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Letter to the Editors

Study of *ABCB1* polymorphism (C3435T) in HIV-1-infected individuals from South India

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Studies on P-glycoprotein expression and function have revealed that a single nucleotide polymorphism (SNP) in the human *ABCB1* gene at 3435 (C > T) results in altered expression and function of P-glycoprotein [1, 2]. There have been reports of lower nelfinavir and efavirenz (EFV) concentrations associated with TT genotypes (mutant) of *ABCB1* C3435T polymorphism [3, 4]. Frequency distribution of this polymorphism is known to vary across populations [3, 5, 6]. We report the genotype distribution of *ABCB1* C3435T in 179 individuals (126 HIV-infected and 53 healthy) from South India. The polymorphism was correlated with plasma 12 h EFV and 2 h nevirapine (NVP) concentrations in 55 and 71 patients, respectively. Plasma EFV and NVP were estimated by HPLC [7, 8]. Genotyping was carried out by PCR-RFLP [9].

The number of TT, CT and CC genotypes, respectively, were 78 (44%), 74 (41%) and 27 (15%); C and T allele frequencies were 0.36 and 0.64, respectively. The difference between observed and expected frequency was not significant ($P > 0.05$) and satisfied Hardy–Weinberg equilibrium. This distribution is different from other populations; TT genotypes in the South Indian population were 44%, which is the highest reported so far (21–32% in Caucasians, 1–7% in Africans, 22% in Chinese, 20% in Japanese and 17% in Filipinos) [3, 5, 6]. The observed distribution was significantly different from that reported by Schaeffeler *et al.* [5] in Caucasian, African-American and Japanese populations ($P < 0.05$). The distribution of this polymorphism was similar in patients and healthy subjects. A limitation of this study was the small sample size. Hence, the allele frequency of this polymorphism needs to be studied in a larger population.

A trend in the plasma EFV concentrations was observed. Patients with the CC genotype had the highest values followed by CT and TT but the differences were not statistically significant (Table 1). Similar findings have been reported by others [3, 4]. Inter-individual variations in plasma concentrations of EFV could be due to an indirect effect of genetic variations in the *ABCB1* gene. This is probably not the only factor, since mutations in the *CYP2B6* gene could lead to altered substrate utilization [10]. Our study has shown that plasma NVP did not differ between genotypes, suggesting that NVP concentrations are not governed by genetic variations in the *ABCB1* gene (Table 1).

Differences in the distribution of the *ABCB1* C3435T polymorphism could impact on HIV-1 disease progression as well as response to antiretroviral therapy in different populations and this needs further study.

Table 1

Plasma EFV and NVP in different genotypes of the *ABCB1* C3435T polymorphism

	Plasma concentration (mean ± SD (μg ml^{-1})) 12 h EFV	2 h NVP
Total number of patients	55	71
Number of males	45	45
Mean age (range) (years)	37 (26–59)	34 (20–48)
CC genotype	5.22 ± 5.32 (10)	8.33 ± 2.78 (11)
CT genotype	3.5 ± 1.83 (22)	8.99 ± 2.64 (26)
TT genotype	2.48 ± 1.29 (23)	7.52 ± 2.65 (34)

n given in parentheses.

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