

Innovation of Pharmacogenomics Solutions



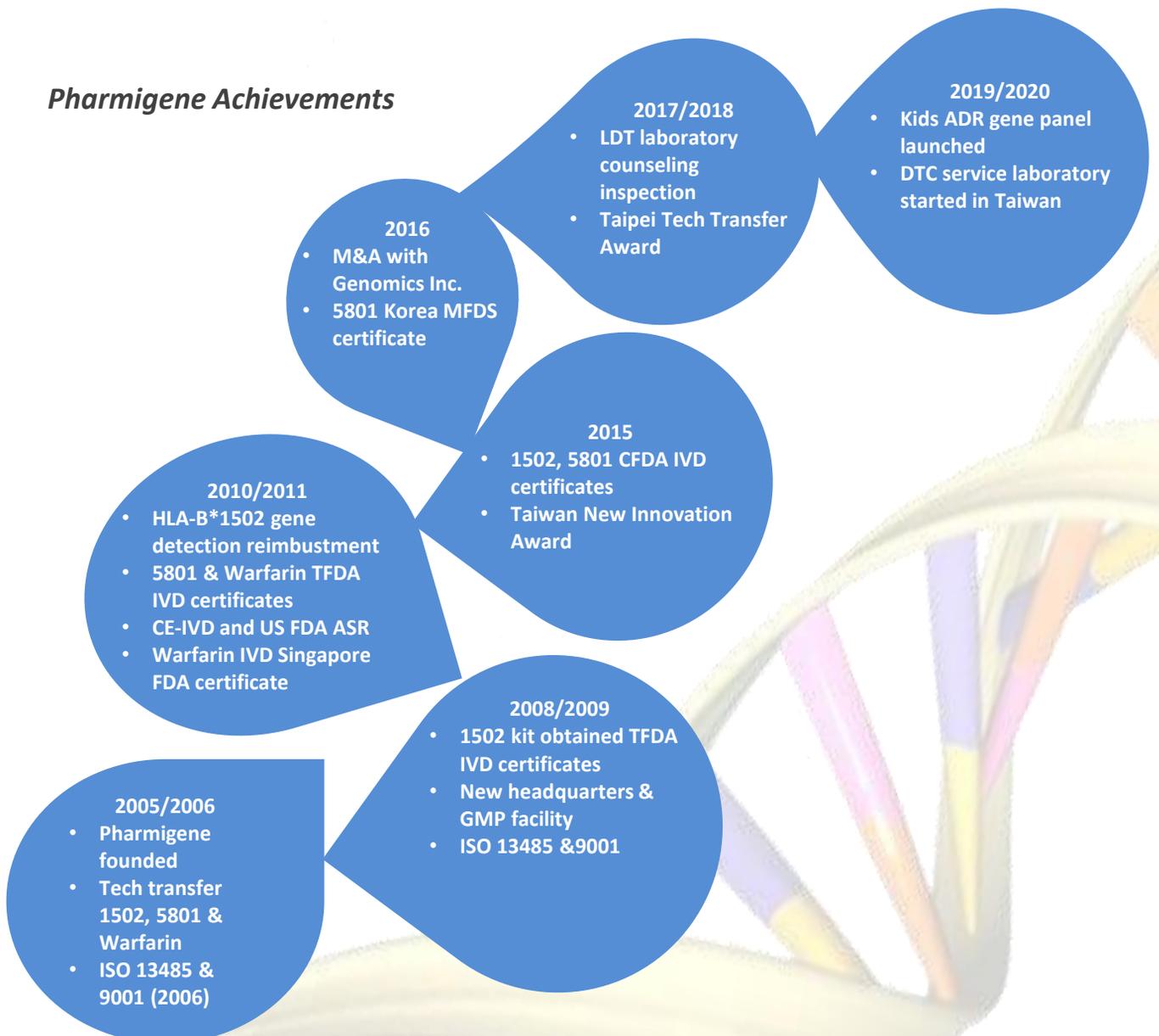
PharmiGENE



About Pharmigene

Pharmigene is established in 2005 and funded by venture capital firms and individuals. Our goal is to innovate and commercialize diagnostic tests that enable individuals to be better informed about their genomic makeup and to make decisions that better their health. We have licensed exclusive world-wide rights and transferred key know-how from Academia Sinica relating to the genetic markers that are associated with adverse drug reactions caused by several popular drugs. We have obtained ISO 13485 and GMP certifications, and are manufacturing our DNA genetic tests under the most stringent guideline. In developing our DNA genetic tests, we also have validated our tests with clinical studies that involved hundreds and thousands of patients. Today our certified DNA genetic tests are available world wide.

