

**Table S5. Haplotype frequencies of CYP2A6 functional allele and rs11878604.**

Possible CYP2A6 alleles <sup>†</sup>	rs11878604			<i>p</i> <sup>‡</sup>
	T	C	Total(%)	
*1, *2 and other functional alleles	35.96	3.37	39.33	<i>reference</i>
*4 (whole deletion)	19.10	2.25	21.35	0.74
*7, *36, *37 (missense SNP in Exon 9)	0.00	14.61	14.61	$4.4 \times 10^{-18}$
*9, *15 (SNP in TATA box)	1.69	19.66	21.35	$1.0 \times 10^{-18}$
*10 (two missense SNPs in Exon 9)	0.00	2.25	2.25	$1.8 \times 10^{-4}$
*13	0.00	0.56	0.56	0.099
*18	0.00	0.56	0.56	0.099
Total(%)	56.75	43.25	100.0	

The phased reference panel data of 1000 Genomes project (phase I; 2011-11-23).

Only the Japanese subjects were used (JPT;  $N = 89$ ).

<sup>†</sup> The CYP2A6 functional alleles were determined by the seven nonsense SNPs of CYP2A6 gene; rs28399468, rs5031017 (rs75344699), rs5031016 (rs60711313), rs61736436, rs1809810, rs28399434 and rs28399433. These SNP genotypes were phased during the imputation study using the Beagle software [33]. The known CYP2A6 functional alleles (<http://cypalleles.ki.se/>) were assigned according to the combination of alleles in the phased haplotypes.

<sup>‡</sup> Significance of association between each functional allele and the mutant allele at rs11878604 was assessed by the Fisher's exact test.