한국인에서 CYP 동효소군과 hPXR의 유전적 다형성 빈도 검색

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Genetic polymorphisms of seven CYPs and a hPXR in Korean population

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Objective : To evaluate genetic polymorphisms of seven CYPs and a hPXR in korean population

Methods : We carried out high throughput screening of genetic polymorphisms for seven CYPs containing a CYP2B6, three CYP2Cs, and two CYP3As, and a hPXR by sequence analysis from an approximate 48 Korean healthy subjects.

Results : In the screening of CYP2B6, the estimated allele frequencies were 3.2% for C64T, 3.4% for G216C, 15.2% for G516T, and 19.8% for A785G, respectively. No subject was found to have C78T, G714A, C732T, C777A, and C1459T variants.

Among CYP2C subfamilies, we analyzed CYP2C8, CYP2C9, and CYP2C19. For CYP2C8, we could not find any subjects with A805T, G416A, and A1196G variants. For CYP2C9, we found just one variant in coding sequence. Three of forty subjects were identified to be heterozygous for CYP2C9*3 with 3.8% allele frequency. Most variants were found in 5' UTR and the allele frequencies were 4.2% for C-1886G, 6.3% for C-1566T, 4.2% for G-1538A, 57.4% for C-1189T, and 4.2% for G-982A, respectively. We also identified four variants in CYP2C19 coding polymorphisms. Seventeen of forty-seven subjects were heterozygous and five were homozygous for CYP2C19*2 which leads to a splicing defect. For CYP2C19*3 which leads to a stop codon at amino acids position 212, four subjects (8.5%) were heterozygous and two (4.4%) were homozygous. Finally for CYP2C19*4, one subject was identified to heterozygous with 1.1% of allele frequency.

Among CYP3A subfamilies, we screened CYP3A4 and CYP3A7 genetic polymorphism. For CYP3A4, two subjects were found as heterozygous for CYP3A4*6 (831insA), which results in frame shift, and the

allele frequency was estimated 2.2%. No subject was found to have other known CYP3A4 variants. In analysis of all known CYP3A7 polymorphisms, no subjects were identified.

We also screened hPXR gene, known as a master regulator of CYP3A4. We found four variants in untranslated region or intron. The estimated allele frequencies were 79.4 % for C-24381A, 6.0% for T3015G, 37.8% for C8055T, and 1.1% for G9976A, respectively.

Conclusion : This result will provide information for future pharmacogenetic studies in Korean population.