BHARATH GENOMIX

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Anbu Rajan**	**SPECIMEN TYPE:**	Buccal Swab	**Kathiresan Muthu**
ACC #:	41001710241297	**COLLECTION DATE:**	1/31/2018	**Mullai** Nursing Home of **Sirkali**
DOB:	9/22/1949	**RECEIVED DATE:**	2/13/2018	
SEX:	Male	**REPORT DATE:**	4/8/2018	

Comprehensive Pharmacogenetic Report

Current Patient Medications

ALBUTEROL SULFATE, Aspirin, Baclofen, Colace, COREG, Depakote, Diclofenac Sodium, Gabapentin, Humalog, Lantus, LISINOPRIL, MiraLAX, PAXIL, Pepcid, Plavix, Provera, Lopid, Propranolol, Acetaminophen, Milk of Magnesia, NITROSTAT

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DOB: 9/22/1949 **SEX:** Male

Diclofenac
Voltaren

Possible Sensitivity to Diclofenac (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e poor metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.

Coreg
Carvedilol

Normal Sensitivity to Carvedilol (CYP2D6: Normal Metabolizer) — **ACTIONABLE**

Carvedilol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.

Depakote
Valproic Acid

Normal Response to Valproic acid — **INFORMATIVE**

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients carrying mutations in mitochondrial DNA polymerase γ (POLG). Valproic acid is contraindicated in patients known to have mitochondrial disorders caused by mutations in mitochondrial DNA polymerase γ (POLG; e.g., Alpers-Huttenlocher Syndrome) and children under two years of age who are suspected of having a POLG-related disorder.

Valproic acid is extensively metabolized in the liver, which occurs primarily by glucuronidation with probable contributions of UGT1A6, UGT1A9, and UGT2B7. This drug is also metabolized by a minor CYP–dependent oxidation pathway, which includes multiple enzymes such as CYP2A6, CYP2C9, and CYP2C19. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on valproic acid response, and no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** enzyme-inducing drugs increase valproic acid clearance 2-fold, and higher doses of this drug are required to maintain therapeutic concentrations when added to a therapy regimen containing enzyme-inducing antiepileptic drugs.

Gabapentin
Neurontin

Normal Response to Gabapentin — **INFORMATIVE**

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Gabapentin is eliminated primarily through renal excretion and is not metabolized by CYPs. Genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Gabapentin can be prescribed at standard label-recommended dosage and administration.

Paxil
Paroxetine

Normal Sensitivity to Paroxetine (CYP2D6: Normal Metabolizer) — **ACTIONABLE**

Paroxetine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

Plavix
Clopidogrel

Normal Response to Clopidogrel (CYP2C19: Normal Metabolizer) — **ACTIONABLE**

Clopidogrel can be prescribed at standard label-recommended dosage.

Propranolol
Inderal

Normal Sensitivity to Propranolol (CYP2D6: Normal Metabolizer) — **ACTIONABLE**

Propranolol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.

Medications outside the scope of the report: Albuterol, Aspirin, Baclofen, Colace, HumaLOG, Lantus, Lisinopril, Miralax, Pepcid, Provera, Lopid, Acetaminophen, Milk of Magnesia, Nitrostat

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A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE**	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE**	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

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Risk Management

Antipsychotic-Induced Tardive Dyskinesia

Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for tardive dyskinesia when treated with antipsychotics.

Monitor the patient for any signs of tardive dyskinesia.

Antipsychotic-Induced Hyperprolactinemia

Moderate Risk of Antipsychotic-induced Hyperprolactinemia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk of hyperprolactinemia when treated with antipsychotics.

Monitor patient closely for signs of hyperprolactinemia. An evaluation of the risk-benefit profile of the antipsychotic medication may be required.

Antipsychotic-Induced Weight Gain

Moderate Risk of Antipsychotic-Induced Weight Gain

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for weight gain when treated with antipsychotics.

Monitor patient closely for signs of weight gain.

Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is negative for both the APOE c.388 T>C (Cys130Arg) and c.526 C>T (Arg176Cys) mutations. The patient's genotype is wild-type, which is the most common genotype in the general population (frequency: >60%).

A patient with wild-type genotype does not have a defect in the apolipoprotein E (APOE), which is an integral structure of lipoprotein particles that have critical roles in blood lipid metabolism and transport. The APOE ε3/ε3 genotype is not associated with increased risk of cardiovascular disease.

No action is needed when a patient is normolipidemic.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia.

Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

Thrombophilia

No Increased Risk of Thrombosis

The patient does not carry the Factor V Leiden G1691A mutation or Factor II G20210A mutation (wild-type).

The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Unless other genetic and/or circumstantial risk factors are present (e.g., smoking or obesity...), estrogen-containing contraceptive and hormone replacement therapy can be used by the patient.

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Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation and one A1298C mutation (compound heterozygous). MTHFR enzyme activity is reduced.

The patient's reduced MTHFR activity is not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

Testing total plasma homocysteine level may be beneficial. Hyperhomocysteinemia can be treated with nutritional supplementation.

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SEX: Male

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	**Antifolates**		Methotrexate (Trexall)	
Cardiovascular	**Angiotensin II Receptor Antagonists**	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)	Losartan (Cozaar, Hyzaar)	
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics	Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)		
	Anticoagulants	Apixaban (Eliquis) Betrixaban (Bevyxxa) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto)	Warfarin (Coumadin)	
	Antiplatelets	Clopidogrel (Plavix) Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)		
	Beta Blockers	Bisoprolol (Zebeta) Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Metoprolol (Lopressor) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		
	Diuretics		Torsemide (Demadex)	
	Statins	Atorvastatin (Lipitor) Lovastatin (Mevacor, Altoprev, Advicor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)	Fluvastatin (Lescol)	
Diabetes	**Meglitinides**	Repaglinide (Prandin, Prandimet)	Nateglinide (Starlix)	
	Sulfonylureas		Chlorpropamide (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)	

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Gastrointestinal	**Antiemetics**	Aprepitant (Emend-oral) Dolasetron (Anzemet) Fosaprepitant (Emend-i.v) Metoclopramide (Reglan) Netupitant-Palonosetron (Akynzeo) Ondansetron (Zofran, Zuplenz) Palonosetron (Aloxi) Rolapitant (Varubi)	Dronabinol (Marinol)	
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		
Infections	**Antifungals**	Amphotericin B (AmBisome, Abelcet) Anidulafungin (Eraxis) Caspofungin (Cancidas) Fluconazole (Diflucan) Isavuconazonium (Cresemba) Itraconazole (Sporanox) Micafungin (Mycamine) Posaconazole (Noxafil) Voriconazole (Vfend)		
	Anti-HIV Agents	Dolutegravir (Tivicay, Triumeq) Raltegravir (Isentress, Dutrebis)		
	Antimalarials	Proguanil (Malarone)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Carisoprodol (Soma) Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)	Tizanidine (Zanaflex)	
	NSAIDs	Ketoprofen (Orudis) Ketorolac (Toradol) Nabumetone (Relafen) Naproxen (Aleve) Sulindac (Clinoril)	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Meloxicam (Mobic) Piroxicam (Feldene)	
	Opioids	Alfentanil (Alfenta) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)	Methadone (Dolophine)	
	Antiaddictives		Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Naltrexone (Vivitrol, Contrave)	
	Anti-ADHD Agents	Amphetamine (Adderall, Evekeo) Atomoxetine (Strattera) Clonidine (Kapvay) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse)	Dexmethylphenidate (Focalin) Methylphenidate (Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER)	

