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PharmGKB Update: II. CYP3A5, Cytochrome P450, Family 3, Subfamily A, Polypeptide 5

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Category: Genotype

PharmGKB Submission Numbers: PS113737, PS115406, PS114503, PS200420, PS201057, PS115245
http://www.pharmgkb.org/do/serve?objId=PA131&objCls=Gene

Date of Submission: May 19, 2003

Project: Pharmacogenetics of Anticancer Agents, St. Jude Children's Research Hospital

HGNC Symbol: CYP3A5
HGNC Name: cytochrome P450, family 3, subfamily A, polypeptide 5
Synonyms: CYP3A5

Gene Ontology Terms: GO:0004497 monooxygenase activity, GO:0005783 endoplasmic reticulum, GO:0005792 microsome, GO:0006118 electron transport, GO:0008202 steroid metabolism, GO:0015034 cytochrome P450 activity, GO:0016020 membrane, GO:0016712 oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen
Locus ID: 1577
GenBank Accession: J04813

Pharmacogenetic Significance: An AG SNP in intron 3 of CYP3A5 results in the introduction of an alternative exon 3A, that introduces a premature stop codon and lack of CYP3A5 protein expression. The nonfunctional homozygous *3 genotype is present in 70% of whites and 30% of blacks.

Pharmacological Significance: CYP3A4 and CYP3A5 together account for approximately 50% of hepatic cytochrome P450 and approximately half of medications that are metabolized by P450 are CYP3A substrates. The two forms are often linked because they have substantial qualitative overlap in substrate specificity, although there are differences among substrates in the relative importance of CYP3A5 versus CYP3A4. CYP3A5 is the predominant form for extrahepatic CYP3A expression. Whereas CYP3A4 is expressed in all adult human livers, CYP3A5 hepatic expression is polymorphic.

Potential Drug Interactions: erythromycin, midazolam, prednisone, itraconazole, ketoconazole, fluconazole, etoposide, teniposide, vincristine, vinblastine, paclitaxel, topotecan, docetaxel, cyclosporine, tacrolimus, grapefruit juice, ritonavir, clarithromycin, quinidine, alprazolam, diazepam, midazolam, triazolam, indinavir, saquinavir, cisapride, astemizole, chlorpheniramine, amlodipine, diltiazem, felodipine, nifedipine, isoldipine, nitrendipine, verapamil, atorvastatin, cerivastatin, lovastatin, buspirone, haloperidol, methadone, pimozide, quinine, sildenafil, tamoxifen, trazodone, vincristine, indinavir, nelfinavir, ritonavir, saquinavir, amiodarone, cimetidine, fluoxetine, fluvoxamine, itraconazole, ketoconazole, mibefradil, nefazodone, troleandomycin, verapamil, isoniazid, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, St. John's wort, troglitazone

Function Characteristics: Liver microsomes from individuals homozygous for the nonfunctional *3 genotype have about half the overall CYP3A catalytic activity toward midazolam, which is a substrate for CYP3A5 and CYP3A4, than individuals with at least one wild-type (*1) CYP3A5 allele.

Summary of Data Submitted:

Size of Sample Set Assayed: 386 (772 chromosomes)
Number of gene regions assayed: 1
Total bases assayed: 2760
Number of variant sites: 3
PCR Primers Reported: 6

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