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LETTER TO THE EDITORS

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Absence of CYP2B6 promoter −82T>C mutation in Chinese as an additional factor for slow metabolism of drugs commonly used in infections

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Mehlotra et al. highlighted the importance of CYP2B6 polymorphism that underlies the variability of the metabolism of an increasing number of pharmaceutical compounds [1]. Specifically, the high allelic frequency of 2B6*6 in some populations is a case in point. We recently examined the prevalence of 2B6*6 in ethnic Chinese and found that it is high at 0.43 [2], a figure not too different from that for West Africans, as reported by Mehlotra et al. We undertook to explore the possible role of promoter polymorphisms, which may contribute to the functional variability of CYP2B6 in the population.

One hundred healthy individual buffy coat samples were collected from local Chinese (ethnic Han population) by the Hong Kong Red Cross Blood Transfusion Service from October to November of 2005. Genomic DNA was isolated from 200 μl of buffy coat sample using the QIAGEN QIAamp DNA Mini Blood Kit (Hilden, Germany) according to the manufacturer's instructions. DNA was finally eluted with 100 μl of Tris-EDTA buffer (10 mM Tris, 1 mM EDTA, pH 8.0) and stored at −20°C for assays. Primers were designed to amplify a genomic fragment in the CYP2B6 promoter region. The primers used in the polymerase chain reaction (PCR) were 5′-ACCCA CACAC CCACA CATTC ACTTG CT-3′ (forward) and 5′-TCCAC ACAGG CTGCA AACTG CTCAG AT-3′ (reverse). PCR reactions were set up in a total volume of 20 μl with Hot Start Taq polymerase (Qiagen, Germany). The PCR was carried out as follows: 95°C for 10 min for the initiation of the reaction, followed by 35 cycles of denaturing at 95°C for 1 min, annealing at 69°C for 1 min, and elongation at 72°C for 1 min. The final elongation step was set at 72°C for 10 min. PCR products were purified using a Promega Wizard SV Gel and PCR Clean-up System (Promega, Madison, WI, USA). The purified PCR products were confirmed to be a single band with expected molecular weight after electrophoresis with 1% agarose gel, and were directly applied for DNA sequencing using the ABI 3700 automated sequencer. Both the sense strand and the antisense strand were sequenced to check and confirm the −82T>C and C64T polymorphisms.

Eighty-six of 100 samples were successfully processed. Results of the C64T polymorphism were obtained from DNA sequencing chromatographs. Seventy-two of the 86 samples were CC wild type alleles, and 14 were CT heterozygous. There was no TT homozygous allele in the sample population. The allelic frequency of C>T was 0.08, which is similar to the data obtained from Caucasians [3]. The −82T>C TATA box promoter polymorphism, which had been reported to be associated with enhanced transcription activities on transfected cells, was distinctly absent [4]. A combination of a high allelic frequency of 2B6*6 and the absence of −82T>C polymorphism suggests that the prevalence of poor metabolizers could be much higher in Chinese compared with Caucasians. CYP2B6 is an important enzyme for the metabolism of therapeutic agents for the human immunodeficiency virus (HIV; for example, Efavirenz, a nonnucleoside reverse transcriptase inhibitor) and malaria (for example, artemisinin), both being infections of a pandemic scale. Although treatment is becoming increasingly accessible in developing countries, recommended regimens have largely been established from studies of Caucasian populations. A generally poorer metabolism would mean a higher tendency of adverse effects during standard treatment, while the reverse would

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lead to lower efficacy. There is clearly a need to optimize treatment for the benefit of individuals in developing countries, where HIV/AIDS and malaria continue to ravage populations.

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