Identification of Novel Genetic Variant on N-Acetyltransferase 2 Gene (*NAT2*) with *In Silico* Functionality among Jordanian Population

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Abstract

Background: Genetic variants of N-acetyltransferase 2 gene (*NAT2*) influence the acetylation capacity of drugs and toxic compounds. The *NAT2* genetic variants and haplotypes weren't fully identified among Jordanian population.

Aims: The present study aims to sequence the *NAT2* gene among a sample of healthy Arab Jordanian volunteers; in order to identify the *NAT2* haplotypes, linkage disequilibrium and novel *NAT2* genetic variants among Jordanian population.

Methods: The present study sequenced the functional exon 2 in *NAT2* gene completely for 68 healthy unrelated Jordanian volunteers.

Results: The allele frequency of known *NAT2* genetic variants 282C>T, 341T>C, 481C>T, 590 G>A and 803A>G were 26.5, 48.5, 35.3, 30.9 and 32.4%, respectively. The most common genetic variant among Jordanian volunteers was *NAT2* 341T>C with a frequency of 27.7% (95% confidence interval 15.7 – 29.8%). The *NAT2* allele frequencies were similar to the white European while different than the Asian and African populations. The most common *NAT2* haplotype was *NAT2*5B* with a frequency of 29.3%. According to the *NAT2* haplotype frequencies, 72% (95% confidence interval 61.4 – 82.7%) of the volunteers were slow encoding *NAT2* haplotype acetylators. The *NAT2*5* represented variants 341T>C and 481C>T were in strong but not in complete linkage disequilibrium ($D' = 0.8$, $r^2 = 0.63$). In addition, this study found a novel *NAT2* 436G>C genetic variant with low frequency (0.7%). However, this novel variant was predicted to be tolerated and not harmful to the NAT2 protein, using *in silico* prediction tools.

Conclusions: The frequency of slow encoding *NAT2* haplotype was high among the Jordanian volunteers which may have effects on drug responses and susceptibility to some diseases, such as cancers. Further intensive *in vitro* and *in vivo* studies are needed to find the effect of the novel *NAT2* genetic variant 436G>C on drug response.

Keywords: Acetylation, *NAT2* gene, genetic variants, Jordanians.