Allele Frequency Distribution

Pharmacodynamic Genes	SNP	Heterozygous Allele Frequency				Homozygous Risk Allele Frequency			
		Heterozygous Genotype	CEU	AFR	ASN	Homozygous Genotype	CEU	AFR	ASN
SLC6A4	*rs63749047*	L/S	48.8%*	17.6%[2]	26.9%[3]	S/S	18.9%*	4.1%[2]	69.3%[3]
	rs25531	A/G	9.4%	34.1%	15.4%	G/G	< 1%	3.7%	< 1%
HTR2C	*rs3813929*	T/C	15.3%	2.0%	12.9%	C/C	31.8%	51.2%	36.4%
DRD2	*rs1799732*	C/DEL	13%[1]	38%[1]	30%[1]	DEL/DEL	< 1%*	9.9%*	< 1%*
CACNA1C	*rs1006737*	G/A	43.5%	51.6%	11.9%	A/A	16.5%	30.1%	< 1%
ANK3	*rs10994336*	C/T	11.8%	2.8%	37.4%	T/T	< 1%	< 1%	5.9%
COMT	*rs4680*	Val/Met	47.1%	38.2%	39.9%	Val/Val	29.4%	50.0%	51.0%
						Met/Met	23.5%	11.8%	9.1%
MTHFR	*rs1801133*	C/T	38.8%	19.1%	44.1%	T/T	11.8%	1.6%	14.7%

CEU = European ancestry, AFR = African ancestry, ASN = Asian ancestry
All frequency data obtained from 1000 genomes project at http://useast.ensembl.org/index.html, unless otherwise noted
* Value derived using Hardy-Weinberg Principle;
http://www.nature.com/scitable/knowledge/library/the-hardy-weinberg-principle-13235724

Pharmacokinetic Genes	Poor Metabolizer Frequency			Intermediate Metabolizer Frequency			Extensive Metabolizer Frequency			Ultra Metabolizer Frequency		
	CEU	AFR	ASN	CEU	AFR	ASN	CEU	AFR	ASN	CEU	AFR	ASN
CYP2D6	~21-22%[4ł]	~8-9%[4ł]	~8-9%[4ł]	~12-13%[4ł]	~26%[4ł]	~41-42%[4ł]	~63-64%[4ł]	~57-58%[4ł]	~47-48%[4ł]	~2-3%[4ł]	~6-7%[4ł]	~2-3%[4ł]
CYP2C19	~2-3%[5€]; ~1-2%[6₮]	~3-6%[7]	~14-15%[6₮]; 13-23%[7]	~25-26%[5€]; 24-25%[6₮]	~25-37%[8£]	~49-50%[6₮]	~43-44%[5€]; ~40%[6₮]	~56%-70[8£]	~36-37%[6₮]	~28-29%[5€]; ~33%[6₮]	~23-24%[9]	~1-2%[9, 6₮]
CYP3A4/5	~85-95%[10,11]	~27-50%[10]; ~23%[11]	~60-73%[10]; ~36%[12¥]	~12-13%[11]	~50%[11]	~52%[12¥]	~10%[13]; ~1%[11]	~70%[13]	~12%[12¥]	n/a	n/a	n/a

CEU = European ancestry, AFR = African ancestry, ASN = Asian ancestry

Metabolizer phenotypes derived as described below:

[ł]The prediction of enzyme activity corresponding to each CYP2D6 haplotype was based on results obtained from previously published studies (for references see http:// www.cypalleles.ki.se/cyp2d6.htm). To assess the differences in CYP2D6 metabolism among regions of the world a conventional classification of phenotypes that is based on the assumption of dominance was used (the phenotype is determined by the most efficient haplotype in the genotype).

[€]Analysis includes the following genotypes; *1/*2, *2/*17, *2/*2, *1/*1, *1/*17, *17/*17.

[₮]Data generated utilizing frequency data from 5 different Asian populations

[£]Data generated utilizing frequency data from 4 different African American populations.

[¥]Analysis includes the following genotypes: *3/*3, *1/*3, and *1/*1.

References

1. The Allele Frequency Database. http://alfred.med.yale.edu/alfred/SiteTable1A_working.asp?siteuid=SI000135J.
2. Lotrich FE, Pollock BG, Ferrell RE. Serotonin transporter promoter polymorphism in African Americans: allele frequencies and implications for treatment. *American journal of pharmacogenomics: genomics-related research in drug development and clinical practice.* 2003; 3(2):145-147.
3. Toyoshima F, Oshima T, Nakajima S, et al. Serotonin transporter gene polymorphism may be associated with functional dyspepsia in a Japanese population. *BMC medical genetics.* 2011; 12:88.
4. Sistonen J, Sajantila A, Lao O, Corander J, Barbujani G, Fuselli S. CYP2D6 worldwide genetic variation shows high frequency of altered activity variants and no continental structure. *Pharmacogenetics and genomics.* Feb 2007;17(2):93-101.
5. Sim SC, Nordin L, Andersson TM, et al. Association between CYP2C19 polymorphism and depressive symptoms. *American journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics.* Sep 2010;153B(6):1160-1166.
6. Myrand SP, Sekiguchi K, Man MZ, et al. Pharmacokinetics/genotype associations for major cytochrome P450 enzymes in native and first- and third-generation Japanese populations: comparison with Korean, Chinese, and Caucasian populations. *Clinical pharmacology and therapeutics.* Sep 2008;84(3):347-361.
7. Kaneko A, Lum JK, Yaviong L, et al. High and variable frequencies of CYP2C19 mutations: medical consequences of poor drug metabolism in Vanuatu and other Pacific islands. *Pharmacogenetics.* Oct 1999;9(5):581-590.
8. Xie HG, Kim RB, Stein CM, Wilkinson GR, Wood AJ. Genetic polymorphism of (S)-mephenytoin 4'-hydroxylation in populations of African descent. *British journal of clinical pharmacology.* Sep 1999;48(3):402-408.
9. Kurose K, Sugiyama E, Saito Y. Population differences in major functional polymorphisms of pharmacokinetics/pharmacodynamics-related genes in Eastern Asians and Europeans: implications in the clinical trials for novel drug development. *Drug metabolism and pharmacokinetics.* 2012;27(1):9-54.
10. Thompson EE, Kuttab-Boulos H, Witonsky D, Yang L, Roe BA, Di Rienzo A. CYP3A variation and the evolution of salt-sensitivity variants. *American journal of human genetics.* Dec 2004;75(6):1059-1069.
11. Miao J, Jin Y, Marunde RL, et al. Association of genotypes of the CYP3A cluster with midazolam disposition in vivo. *The pharmacogenomics journal.* Oct 2009;9(5):319-326.
12. Goh BC, Lee SC, Wang LZ, et al. Explaining interindividual variability of docetaxel pharmacokinetics and pharmacodynamics in Asians through phenotyping and genotyping strategies. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Sep 1 2002;20(17):3683-3690.
13. Wojnowski L, Kamdem LK. Clinical implications of CYP3A polymorphisms. *Expert opinion on drug metabolism & toxicology.* Apr 2006;2(2):171-182.