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Tapping untapped: Exploring role of ALDH in pharmacogenetic and toxicogenetic studies

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The response to a xenobiotic may be influenced by polymorphic genes of metabolizing enzymes and transporters. We had previously reported, selected genotype profiles for the breast cancer patients on fluorouracil, doxorubicin and cyclophosphamide (FAC) in a Pakistani set of population and compared them with allele frequencies in North America, Europe, Africa, China and other regions as represented in HapMap database. Our current study explores the previously reported as well as additional genotypes in healthy adults from different population subgroups at Karachi which remains unreported so far. We included 155 healthy adults after informed consent and institutional approval. The DNA was extracted from saliva collected and stored in Oragene-DNA[®] kits. Relevant SNPs of genes involved in drug metabolism and transport were genotyped either through restriction fragment length polymorphism or pyrosequencing after PCR amplification. We genotyped selected drug metabolizing enzymes involved in Phase-I metabolism (CYP1A1*2A/*3, CYP1A1*2C, CYP2B6*4, CYP2B6*6, CYP2C9*2, CYP2C19*2, CYP2C19*17, CYP2D6*4, CYP2D6*10, CYP3A4*22 and CYP3A5*3), Phase-II metabolism (ALDH3A1, GSTA1-69, GSTM1) and efflux transporters (ABCB1 1236, ABCB1 2677, ABCB1 3435, ABCC2-24, ABCC2 3972, ABCC2 1249) along with such frequencies in other population sets represented in HapMap. Interestingly, we found that although there were certain differences in allele frequencies, most notably, ALDH2 variant allele frequency is much higher in our population, thus drawing possible implications regarding environmental toxicity, atherosclerosis and other situations marked by oxidative stress. The presentation would emphasize upon the fact that molecular research outcome from one field could be used in other disciplines because of biological overlap.

Biography

Nasir Ali Afsar is a Pharmacologist and is a Member of British Pharmacological Society, Canadian Society of Pharmacology and Therapeutics, Association of Medical Education in Europe as well as Certified Researcher in Medical Education by American Association of Medical Colleges. He is affiliated to Academia since 1999 in different capacities. His research interest includes pharmacogenetics, clinical pharmacology, clinical simulation and medical education. He has several publications, invited lectures as well as conference presentations to his credit and serves as a peer Reviewer and Editorial Board Member of repute.

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