PositiveMed™

Positive Bioscience

PATIENT		PHYSICIAN	
Name :	XXXXX	Name :	
Gender :	M	Institute :	
Date of Birth :	01/Jul/1967		

Sample Type :	Whole Blood	Sample Collection Date :	14/Jan/2017	Report Date :	13/Feb/2017	Sample ID :	PB_PG_PP_2016_20

ACE-inhibitor

Drug	Recommended	Response	Gene - Genotype
Perindopril	⚠	Poor, Adverse event – MI, Stroke	AGTR1 – AA
Quinapril	✓	Better	AGT – GG
Captopril	✓	Better	AGTR1 - AC
Benazepril	✗	Poor	AGT - AA

Attention Deficit Hyperactivity Disorder (ADHD)

Drug	Recommended	Response	Gene - Genotype
Amitriptyline	✗	Poor	CYP2C19*2/*2
Amphetamine	✓	Mild response	COMT– AG
Dextroamphetamine	✓	Mild response	COMT– AG
Dexmethylphenidate	✓	Mild response	COMT – AG
Methylphenidate	✓	Mild response	COMT – AG

Angiotensin Receptor Blockers (ARBs)

Drug	Recommended	Response	Gene – Genotye
Candesartan	✗	Poor	AGTR1 – AC
Irbesartan	✓	Typical	EDN1 - GT
Losartan	✓	Typical	CYP2C9 - AA

Anti-HIV Agents

Drug	Recommended	Response	Gene – Genotye
Abacavir	✓	Typical	HLA-B*5701 (Non-carrier)
Nelfinavir	✗	Poor	CYP2C19*2/*2
Nevirapine	✗	Poor	CYP2B6 - AC

Anti-Hyperlipidemic

Drug	Recommended	Response	Gene – Genotye
Ezetimibe	✓	Typical	UGT1A1 - GG

Anti-Infective Agents

Drug	Recommended	Response	Gene - Genotype
Chloramphenicol	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Ciprofloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Dapsone	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Dolutegravir	✓	Typical	UGT1A1 - GG
Efavirenz	✓	Typical	CYP2B6 - AG
Gemifloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Hydroxychloroquine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Indinavir	✓	Typical	UGT1A1 - GG
Isoniazid	✓	Intermediate - Dose reduction needed	NAT2*4/*5D
Levofloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Mafenide	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Moxifloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Nalidixic acid	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Nitrofurantoin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Norfloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Ofloxacin	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
PEG IFN alpha	✓	Better	IFNL3 - CC
Primaquine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Proguanil	✗	Poor	CYP2C19*2/*2
Quinine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Sulfamethoxazole	✓	Intermediate - Dose reduction needed	NAT2*4/*5D
SMZ/TPM	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Voriconazole	✗	Poor	CYP2C19*2/*2

Anti-Inflammatory Agents

Drug	Recommended	Response	Gene - Genotype
Mesalamine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Sulfasalazine	✓	Intermediate - Dose reduction needed	NAT2*4/*5D
Chloroquine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Fluticasone Propionate	✓	Better	GLCCI1 - AA
Budesonide	✓	Better	GLCCI1 - AA
Adalimumab	✗	Poor	ATG16L1 -CC
Infliximab	✗	Poor	TRAILR1 - CG
Etanercept	✗	Poor	TRAILR1 - CG

Antiarrhythmics

Drug	Recommended	Response	Gene - Genotype
Amiodarone	✓	Typical	NOS1AP- GG
Flecainide	✓	Typical	CYP2D6*1/*1
Mexiletine	✗	Poor	CYP2D6*1/*10
Propafenone	✓	Better	CYP2D6*1/*10
Timolol	⚠	Poor - Adverse event Bradychardia	CYP2D6*1/*2

Anticoagulants

Drug	Recommended	Response	Gene - Genotype
Acenocoumarol	✓	Dosage – High dose	VKORC1 – CC
Phenprocoumon	✓	Dosage – High dose	VKORC1 – CC
Warfarin	✓	Dosage – Typical	VKORC1 – CC

Anticonvulsants

Drug	Recommended	Response	Gene - Genotype
Carbamazepine	✓	Typical	HLA-B (Non-carrier)
Eslicarbazepine	✓	Typical	HLA-B (Non-carrier)
Fosphenytoin	✓	Typical	HLA-B (Non-carrier)
Lamotrigine	✓	Typical	HLA-B (Non-carrier)
Oxcarbazepine	✓	Typical	HLA-B (Non-carrier)
Phenobarbital	✓	Typical	HLA-B (Non-carrier)
Zonisamide	✓	Extensive metabolizer	CYP3A4*1/*1

Antidepressants

Drug	Recommended	Response	Gene - Genotype
Amoxapine	✓	Typical	CYP2D6*1/*1
Bupropion	✗	Poor	CYP2B6*1/*4
Citalopram	✗	Poor	CYP2C19*2/*2
Clomipramine	✗	Poor	CYP2C19*2/*2
Desipramine	✗	Poor	CYP2C19*2/*2
Diazepam	✗	Poor	CYP2C19*2/*2
Doxepin	✗	Poor	CYP2C19*2/*2
Duloxetine	✓	Better	ABCB1 - AG
Escitalopram	✗	Poor	CYP2C19*2/*2
Fluoxetine	✗	Poor	CYP2C19*2/*2
Fluvoxamine	✓	Typical	CYP2D6*1/*1
Imipramine	✗	Poor	CYP2C19*2/*2
Maprotiline	✓	Typical	CYP2D6*1/*1
Nefazodone	✓	Typical	CYP2D6*1/*1
Nortriptyline	✗	Poor	CYP2C19*2/*2
Paroxetine	✓	Typical	CYP2D6*1/*1
Protriptyline	✓	Typical	CYP2D6*1/*1
Sertraline	✗	Poor	CYP2C19*2/*2
Trazodone	✓	Typical	CYP2D6*1/*1
Trimipramine	✗	Poor	CYP2C19*2/*2
Venlafaxine	✓	Ultra-rapid: Dosage can be increased	CYP2D6*1/*1
Vortioxetine	✓	Typical	CYP2D6*1/*1

Antiepileptics

Drug	Recommended	Response	Gene - Genotype
Brivaracetam	✗	Poor	CYP2C19*2/*2
Phenytoin	✓	Typical	CYP2C9*1/*1
Primidone	✓	Typical	CYP2C9*1/*1

Antihypertensives

Drug	Recommended	Response	Gene - Genotype
Enalapril	✓	Typical	CES1 – GG
Hydralazine	✗	Poor	GNB3 – CC
Verapamil	✓	Typical	CACNA1C – AA

Antipsychotics

Drug	Recommended	Response	Gene - Genotype
Aripiprazole	✗	Poor	DRD2 - GG
Brexpiprazole	✓	Typical	CYP2D6*1/*1
Clozapine	⚠	Poor - Risk of AE, Seizures	CYP1A2 - AA
Haloperidol	✓	Typical	CYP2D6*1/*1
Iloperidone	⚠	Poor - Risk of AE, Increased QT	NRG3 - GG
Olanzapine	✗	Poor	CYP1A2 - AA
Perphenazine	✓	Intermediate	CYP2D6*1/*10
Pimozide	✓	Typical	CYP2D6*1/*1
Risperidone	✗	Poor	HTR2A - AC
Thioridazine	✓	Typical	CYP2D6*1/*1
Tetrabenazine	✓	Typical	CYP2D6*1/*1

Antiviral Agents

Drug	Recommended	Response	Gene - Genotype
Atazanavir	✓	Typical	UGT1A1 -GG

Beta Blockers

Drug	Recommended	Response	Gene - Genotype
Atenolol	✓	Better	CACNA1C – AG
Carvedilol	✓	Better	ARDB1 – GG
Metoprolol	✓	Typical	CYP2D6*1/*1
Propranolol	✓	Intermediate	CYP2D6*1/*10
Salbutamol	✗	Poor	ADRB2 - CT
Salmeterol	✗	Poor	ADRB2 – AG

Benzodiazepines

Drug	Recommended	Response	Gene - Genotype
Clobazam	✓	Better with typical risk of AE	CYP2C19*2/*2

Biguanides

Drug	Recommended	Response	Gene - Genotype
Metformin	✗	Poor	MATE2 - AC

Calcium channel Blockers

Drug	Recommended	Response	Gene - Genotype
Amlodipine	✗	Poor	NOS1AP- AG
Diltiazem	✓	Better	ACBD4 - AT
Nifedipine	✓	Better	CYP3A5 - AG

Catecholamines

Drug	Recommended	Response	Gene - Genotype
Catecholamines	✓	Dosage – High dose	ADRB1 – GG

Cholesteryl Ester Transfer Protein Inhibitors

Drug	Recommended	Response	Gene - Genotype
Dalcetrapib	✓	Typical	ADCY9 – AG

Cholinesterase Inhibitors

Drug	Recommended	Response	Gene - Genotype
Donepezil	✓	Typical	CYP2D6*1/*10
Galantamine	✓	Typical	CYP2D6*1/*1

Diphosphonates

Drug	Recommended	Response	Gene - Genotype
Etidronate	✓	Better	VDR -AG

Diuretics

Drug	Recommended	Response	Gene - Genotype
Chlorthalidone	✓	Better	NOS1AP- AG
Hydrochlorothiazide	✓	Typical risk for AE	KCNJ1 – GG
Isosorbide	✗	Poor	GNB3 – CC
Torsemide	✓	Typical	CYP2C9*1/*1

DPP-4 inhibitors

Drug	Recommended	Response	Gene - Genotype
Linagliptin	✓	Better	TCF7L2 – CC
Sitagliptin	✓	Better	GLP1R – GG
Vildagliptin	✓	Better	GLP1R – GG

Estrogen Antagonists

Drug	Recommended	Response	Gene - Genotype
Raloxifene	✓	Better	VDR -AC

Fibrate

Drug	Recommended	Response	Gene - Genotype
Fenofibrate	✓	Typical	PPARA - CG

Hormone

Drug	Recommended	Response	Gene - Genotype
Insulin	✓	Typical	TCF7L2 - GG
Liraglutide	✗	Poor	GLP1R – GG

Immunosuppressants

Drug	Recommended	Response	Gene - Genotype
Azathioprine	✓	Typical risk of AE	NUDT15 - CC
Cyclosporine	✓	Typical	ABCB1- AG
Leflunomide	✓	Typical risk of AE	CYP1A2*1F-AA

Meglitinides

Drug	Recommended	Response	Gene - Genotype
Nateglinide	✓	Typical risk of AE	CYP2C9*1 – AA
Repaglinide	✓	Typical	KCNQ1 - AA

Muscle Relaxants

Drug	Recommended	Response	Gene - Genotype
Carisoprodol	✗	Poor	CYP2C19*2/*2
Zolpidem	✗	Poor	CYP2C19*2/*2

Non-Steroidal Anti-inflammatory Drugs

Drug	Recommended	Response	Gene - Genotype
Aspirin	✓	Typical	PTGS1 - AA
Celecoxib	✓	Typical	CYP2C9*1/*1
Diclofenac	✓	Typical	CYP2C9*1/*1
Flurbiprofen	✓	Typical	CYP2C9*1/*1
Ibuprofen	✓	Typical	CYP2C8*1/*1
Meloxicam	✓	Typical	CYP2C9*1/*1
Naproxen	✓	Typical	CYP2C9*1/*1
Piroxicam	✓	Typical	CYP2C9*1/*1

Opioids

Drug	Recommended	Response	Gene - Genotype
Alfentanil	✓	Typical	CYP3A5 *1/*3
Codeine	✓	Typical	CYP2D6 *1/*1
Dihydrocodeine	✓	Typical	CYP2D6 *1/*1
Fentanyl	✓	High dose needed	CYP3A4 - AA
Hydrocodone	✓	Typical	CYP2D6 *1/*1
Methadone	✓	Typical	CYP2B6 -AG
Meperidine	✓	Typical	CYP2B6 - AG
Oxycodone	✓	Typical	CYP2D6 *1/*1
Paracetamol	✓	Typical	SULT1A1 - AA
Sufentanil	✗	Poor	OPRM1 -AG
Tramadol	✓	Typical	CYP2D6*1/*1

Osmotic Laxatives

Drug	Recommended	Response	Gene - Genotype
PEG-3350	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT

Platelet Aggregation Inhibitors

Drug	Recommended	Response	Gene - Genotype
Clopidogrel	✗	Poor: Alternative antiplatelet therapy needed	CYP2C19*2/*2
Prasugrel	✓	Typical	CYP2C19 – CC
Ticagrelor	✗	Poor	SLCO1B1 - TT

PPARG - agonist

Drug	Recommended	Response	Gene - Genotype
Muraglitazar	✓	Typical risk of AE	REN - CC

Proton pump inhibitors

Drug	Recommended	Response	Gene - Genotype
Dexlansoprazole	✓	Better	CYP2C19*2/2
Esomeprazole	✓	Better	CYP2C19*2/*2
Lansoprazole	✓	Better	CYP2C19 *2/*2
Omeprazole	✓	Better	CYP2C19 *2/*2
Pantoprazole	✓	Better	CYP2C19 *2/*2
Rabeprazole	✓	Better	CYP2C19*2/*2

