NOVEL HUMAN CYP2A6 ALLELES, CYP2A6*1F AND CYP2A6*1G, CONFOUND GENE DELETION ANALYSIS

Tatsuki Fukami¹, Miki Nakajima¹, Ryoko Yoshida¹, Miki Katoh¹, Howard L. McLeod³ and Tsuyoshi Yokoi¹,²
¹Graduate School of Natural Science and Technology, ²Graduate School of Medical Science, Kanazawa University, Kakuma, Kanazawa 920-1192, Japan and ³Washington University School of Medicine, St. Louis, MO 63110, USA

CYP2A6 is a major enzyme responsible for the metabolism of nicotine and coumarin in humans. There are genetic polymorphisms in the human CYP2A6 gene and a relationship with smoking habits as well as the incidence of lung cancer has been reported. CYP2A6*4 is a whole gene deleted allele that completely lacks enzymatic activity. An unequal crossover junction is located in the 3'-flanking region in the CYP2A6*4A allele, whereas the junction is located in either intron 8 or exon 9 in the CYP2A6*4D allele. In the present study, a novel genotyping method to distinguish between two different whole deleted alleles of CYP2A6*4A and CYP2A6*4D was established. In the process, two novel alleles, CYP2A6*1F and CYP2A6*1G, were found. The CYP2A6*1F has a single nucleotide polymorphism (SNP) of C5717T in exon 8, and the CYP2A6*1G has two SNPs, C5717T in exon 8 and A5825G in intron 8. The SNP of C5717T is a synonymous mutation. Since the CYP2A6*1F produces a recognition site of the restriction enzymes that is the same as CYP2A6*4D, the presence of the CYP2A6*1F allele could cause a mistyping as the CYP2A6*4D allele. Using our improved genotyping method, the allele frequencies of CYP2A6*4A, CYP2A6*4D, CYP2A6*1F and CYP2A6*1G in Caucasians (n = 187) were 3.2%, 0%, 1.6% and 0.5%, respectively. However, they were 0.4%, 0.4%, 0% and 4.0% in African-Americans (n = 139), respectively. CYP2A6*4D, CYP2A6*1F, and CYP2A6*1G alleles were not found in Japanese and Koreans.