KAILOS GENETICS

Kailos™ Test Results
Dr. Ronald McGlennen, Medical Director
CLIA#: 01D2016114

601 Genome Way
Huntsville, AL 35806
256-327-9800 (Ph), 256-327-9810 (Fax)

PATIENT: Doe, John (M) **COLLECTED:** 02/21/2017 **SAMPLE TYPE:** Buccal **ACCESSION:** LKG-900017
DOB: 1985-01-01 **RECEIVED:** 02/21/2017 **PHYSICIAN:** Dr. Example
PATIENT ID: **REPORTED:** 03/08/2017 **PRACTICE:** Example Practice

QUICK SUMMARY

ADHD	RESULTS
Amphetamine (ADDERALL®) Dexmethylphenidate (FOCALIN®) Dextroamphetamine (DEXEDRINE®, PROCENTRA®, DEXTROSTAT®) Lisdexamfetamine (VYVANSE®) Methylphenidate (RITALIN®, CONCERTA®, DAYTRANA®, METADATE®)	Risk of reduced response. Select alternative drug.
Atomoxetine (STRATTERA®)	Be alert to adverse drug events.
Clonidine (KAPVAY®, CATAPRES®, DURACLON®, NEXICLON™)	Consider label recommended dosage if no contraindication.

ANTIARRHYTHMICS	
Digoxin (LANOXIN®, DIGITEK®)	Consider label recommended dosage if no contraindication.
Flecainide (TAMBACOR™)	Reduce dose by 50%, record ECG, monitor plasma concentration.
Propafenone (RYTHMOL SR®)	Reduce dose by 70%, record ECG, monitor plasma concentration.

ANTICOAGULANTS	
Warfarin (COUMADIN®)	The FDA recommends a daily dosage of 5-7 mg/day. This patient also has VKORC1 variants that could further alter dosing considerations.

ANTIDEPRESSANTS	
Amitriptyline (ELAVIL®) Clomipramine (ANAFRANIL®) Desipramine (NORPRAMIN®) Doxepin (SINEQUAN®) Imipramine (TOFRANIL™) Nortriptyline (PAMELOR™) Trimipramine (SURMONTIL®)	Avoid tricyclic use. If a tricyclic is warranted utilize therapeutic drug monitoring to guide dose adjustment.
Citalopram (CELEXA®) Escitalopram (LEXAPRO®)	Consider alternative drug not metabolized by CYP2C19.
Duloxetine (CYMBALTA®) Sertraline (ZOLOFT®)	Consider label recommended dosage if no contraindication.
Paroxetine (PAXIL®, PEXEVA®)	Consider alternative drug not metabolized by CYP2D6 or consider reduced dose.
Venlafaxine (EFFEXOR®)	Consider alternative drug not metabolized by CYP2D6.

ANTIDIABETICS	
Repaglinide (PRANDIN®) Tolbutamide (ORINASE®)	Consider label recommended dosage if no contraindication.

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ANTIEPILEPTICS

Mephenytoin (MESANTOIN®) Phenytoin (DILANTIN®) Valproic Acid (DEPAKOTE®, STAVZOR®)	✅ Consider label recommended dosage if no contraindication.

ANTIHYPERTENSIVES

Atenolol (TENORMIN®)	⚠️ Increased risk of cardiovascular events. Risk of decreased efficacy in women. Risk of reduced response.
Benazepril (LOTENSIN®) Imidapril (TANATRIL®)	⚠️ Risk of reduced response.
Enalapril (VASOTEC®, EPANED™) Irbesartan (AVAPRO®) Losartan (COZAAR®, HYZAAR®) Timolol (TIMOPTIC®, ISTALOL®, BETIMOL®)	✅ Consider label recommended dosage if no contraindication.
Metoprolol (LOPRESSOR®, TOPROL XL®)	🚫 Select alternative drug or consider dose reduction.
Verapamil (COVERA®, CALAN®, VERELAN®)	⚠️ Increased risk of cardiovascular events.

ANTIPSYCHOTICS

Aripiprazole (ABILIFY®)	⚠️ Consider reducing maximum dose.
Clozapine (CLOZARIL®, FAZACLO®)	⚠️ Increased risk of seizure. Risk of reduced response.
Haloperidol (HALDOL®)	🚫 Reduce dose by 50% or select alternative drug.
Olanzapine (ZYPREXA®)	⚠️ Risk of decreased AUC. Risk of increased social and clinical needs. Risk of reduced response. Risk of weight gain.
Risperidone (RISPERDAL®)	🚫 Select alternative drug or be extra alert to ADEs.

BENZODIAZEPINES

Diazepam (VALIUM®)	✅ Consider label recommended dosage if no contraindication.

CHEMOTHERAPEUTICS

Capecitabine (XELODA®) Cisplatin (PLATINOL®) Cyclophosphamide (CYTOXAN®) Mercaptopurine (PURINETHOL®, PURIXAN®) Tegafur Thioguanine (TABLOID®)	✅ Consider label recommended dosage if no contraindication.
Fluorouracil (EFUDEX®, CARAC®, FLUOROPLEX®, ADRUCIL®) Leucovorin (FUSILEV®) Oxaliplatin (ELOXATIN®)	⚠️ Risk of reduced response.
Methotrexate (RASUVO®, OTREXUP™, TREXALL™)	⚠️ Increased risk of toxicity. Risk of reduced clearance.
Paclitaxel (ABRAXANE®)	⚠️ Increased risk of toxicity.
Tamoxifen (NOLVADEX®, SOLTAMOX®)	🚫 Increased risk for relapse. Consider aromatase inhibitor.

CORTICOSTEROIDS

Prednisone (DELTASONE®, STERAPRED®)	✅ Consider label recommended dosage if no contraindication.

CYSTIC FIBROSIS

Ivacaftor (KALYDECO®)	⛔ Ivacaftor is not recommended. Select an alternative drug.

GENERAL ANESTHETICS

Desflurane (SUPRANE®) Isoflurane (FORANE®) Sevoflurane (ULTANE®, SOJOURN®) Succinylcholine (ANECTINE®, QUELICIN®)	✅ Consider label recommended dosage if no contraindication.
Nitrous Oxide (NITRONOX)	⚠️ Higher homocysteine levels after anesthesia.

HEPATITIS ANTIVIRALS

Peginterferon-alfa (PEGASYS®, PEGINTRON®, SYLATRON®) Ribavirin (COPEGUS®, REBETOL®)	✅ Consider label recommended dosage if no contraindication.

HIV/AIDS

Efavirenz (SUSTIVA®) Nelfinavir (VIRACEPT®) Nevirapine (VIRAMUNE®)	✅ Consider label recommended dosage if no contraindication.

IMMUNOSUPPRESSANTS

Azathioprine (IMURAN®) Tacrolimus (PROGRAF®)	✅ Consider label recommended dosage if no contraindication.
Cyclosporine (SANDIMMUNE®)	⚠️ Risk of decreased metabolism. Increased risk of adverse events. Risk of increased intracellular and blood concentration.
Sirolimus (RAPAMUNE®)	⚠️ Risk of increased cholesterol.

MUSCLE RELAXANTS

Carisoprodol (SOMA®)	✅ Consider label recommended dosage if no contraindication.

NSAIDS

Celecoxib (CELEBREX®) Diclofenac (VOLTAREN®, CATAFLAM®)	✅ Consider label recommended dosage if no contraindication.

OPIOIDS

Codeine (TYLENOL® #3) Hydrocodone (LORTAB®, VICODIN®) Oxycodone (OXYCONTIN®, PERCOCET®) Tramadol (ULTRAM®)	⛔ Consider alternative analgesics such as morphine or a nonopioid. Patient has greatly reduced metabolism of narcotic analgesics, leading to insufficient pain relief.

PLATELET AGGREGATION INHIBITORS

Clopidogrel (PLAVIX®)	⚠️ Be alert to increased platelet inhibition, decreased residual platelet aggregation, and increased risk of bleeding complications.