Pharmigene Achievements



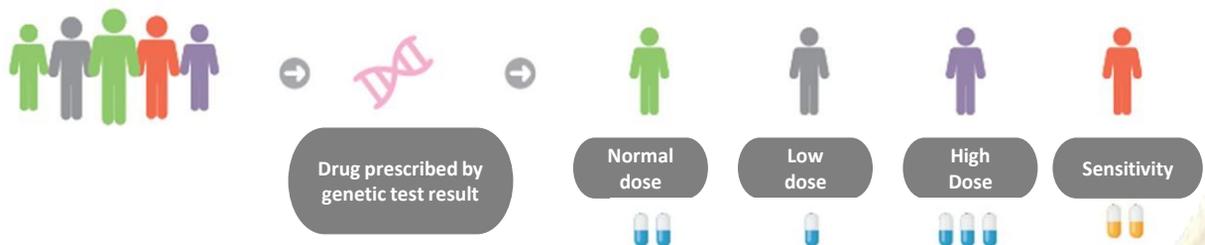
“Pharmacogenomics is the study of how genes affect a person’s response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that will be tailored to a person’s genetic makeup.”

(ref: What is pharmacogenomics? <https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics>)

Before, drug can only be prescribed by indications



Now, drug can be prescribed not only by indication but also by pharmacogenomics result



Drug Sensitivity:

Drug sensitivity is the abnormal reaction of human immune system caused by medication. Any medication may have the possibility to induce the immune storm – drug sensitivity. The symptoms of drug sensitivity vary like hives, rash or fever. Sometimes, severe events such as Stevens-Johnson syndrome or Toxic epidermal necrolysis can occur and may cause death.

Drug metabolism:

Drug metabolism is the pathway to break down drug compounds inside the body into the functional molecules. Drug metabolism rates vary among patients and the speed can be determined by gene. Different genotypes can cause huge differences in dosage of drug among patients. For example, warfarin, a common use anti-coagulant, can be dosed more than 6 times higher in a mutant type patient than in a wild type one.

Stevens-Johnson syndrome/Toxic epidermal necrolysis:

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are two of the most serious and life-threatening cutaneous adverse drug reactions with a 10 – 50% mortality rate. Although these symptoms are rare, serious disorders of the skin and mucous membranes, these symptoms start with flu-like symptoms, followed by a painful rash that spreads and blisters. SJS is defined as skin detachment of < 10% and TEN as skin detachment greater than 30%.

Carbamazepine induced Stevens-Johnson Syndrome /Toxic Epidermal Necrolysis in at-risk populations:

Carbamazepine (CBZ) is among the most commonly used antiepileptic drug and pain management drug. However, serious and sometimes life-threatening reactions, including Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN), have been reported with CBZ. The risk of SJS and TEN exists in all patients, but in patients of certain Asian ancestry the risk can be significantly higher. Studies have shown that the **HLA-B*1502** allele found in Asian population and **HLA-A*3101** allele found in Caucasian population has strong association with SJS and TEN.

Allopurinol induced Hypersensitivity Syndrome, Stevens-Johnson Syndrome & Toxic Epidermal Necrolysis in at-risk populations:

Allopurinol is among the most commonly used drug to treat hyperuricemia and its complications. However, severe cutaneous adverse reactions (SCARs), including Hypersensitivity Syndrome (HSS), Stevens-Johnson Syndrome (SJS), and Toxic Epidermal Necrolysis (TEN), have been reported with usage of Allu. The risk of SCARs exists in all patients, but in patients of certain genetic variants the risk can be significantly higher. Studies have shown that the **HLA-B*5801** allele found in European ancestry, Chinese Han, Japanese, & Thai populations has strong association with SCARs.

Abacavir induced Hypersensitivity Syndrome in at-risk populations:

Abacavir is the drug to treat HIV-1 infection. Studies have shown that people who carry **HLA-B*5701** allele has higher risk to induce hypersensitivity syndrome by taking Abacavir.