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychotropic	**Anticonvulsants**	Brivaracetam (Briviact) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)	Fosphenytoin (Cerebyx) Phenytoin (Dilantin)	
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		
	Antidepressants	Amitriptyline (Elavil) Amoxapine (Amoxapine) Citalopram (Celexa) Clomipramine (Anafranil) Desipramine (Norpramin) Desvenlafaxine (Pristiq) Doxepin (Silenor) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Imipramine (Tofranil) Levomilnacipran (Fetzima) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Sertraline (Zoloft) Trazodone (Oleptro) Trimipramine (Surmontil) Venlafaxine (Effexor) Vilazodone (Viibryd) Vortioxetine (Trintellix)		

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NAME: **Anbu Rajan**
ACC #: 410017102
41297 **DOB:** 9/22/1949
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify, Aristada) Asenapine (Saphris) Brexpiprazole (Rexulti) Cariprazine (Vraylar) Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Perphenazine (Trilafon) Pimavanserin (Nuplazid) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Clozapine (Clozaril) Olanzapine (Zyprexa)	
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin) Diazepam (Valium)		
	Other Neurological Agents	Deutetrabenazine (Austedo) Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi) Valbenazine (Ingrezza)	Tetrabenazine (Xenazine)	
Rheumatology	**Anti-Hyperuricemics and Anti-Gout Agents**	Colchicine (Mitigare) Febuxostat (Uloric)	Lesinurad (Zurampic)	
	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	**Immunosuppressants**	Tacrolimus (Prograf)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Urologicals	**5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia**	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex) Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Tolterodine (Detrol) Trospium (Sanctura)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		

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Dosing Guidance

Bupropion
Wellbutrin, Zyban, Aplenzin, Contrave

Possibly Decreased Response to Bupropion (CYP2B6: Intermediate Metabolizer) — **INFORMATIVE**

Bupropion is metabolized to its active metabolite hydroxybupropion by CYP2B6. This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. Individuals who are CYP2B6 intermediate metabolizers may or may not have lower blood levels of hydroxybupropion which may or may not result in a reduced response to bupropion treatment. Bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment.

Bupropion
Wellbutrin, Zyban, Aplenzin, Contrave

Decreased Response to Bupropion for Smoking Cessation (ANKK1: Altered DRD2 function) — **INFORMATIVE**

Smoking Cessation: The patient's genotype result is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

Celecoxib
Celebrex

High Sensitivity to Celecoxib (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

Consider starting at half the lowest recommended dose, and evaluate response the first week. Be alert to gastrointestinal adverse events. Consider alternative medication for the management of Juvenile Rheumatoid Arthritis.

Chlorpropamide
Diabenese

Possible Sensitivity to Chlorpropamide (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

Subjects with reduced CYP2C9 activity may have increased chlorpropamide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, chlorpropamide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of plasma glucose levels.

Clozapine
Clozaril

Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — **INFORMATIVE**

Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexmethylphenidate
Focalin

Unfavorable Response to Dexmethylphenidate (ADRA2A: Homozygous for C Allele) — **INFORMATIVE**

The patient carries two C alleles of the ADRA2A –1291 C>G polymorphism. Preliminary studies suggest that this genotype may be associated with an unfavorable response to dexmethylphenidate in children and adolescents with the attention-deficit and hyperactivity disorder of inattentive type.

Dexmethylphenidate
Focalin

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

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Diclofenac
Voltaren

Possible Sensitivity to Diclofenac (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e poor metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.

Dronabinol
Marinol

Possible Sensitivity to Dronabinol (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

The patient has a substantial reduction in CYP2C9 metabolic activity (CYP2C9 poor metabolizer). Increased drug exposure may occur in this patient leading to prolonged sedation. Consider standard label-recommended dosing and close monitoring for adverse effects.

Flurbiprofen
Ansaid

Increased Sensitivity to Flurbiprofen (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

At standard dosage, plasma concentrations of flurbiprofen are expected to be high, resulting in an increased risk of gastrointestinal toxicity. Administer flurbiprofen with caution and reduce dose if necessary.

Fluvastatin
Lescol

Increased Sensitivity to Fluvastatin (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myotoxicity/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose as needed. Other adverse events and predisposing factors include advanced age (≥65), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female gender.

Fosphenytoin
Cerebyx

High Sensitivity to Fosphenytoin (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

In CYP2C9 poor metabolizers, the plasma concentrations of phenytoin are expected to increase, resulting in an increased risk of severe neurological toxicity. This risk increases further in individuals who are also CYP2C19 poor metabolizers. **Consider a standard loading dose, and reduce the maintenance dose by 50%**. Evaluate response and serum concentrations after 7-10 days. **Be alert to neurological concentration-related adverse events.**

Glimepiride
Amaryl

Possible Sensitivity to Glimepiride (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

Subjects with reduced CYP2C9 activity may have increased glimepiride plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glimepiride can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of plasma glucose levels.

Glipizide
Glucotrol

Possible Sensitivity to Glipizide (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

Subjects with reduced CYP2C9 activity may have increased glipizide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glipizide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of glucose plasma levels.

Glyburide
Micronase

Possible Sensitivity to Glyburide (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

Subjects with reduced CYP2C9 activity may have increased glyburide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glyburide can be prescribed according to standard label-recommended dosage and administration with frequent monitoring of glucose plasma levels.

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Ibuprofen
Advil, Motrin

Possible Sensitivity to Ibuprofen (CYP2C9: Poor Metabolizer) — INFORMATIVE

Ibuprofen is extensively metabolized into hydroxylate or carboxylate metabolites by CYP2C8 and CYP2C9. Diminished ibuprofen clearance has been found in CYP2C9 poor metabolizers and those with decreased CYP2C8 activity. This change in clearance may result in elevated concentrations of the drug inadvertently leading to adverse events. Although, dosage adjustment is not necessary in a patient identified as a CYP2C9 poor metabolizer, a lower dose and a closer monitoring for increased gastrointestinal adverse events may be considered.

Indomethacin
Indocin

Possible Sensitivity to Indomethacin (CYP2C9: Poor Metabolizer) — INFORMATIVE

Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethylindomethacin, a reaction catalyzed by CYP2C9. At standard dosage, plasma concentrations of indomethacin are expected to be high resulting in an increased risk of gatrointestinal toxicity. To minimize the potential risk for an adverse event, the lowest effective dose should be used for the shortest possible duration.

Lesinurad
Zurampic

Possible Sensitivity to Lesinurad (CYP2C9: Poor Metabolizer) — ACTIONABLE

The patient has a substantial reduction in CYP2C9 metabolic activity (CYP2C9 poor metabolizer). Increased drug exposure may occur in this patient leading to an increased risk for adverse events. Consider using lesinurad with caution and with close monitoring for adverse effects.

Losartan
Cozaar, Hyzaar

Possible Decreased Response to Losartan (CYP2C9: Poor Metabolizer) — INFORMATIVE

Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a reduced exposure to losartan's active metabolite and a possible reduced hypotensive effect. Losartan can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.

Meloxicam
Mobic

Increased sensitivity to Meloxicam (CYP2C9: Poor Metabolizer) — INFORMATIVE

CYP2C9 poor metabolizers have a higher risk of experiencing gastrointestinal toxicities when taking meloxicam at standard doses. To minimize the potential risk of adverse events in these patients, **the lowest effective dose should be used for the shortest possible duration.**

Methadone
Dolophine

Possible Sensitivity to Methadone (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Based on currently available evidence, S-methadone plasma concentrations may increase, resulting in higher risk of cardiac arrhythmias and QTc prolongation. Consider lower starting doses of methadone, and adjust dosing based on the clinical response.

Methotrexate
Trexall

Increased risk for methotrexate toxicity (MTHFR: Reduced MTHFR Activity) — INFORMATIVE

The patient carries the MTHFR 677 T allele resulting in a reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens might have an increased likelihood of treatment interruptions due to methotrexate toxicity. Consider at least a 25% reduction in methotrexate starting dose, followed by titration based on toxicity. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between the MTHFR 677 T allele and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.