PROTON PUMP INHIBITORS

Lansoprazole (PREVACID®) Omeprazole (PRILOSEC®) Pantoprazole (PROTONIX®)	✅ Consider label recommended dosage if no contraindication.

STATINS

Atorvastatin (LIPITOR®) Rosuvastatin (CRESTOR®)	⚠️ Risk of reduced response.
Fluvastatin (LESCOL®) Lovastatin (ALTOPREV®, MEVACOR®)	✅ Consider label recommended dosage if no contraindication.
Pravastatin (PRAVACHOL®)	⚠️ Increased risk of nonfatal myocardial infarction and fatal coronary heart disease. Risk of reduced response.
Simvastatin (ZOCOR®, SIMCOR®)	🚫 Intermediate myopathy risk. Consider lower dose or select an alternative statin.

THROMBOPHILIA

Thrombophilia	✅ Patient is negative for the Factor V Leiden and Factor II Prothrombin variants.

IMPORTANT

This Quick Summary provides a brief overview of the predicted response of the patient. This information is based solely on the genotype information and is not based on a complete patient profile. Detection or absence of variants does not replace the need for therapeutic monitoring. Physicians should consider the information contained in the Details section, as well as consider current prescriptions, family history, presenting symptoms, and other factors before making any clinical or therapeutic decisions.

✅ No negative assertions based on genotype.

⚠️ Genotype may present increased risk or decreased effectiveness; prescribe with caution.

🚫 Genotype may present increased risk or decreased effectiveness; select alternative drug.

GENE SUMMARY

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*4/*4	🚫 Poor Metabolizer
CYP2C19	*1/*17	⚠️ Rapid Metabolizer
CYP2C9	*1/*1	✅ Extensive (Normal) Metabolizer
CYP3A4	*1/*22	⚠️ Reduced Metabolizer
TPMT	*1/*1	✅ Extensive (Normal) Metabolizer
DPYD	*1/*5	✅ Extensive (Normal) Metabolizer
F2/F5	Negative	✅ Normal Thrombophilia Risk
COMT	MET/MET	🚫 Reduced Stimulant Response

DETAILED INFORMATION

Amitriptyline	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Amitriptyline. Patient may have increased metabolism of Amitriptyline when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	
	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Amitriptyline. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	
	ABCB1 rs2235015 C/C (WT)	Evidence ★
	Patients with the wild-type genotype and depression who are treated with amitriptyline may be less likely to experience remission as compared to patients with the heterozygous or homozygous genotype.	
Amphetamine	COMT rs4680 A/A (HOM) — *Reduced stimulant response.*	Evidence ★★
	The patient has the homozygous genotype (MET/MET), which is associated with reduced function in metabolizing dopamine and norepinephrine in the prefrontal cortex. The patient may respond poorly to the increased dopamine levels generated by stimulants.	
	OPRM1 rs2281617 C/C (WT) OPRM1 rs510769 C/C (WT)	Evidence ★
	Patients may have normal Euphoria, Energy and Stimulation scores after amphetamine exposure. Consider label recommended dosage of Amphetamine if no contraindication.	
Aripiprazole	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Aripiprazole. The label has dosing recommendation in patients who are classified as CYP2D6 poor metabolizers (PM): The aripiprazole dose in PM patients should initially be reduced to one-half (50%) of the usual dose and then adjusted to achieve a favorable clinical response. The dose of aripiprazole for PM patients who are administered a strong CYP3A4 inhibitor should be reduced to one-quarter (25%) of the usual dose.	
	DRD2 rs6277 A/A (HOM) DRD2 rs1799732 TG/TG (HOM)	Evidence ★
	Consider label recommended dosage of Aripiprazole if no contraindication.	
Atenolol	CACNA1C rs1051375 A/A (HOM)	Evidence ★
	Patients with the homozygous genotype, hypertension and stable coronary artery disease, are more likely to benefit from treatment with verapamil compared to treatment with atenolol.	
	GNB3 rs5443 T/T (HOM)	Evidence ★
	Patients with the homozygous genotype and essential hypertension who are treated with atenolol may have a decreased response as compared to patients with the wild-type genotype.	

DETAILED INFORMATION

	NR1H3 rs11039149 A/G (HET) Patients with the heterozygous genotype and hypertension and coronary artery disease who are treated with atenolol may have an increased risk for cardiovascular events as compared to patients with the wild-type genotype.		Evidence ★
	GNB3 rs2301339 A/A (HOM) Women with the homozygous genotype and hypertension may have smaller decreases in systolic blood pressure when treated with atenolol as compared to women with the wild-type genotype. No significant results were seen when considering men only.		Evidence ★
	AGT rs5051 T/T (HOM) EDN1 rs5370 G/G (WT) Consider label recommended dosage of Atenolol if no contraindication.	AGT rs699 G/G (HOM) LDLR rs688 C/C (WT)	Evidence ★
Atomoxetine	CYP2D6 *4/*4 CYP2D6 metabolizers have higher plasma concentrations of atomoxetine compared with individuals who have two copies of normal activity alleles. The DPWG recommends that poor metabolizers be given the standard dose of atomoxetine, but physicians should be aware of adverse drug events.	*Poor metabolizer.*	Evidence ★★
	SLC6A2 rs3785143 C/C (WT) Consider label recommended dosage of Atomoxetine if no contraindication.	SLC6A2 rs12708954 C/A (HET)	Evidence ★
Atorvastatin	ABCB1 rs2032582 A/A (WT) Patients with this genotype who are treated with atorvastatin may have a reduced response (as measured by lower reductions in LDL-cholesterol).		Evidence ★
	SLCO1B1 rs4149056 T/C (HET) Patient may have 1) lower oral clearance and higher plasma concentrations of atorvastatin, and 2) an increased risk of composite adverse events compared to the wild type.		Evidence ★
	ABCB1 rs1045642 A/A (WT) RYR1 rs118192172 C/C (WT) Consider label recommended dosage of Atorvastatin if no contraindication.	ABCG2 rs2231142 G/T (HET)	Evidence ★
Azathioprine	TPMT *1/*1 Consider label recommended dosage of Azathioprine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★★★
Benazepril	AGT rs5051 T/T (HOM) Patients with the homozygous genotype and hypertension may have a poorer response to treatment with benazepril as compared to patients with the wild-type genotype.		Evidence ★
Capecitabine	DPYD *1/*5 Consider label recommended dosage of Capecitabine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★★★
	DPYD rs2297595 T/T (WT) MTHFR rs1801131 T/T (WT) Consider label recommended dosage of Capecitabine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★★
	DPYD rs67376798 T/T (WT) Consider label recommended dosage of Capecitabine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★
Carisoprodol	CYP2C19 *1/*17 Consider label recommended dosage of Carisoprodol if no contraindication.	*Rapid metabolizer.*	Evidence ★★★

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Celecoxib	CYP2C9 *1/*1 — *Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Celecoxib if no contraindication.	
	AGT rs699 G/G (HOM)	Evidence ★
	Consider label recommended dosage of Celecoxib if no contraindication.	
Cisplatin	TPMT *1/*1 — *Extensive (normal) metabolizer.*	Evidence ★
	ABCB1 rs1045642 A/A (WT) MTHFR rs1801133 G/A (HET)	
	Consider label recommended dosage of Cisplatin if no contraindication.	
Citalopram	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Rapid Metabolizer of Citalopram. The patient may have increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure. The CPIC Guideline recommends considering an alternative drug not predominantly metabolized by CYP2C19.	
	GRIK4 rs1954787 C/C (HOM)	Evidence ★★★
	Consider label recommended dosage of Citalopram if no contraindication.	
	HTR2A rs7997012 A/G (HET)	Evidence ★★
	Consider label recommended dosage of Citalopram if no contraindication.	
	ABCB1 rs2235015 C/C (WT)	Evidence ★
	Patients with the wild-type genotype and depression who are treated with citalopram may be less likely to experience remission as compared to patients with the heterozygous or homozygous genotype.	
	HTR2A rs6313 G/G (WT)	Evidence ★
	Patients with the wild-type genotype and major depression may have increased risk of heart palpitations when treated with citalopram as compared to patients with the homozygous genotype.	
Clomipramine	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Clomipramine. Patient may have increased metabolism of Clomipramine when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	
	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Clomipramine. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	
Clonidine	GNB3 rs5443 T/T (HOM)	Evidence ★
	Consider label recommended dosage of Clonidine if no contraindication.	