Pharmigene Products for drug sensitivity related genes:

Product Name	Catalog #	Pack Size	Sample Size	Regulation	Description
PG1502 Detection Kit	PG-1502C-024	24 reactions	10 samples	TFDA NMPA HSA CE IVD	HLA-B*1502 gene has been found a strong association with carbamazepine induced server cutaneous adverse reactions such as Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. HLA-B*1502 gene is common in south-east Asia, South China and Taiwan.
	PG-1502C-048	48 reactions	20 samples		
	PG-1502C-096	96 reactions	40 samples		
PG1502 Companion Kit-RT	PG-1513C-012	12 reactions	10 samples	RUO	HLA-B*1513 gene is common (8~15%) in south-east Asians. Using this kit to distinguish HLA-B*1502 and HLA-B*1513 can help physicians identifying the patient from south-east Asia who has high risk to take carbamazepine.
	PG-1513C-024	24 reactions	20 samples		
	PG-1513C-048	48 reactions	40 samples		
PG5801 Detection Kit	PG-5801C-024	24 reactions	10 samples	TFDA NMPA HSA CE IVD Korea MFDS	HLA-B*5801 gene has been found a strong association with Allopurinol induced server cutaneous adverse reactions such as Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis.
	PG-5801C-048	48 reactions	20 samples		
	PG-5801C-096	96 reactions	40 samples		
PG5701 Detection Kit	PG-5701C-024	24 reactions	10 samples	CE IVD	HLA-B*5701 gene has been found a strong association with Abacavir, a drug for HIV treatment, induced hypersensitivity.
	PG-5701C-048	48 reactions	20 samples		
	PG-5701C-096	96 reactions	40 samples		
PG3101 Detection Kit	PG-3101C-024	24 reactions	10 samples	RUO	HLA-A*3101 gene has also been found an association with Carbamazepine induced server cutaneous adverse reactions. HLA-A*3101 gene is common in Japan, Korea, Europe and America.
	PG-3101C-048	48 reactions	20 samples		
	PG-3101C-096	96 reactions	40 samples		
PG1301 Detection Kit	PG-1301C-024	24 reactions	10 samples	RUO	HLA-A*1301 gene has also been found an association with co-trimoxazole (Baktar), Dapsone and Phenytoin induced server cutaneous adverse.
	PG-1301C-048	48 reactions	20 samples		
	PG-1301C-096	96 reactions	40 samples		

* TFDA means Taiwan food and drug administration.

* NMPA means National Medical Products Administration in China.

* HSA means health Science Authority in Singapore.

* CE-IVD products are capable to sell in most EU countries.

Drug metabolism:

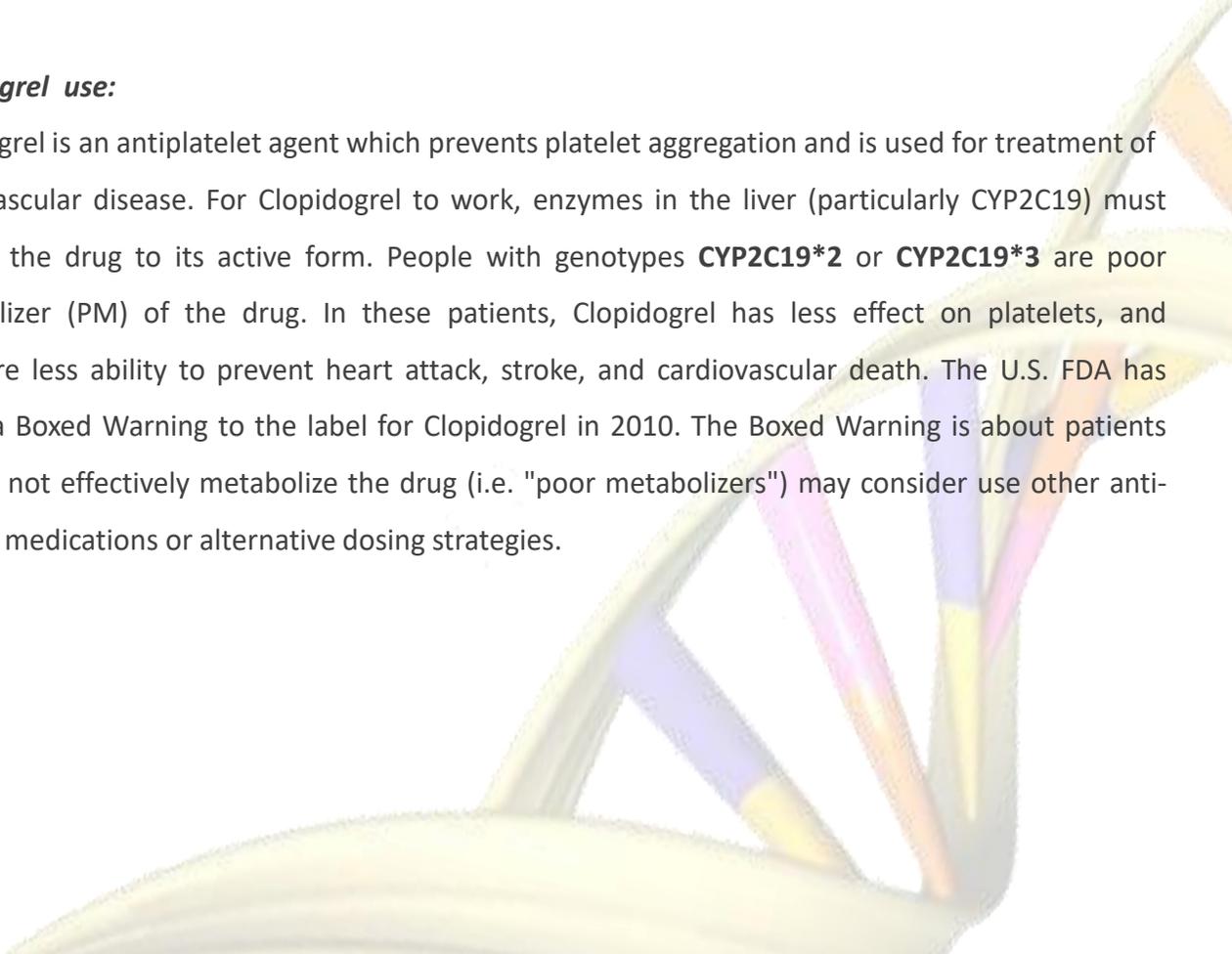
Drug metabolism has been recognized as the most important part to evaluate the real factor for drug efficiency. Drug metabolism is the metabolic breakdown of drugs by living organisms, usually through specialized enzymatic systems modulated by genes. Many of the major pharmacokinetic interactions between drugs are due to hepatic cytochrome P450 (P450 or CYP) enzymes being affected by previous administration of other drugs. The ability of CYP enzymes can be illustrated by genotyping.

Warfarin Dosing:

Warfarin is a widely prescribed anticoagulant for the prevention of thromboembolic diseases for subjects with deep vein thrombosis, atrial fibrillation or mechanical heart valve replacement. However, Warfarin treatment is problematic because the dose requirement for Warfarin is highly variable. Incorporation of **VKORC1-1639** and **CYP2C9*2/*3** genotypes, age, body weight and gender can estimate the Warfarin dose.

Clopidogrel use:

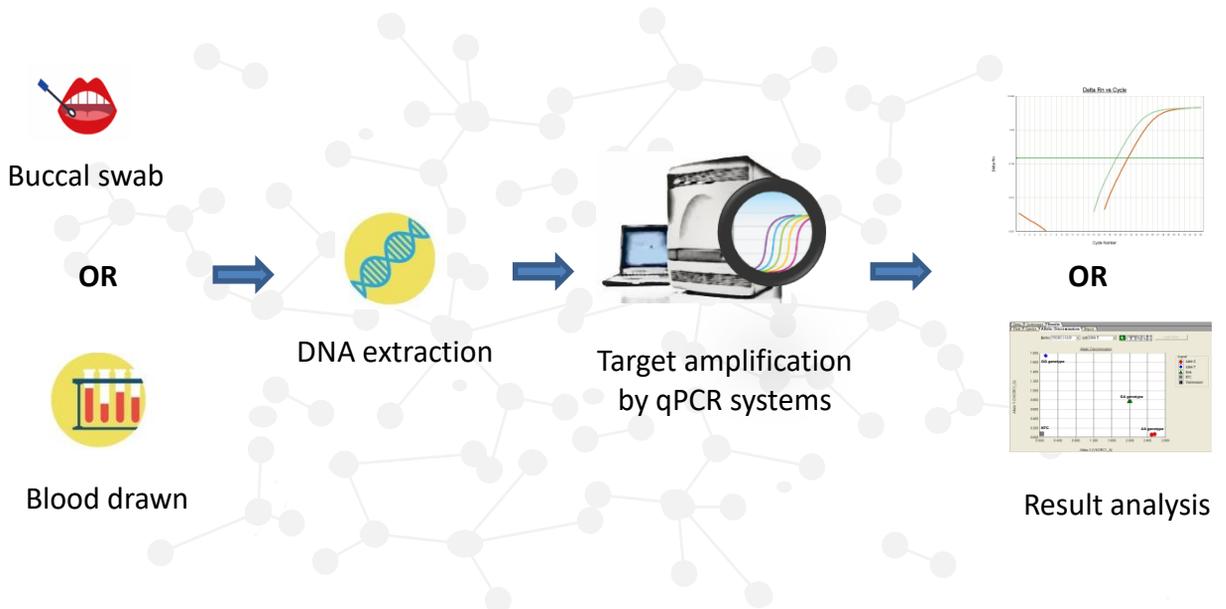
Clopidogrel is an antiplatelet agent which prevents platelet aggregation and is used for treatment of cardiovascular disease. For Clopidogrel to work, enzymes in the liver (particularly CYP2C19) must convert the drug to its active form. People with genotypes **CYP2C19*2** or **CYP2C19*3** are poor metabolizer (PM) of the drug. In these patients, Clopidogrel has less effect on platelets, and therefore less ability to prevent heart attack, stroke, and cardiovascular death. The U.S. FDA has added a Boxed Warning to the label for Clopidogrel in 2010. The Boxed Warning is about patients who do not effectively metabolize the drug (i.e. "poor metabolizers") may consider use other antiplatelet medications or alternative dosing strategies.



Product Name	Catalog #	Pack Size	Sample Size	Regulation	Description
PG1639 Detection kit	PG-1639C-012	12 reactions	10 samples	TFDA CE IVD HSA	VKORC1-1639 SNP has been found a strong linkage with the maintain dosage of warfarin, a wide use anticoagulant. To test the different SNP type of VKORC1-1639 with CYP2C9*2(0430) and CYP2C9*3(1075) can help physician adjust the starting dose of warfarin and then quickly reach the maintain dose.
	PG-1639C-024	24 reactions	20 samples		
	PG-1639C-048	48 reactions	40 samples		
	PG-1639C-096	96 reactions	80 samples		
PG0430 Detection kit	PG-0430C-012	12 reactions	10 samples	TFDA CE IVD HSA	CYP2C9*2(0430) SNP has been found a strong linkage with the maintain dosage of warfarin, a wide use anticoagulant. To test the different SNP type of CYP2C9*2(0430) with VKORC1-1639 and CYP2C9*3(1075) can help physician adjust the starting dose of warfarin and then quickly reach the maintain dose.
	PG-0430C-024	24 reactions	20 samples		
	PG-0430C-048	48 reactions	40 samples		
	PG-0430C-096	96 reactions	80 samples		
PG1075 Detection kit	PG-1075C-012	12 reactions	10 samples	TFDA CE IVD HSA	CYP2C9*3(1075) SNP has been found a strong linkage with the maintain dosage of warfarin, a wide use anticoagulant. To test the different SNP type of CYP2C9*3(1075) with VKORC1-1639 and CYP2C9*2(0430) can help physician adjust the starting dose of warfarin and then quickly reach the maintain dose.
	PG-1075C-024	24 reactions	20 samples		
	PG-1075C-048	48 reactions	40 samples		
	PG-1075C-096	96 reactions	80 samples		
PG0681 Detection kit	PG-0681C-012	12 reactions	10 samples	RUO	Clopidogrel is an antiplatelet agent which prevents platelet aggregation and is used for treatment of cardiovascular disease. For Clopidogrel to work, enzymes in the liver (particularly CYP2C19) must convert the drug to its active form. People with genotypes CYP2C19*2(0681) or CYP2C19*3(0636) are poor metabolizer (PM) of the drug and should avoid taking Clopidogrel.
	PG-0681C-024	24 reactions	20 samples		
	PG-0681C-048	48 reactions	40 samples		
	PG-0681C-096	96 reactions	80 samples		
PG0636 Detection kit	PG-0636C-012	12 reactions	10 samples	RUO	Clopidogrel is an antiplatelet agent which prevents platelet aggregation and is used for treatment of cardiovascular disease. For Clopidogrel to work, enzymes in the liver (particularly CYP2C19) must convert the drug to its active form. People with genotypes CYP2C19*2(0681) or CYP2C19*3(0636) are poor metabolizer (PM) of the drug and should avoid taking Clopidogrel.
	PG-0636C-024	24 reactions	20 samples		
	PG-0636C-048	48 reactions	40 samples		
	PG-0636C-096	96 reactions	80 samples		