Methylphenidate
Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER

Unfavorable Response to Methylphenidate (ADRA2A: Homozygous for C Allele) — INFORMATIVE

The patient carries two C alleles of the ADRA2A –1291 C>G polymorphism. Preliminary studies suggest that this genotype may be associated with an unfavorable response to methylphenidate in children and adolescents with the attention-deficit and hyperactivity disorder of inattentive type.

PATIENT INFORMATION

NAME: Anbu Rajan
ACC #: 41001710241297
DOB: 9/22/1949
SEX: Male

Methylphenidate
Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Naltrexone
Vivitrol, Contrave

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) — **INFORMATIVE**

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

Nateglinide
Starlix

Possible Sensitivity to Nateglinide (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

The patient's genotype predicts a reduced CYP2C9 activity, which may result in a slightly increased risk for hypoglycemia. Nateglinide can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.

Olanzapine
Zyprexa

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — **INFORMATIVE**

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Phenytoin
Dilantin

High Sensitivity to Phenytoin (CYP2C9: Poor Metabolizer) — **ACTIONABLE**

In CYP2C9 poor metabolizers, the plasma concentrations of phenytoin are expected to increase, resulting in an increased risk of severe neurological toxicity. This risk increases further in individuals who are also CYP2C19 poor metabolizers. **Consider a standard loading dose, and reduce the maintenance dose by 50%**. Evaluate response and serum concentrations after 7-10 days. **Be alert to neurological concentration-related adverse events.**

Piroxicam
Feldene

Increased Sensitivity to Piroxicam (CYP2C9: Poor Metabolizer) — **INFORMATIVE**

At standard dosage, plasma concentrations of piroxicam are expected to be high, resulting in an increased risk of gastrointestinal toxicity. Administer piroxicam with caution and reduce dose if necessary.

Tetrabenazine
Xenazine

Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer) — **ACTIONABLE**

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 normal metabolizers is 100 mg, with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine
Zanaflex

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility) — **INFORMATIVE**

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

PATIENT INFORMATION

NAME: **Anbu Rajan**
ACC #: 41001710241297
DOB: 9/22/1949
SEX: Male

Tolbutamide
Orinase

Possible Sensitivity to Tolbutamide (CYP2C9: Poor Metabolizer) **ACTIONABLE**

Subjects with reduced CYP2C9 activity may have increased tolbutamide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, tolbutamide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of glucose plasma levels.

Torsemide
Demadex

Possible Sensitivity to Torsemide (CYP2C9: Poor Metabolizer) **INFORMATIVE**

The patient's genotype predicts a reduced CYP2C9 function, which may result in reduced torsemide clearance. There is insufficient data to whether such change has a significant clinical impact and whether the diuretic effects are more pronounced in patients with this phenotye. Torsemide can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.

Warfarin
Coumadin

Very High Sensitivity to Warfarin (CYP2C9 *3/*3 VKORC1 -1639G>A G/A) **ACTIONABLE**

Initiation Therapy: the expected therapeutic **dose is substantially lower than the usual one.** Consider using the following warfarin dose range provided in the FDA-approved label: **0.5-2 mg/day.** OR consider using a personalized dose as calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is more than 2-4 weeks. Frequent INR monitoring is recommended.

