**Client ID: Vas8234mdu9i0**
August 19, 2020

## Personalized Pharmacogenomic Overview

Pharmacogenomics combines pharmacology (the study of drugs) and genomics (the study of genes and their functions) and involves how a person's DNA can affect their response to drugs. This overview provides insights on specific variations identified in your DNA that may alter your clinical response to certain medications. For most drugs, multiple genes are responsible for drug response, the appropriate dose level, and/or the toxicity associated with taking the drug. MyGenome$_{Rx}$ analyzes your DNA at over 1 million locations (rsID) from 2038 different genes to determine if there are single nucleotide polymorphism (SNPs) or variations in your DNA. Some of the genes screened are related to pharmacokinetics (absorption, bioavailability, distribution, metabolism, and excretion), other are involved in pharmacodynamics (drug action and drug effect). Multiple genes can alter your response to a single medication.

**The following star alleles were identified.** There are cards on the final page of this report that can be removed and carried with you as a reference for your healthcare providers.

CYP2B6 ?/*6

CYP2C19 *19/*19

CYP3A5 *3/*3

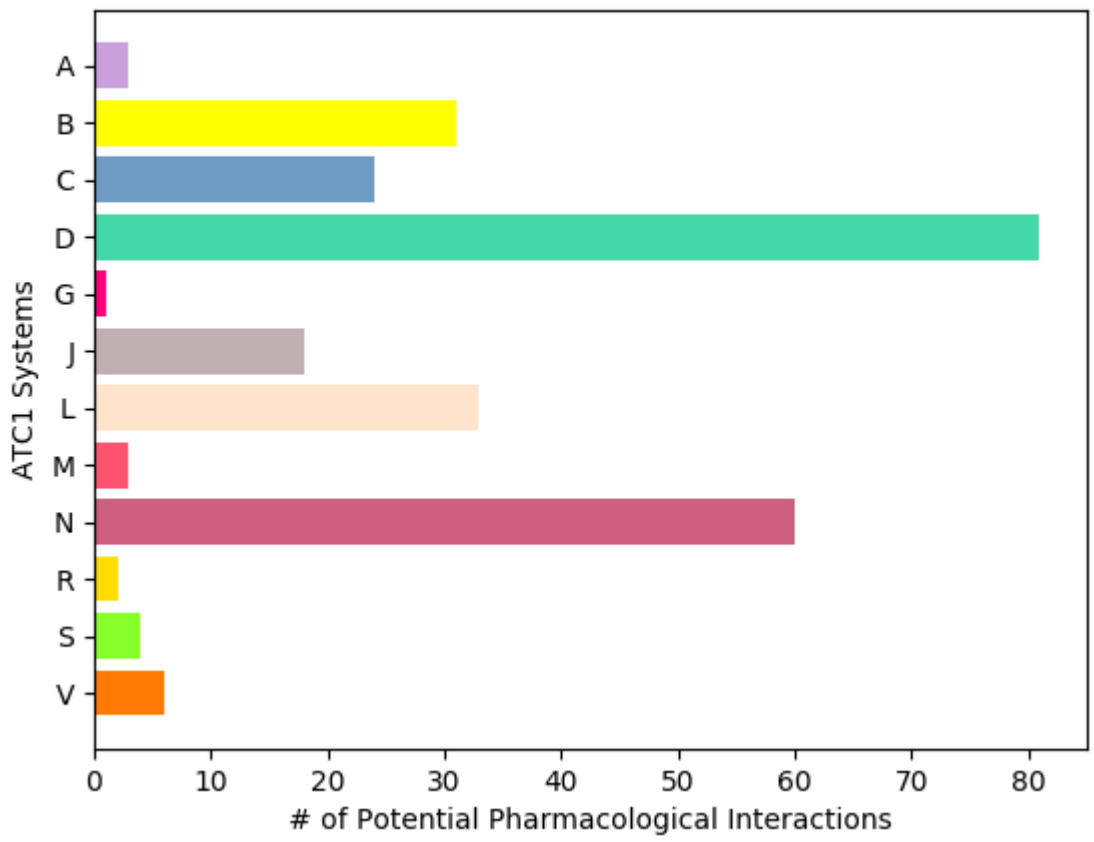
SLCO1B1 ?/*1B

*^A person can only be identified as *1 if all variant alleles have been tested; this in not the case with direct-to-consumer genetic testing.*

*? – denotes that a star allele is present, but without further DNA analysis determination of which star allele is not possible*

The star (*) allele nomenclature system is used to describes haplotype patterns at the gene level. The *1 allele almost always denotes the most common allele found in all populations. All other * alleles carry one or more variants. An rsID is used to identify the genomic position of the variants. Many *alleles are defined by a single rsID, others are a combination of multiple rsIDs. If you are a *1/*1 you have a functional gene, but to report this requires testing every possible variant. For example, CYP3A5*3 is a nonfunctional variant of CYP3A5. The CYP3A5*3 allele is defined by rs776746; the reference genotype at this position is AA. If an AG is present at this position the person would be a carrier for one CYP3A5*3 allele, if a GG is present the person has two CYP3A5*3 alleles. A person could only be identified as CYP3A5*1/ CYP3A5*1 if all possible variants of CYP3A5 have been interrogated, not just the rs776746 position. The positions interrogated are dependent on the platform used by the genetic testing companies. Further information can be found in the FAQ section of the MyGenome$_{Rx}$ website.

Analysis of your DNA identified a total of **266 potential pharmacogenomic interactions**. These have been classified based on organ or system on which the medication acts (ATC1 Systems). This information is provided below in a color coded, rank ordered graphic divided into the 14 categories of the Anatomical Therapeutic Chemical (ATC) systems.




The tables below provide detailed information (gene, rsID, reference genotype, and genotype present) for each of the variant gene-drug interactions identified. The **reference genotype** refers to the bases found in the reference genome. The **genotype present** refers to the bases identified in the raw DNA file at the same position. In some cases the reference genotype and the genotype present match. This indicates that the reference genotype has been associated with a phenotype. In other cases the reference genotype and the genotype present do not match. For these, the genotype present has been associated with a phenotype.For the overview, information is included for genetic variant drug combinations that fall into PharmGKB Level 1 and Level 2. These clinical annotation levels have the most evidence, and in some cases medication guidelines have been established. If no Level 1 or Level 2 pharmacogenomic interactions were identified for medications that target an organ/system this is noted. Further information on the ATC system and PharmGKB Evidence Levels can be found at the end of the report.

The educational information provided in the overview is specific to the raw DNA file that was uploaded. When combined with the Detailed Drug Gene Report, and in collaboration with healthcare providers, MyGenome$_{Rx}$ services can help optimize your drug therapy choices. However, there are additional non- genetic factors that influence drug response such as age, weight, gender, race, diet, smoking status, comorbidities, and whether you are taking other medications.

IT IS IMPORTANT THAT YOU DISCUSS THE RESULTS IN THIS REPORT WITH YOUR PHYSICIAN BEFORE STARTING, STOPPING OR MAKING ANY OTHER CHANGES TO YOUR PRESCRIPTION REGIMEN, YOUR TREATMENT OR ANY THERAPIES WITH WHICH YOU ARE INVOLVED.

## A: ALIMENTARY (GI) TRACT AND METABOLISM

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTIEMETICS AND ANTINAUSEANTS | ABCB1 | rs1045642 | AA | AA |
| DRUGS USED IN DIABETES | CYP2C8 | rs10509681 | TT | TT |
| | KCNJ11 | rs5219 | TT | CC |

## B: BLOOD AND BLOOD FORMING ORGANS

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTITHROMBOTIC AGENTS | CALU | rs339097 | AA | AA |
| | CES1 | rs71647871 | CC | CC |
| | CYP2C19 | rs12248560 | CC | CC |
| | CYP2C19 | rs28399504 | AA | AA |
| | CYP2C19 | rs4244285 | GG | GG |
| | CYP2C19 | rs4986893 | GG | GG |
| | CYP2C9 | rs1057910 | AA | AA |
| | CYP2C9 | rs1799853 | CC | CC |
| | CYP2C9 | rs28371686 | CC | CC |
| | CYP2C9 | rs4917639 | AA | AA |
| | CYP2C9 | rs7900194 | GG | GG |
| | CYP4F2 | rs2108622 | CC | CT |
| | GGCX | rs11676382 | CC | CC |
| | VKORC1 | rs17708472 | GG | GG |
| | VKORC1 | rs2359612 | AA | GG |
| | VKORC1 | rs2884737 | AA | AA |
| | VKORC1 | rs7196161 | GG | AA |
| | VKORC1 | rs7294 | CC | TT |
| | VKORC1 | rs8050894 | CC | CC |
| | VKORC1 | rs9923231 | CC | CC |
| | VKORC1 | rs9934438 | GG | GG |

## C: CARDIOVASCULAR

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| CARDIAC THERAPY | ABCB1 | rs1045642 | AA | AA |
| DIURETICS | ADD1 | rs4961 | GG | GT |
| | NEDD4L | rs4149601 | GG | GG |
| | PRKCA | rs16960228 | GG | AG |
| | YEATS4 | rs7297610 | CC | CC |
| LIPID MODIFYING AGENTS | ABCG2 | rs2231142 | GG | GG |
| | APOA5 | rs662799 | GG | AA |
| | APOE | rs7412 | CC | CC |
| | CETP | rs1532624 | CC | AC |
| | FDPS | rs2297480 | TT | TT |
| | KIF6 | rs20455 | AA | AA |
| | LPA | rs10455872 | AA | AA |
| | SLCO1B1 | rs4149015 | GG | AG |
| | SLCO1B1 | rs4149056 | TT | TT |

## D: DERMATOLOGICALS

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE | SLC28A3 | rs7853758 | GG | AG |
| | SLC28A3 | rs885004 | GG | AG |
| ANTIFUNGALS FOR DERMATOLOGICAL USE | ABCB1 | rs1045642 | AA | AA |
| | ANKK1 | rs1800497 | GG | GG |
| | COMT | rs13306278 | CC | CC |
| | COMT | rs4680 | GG | GG |
| | DRD2 | rs1799978 | TT | TT |

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| | DRD2 | rs1800497 | GG | GG |
| | F5 | rs6025 | TT | CC |
| | FLT3 | rs1933437 | GG | AA |
| | HAS3 | rs2232228 | AA | AG |
| | HTR1A | rs6295 | CC | CG |
| | HTR2A | rs7997012 | AA | GG |
| | HTR2C | rs1414334 | CC | G |
| | HTR2C | rs3813929 | CC | C |
| | ITPA | rs1127354 | CC | CC |
| | ITPA | rs7270101 | AA | AA |
| | LTC4S | rs730012 | AA | AA |
| | MC4R | rs17782313 | TT | TT |
| | MC4R | rs489693 | CC | CC |
| | NAT2 | rs1041983 | CC | CC |
| | NAT2 | rs1799930 | GG | GG |
| | NQO1 | rs1800566 | GG | GG |
| | SLC28A3 | rs7853758 | GG | AG |
| | SLC28A3 | rs885004 | GG | AG |
| | SLCO1B1 | rs4149056 | TT | TT |
| | TCF7L2 | rs7903146 | CC | CT |
| | TXNRD2 | rs13306278 | CC | CC |
| ANTIPSORIATICS | ITPA | rs7270101 | AA | AA |
| | SLCO1B1 | rs11045879 | TT | TT |
| EMOLLIENTS AND PROTECTIVES | HTR2C | rs1414334 | CC | G |
| | TCF7L2 | rs7903146 | CC | CT |

## G: GENITO-URINARY SYSTEM

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| UROLOGICALS | GNB3 | rs5443 | CC | CT |

## H: HORMONES, EXCLUDING SEX HORMONES AND INSULINS

No Level 1 or Level 2 pharmacogenomic interactions were identified for this organ/system.

## J: ANTIINFECTIVES FOR SYSTEMIC USE

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTIMYCOBACTERIALS | NAT2 | rs1799930 | GG | GG |
| ANTIVIRALS FOR SYSTEMIC USE | ABCB1 | rs1045642 | AA | AA |
| | CCHCR1 | rs746647 | AA | AA |
| | CYP2B6 | rs2279343 | AA | AG |
| | CYP2B6 | rs2279345 | TT | CT |
| | CYP2B6 | rs28399499 | TT | TT |
| | CYP2B6 | rs3745274 | GG | GT |
| | IFNL3 | rs11881222 | AA | AA |
| | IFNL3 | rs12979860 | CC | CC |
| | IFNL3 | rs8099917 | TT | TT |
| | IFNL4 | rs12979860 | CC | CC |
| | ITPA | rs1127354 | CC | CC |
| | ITPA | rs7270101 | AA | AA |
| | UGT1A1 | rs887829 | CC | CC |

## L: ANTINEOPLASTIC (ONCOLOGY) AND IMMUNOMODULATING AGENTS

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTINEOPLASTIC AGENTS | ABCB1 | rs1045642 | AA | AA |
| | DPYD | rs3918290 | CC | CC |
| | DPYD | rs55886062 | AA | AA |

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| | DPYD | rs67376798 | TT | TT |
| | EGF | rs4444903 | AA | AG |
| | FCGR2A | rs1801274 | AA | AG |
| | FLT3 | rs1933437 | GG | AA |
| | GSTP1 | rs1695 | AA | AA |
| | MTHFR | rs1801133 | GG | AA |
| | MTRR | rs1801394 | AA | AG |
| | NQO1 | rs1800566 | GG | GG |
| | NT5C2 | rs11598702 | TT | CT |
| | SEMA3C | rs7779029 | TT | TT |
| | SLC28A3 | rs7853758 | GG | AG |
| | SLC28A3 | rs885004 | GG | AG |
| | SLCO1B1 | rs11045879 | TT | TT |
| | SOD2 | rs4880 | AA | AG |
| | UGT1A1 | rs4148323 | GG | GG |
| | UMPS | rs1801019 | GG | CG |
| | XPC | rs2228001 | GG | TT |
| IMMUNOSTIMULANTS | IFNL3 | rs12979860 | CC | CC |
| | ITPA | rs1127354 | CC | CC |
| | ITPA | rs7270101 | AA | AA |
| IMMUNOSUPPRESSANTS | CYP3A4 | rs2740574 | CC | TT |
| | CYP3A5 | rs776746 | CC | CC |
| | ITPA | rs7270101 | AA | AA |

## M: MUSCULO-SKELETAL SYSTEM

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTIGOUT PREPARATIONS | ABCG2 | rs2231142 | GG | GG |

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS | CYP2C9 | rs1057910 | AA | AA |

## N: NERVOUS SYSTEM

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ANALGESICS | COMT | rs4680 | GG | GG |
| | GP1BA | rs6065 | CC | CC |
| | LTC4S | rs730012 | AA | AA |
| | OPRD1 | rs678849 | CC | CC |
| | PTGS1 | rs10306114 | AA | AA |
| | RYR1 | rs28933396 | GG | GG |
| | RYR1 | rs63749869 | GG | GG |
| ANESTHETICS | ABCB1 | rs1045642 | AA | AA |
| | RYR1 | rs28933396 | GG | GG |
| | RYR1 | rs63749869 | GG | GG |
| ANTIEPILEPTICS | EPHX1 | rs1051740 | TT | CT |
| | EPHX1 | rs2234922 | AA | AA |
| | SCN1A | rs3812718 | CC | CC |
| OTHER NERVOUS SYSTEM DRUGS | CHRNA3 | rs1051730 | GG | AG |
| | CHRNA3 | rs578776 | GG | GG |
| | CHRNA5 | rs16969968 | GG | AG |
| | COMT | rs4680 | GG | GG |
| | CYP2B6 | rs3745274 | GG | GT |
| | OPRD1 | rs2236857 | None | CC |
| | OPRD1 | rs3766951 | None | CC |
| | OPRM1 | rs510769 | CC | CT |
| PSYCHOANALEPTICS | ADORA2A | rs2298383 | CC | CT |

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| | COMT | rs13306278 | CC | CC |
| | CYP2C19 | rs12248560 | CC | CC |
| | CYP2C19 | rs4244285 | GG | GG |
| | HTR1A | rs6295 | CC | CG |
| | HTR2A | rs7997012 | AA | GG |
| | TXNRD2 | rs13306278 | CC | CC |
| PSYCHOLEPTICS | DRD2 | rs1799978 | TT | TT |
| | MC4R | rs17782313 | TT | TT |
| | MC4R | rs489693 | CC | CC |

## P: ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS

No Level 1 or Level 2 pharmacogenomic interactions were identified for this organ/system.

## R: RESPIRATORY SYSTEM

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES | ADRB2 | rs1042713 | GG | AG |
| OTHER RESPIRATORY SYSTEM PRODUCTS | CFTR | rs11971167 | GG | GG |

## S: SERSORY ORGANS

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| OPHTHALMOLOGICALS | CYP2C9 | rs1057910 | AA | AA |
| | CYP3A5 | rs776746 | CC | CC |
| | DRD2 | rs1076560 | CC | CC |
| | PTGFR | rs3753380 | TT | TT |

## V: VARIOUS

| Variant Gene-Drug Interactions | Gene | rsID | Reference Genotype | Genotype Present |
|---|---|---|---|---|
| ALL OTHER THERAPEUTIC PRODUCTS | ANKK1 | rs1800497 | GG | GG |
| | OPRM1 | rs1799971 | AA | AA |
| DIAGNOSTIC AGENTS | CYP2C8 | rs10509681 | TT | TT |
| | TCF7L2 | rs7903146 | CC | CT |
| THERAPEUTIC RADIOPHARMACEUTICALS | CYP2C9 | rs1057910 | AA | AA |

The information provided in the tables is for Variant Gene-Drug Interactions classified as Clinical Evidence Level 1 or Level 2 by PharmGKB[1]. PharmGKB is an NIH funded knowledgebase (https://www.pharmgkb.org/) that aggregates, curates, integrates, and disseminates information on the impact of human genetic variation on drug response. Level 1 annotations are used for a variant drug combination where the preponderance of evidence shows an association or has been recognized in a Clinical Pharmacogenetics Implementation Consortium (CPIC) or medical society endorsed pharmacogenomics guideline, implemented at a Pharmacogenomics Research Network (PGRN) site, or in a major health system. The association must be replicated in more than one cohort with significant p- values, and preferably will have a strong effect size. Level 2 annotations are used for a variant-drug combination with known pharmacogenes, so functional significance is likely. Level 2 annotations are also used for a variant-drug combination with moderate evidence of an association. For example, when the association has been replicated but there may be some studies that do not show statistical significance, and/or the effect size may be small. If no Level 1 or Level 2 pharmacogenomic interactions were identified for an organ/system this is noted. More information on the rsIDs (reference SNP cluster ID numbers)[2] can be found using the NCBI dbSNP database (https://www.ncbi.nlm.nih.gov/snp/).

The Personalized Pharmacogenomic Overview provides information for Variant Gene-Drug Interactions classified as Clinical Evidence Level 1 or Level 2 by PharmGKB at ATC2. The Anatomical Therapeutic Chemical (ATC) system classifies active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties and is controlled by the World Health Organization[3] (https://www.who.int/classifications/atcddd/en/). The first level (ATC1) indicates the anatomical main group and consists of one letter: A, GI (Alimentary) tract and metabolism; B, Blood and blood forming organs; C, Cardiovascular system; D, Dermatologicals: G, Genito-urinary system and sex hormones; H, Systemic hormonal preparations excluding sex hormones and insulin; J, Antiinfectives; L, Oncology and immunomodulating agents; M, Musculoskeletal system; N, Nervous system; P, Antiparasitic products, insecticides, and repellents; R, Respiratory system; S, sensory organs; V, various. A single drug may have more than one ATC code, and thus be listed in more than one ATC group. For example, aspirin is listed in categories A (for local oral treatment, B (for use as a platelet inhibitor, N (for use as analgesic and antipyretic); and C (when in combination with perindopril and amlodipine). The second level (ATC2) provides information on the pharmacological or therapeutic subgroup that drugs are used to treat. Some rsIDs are present more than once. For example, if the raw DNA file indicated a CC genotype is resent for rsID 6065 (GP1BA gene), notations would be seen in the tables for categories A

(Stomatological preparations), B (Antithrombotic Agents), and N (Analagesic) as PharmGKB has a Level 2 clinical annotation for aspirin suggesting individuals with a CC genotype at rsID 6065 may have an increased risk for aspirin resistance. If information on specific Variant Gene-Drug Interactions is needed, a personalized Drug-Gene report should be run that includes information on the client's current medication list.

PLEASE READ THE DISCLAIMERS BELOW

*** Status of Evidence Levels**

The PharmGKB Database and Evidence Levels referenced in this Report are based on information available to MyGenome$_{Rx}$ as of the date of this Report. These Evidence Levels may change over time as additional research is completed, additional links between genes and treatment outcomes are identified, studies are evaluated and confirmed by the scientific community, and additional knowledge of gene interactions with pharmaceuticals are understood.

**** General Disclaimer**

The Personalized Pharmacogenomic Overview is an educational tool, to be used in collaboration with your healthcare providers. MyGenome$_{Rx}$ services can help an individual optimize their drug therapy choices. However, this overview is not intended to be a substitute for professional medical advice, diagnosis, or treatment, and nothing in this Report or the services provided by MyGenome$_{Rx}$ should be construed as medical advice or the practice of medicine by MyGenome$_{Rx}$. You should seek the advice of your physicians, pharmacists, or other qualified health care providers with any questions you may have regarding a medical condition or a medication and before starting, stopping or making other changes to your prescription regimen, your treatment or any therapies with which you are involved.

*1 Whirl-Carrillo M, McDonagh E M, Hebert J M, Gong L, Sangkuhl K, Thorn C F, Altman R B, Klein T E. Pharmacogenomics knowledge for personalized medicine. Clinical pharmacology and therapeutics. 2012. 92:414-7 PMID: 22992668*

*2 Kitts, A and Sherry, S. Chapter 5. The Single Nucleotide Polymorphism Database (dbSNP) of Nucleotide Sequence Variation. The NCBI Handbook. McEntyre J, Ostell J, editors. Bethesda (MD): National Center for Biotechnology Information (US); 2002*

*3 The Selection and Use of Essential Medicines. World Health Organization technical report series. 2015; (994):vii-xv, 1-54. PMID: 27183787*

STAR ALLELES IDENTIFIER

CYP2B6 ?/*6

CYP2C19 *19/*19

CYP3A5 *3/*3

SLCO1B1 ?/*1B

? - a star allele is present, but further DNA analysis is needed to determine which star allele is present

This information came from analysis of my at home genetic raw DNA file.

$MyGenome_{Rx}$ PO Box 1642 Palatine, IL 60078

STAR ALLELES IDENTIFIER

CYP2B6 ?/*6

CYP2C19 *19/*19

CYP3A5 *3/*3

SLCO1B1 ?/*1B

? - a star allele is present, but further DNA analysis is needed to determine which star allele is present

This information came from analysis of my at home genetic raw DNA file.

$MyGenome_{Rx}$ PO Box 1642 Palatine, IL 60078