DETAILED INFORMATION

Clopidogrel	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★★
	The patient is a rapid metabolizer of Clopidogrel. The US Food and Drug Administration suggests label-recommended dosage and administration of Clopidogrel. The CPIC Dosing Guidelines report risk of increased platelet inhibition and decreased residual platelet aggregation. Ultrarapid metabolizers may also be associated with an increased risk of bleeding complications.	
	CES1 rs71647871 C/C (WT)	Evidence ★★
	Consider label recommended dosage of Clopidogrel if no contraindication.	
	CYP1A2 rs762551 A/A (HOM)	Evidence ★
	Patient may have decreased on-treatment platelet reactivity when treated with clopidogrel as compared to patients with the wild-type genotype.	
	ABCB1 rs1045642 A/A (WT)	Evidence ★
	People with this genotype may have an increased risk of major adverse cardiovascular events (MACE such as cardiovascular death, myocardial infarction, or stroke) when treated with clopidogrel in people with acute coronary syndrome or myocardial infarction as compared to people with homozygous genotypes. Contradictory findings have been reported in the literature.	
	CYP3A4 rs2242480 C/C (WT) — *Reduced metabolizer.*	Evidence ★
	Consider label recommended dosage of Clopidogrel if no contraindication.	
Clozapine	COMT rs4680 A/A (HOM) — *Reduced stimulant response.*	Evidence ★
	Patients with the homozygous genotype and schizophrenia may have a poorer response when treated with clozapine as compared to patients with the wild-type genotype.	
	CYP1A2 rs762551 A/A (HOM)	Evidence ★
	Patients with the homozygous genotype and schizophrenia may have an increased risk for seizures when treated with clozapine as compared to patients with wild-type or heterozygous genotype.	
	HTR1A rs6295 C/G (HET)	Evidence ★
	Patients with the heterozygous genotype and schizophrenia may have a poorer response when treated with clozapine as compared to patients with the homozygous genotype.	
	DRD2 rs6277 A/A (HOM) DRD2 rs1799732 TG/TG (HOM) DRD2 rs1079598 A/A (WT) MTHFR rs1801131 T/T (WT)	Evidence ★
	Consider label recommended dosage of Clozapine if no contraindication.	

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Codeine	CYP2D6 *4/*4 *Poor metabolizer.* The genotype predicts that the patient is a Poor Metabolizer for Codeine. Patient may have greatly reduced morphine formation following codeine administration, leading to insufficient pain relief. CPIC Dosing Guidelines recommend avoiding codeine use due to lack of efficacy. Consider alternative analgesics such as morphine or a nonopiod. Consider avoiding tramadol. The Dutch Pharmacogenetics Working Group Guideline suggests selecting an alternative drug (e.g., acetaminophen, NSAID, morphine-not tramadol or oxycodone) or be alert to symptoms of insufficient pain relief. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.	Evidence ★★★
Cyclophosphamide	MTHFR rs1801133 G/A (HET) Consider label recommended dosage of Cyclophosphamide if no contraindication.	Evidence ★★
Cyclosporine	CYP3A5 *3/*3 Consider label recommended dosage of Cyclosporine if no contraindication.	Evidence ★★
	ABCB1 rs1045642 A/A (WT) Patients with this genotype may have increased intracellular and blood concentration of cyclosporine with transplantation. However contradictory findings have been reported for no association between this variant and dose/efficacy of cyclosporine.	Evidence ★
	CYP3A4 rs35599367 G/A (HET) *Reduced metabolizer.* Patients with the heterozygous genotype and organ transplantation administered cyclosporine may have a 1) decreased metabolism of cyclosporine 2) decreased clearance of cyclosporine and 3) an increased risk in adverse events (e.g. graft rejection or kidney function) all as compared to patients with the wild-type genotype. However, these issues are not as significant as they are in the homozygous genotype.	Evidence ★
Desflurane	RYR1 rs118192161 C/C (WT) RYR1 rs118192162 A/A (WT) RYR1 rs118192175 C/C (WT) RYR1 rs118192176 G/G (WT) RYR1 rs121918593 G/G (WT) RYR1 rs121918594 G/G (WT) RYR1 rs121918595 C/C (WT) RYR1 rs121918592 G/G (WT) RYR1 rs118192172 C/C (WT) RYR1 rs118192163 G/G (WT) RYR1 rs118192177 C/C (WT) RYR1 rs28933397 C/C (WT) RYR1 rs118192167 A/A (WT) RYR1 rs118192170 T/T (WT) Consider label recommended dosage of Desflurane if no contraindication.	Evidence ★
Desipramine	CYP2C19 *1/*17 *Rapid metabolizer.* The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Desipramine. Patient may have increased metabolism of Desipramine when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★★

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	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Desipramine. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.		
Dexmethylphenidate	COMT rs4680 A/A (HOM)	*Reduced stimulant response.*	Evidence ★★
	The patient has the homozygous genotype (MET/MET), which is associated with reduced function in metabolizing dopamine and norepinephrine in the prefrontal cortex. The patient may respond poorly to the increased dopamine levels generated by stimulants.		
	ADRA2A rs1800544 C/C (HOM)		Evidence ★
	Pediatric ADHD Patients with the homozygous genotype may have a poorer response to methylphenidate treatment as compared to pediatric patients with the wild-type or heterozygous genotype.		
	DRD3 rs6280 T/T (HOM)		Evidence ★
	Patients with the homozygous genotype and autism spectrum disorders may have a lesser tolerance for methylphenidate treatment as compared to patients with the wild-type genotype.		
	DRD1 rs4532 C/C (WT)		Evidence ★
	Patients with the wild-type genotype and attention deficit hyperactivity disorder (ADHD) may have an increased severity of social withdrawal or nausea when treated with methylphenidate as compared to patients with the heterozygous or homozygous genotype.		
	CES1 rs71647871 C/C (WT)		Evidence ★
	Consider label recommended dosage of Methylphenidate if no contraindication.		
Dextroamphetamine	COMT rs4680 A/A (HOM)	*Reduced stimulant response.*	Evidence ★★
	The patient has the homozygous genotype (MET/MET), which is associated with reduced function in metabolizing dopamine and norepinephrine in the prefrontal cortex. The patient may respond poorly to the increased dopamine levels generated by stimulants.		
	DRD1 rs4532 C/C (WT)		Evidence ★
	Patients with the wild-type genotype and ADHD may have an increased severity of social withdrawal or nausea when treated with dextroamphetamine as compared to patients with the heterozygous or homozygous genotype.		
Diazepam	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★
	The patient is a rarapid metabolizer of diazepam and should have increased metabolism of diazepam (lower AUC and higher clearance of diazepam) compared to poor metabolizers. The patient should emerge from anesthesia more rapidly than poor metabolizers.		
Diclofenac	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Diclofenac if no contraindication.		
	AGT rs699 G/G (HOM)		Evidence ★
	Consider label recommended dosage of Diclofenac if no contraindication.		

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Digoxin	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Digoxin if no contraindication.	Evidence ★★
Doxepin	CYP2C19 *1/*17 *Rapid metabolizer.* The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Doxepin. Patient may have increased metabolism of Doxepin when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★★
	CYP2D6 *4/*4 *Poor metabolizer.* The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Doxepin. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★★
Duloxetine	DRD3 rs963468 A/A (HOM) Consider label recommended dosage of Duloxetine if no contraindication.	Evidence ★
Efavirenz	CYP3A5 *3/*3 Consider label recommended dosage of Efavirenz if no contraindication.	Evidence ★★
	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Efavirenz if no contraindication.	Evidence ★
Enalapril	CES1 rs71647871 C/C (WT) Consider label recommended dosage of Enalapril if no contraindication.	Evidence ★
Escitalopram	CYP2C19 *1/*17 *Rapid metabolizer.* The genotype predicts that the patient is a Rapid Metabolizer of Escitalopram. The patient may have increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure. The CPIC Guideline recommends considering an alternative drug not predominantly metabolized by CYP2C19.	Evidence ★★★
	CYP1A2 rs4646427 T/T (WT) CYP1A2 rs2069526 T/T (WT) HTR2A rs9316233 C/C (WT) CYP1A2 rs4646425 C/C (WT) HTR2A rs6311 C/C (WT) HTR2C rs6318 G/G (WT) Consider label recommended dosage of Escitalopram if no contraindication.	Evidence ★
Flecainide	CYP2D6 *4/*4 *Poor metabolizer.* The genotype predicts that the patient is a Poor Metabolizer for Flecainide. The Dutch Pharmacogentics Working Group Guideline recommends reducing dose by 50%, record ECG, monitor plasma concentration. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	Evidence ★★★
Fluorouracil	MTHFR rs1801131 T/T (WT) Patients with the wild-type genotype and colorectal cancer who are treated with FOLFOX therapy (includes fluorouracil, leucovorin, oxaliplatin) may have a reduced response to treatment as compared to patients with the heterozygous and homozygous genotype.	Evidence ★★

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	DPYD *1/*5 DPYD rs2297595 T/T (WT) Consider label recommended dosage of Fluorouracil if no contraindication.	*Extensive (normal) metabolizer.* *Extensive (normal) metabolizer.*	Evidence ★★
	DPYD rs17376848 A/A (WT) DPYD rs115232898 T/T (WT) ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Fluorouracil if no contraindication.	*Extensive (normal) metabolizer.* *Extensive (normal) metabolizer.*	Evidence ★
Fluvastatin	ABCG2 rs2231142 G/T (HET) SLCO1B1 rs11045819 C/C (WT) Consider label recommended dosage of Fluvastatin if no contraindication.	RYR1 rs118192172 C/C (WT)	Evidence ★
Haloperidol	CYP2D6 *4/*4 The genotype predicts that the patient is a Poor Metabolizer for Haloperidol. The Dutch Pharmacogentics Working Group Guideline recommends reducing dose by 50% or selecting alternative drug (e.g., pimozide, flupenthixol, fluphenazine, quetiapine, olanzapine, clozapine).	*Poor metabolizer.*	Evidence ★★★
	COMT rs4680 A/A (HOM) Consider label recommended dosage of Haloperidol if no contraindication.	*Reduced stimulant response.*	Evidence ★
Hydrocodone	CYP2D6 *4/*4 The genotype predicts that the patient is a Poor Metabolizer for Hydrocodone. This may lead to greatly reduced morphine formation following Hydrocodone administration leading to insufficient pain relief. The CPIC codeine guidelines suggest avoiding use of analgesics metabolized by CYP2D6 (such as Codeine, Hydrocodone, Oxycodeine, Tramadol) and consider alternative analgesics such as morphine or a non-opioid.	*Poor metabolizer.*	Evidence ★★★
Imidapril	AGT rs5051 T/T (HOM) Patients with the homozygous genotype and hypertension may have a poorer response to treatment with imidapril as compared to patients with the wild-type genotype.		Evidence ★
Imipramine	CYP2C19 *1/*17 The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Imipramine. Patient may have increased metabolism of Imipramine when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	*Rapid metabolizer.*	Evidence ★★★
	CYP2D6 *4/*4 The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Imipramine. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	*Poor metabolizer.*	Evidence ★★★
Irbesartan	AGT rs699 G/G (HOM) Consider label recommended dosage of Irbesartan if no contraindication.	EDN1 rs5370 G/G (WT)	Evidence ★

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Isoflurane	RYR1 rs118192161 C/C (WT) RYR1 rs118192162 A/A (WT) RYR1 rs118192175 C/C (WT) RYR1 rs118192176 G/G (WT) RYR1 rs121918593 G/G (WT) RYR1 rs121918594 G/G (WT) RYR1 rs121918595 C/C (WT)	RYR1 rs121918592 G/G (WT) RYR1 rs118192172 C/C (WT) RYR1 rs118192163 G/G (WT) RYR1 rs118192177 C/C (WT) RYR1 rs28933397 C/C (WT) RYR1 rs118192167 A/A (WT) RYR1 rs118192170 T/T (WT)	Evidence ★
	Consider label recommended dosage of Isoflurane if no contraindication.		
Ivacaftor	CFTR		Evidence ★★
	The patient may not respond to Ivacaftor treatment. The FDA-approved drug labeling information and CPIC guidelines indicate use of ivacaftor in cystic fibrosis patients with at least one copy of a list of 10 CFTR genetic variants. This patient does not have one of these variants and may have an unknown response to ivacaftor treatment, as response may depend on the presence of other CFTR variants.		
Lansoprazole	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Lansoprazole if no contraindication.		
Leucovorin	MTHFR rs1801131 T/T (WT)		Evidence ★★
	Patients with the wild-type genotype and colorectal cancer who are treated with FOLFOX therapy (includes fluorouracil, leucovorin, oxaliplatin) may have a reduced response to treatment as compared to patients with the heterozygous and homozygous genotype.		
Lisdexamfetamine	COMT rs4680 A/A (HOM)	*Reduced stimulant response.*	Evidence ★★
	The patient has the homozygous genotype (MET/MET), which is associated with reduced function in metabolizing dopamine and norepinephrine in the prefrontal cortex. The patient may respond poorly to the increased dopamine levels generated by stimulants.		
Losartan	CYP2C9 rs1057910 A/A (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Losartan if no contraindication.		
Lovastatin	CYP3A5 rs776746 C/C (WT)	RYR1 rs118192172 C/C (WT)	Evidence ★
	Consider label recommended dosage of Lovastatin if no contraindication.		
Mephenytoin	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★
	Consider label recommended dosage of Mephenytoin if no contraindication.		
Mercaptopurine	TPMT *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Mercaptopurine if no contraindication.		
	MTHFR rs1801133 G/A (HET)		Evidence ★
	Patients with this genotype and with Precursor Cell Lymphoblastic Leukemia-Lymphoma may have increased likelihood of treatment interruptions when treated with mercaptopurine as compared to patients with the wild-type genotype.		
Methotrexate	ABCB1 rs1045642 A/A (WT)		Evidence ★★
	Patients with this genotype and lymphoma or leukemia who are treated with methotrexate may have increased concentrations of the drug and may have an increased risk of toxicity.		

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	SLCO1B1 rs4149056 T/C (HET) Pediatric patients with this genotype and acute lymphoblastic leukemia may have decreased clearance of methotrexate as compared to patients with the wild-type genotype.	Evidence ★
	MTHFR rs1801133 G/A (HET) SLCO1B1 rs2306283 A/G (HET) Consider label recommended dosage of Methotrexate if no contraindication.	Evidence ★
Methylphenidate	COMT rs4680 A/A (HOM) *Reduced stimulant response.* The patient has the homozygous genotype (MET/MET), which is associated with reduced function in metabolizing dopamine and norepinephrine in the prefrontal cortex. The patient may respond poorly to the increased dopamine levels generated by stimulants.	Evidence ★★
	ADRA2A rs1800544 C/C (HOM) Pediatric ADHD Patients with the homozygous genotype may have a poorer response to methylphenidate treatment as compared to pediatric patients with the wild-type or heterozygous genotype.	Evidence ★
	DRD3 rs6280 T/T (HOM) Patients with the homozygous genotype and autism spectrum disorders may have a lesser tolerance for methylphenidate treatment as compared to patients with the wild-type genotype.	Evidence ★
	DRD1 rs4532 C/C (WT) Patients with the wild-type genotype and attention deficit hyperactivity disorder (ADHD) may have an increased severity of social withdrawal or nausea when treated with methylphenidate as compared to patients with the heterozygous or homozygous genotype.	Evidence ★
	CES1 rs71647871 C/C (WT) Consider label recommended dosage of Methylphenidate if no contraindication.	Evidence ★
Metoprolol	CYP2D6 *4/*4 *Poor metabolizer.* The patient is a CYP2D6 poor metabolizer. Poor metabolizers will have increased (several-fold) metoprolol blood levels, decreasing metoprolol's cardioselectivity. The DPWG Guidelines indicate a risk of heart failure, and recommend selecting an alternative drug (e.g., bisoprolol, carvedilol) or reduce dose by 75% and be alert to ADEs (e.g., bradycardia, cold extremities).	Evidence ★★★
Nelfinavir	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Nelfinavir if no contraindication.	Evidence ★
Nevirapine	CYP3A5 *3/*3 Patients with the CYP3A5 *3/*3 genotype and HIV infection who are treated with nevirapine may have increased clearance of the drug as compared to patients with the *1/*3 or *1/*1 genotype. Association with clearance was not found in a larger cohort in a separate study. Patients may also have differences in alanine aminotransferase levels, but association with toxicity has not been reported.	Evidence ★★
	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Nevirapine if no contraindication.	Evidence ★★
Nitrous Oxide	MTHFR rs1801133 G/A (HET) Patients with the heterozygous rs1801133 genotype who undergo elective surgery with nitrous oxide anesthesia may have higher plasma total homocysteine concentrations.	Evidence ★

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	MTHFR rs1801131 T/T (WT) Consider label recommended dosage of Nitrous Oxide if no contraindication.	Evidence ★
Nortriptyline	CYP2C19 *1/*17 *Rapid metabolizer.* The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Nortriptyline. Patient may have increased metabolism of Nortriptyline when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★★
	CYP2D6 *4/*4 *Poor metabolizer.* The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Nortriptyline. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★★
	ABCB1 rs1045642 A/A (WT) Patients with the wild-type genotype and depression who are treated with nortriptyline may have a higher likelihood to develop postural hypotension as compared to patients with the heterozygous or homozygous genotype.	Evidence ★
	GNB3 rs5443 T/T (HOM) Consider label recommended dosage of Nortriptyline if no contraindication.	Evidence ★
Olanzapine	HTR2C rs3813929 C/C (WT) Consider label recommended dosage of Olanzapine if no contraindication.	Evidence ★★
	ABCB1 rs1045642 A/A (WT) Patients with the wild-type genotype and Psychotic Disorders who are treated with olanzapine may have increased social and clinical needs as compared to patients with the heterozygous or homozygous genotype.	Evidence ★
	CYP1A2 rs762551 A/A (HOM) Patients with the homozygous genotype and psychiatric disorders who are treated with olanzapine may have decreased response to olanzapine.	Evidence ★
	CYP3A5 rs776746 C/C (WT) Individuals with the homozygous genotype may have decreased area under the curve (AUC) of olanzapine as compared to Individuals with the heterozygous or wild-type genotype.	Evidence ★
	DRD3 rs6280 T/T (HOM) Patients with the homozygous genotype and schizophrenia who are treated with olanzapine may have reduced positive symptom improvement and positive symptom remission as compared to patients with the wild-type genotypes.	Evidence ★
	HTR2C rs1414334 G/G (HOM) Women with the homozygous genotype and mental disorders (excluding schizophrenia) may have greater weight gain when treated with olanzapine as compared to women with the wild-type genotype.	Evidence ★

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	HTR1A rs10042486 C/T (HET) Patients with the heterozygous genotype and schizophrenia may have a poorer response when treated with olanzapine as compared to patients with the homozygous genotype.		Evidence ★
	HTR2C rs518147 G/G (WT) Patients with this genotype and schizophrenia who are treated with olanzapine may have an increased risk of weight gain as compared to patients with the CC genotype. However, contradictory findings are reported.		Evidence ★
	GNB3 rs5443 T/T (HOM) Patients with the homozygous genotype and Schizophrenia who are treated with olanzapine may have an increased risk of weight gain as compared to patients with the wild-type genotype.		Evidence ★
	TPMT rs1142345 T/T (WT) DRD2 rs1799732 TG/TG (HOM) DRD2 rs1079598 A/A (WT) HTR2A rs6313 G/G (WT) HTR2C rs6318 G/G (WT) DRD2 rs6277 A/A (HOM) DRD2 rs1799978 T/T (WT) HTR2A rs7997012 A/G (HET) MTHFR rs1801131 T/T (WT) Consider label recommended dosage of Olanzapine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★
Omeprazole	CYP2C19 *1/*17 Consider label recommended dosage of Omeprazole if no contraindication.	*Rapid metabolizer.*	Evidence ★★★
Oxaliplatin	MTHFR rs1801131 T/T (WT) Patients with the wild-type genotype and colorectal cancer who are treated with FOLFOX therapy (includes fluorouracil, leucovorin, oxaliplatin) may have a reduced response to treatment as compared to patients with the heterozygous and homozygous genotype.		Evidence ★★
	DPYD rs67376798 T/T (WT) Consider label recommended dosage of Oxaliplatin if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★
Oxycodone	CYP2D6 *4/*4 The genotype predicts that the patient is a Poor Metabolizer for Oxycodone. Consider using an alternate drug rather than oxycodone (not codeine or tramadol) or be alert to insufficient pain relief. The Dutch Pharmacogenetics Working Group Guideline indicates that there is insufficient data to allow calculation of dose adjustment. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.	*Poor metabolizer.*	Evidence ★★
Paclitaxel	ABCB1 rs1045642 A/A (WT) Patients with this genotype may have increased risk of Neutropenia and Neurotoxicity Syndromes when treated with paclitaxel in cancer patients as compared to patients with homozygous genotype GG.		Evidence ★
	CYP3A4 rs67666821 G/G (WT) CYP3A4 rs72552799 C/C (WT) CYP3A5 rs776746 C/C (WT) Consider label recommended dosage of Paclitaxel if no contraindication.	*Reduced metabolizer.* *Reduced metabolizer.*	Evidence ★

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Pantoprazole	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Pantoprazole if no contraindication.		
Paroxetine	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer of Paroxetine. The patient may have greatly reduced metabolism when compared to extensive metabolizers, and higher plasma concentrations may increase the probability of side effects. The CPIC Guideline recommends selecting alternative drug not predominantly metabolized by CYP2D6 or if paroxetine use warranted, consider a 50% reduction of recommended starting dose and titrate to response.		
	HTR1A rs6295 C/G (HET)		Evidence ★★
	Patients with the heterozygous genotype with panic disorder who are treated with paroxetine may have a reduced response at 4 weeks of treatment as compared to patients with the homozygous genotype.		
	CYP1A2 rs762551 A/A (HOM)		Evidence ★
	Patients with homozygous genotype may require an increased dose of paroxetine and may have an increased risk of fatigue when treated with paroxetine as compared to patients with the wild-type genotype.		
	ABCB1 rs2235015 C/C (WT)		Evidence ★
	Patients with the wild-type genotype and depression who are treated with paraxetine may be less likely to experience remission as compared to patients with the heterozygous or homozygous genotype.		
	HTR2A rs6313 G/G (WT)		Evidence ★
	Patients with the wild-type genotype and depression who are treated with paroxetine may have an increased risk of adverse drug reactions as compared to patients with the heterozygous or homozygous genotype.		
	HTR1A rs10042486 C/T (HET)		Evidence ★
	Patients with the heterozygous genotype and Major Depressive Disorder who are treated with paroxetine may have decreased response to treatment as compared to patients with the wild-type genotype.		
	DRD3 rs6280 T/T (HOM)		Evidence ★
	Patients with the homozygous genotype and major depressive disorder may have a reduced response when treated with paroxetine as compared to patients with the heterozygous or wild-type genotype.		
	COMT rs4680 A/A (HOM)	*Reduced stimulant response.*	Evidence ★
	CYP1A2 rs2470890 T/T (HOM) CYP1A2 rs4646427 T/T (WT)		
	Consider label recommended dosage of Paroxetine if no contraindication.		
Peginterferon-alfa	IFNL3 rs12979860 C/C (WT) IFNL3 rs8099917 T/T (WT)		Evidence ★★★
	Consider label recommended dosage of Peginterferon-alfa if no contraindication.		
	IFNL3 rs8103142 T/T (WT)		Evidence ★
	Consider label recommended dosage of Peginterferon-alfa if no contraindication.		
Phenytoin	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Phenytoin if no contraindication.		

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	CYP2C9 rs9332131 A/A (WT) *Extensive (normal) metabolizer.* ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Phenytoin if no contraindication.	Evidence ★
Pravastatin	SLCO1B1 rs4149056 T/C (HET) Patient may have increased plasma concentrations of pravastatin and may have a smaller reduction in total cholesterol. Note that this has not been found in all studies, and the association between this variant and pravastatin response remains unclear.	Evidence ★★
	ABCB1 rs2032582 A/A (WT) Patients with this genotype and Acute Coronary Syndrome who are treated with pravastatin may have a reduced response (as measured by lower reductions in LDL-cholesterol).	Evidence ★
	MTHFR rs1801133 G/A (HET) Patients with this genotype may have an increased risk of nonfatal myocardial infarction and fatal coronary heart disease compared to the wild-type genotype.	Evidence ★
	RYR1 rs118192172 C/C (WT) SLCO1B1 rs4149015 G/G (WT) Consider label recommended dosage of Pravastatin if no contraindication.	Evidence ★
Prednisone	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of prednisone if no contraindication.	Evidence ★
Propafenone	CYP2D6 *4/*4 *Poor metabolizer.* The genotype predicts that the patient is a Poor Metabolizer for Propafenone. The Dutch Pharmacogenetics Working Group Guideline recommends reducing dose by 70%, recording ECG, and monitoring plasma concentration. Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.	Evidence ★★★
Repaglinide	SLCO1B1 rs4149056 T/C (HET) Consider label recommended dosage of Repaglinide if no contraindication.	Evidence ★
Ribavirin	IFNL3 rs12979860 C/C (WT) IFNL3 rs8099917 T/T (WT) Consider label recommended dosage of Ribavirin if no contraindication.	Evidence ★★★
	IFNL3 rs8103142 T/T (WT) Consider label recommended dosage of Ribavirin if no contraindication.	Evidence ★
Risperidone	CYP2D6 *4/*4 *Poor metabolizer.* The DPWG Pharmacogenetics Working Group has evaluated therapeutic dose recommendations for risperidone based on CYP2D6 genotypes and recommends selecting an alternative drug or being extra alert to Adverse Drug Events and adjusting dose to clinical response for patients who are CYP2D6 poor, intermediate, or ultrarapid metabolizers.	Evidence ★★★
	DRD3 rs6280 T/T (HOM) Patients with the homozygous genotype may have smaller reductions in Autism Treatment Evaluation Checklist (ATEC) scores, indicating poorer response to risperidone in Children with Autism, compared to patients with the wild-type or heterozygous genotype.	Evidence ★

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	HTR2A rs6311 C/C (WT) Patients with the wild-type genotype may have poorer response to risperidone in children with autism as compared to patients with the heterozygous or homozygous genotype.	Evidence ★
	HTR1A rs10042486 C/T (HET) Patients with the heterozygous genotype and schizophrenia may have a poorer response when treated with risperidone as compared to patients with the homozygous genotype.	Evidence ★
	ABCB1 rs1128503 A/A (WT) DRD2 rs1799732 TG/TG (HOM) DRD3 rs167771 A/A (HOM) HTR2A rs6313 G/G (WT) HTR2C rs3813928 G/G (WT) Consider label recommended dosage of Risperidone if no contraindication.	Evidence ★
Rosuvastatin	SLCO1B1 rs4149056 T/C (HET) Patients with this genotype may have increased plasma concentrations of rosuvastatin. However, no association is seen between genotypes of this variant and change in LDL-cholesterol levels in response to rosuvastatin treatment.	Evidence ★★
	ABCG2 rs2231142 G/T (HET) Consider label recommended dosage of Rosuvastatin if no contraindication.	Evidence ★★
	RYR1 rs118192172 C/C (WT) Consider label recommended dosage of Rosuvastatin if no contraindication.	Evidence ★
Sertraline	CYP2C19 *1/*17 *Rapid metabolizer.* HTR1A rs6295 C/G (HET) Consider label recommended dosage of Sertraline if no contraindication.	Evidence ★★★
Sevoflurane	RYR1 rs118192161 C/C (WT) RYR1 rs121918592 G/G (WT) RYR1 rs118192162 A/A (WT) RYR1 rs118192172 C/C (WT) RYR1 rs118192175 C/C (WT) RYR1 rs118192163 G/G (WT) RYR1 rs118192176 G/G (WT) RYR1 rs118192177 C/C (WT) RYR1 rs121918593 G/G (WT) RYR1 rs28933397 C/C (WT) RYR1 rs121918594 G/G (WT) RYR1 rs118192167 A/A (WT) RYR1 rs121918595 C/C (WT) RYR1 rs118192170 T/T (WT) Consider label recommended dosage of Sevoflurane if no contraindication.	Evidence ★
Simvastatin	SLCO1B1 rs4149056 T/C (HET) This patient has one copy of a wild type (normal function) allele and one copy of a decreased function allele. Based on the genotype result, this patient is predicted to have intermediate SLCO1B1 function. This patient may be at risk for an adverse response to medications that are affected by SLCO1B1. If simvastatin is prescribed to a patient with intermediate SLCO1B1 function, there is an increased risk for developing simvastatin-associated myopathy; such patients may need a lower starting dose of simvastatin or an alternate statin agent. Please consult a clinical pharmacist for more specific information about how SLCO1B1 function influences drug dosing. The CPIC Guidelines recommend prescribing a lower dose or considering an alternative statin (e.g. pravastatin or rosuvastatin) and consider routine CK surveillance.	Evidence ★★★
	ABCB1 rs2032582 A/A (WT) Consider label recommended dosage of Simvastatin if no contraindication.	Evidence ★★

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	SLCO1B1 rs4149081 G/A (HET) Patients with this genotype and Coronary Disease may have higher LDL-C reduction as compared to patients with the wild-type genotype.	Evidence ★
	CYP3A5 rs776746 C/C (WT) Patients with this genotype may have higher plasma concentrations and reduced clearance of simvastatin as compared to patients with the homozygous genotype. This does not seem to affect response to treatment or risk of myalgia.	Evidence ★
	ABCB1 rs1045642 A/A (WT) ABCG2 rs2231142 G/T (HET) RYR1 rs118192172 C/C (WT) Consider label recommended dosage of Simvastatin if no contraindication.	Evidence ★
Sirolimus	CYP3A5 *3/*3 Consider label recommended dosage of Sirolimus if no contraindication.	Evidence ★★
	ABCB1 rs1045642 A/A (WT) Patients with this genotype who underwent kidney transplantation may been shown to have increased total and low-density lipoprotein cholesterol when treated with sirolimus as compared to patients with the GG genotype	Evidence ★
Succinylcholine	RYR1 rs118192161 C/C (WT) RYR1 rs121918592 G/G (WT) RYR1 rs118192162 A/A (WT) RYR1 rs118192172 C/C (WT) RYR1 rs118192175 C/C (WT) RYR1 rs118192163 G/G (WT) RYR1 rs118192176 G/G (WT) RYR1 rs118192177 C/C (WT) RYR1 rs121918593 G/G (WT) RYR1 rs28933397 C/C (WT) RYR1 rs121918594 G/G (WT) RYR1 rs118192167 A/A (WT) RYR1 rs121918595 C/C (WT) RYR1 rs118192170 T/T (WT) Consider label recommended dosage of Succinylcholine if no contraindication.	Evidence ★
Tacrolimus	CYP3A5 *3/*3 Consider label recommended dosage of Tacrolimus if no contraindication.	Evidence ★★★
	ABCB1 rs1045642 A/A (WT) Consider label recommended dosage of Tacrolimus if no contraindication.	Evidence ★
Tamoxifen	CYP2D6 *4/*4 *Poor metabolizer.* Patient is a CYP2D6 Poor Metabolizer. Tamoxifen is a pro-drug requiring metabolic activation by CYP2D6. The DPWG Guidelines warn of an increased risk for relapse of breast cancer. Consider aromatase inhibitor for postmenopausal women.	Evidence ★★★
Tegafur	DPYD *1/*5 *Extensive (normal) metabolizer.* Consider label recommended dosage of Tegafur if no contraindication.	Evidence ★★
Thioguanine	TPMT *1/*1 *Extensive (normal) metabolizer.* Consider label recommended dosage of Thioguanine if no contraindication.	Evidence ★★★
Thrombophilia	F2 rs1799963 G/G (WT) The patient does not carry the Prothrombin (Factor II: G20210A) Mutation, a common genetic marker associated with inherited thrombophilia.	Evidence ★★★
	F5 rs6025 C/C (HOM) The patient does not carry the Factor V Leiden (G1691A) Mutation, a common genetic marker associated with inherited thrombophilia.	Evidence ★★★
Timolol	ADRB1 rs1801252 A/A (WT) Consider label recommended dosage of Timolol if no contraindication.	Evidence ★

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Tolbutamide	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Tolbutamide if no contraindication.		
Tramadol	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Tramadol. The Dutch Pharmacogenetics Working Group Guideline recommends selecting an alternative drug, not oxycodone or codeine, or be alert to symptoms of insufficient pain relief. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.		
Trimipramine	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2C19 Rapid Metabolizer of Trimipramine. Patient may have increased metabolism of Trimipramine when compared to extensive metabolizers. The CPIC Guidelines recommends considering an alternative drug not metabolized by CYP2C19. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments.		
	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts the patient is a CYP2D6 Poor Metabolizer of Trimipramine. Patient may have a greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. The CPIC Guidelines recommend avoiding tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.		
Valproic Acid	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Valproic Acid if no contraindication.		
Venlafaxine	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer of venlafaxine. The Dutch Pharmacogenetics Working Group Guideline indicates that there is insufficient data to allow calculation of dose adjustment, and recommends selecting an alternative drug (e.g., citalopram, sertraline) or adjust dose to clinical response and monitor (O-desmethyl)venlafaxine plasma concentration.		
	ABCB1 rs1045642 A/A (WT)		Evidence ★
	Patients with the wild-type genotype and depressive disorder may have decreased response to venlafaxine compared to patients with the homozygous genotype.		
	COMT rs4680 A/A (HOM)	*Reduced stimulant response.*	Evidence ★
	Patients with this genotype who are treated Depressive Disorder may have a decreased response to venlafaxine. However, patients with this genotype who are treated for Anxiety Disorders may have an increased response to venlafaxine.		
	ABCB1 rs2235015 C/C (WT)		Evidence ★
	Patients with the wild-type genotype and depression who are treated with venlafaxine may be less likely to experience remission as compared to patients with the heterozygous or homozygous genotype.		

DETAILED INFORMATION

	HTR2A rs7997012 A/G (HET) Consider label recommended dosage of Venlafaxine if no contraindication.	Evidence ★
Verapamil	NR1H3 rs11039149 A/G (HET) Patients with the heterozygous genotype and hypertension and coronary artery disease who are treated with verapamil may have an increased risk for cardiovascular events as compared to patients with the wild-type genotype.	Evidence ★
	CACNA1C rs1051375 A/A (HOM) KCNIP1 rs11739136 C/C (WT) Consider label recommended dosage of Verapamil if no contraindication.	Evidence ★
Warfarin	CYP2C9 *1/*1. VKORC1 rs9923231 C/T (HET) *Extensive (normal) metabolizer.* The CYP2C9 *1/*1 genotype is a fully functional, extensive (normal) metabolizer of Warfarin, and the VKORC1 heterozygous variant is associated with increased sensitivity to Warfarin. Recommended daily warfarin doses (mg/day) to achieve a therapeutic INR based on CYP2C9 and VKORC1 genotype using the warfarin product insert approved by the United States Food and Drug Administration: 5-7 mg / day.	Evidence ★★★
	VKORC1 rs7294 C/T (HET) Patients with the heterozygous rs7294 genotype who are treated with warfarin may require a higher dose as compared to patients with the wild-type genotype.	Evidence ★★★
	VKORC1 rs9934438 G/A (HET) Patients with the heterozygous rs9934438 genotype who are treated with warfarin may require a lower dose as compared to patients with the wild-type genotype.	Evidence ★★★
	VKORC1 rs8050894 C/G (HET) Patients with the heterozygous rs8050894 genotype who are treated with warfarin may require a lower dose as compared to patients with the wild-type genotype.	Evidence ★★
	VKORC1 rs2359612 A/G (HET) Patients with the heterozygous rs2359612 genotype who are treated with warfarin may require a higher dose as compared to patients with the wild-type genotype but a lower dose as compared to patients with the homozygous genotype.	Evidence ★★
	CYP2C9 rs7900194 G/G (WT) *Extensive (normal) metabolizer.* CYP2C9 rs56165452 T/T (WT) *Extensive (normal) metabolizer.* CYP2C9 rs28371686 C/C (WT) *Extensive (normal) metabolizer.* VKORC1 rs17708472 G/G (WT) Consider label recommended dosage of Warfarin if no contraindication.	Evidence ★★
	CYP2C9 rs28371685 C/C (WT) *Extensive (normal) metabolizer.* CYP2C9 rs9332131 A/A (WT) *Extensive (normal) metabolizer.* Consider label recommended dosage of Warfarin if no contraindication.	Evidence ★

KEY FOR VARIANT-DRUG COMBINATION EVIDENCE

★★★ Replicated in multiple studies with statistical significance and strong effect size.
★★ Replicated in multiple studies with and without statistical significance and effect size may be minimal.
★ Not yet replicated or replicated but lacking clear evidence of an association.
Notable information is available and special considerations may be of interest when prescribing for this genotype.
Literature does not indicate additional risks, benefits, or prescription changes to consider for this genotype.

REPORTED GENOTYPES

This panel performs genotyping analysis on key genes and variant hot-spot regions, focused on analyzing loci documented as altering the effectiveness of drug metabolism. Key genotyping results include the following:

ABCB1
rs1045642:A/A Wild
rs2032582:A/A Wild
rs1128503:A/A Wild
rs2235015:C/C Wild

ABCG2
rs2231142:G/T Het

ADRA2A
rs1800544:C/C Hom

ADRB1
rs1801252:A/A Wild

AGT
rs5051:T/T Hom
rs699:G/G Hom

CACNA1C
rs1051375:A/A Hom

CES1
rs71647871:C/C Wild

CFTR
rs267606723:G/G Wild
rs193922525:G/G Wild
rs199826652:TCT/TCT Wild
rs75527207:G/G Wild
rs121908755:G/G Wild
rs80282562:G/G Wild
rs121908757:A/A Wild
rs121909005:T/T Wild
rs121909013:G/G Wild
rs74503330:G/G Wild
rs121909041:T/T Wild

COMT
rs4680:A/A Hom

CYP1A2
rs2069526:T/T Wild
rs2470890:T/T Hom
rs4646425:C/C Wild
rs4646427:T/T Wild
rs762551:A/A Hom

CYP2C19
CYP2C19 *1/*17
rs4244285:G/G Wild
rs4986893:G/G Wild
rs28399504:A/A Wild
rs56337013:C/C Wild
rs72552267:G/G Wild
rs72558186:T/T Wild
rs41291556:T/T Wild
rs17884712:G/G Wild
rs6413438:C/C Wild
rs55640102:A/A Wild
rs12248560:C/T Het

CYP2C9
CYP2C9 *1/*1
rs1799853:C/C Wild
rs1057910:A/A Wild
rs28371686:C/C Wild
rs9332131:A/A Wild
rs7900194:G/G Wild
rs28371685:C/C Wild
rs56165452:T/T Wild

CYP2D6
CYP2D6 *4/*4
rs16947:G/G Hom
rs1135840:G/G Wild
rs35742686:T/T Wild
rs1135824:T/T Wild
rs1065852:A/A Hom
rs3892097:T/T Hom
rs5030655:A/A Wild
rs5030867:T/T Wild
rs5030865:C/C Wild
rs5030656:CTT/CTT Wild
rs5030863:C/C Wild
rs5030862:C/C Wild
rs72549357:C/C Wild
rs28371706:G/G Wild
rs59421388:C/C Wild
rs769258:C/C Wild
rs28371725:C/C Wild
rs28371696:C/C Wild
rs28371717:C/C Wild

CYP3A4
CYP3A4 *1/*22
rs12721627:G/G Wild
rs2242480:C/C Wild
rs12721629:G/G Wild
rs4987161:A/A Wild
rs72552799:C/C Wild
rs67784355:G/G Wild
rs4986909:G/G Wild
rs35599367:G/A Het
rs67666821:G/G Wild

CYP3A5
CYP3A5 *3/*3
rs776746:C/C Wild

DPYD
DPYD *1/*5
rs67376798:T/T Wild
rs3918290:C/C Wild
rs55886062:A/A Wild
rs2297595:T/T Wild
rs17376848:A/A Wild
rs1801159:T/C Het
rs1801158:C/C Wild
rs115232898:T/T Wild

DRD1
rs4532:C/C Wild

DRD2
rs1079598:A/A Wild
rs1799732:TG/TG Hom
rs1799978:T/T Wild
rs6277:A/A Hom

DRD3
rs167771:A/A Hom
rs6280:T/T Hom
rs963468:A/A Hom

EDN1
rs5370:G/G Wild

F2
rs1799963:G/G Wild

F5
rs6025:C/C Hom

GNB3
rs2301339:A/A Hom
rs5443:T/T Hom

GRIK4
rs1954787:C/C Hom

HTR1A
rs10042486:C/T Het
rs6295:C/G Het

HTR2A
rs7997012:A/G Het
rs9316233:C/C Wild
rs6313:G/G Wild
rs6311:C/C Wild

HTR2C
rs1414334:G/G Hom
rs3813928:G/G Wild
rs3813929:C/C Wild
rs518147:G/G Wild
rs6318:G/G Wild

IFNL3
rs12979860:C/C Wild
rs8099917:T/T Wild
rs8103142:T/T Wild

KCNIP1
rs11739136:C/C Wild

LDLR
rs688:C/C Wild

MTHFR
rs1801133:G/A Het
rs1801131:T/T Wild

NR1H3
rs11039149:A/G Het

OPRM1
rs2281617:C/C Wild
rs510769:C/C Wild

RYR1
rs118192161:C/C Wild
rs121918592:G/G Wild
rs118192162:A/A Wild
rs118192172:C/C Wild
rs118192175:C/C Wild
rs118192163:G/G Wild
rs118192176:G/G Wild
rs118192177:C/C Wild
rs121918593:G/G Wild
rs28933397:C/C Wild
rs121918594:G/G Wild
rs118192167:A/A Wild
rs121918595:C/C Wild
rs118192170:T/T Wild

SLC6A2
rs3785143:C/C Wild
rs12708954:C/A Het

601 Genome Way
Huntsville, AL 35806
256-327-9800 (Ph), 256-327-9810 (Fax)

SLCO1B1
rs4149056:T/C Het
rs11045819:C/C Wild
rs2306283:A/G Het
rs4149015:G/G Wild
rs4149081:G/A Het

TPMT
TPMT *1/*1
rs1142345:T/T Wild
rs1800584:C/C Wild
rs1800460:C/C Wild
rs1800462:C/C Wild

VKORC1
rs9923231:C/T Het
rs9934438:G/A Het
rs17708472:G/G Wild
rs2359612:A/G Het
rs7294:C/T Het
rs8050894:C/G Het

Reported genotype calls are all displayed with respect to the positive DNA strand. Variants indicated as homozygous (Hom) or heterozygous (Het) differ from the GRCh37/hg19 reference sequence (Wild). This report is limited to the following star-alleles: CYP2D6: *1, *2, *3, *3B, *4, *5, *6C, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *29, *33, *35A, *41, *45A & *46. CYP2C19: *1, *2, *3, *4B, *4, *5, *6, *7, *8, *9, *10, *12 & *17. CYP2C9: *1, *2 & *3. CYP3A5: *1 & *3. CYP3A4: *1, *8, *11, *12, *13, *16, *17 & *22. TPMT: *1, *2, *3A, *3C, *3B & *4. DPYD: *1, *2, *4, *5, *13 & rs67376798A. Any genotype identified as a default star-allele (CYP2D6 *2, CYP2C19 *1, CYP2C9 *1, CYP3A5 *3, CYP3A4 *1, TPMT *1, DPYD *1) indicates the absence only of the other alleles listed and does not imply that other variants in the gene are absent. Full allele deletions and duplications are only analyzed for the CYP2D6 gene. This test does not report polymorphisms other than those specifically listed, and mutations in other genes associated with drug metabolism will not be detected. Rare diagnostic errors may occur if variations occur in primer site locations.

DISCLAIMER

The information presented on this report is provided as supplementary health information. The results presented are intended for use by a physician, pharmacist or other healthcare professional to advise a patient on the use of prescribed medications. This test is not a 510k cleared test, but managed by CMS and FDA under the Clinical Laboratory Improvement Amendment (CLIA) as a LDT. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided. Results are dependent on adequate specimen collection and processing.

METHODOLOGY

Genomic DNA is extracted from dry buccal swabs using magnetic particle processing. DNA from patient samples are amplified with primers specific for ABCB1, ABCG2, ADRA2A, ADRB1, AGT, CACNA1C, CES1, CFTR, COMT, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, DPYD, DRD1, DRD2, DRD3, EDN1, F2, F5, GNB3, GRIK4, HTR1A, HTR2A, HTR2C, IFNL3, KCNIP1, LDLR, MTHFR, NR1H3, OPRM1, RYR1, SLC6A2, SLCO1B1, TPMT & VKORC1 using Nested Patch PCR (Varley, et. al.). Positive and negative controls are used with each run. Patient samples, positive, and negative controls are sequenced using a MiSeq (Illumina). Sequences are analyzed using alignment and base call algorithms with Kailos Blue Software for the presence or absence of single nucleotide base changes, insertions and deletions. LR-PCR utilized for confirmation of CYP2D6 duplications and deletions. Results and recommendations are compiled as part of a medical report.

Genetic testing was performed in the Kailos Genetics CLIA facility at 601 Genome Way; Huntsville, Al. 35806. CLIA#: 01D2016114. Medical Director: Ronald McGlennen MD, FCAP, FACMG, ABMG.

This report was reviewed and approved for release by CLIA Lab Manager & Supervisor: Michele R. Erickson-Johnson, PhD, MB (ASCP)^{CM}

REFERENCES

M.V. Relling, T.E. Klein. "CPIC: Clincial Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network." Clinical Pharmacology & Therapeutics (2011) 89(3): 464-467.

J.J. Swen, M. Nijenhuis, A. de Boer, L. Grandia, A.H. Maitland-van der Zee, H. Mulder, G.A. Rongen, R.H. van Schaik, T. Schalekamp, D.J. Touw, J. van der Weide, B. Wilffert, V.H. Deneer, H.J. Guchelaar. "Pharmacogenetics: from bench to byte--an update of guidelines." Clinical Pharmacology & Therapeutics (2011) 89(5): 662-673.

K.E. Varley, R.D. Mitra. "Nested Patch PCR Enables Highly Multiplexed Mutation Discovery in Candidate Genes." Genome Research (2008) 18: 1844-1850.

M. Whirl-Carrillo, E.M. McDonagh, J. M. Hebert, L. Gong, K. Sangkuhl, C.F. Thorn, R.B. Altman and T.E. Klein. "Pharmacogenomics Knowledge for Personalized Medicine" Clinical Pharmacology & Therapeutics (2012) 92(4): 414-417.