The Nudix Hydrolase (*NUDT15)* Gene Variants among Jordanian Population

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Abstract

Background: Nudix Hydrolase 15 gene (*NUDT15*) encodes nucleotide triphosphate diphosphatase which metabolizes the purine analog drugs, such as anticancer thiopurine and anti-gout allopurinol. Genetic variants on *NUDT15* gene effect on drug dephosphorylation and hence susceptibility to drug-induced toxicity. The *NUDT15* gene has been genotyped in many ethnic groups but still has not been genotyped among Middle Eastern Arab Jordanian population.

Aim: The current study aims to identify *NUDT15* genetic variants among Jordanian Arab population.

Method: The DNA samples were isolated from the leukocytes of 85 healthy, unrelated Jordanian Arab volunteers. The total 3 exons of *NUDT15* gene, in addition to some parts of intron 1, 2 and the 3' untranslated region (3'UR), were amplified using polymerase chain reaction (PCR). Then, the PCR products were purified and sequenced using Applied Biosystems Model (ABI3730x1).

Results: Six *NUDT15* genetic variants were found among the volunteers as following: The novel synonymous 36A>G (6%, 95%CI= 3- 9%) on exon 1, the intronic IVS1 +116C>T in intron 1 (0.6%, 95%CI= 0-2%), the non-synonymous 415C>T (0.6%, 95%CI= 0-2%) and novel non-synonymous 404C>A (0.6%, 95%CI= 0-2%) on exon 3, and novel 502G>A (2%, 95%CI= 0.5-4%) and 588T>C (0.6%, 95%CI= 0-2%) variants on 3'UR. It is found that the most common allele among Jordanians is *NUDT15 36A>G*. The *In silico* softwares predicted that novel *NUDT15 404C>A* has harmful effects on *NUDT15* stability and function.

Furthermore, the frequency of *NUDT15* IVS1 +116C>T, among Jordanians, was significantly (p value > 0.05) different than what was reported among other ethnic populations, while the frequency of 415C>T variants was similar to Europeans but significantly (p value > 0.05) lower than Asians and Indians.

Conclusions: The frequency of *NUDT15* genetic variants is low among the Jordanian volunteers and it is significantly different than other ethnic groups. The findings of this study may increase our understanding of the inter-individual variation in the response to purine analog drugs. Further clinical studies are needed to investigate the influence of novel *NUDT15 404C>A* on drug metabolism and response.

Keywords: *NUDT15*, Jordanians, genetic variants, dephosphorelation