Adalberto Rezende Santos, J Pharm Drug Deliv Res 2016, 5:4(Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.011

Pharmacogenetics research in different disease models: Genetic diversity in an ethnic admixture population

Adalberto Rezende Santos
Oswaldo Cruz Institute, Brazil

In humans, the enzyme N-acetyltransferase2 (NAT2), coded by *NAT2* gene, is the main metabolizer of isoniazid, dapsone and hydralazine, used for the treatment of tuberculosis, leprosy and resistant hypertension, highly incident diseases in Brazil. We studied *NAT2* in different Brazilian populations for these three diseases. In the first study, we showed the predominance of *NAT2* slow acetylation alleles in Rio and Goias states. However, population from Rio showed a higher heterogeneity in *NAT2* allele distribution and significant higher frequency of intermediate phenotype. We identified six new SNPs allowing characterization of seven new alleles. Further, we performed an *in silico* molecular modeling and structural protein analyses of *NAT2*. The results strongly indicates the direct involvement of the new SNP (152G>T-Gly51Val) in substrate recognition, SNP (203G>A-Cys68Tyr) in the modification of the catalytic site by the loss of a functional group and SNPs (458C>T, 578C>T, 683C>T and 838G>A) in enzyme degradation, all altering the acetylation activity to slow acetylation. In a subsequent study to evaluate the influence of *CYP2E1, GSTT1, GSTM1* and *NAT2* genotypes on isoniazid-induced hepatitis in TB patients, we found that only the NAT2 slow acetylation phenotype represented a risk factor for the occurrence of this outcome during TB treatment. In a more recent study, the influence of the acetylation phenotypes in anti-hypertensive effect of hydralazine in patients with RH was evaluated. Again, the predominance of slow acetylation phenotype was observed and only slow acetylators had significant blood pressure reductions after hydralazine use, however, with a high incidence of ADRs.

Biography

Adalberto Rezende Santos is PhD in Cellular and Molecular Biology from Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. Actually, he is a Senior Investigator and Head of the Laboratory of Molecular Biology Applied to Mycobacteria of Oswaldo Cruz Institute, Supervisor at the post-graduation programs of Cellular, Molecular Biology, and Clinical Medicine from Fiocruz and Federal University of Rio de Janeiro respectively. He is *ad hoc* consultant of the Executive Secretariat of Science Technology and Environment and of the Ministry of Health, Brazil. He is also referee of the *Journal of Infectious Diseases and Pharmacogenomics*.

adalbertorezende@yahoo.com.br

Notes: