Candidate HLA genes for prediction of co-trimoxazole-induced severe cutaneous reactions

Kongpan, Thachanan[a]; Mahasirimongkol, Surakameth[e]; Konyoung, Parinya[g]; Kanjanawart, Sirimas[a]; Chumworathayi, Pansu[b]; Wichukchinda, Nuanjun[e]; Kidkeukarun, Runglak[i]; Preechakul, Suphanlinee[j]; Khunarkornsiri, Usanee[g]; Bamrungram, Warawut[k]; Supharatwattanakun, Butsaban[l]; Mootsikapun, Piroon[c]; Kwangsukstid, Supanida[h]; Denjanta, Sukanda[m]; Vannaprasaht, Suda[a]; Rungapiromnan, Watcharee[f]; Suwankesawong, Wimon[f]; Tassaneeyakul, Wongwiwat[d]; Tassaneeyakul, Wichittra[a]

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Background Co-trimoxazole is a sulfonamide-containing antibiotic that is effective in the treatment of several infections and for prophylaxis of *Pneumocystis jiroveci* pneumonia. This drug has been reported as a common culprit drug for the Stevens–Johnson syndrome (SJS) and for toxic epidermal necrolysis (TEN). Human leukocyte antigens (HLAs) play a key role in the immunopathogenesis of severe cutaneous reactions induced by several drugs. This study investigated the association between the *HLA* class *I* and *HLA-DRB1* polymorphisms and co-trimoxazole-induced SJS/TEN in a Thai population.

Methods Forty-three patients with co-trimoxazole-induced SJS/TEN and 91 co-trimoxazole-tolerant patients were enrolled in the study. *HLA* class *I* and *HLA-DRB1* were genotyped using the reverse sequence-specific oligonucleotide probe method.

Results The frequencies of three alleles of HLA, namely *HLA-B*15:02*, *HLA-C*06:02*, and *HLA-C*08:01*, were significantly higher in the co-trimoxazole-induced SJS/TEN group compared with controls. The risks for co-trimoxazole-induced SJS/TEN in patients with the *HLA-B*15:02*, *HLA-C*06:02*, or *HLA-C*08:01* allele were about 3–11-fold higher when compared with those who did not carry one of these alleles. Individuals who carried the *HLA-B*15:02-C*08:01* haplotype had a 14-fold higher risk for co-trimoxazole-induced SJS/TEN.

Conclusion Evidence of associations between co-trimoxazole-induced SJS/TEN and HLA alleles including *HLA-B*15:02*, *HLA-C*06:02*, and *HLA-C*08:01* were found in the study population. These findings may suggest that apart from the HLA molecules, other molecules involved in the molecular pathogenesis of these severe cutaneous adverse drug reactions may play an important role in the susceptibility of individuals to SJS/TEN caused by co-trimoxazole.

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[a]Department of Pharmacology

[b]Pharmacy Unit

[c]Department of Medicine, Faculty of Medicine

[d]Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen

[e]Medical Genetics Center, Medical Life Science Institute, Department of Medical Sciences, Ministry of Public Health

[f]Health Product Vigilance Center, Food and Drug Administration, Ministry of Public Health, Nonthaburi

[g]Pharmacy Unit

[h]Department of Medicine, Udon Thani Hospital, Udon Thani

[i]Buddhachinaraj Hospital, Phitsanulok

[j]Lampang Hospital, Lampang

[k]Rayong Hospital, Rayong

[l]Songkhla Hospital, Songkhla

[m]Chiangraiprachanukroh Hospital, Chiangrai, Thailand

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Correspondence to Wichittra Tassaneeyakul, PhD, Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand Tel: +66 81 6594623; fax: +66 43 348397; e-mails: wichitt@kku.ac.th, wichittra.tassaneeyakul@gmail.com

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