Ethnic differences in allelic frequency of two flavin-contaning monooxygenase 3 (*FMO3*) polymorphisms : in vivo and in vitro effects

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In hepatic FMO drug-metabolizing enzyme systems, FMO3 is the major enzyme present in adult huam liver. In the present study, we report that the frequency of each individual allele varies significantly among three different populations, resulting in large differences in the frequency of the cis-linked heterozygous FMO3 genotype.

Genomic DNA samples from 210 Korean, 188 African-American, and 52- Caucasian-American volunteers were examined for the presence of the FMO3 mutant alleles (Glu159Lys, Glu308Gly).

Our study demonstrates a marked inter-ethnic difference in the allelic frequencies of two relatively common FMO3 sequence variants. Most importantly, our results provide strong evidence that these two missense mutations fail to alter enzyme activity individually, but do so significantly when they occur together in cis. Kinetic analysis revealed also that the Vmax/Km value 'hd' cis-variant protein only was decreased.

Taken together with the large inter-population differences in allelic frequencies for the two FMO3 sequence variants, we predict that these two variants contribute significantly to the variations of the drug-metabolizing system observed in FMO activity between different ethnic groups.