BHARATH GENOMIX

PATIENT INFORMATION

NAME: **Anbu Rajan**
ACC #:41001710241297
DOB: 9/22/1949
SEX: Male

Test Details

Gene	Genotype	Phenotype	Alleles Tested
ADRA2A	C-1291G C/C	**Homozygous for C Allele**	C-1291G
ANKK1/DRD2	DRD2:Taq1A A/G	**Altered DRD2 function**	DRD2:Taq1A
Apolipoprotein E	ε3/ε3	**Normal APOE function**	ε2, ε4, (ε3 is reference)
COMT	Val158Met A/G	**Intermediate COMT Activity**	Val158Met
CYP1A2	*1A/*1F	**Normal Metabolizer - Higher Inducibility**	*1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W
CYP2B6	*1/*6	**Intermediate Metabolizer**	*7, *16, *2, *3, *5, *6, *9, *18, *28
CYP2C19	*1/*1	**Normal Metabolizer**	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17
CYP2C9	*3/*3	**Poor Metabolizer**	*2, *3, *5, *6, *8, *11, *27
CYP2D6	*2/*9	**Normal Metabolizer**	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *17, *29, *35, *41, *56A, *56B, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1/*1	**Normal Metabolizer**	*2, *3, *12, *17, *22
CYP3A5	*3/*3	**Poor Metabolizer**	*1D, *3, *3C, *6, *7
DRD2	rs2283265 C/A	**Heterozygous for rs2283265 A allele**	-241A>G, rs2283265
DRD2	-241A>G T/T	**Homozygous for rs1799978 T Allele**	-241A>G, rs2283265
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	**No Increased Risk of Thrombosis**	20210G>A, 1691G>A
MTHFR	677C>T CT	**Reduced MTHFR Activity**	1298A>C, 677C>T
MTHFR	1298A>C AC 677C>T CT	**No Increased Risk of Hyperhomocysteinemia**	1298A>C, 677C>T
OPRM1	A118G A/A	**Normal OPRM1 Function**	A118G
SLCO1B1	521T>C T/T	**Normal Function**	521T>C, 388A>G
VKORC1 and CYP2C9	-1639G>A G/A, *3/*3	**Very High Sensitivity to Warfarin**	-1639G>A

BHARATH GENOMIX

PATIENT INFORMATION

NAME: **Anbu Rajan**
ACC #: 41001710241297
DOB: 9/22/1949
SEX: Male

Bharath Genomics Laboratoy

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Disclaimer: *Only a physician, pharmacist or other healthcare professional should advise a patient on the use of information in this report.*
Methodology: *Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.*
Limitations: *This test will not detect all the known mutations that result in altered or inactive tested genes. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has intermediate or high sensitivity phenotypes due to the presence of an undetected polymorphism or due to drug-drug interactions.*
Methodology: *PCR amplification and bead array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.*
Limitations: *This test will not detect all the known mutations that result in altered or inactive tested genes. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has intermediate or high sensitivity phenotypes due to the presence of an undetected polymorphism or due to drug-drug interactions.*
Disclaimer: *Only a physician, pharmacist, or other healthcare professional should advise a patient on the use of information in the report. The tests listed in this report were developed and their performance characteristics determined by ExcelTox Laboratories. All tests are not FDA approved; CYP2D6 and CYP2C19 have been approved by the U.S. Food and Drug Administration (FDA). However, FDA approval is not required for clinical use of these tests. This laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.*
This customized pharmacogenomic (PGx) report, including medication dosing guidelines, and interpretation for drugs and their interactions was generated via Translational Software using patient genetic test results obtained by Exceltox laboratories.31

Software Disclaimer: *The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.*
The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed byou inhouse Software . The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

BHARATH GENOMIX

PATIENT INFORMATION

NAME: Anbu Rajan
ACC #: 410017102
41297 **DOB:** 9/22/1949
SEX: Male

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS
Name: Larry Newell
DOB: 9/22/1949
ACC #: 41001710241297

Pharmacogenetic Test Summary

ADRA2A	C-1291G C/C	Homozygous for C Allele
ANKK1/DRD2	DRD2:Taq1A A/G	Altered DRD2 function
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CYP3A5	*3/*3	Poor Metabolizer
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Factor II	20210G>A GG	Normal Thrombosis Risk
Factor V Leiden	1691G>A GG	Normal Thrombosis Risk
MTHFR	677C>T CT	Reduced MTHFR Activity
MTHFR	1298A>C AC	Reduced MTHFR Activity
OPRM1	A118G A/A	Normal OPRM1 Function
SLCO1B1	521T>C T/T	Normal Function
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity

For a complete report contact
bharathGenomix **bhrathgenomix.com**