Pyridine

Drug	Recommended	Response	Gene - Genotype
Phenazopyridine	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT

Respiratory System Agents

Drug	Recommended	Response	Gene - Genotype
Methacholine	✗	Poor	ADRB2 – AG
Montelukast	✓	Typical	LTA4H - AA
Pitrakinra	✓	Better	IL4R -GG
Tiotropium	✗	Poor	ADRB2 – AG

Serotonin 5 - HT3 receptor antagonists

Drug	Recommended	Response	Gene - Genotype
Ondansetron	✓	Typical	CYP2D6*1/*1

Statins

Drug	Recommended	Response	Gene - Genotype
Atorvastatin	✓	Better	APOE – AG
Fluvastatin	✓	Typical	ABCB1 - AT
Lovastatin	✓	Typical	CYP3A5 – CT
Pitavastatin	✓	Better	SLCO1B1 - CC
Pravastatin	✓	Typical	NPC1L1 - AA
Rosuvastatin	✓	Typical	SLCO1B1 – TT
Simvastatin	✓	Typical	SLCO1B1 - TT

Sulfonylureas

Drug	Recommended	Response	Gene - Genotype
Chlorpropamide	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Gliclazide	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Glimepiride	✗	Poor	CYP2C9*1/*1
Glipizide	✓	Typical	CYP2C9*1/*1
Tolazamide	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Tolbutamide	✗	Poor; Risk of AE: Acute hemolysis	G6PD - TT
Glibenclamide (Glyburide)	✗	Poor; Risk of AE: Acute hemolysis	G6PD – TT

Thiazolidinediones

Drug	Recommended	Response	Gene - Genotype
Pioglitazone	✗	Poor	PPARG – CC
Rosiglitazone	✓	Better	LPIN1 - CG
Troglitazone	✗	Poor	CDKN2A/B – TT

Vasodilators

Drug	Recommended	Response	Gene - Genotype
Cilostazol	✓	Better response and can be used as an alternative to Clopidogrel in DES-treated patients during maintenance therapy.	CYP2C19*2/*2

Legends for Pharmacogenomics

Recommended

✓ This indicates a positive recommendation representing either a typical/normal or a better therapy outcome

✗ This indicates a negative recommendation representing a poor/low response as therapy outcome or in case of severe adverse events due to therapy. Alternative medications can be considered here

⚠ This indicates a recommendation wherein the therapy needs to be monitored with caution as it bears a typical risk of occurrence of adverse events

Response

1. **Typical** – This indicates that the rate of metabolism as well as efficacy of the drug would be normal
2. **Better** – This indicates that the drug would show an efficacy better than the normal and hence therapeutic outcome could be positive
3. **Poor** – This indicates that the rate of metabolism or the efficacy of the drug would be poor and hence the chances of therapeutic failure is high
4. **Adverse event** – This indicates that therapy with the drug will result in unfavorable clinical manifestations and hence caution needs to be exercised
5. **Dosage -** This indicates the recommendation for alteration of standard dosage as per studies correlating dosage effect with genotype

Gene – Genotype

This part of the report highlights the result of the genetic analysis based on which relevant conclusions pertaining to risk, drug efficacy and nutrigenetics have been drawn. Gene refers to the molecular region which has been proven to cause a significant effect, while genotype refers to the signature at a particular loci in that gene.

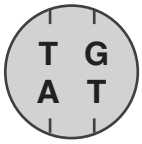
Testing Methodology

Sample : Whole Blood

3 - 5 mL of whole blood in EDTA tube

Wet-lab Analysis :

- DNA extraction
- QC analysis – QIAgen technology / Nano drop
- Microchipping Illumina analysis*



Data Analysis :

- Variant prioritization using inhouse proprietary "Algorithm"
- Risk estimation using our inhouse proprietary "Risk calculator"
- Pharmacogenetics and Nutrigenetics recommendations using our inhouse proprietary "Algorithm" and "Database"

Microchipping Technology

The Illumina human genotyping arrays are popular and led support for a variety of analysis extending from whole-genome, targeted genome as well as exome analyses. The BeadChip arrays as well as the Infinium assay technologies provide high-density genomic coverage and delivers exceptional data quality. The popularity of this technology has been attributed to its three virtues, being; sensitivity, specificity and reproducibility.