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- HSA means health Science Authority in Singapore.
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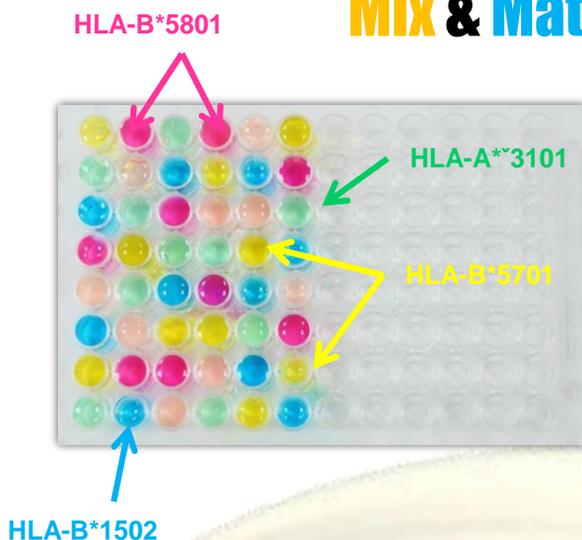
Instructions for performing Pharmigene Products:



What Pharmigene products offer :

- 1000 + real DNA samples includes Caucasians and Asians, and tested & validated by DNA sequencing.
- Over 99+% sensitivity & over 99% specificity compared with sequencing data.
- genomic DNA to results in ~2 hours.
- Compatible with most real-time PCR systems.
- Unique design to perform different genotyping tests at one time.

Mix & Match Design...

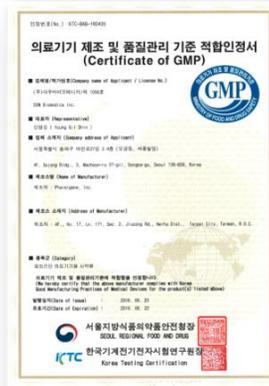


**making your
real-time PCR testing
easier & faster!**

PGx information

gene	Drugs	Type	Notes
HLA-B*1502	carbamazepine	sensitivity	Test required in Asian descents.
	oxcarbazepine		Test recommendation
	fosphenytoin , phenytoin		Actionable PGx in Asian descents.
HLA-B*5801	allopurinol	sensitivity	Actionable PGx
HLA-B*5701	Abacavir, dolutegravir , lamivudine	sensitivity	Test required
	flucloxacillin		Actionable PGx of increased risk for drug-induced liver damage
	pazopanib		Actionable PGx of increased risk of ALT > 3 x ULN and ALT > 5 x ULN (index of hepatitis)
HLA-A*3101	carbamazepine	sensitivity	Actionable PGx in Caucasian descents.
HLA-B*1301	co-trimoxazole (Baktar), Dapsone, Phenytoin	sensitivity	Actionable PGx of increased risk for drug-induced severe cutaneous adverse.
VKORC1	Warfarin	metabolism	Actionable PGx for dosing adjustment
CYP2C9*2	siponimod	metabolism	Test required for dosing adjustment
	Warfarin		Actionable PGx for dosing adjustment
	Celecoxib		
	meloxicam		
	acenocoumarol		
	piroxicam		
CYP2C9*3	siponimod	metabolism	Test required for dosing adjustment
	Warfarin		Actionable PGx for dosing adjustment
	Celecoxib		
	meloxicam		
	lesinurad		
	acenocoumarol		
	piroxicam		
CYP2C19*2	clopidogrel	metabolism	Actionable PGx for dosing adjustment
CYP2C19*3	clopidogrel	metabolism	Actionable PGx for dosing adjustment

Pharmigene's Quality Systems:



Products certificates:





PharmiGENE

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