletion of exon 5,6 and 7 in one patient as well as a point mutation and deletion (c.363delCT/ c.1238T>C).

Conclusion: Computational approaches were used to analyze these novel mutations in terms of their impact on protein structure. Computational structural modeling indicated that these mutations might affect structural stability and multimeric assembly of branched-chain keto acid dehydrogenase complex (BCKDC).

Biography

Hassan Saeiahan is a Medical Genetics Master's student in Iran University of Medical Science, Tehran, Iran. He has the honor of 1st grade and highest GPA in the field of Animal Biology (BSc) and obtained Silver medal at National Biology Olympiad 2017. He also got 9th rank in cellular and molecular biology master's entrance exam. He has also done several researches about natural drugs and drug side effects and published a book and several papers at renowned journals.

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