Pharmacogenetic: screening relevant polymorphisms on antiretroviral therapy in a HIV Portuguese population.

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Several factors cause heterogeneity of response to antiretroviral therapy. Genetic polymorphisms, particularly in metabolizing enzyme, cytochrome P450 isoenzymes and transport proteins MDR, MR P and SLC, may cause pharmacokinetic variability in some ARVs, leading to viral failure, drug toxicity and may explain the interpatient variability for drug absorption pathways.

Objectives

Characterize the genetic profile of HIV-infected patients in the Portuguese Population, from Santa Maria Hospital, Lisbon, Portugal.

Single-Nucleotide Polymorphism

A total of 15 SNP, with pharmacogenetics relevance, located at 9 different genes, were genotyped by Microarray analysis. The SNP were selected based on their involvement in drug metabolism and according to the collection provided by the TaqMan® Drug Metabolism Genotyping Assays.

Experimental Methods

Sample: 1 ml blood of 27 patients infected with HIV1 or co-infected with HBV/C.

Extraction DNA: PerfectPure DNA Blood Kit (5Prime). OpenArray Technology

Microarray: Genotype frequencies for the gene/SNP are not the same among the groups Caucasian and African (p-value < .05). As an example we show 2 SNPs with significance CAR NR1I3 rs2307424 (p<0.005) and CYP3A5 rs776746 (p=0.001), table 1.

Results

All SNP were in Hardy-Weinberg equilibrium except for CAR NR1I3 rs2307424 (p=0.048), CYP2A6 rs28399435 (p= 0.000) and CYP3A5 rs776746 (p=0.001), table 1.

Genotype frequencies for the gene/SNP are not the same among the groups Caucasian and African (p-value < .05). As an example we show 2 SNPs with significance CAR NR1I3 rs2307424 (p=0.005) and CYP3A5 rs776746 (p=0.001), table 2.

The comparison of SNP frequencies by gender doesn't show statistical significance, except for CYP3A5 rs776746 (allele frequencies p<0.049) (genotype frequencies p=0.007), table 3.

Population Characteristics

Is composed of 367 individuals infected with HIV-1 receiving ARV therapy. In terms of gender, 253 are male and 114 are female. In relation to the race are 275 Caucasian, 114 African and 38 unknown.

Conclusion

With the profile obtained by genetic characterization, performed in this study, we can conclude that the gene CYP3A5 rs776746 evidenced more heterogeneity in the population, according to the literature. CYP3A5*3 (rs776746) the most common non-functional allele of the gene. Seems to be an import contributor to individual and inter rational variation in CYP3A5 mediated metabolism of drugs.

Our study revealed a significant frequency of risk alleles associated with drug efficacy, safety and recommend dosage, namely CYP2A6, CAR N and CYP3A5 rs776746. And therefore could provide clinical useful information on ART in HIV Portuguese population.

Acknowledgements

This work was supported with Project INTELEGEN PTDC/DTP-FTO/1747/2012 from Fundação para a Ciência e Tecnologia, Lisbon, Portugal.