SPMED™ Genotyping Kit : CYP2D6

Qualitative genetic testing to be used as aid to clinicians in determining therapeutic strategy and treatment dose for metabolized by the CYP2D6 gene.

Cytochrome P450 2D6 Overview
Clinical Relevance

- **The cytochrome P450 (CYP)** family of enzymes performs the primary **metabolism of many drugs** in the human body.
- One of the key CYP enzymes, **CYP2D6**, is responsible for the metabolism and elimination of approximately **20-25% of clinically used drugs**[1] (Table 1).

Table 1.

Common drug substrates and clinically important inhibitor of CYP2D6[1-3]

Categories	Drugs
Beta-blockers	Alprenolol, Bufuralol, Carvedilol*, Metoprolol*, Propranolol*, Timolol
Tricyclic antidepressants (TCAs)	Amitriptyline*, Clomipramine*, Desipramine*, Doxepine*, Imipramine*, Nortriptyline*, Protriptyline*
Antiarrhythmic agents	Flecainide, Mexiletine, Propafenone*, Quinidine*
Antipsychotic agents and SSRIs+	Aripiprazole*, Atomoxetine*, Clozapine*, Escitalopram*, Fluoxetine*, Fluvoxamine*, Haloperidol, Iloperidone*, Risperidone*, Paroxetine*, Perphenazine*, Venlafaxine*
Others	Codein*, Dextromethorphan*, Eliglustat*, Tramadol*

*Pharmacogenomic Biomarkers in FDA
+SSRIs denotes selective serotonin-reuptake inhibitors.

- More than 100 CYP2D6 variant alleles have been identified[4].
- Genetic polymorphisms of CYP2D6 could greatly affect CYP2D6 activity and lead to differences among individuals in drug efficacy or occurrance of side effects[5].
- Identification of patient's CYP2D6 genotypes can help clinicians tailor drug treatment to patients by selection of appropriate therapies. These measures may improve treatment outcome by ensuring maximum drug efficacy with minimal adverse drug reactions[6].

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Genetic Variation

- "SPMED™ Genotyping Kit: CYP2D6" consist of easy-to-handle reagents to detect CYP2D6 genetic polymorphisms simutaneously.
- This kit comprehensively cover most mutations existed in each ethnicity(allele coverage about 99.5%), including deletion and duplication of gene.
- Detected CYP2D6 genotype through this kit is meaningful variants associated drug metabolism in multi-ethnic groups[7-8].

Table 2.

CYP2D6 allele frequencies in various populations[7-8]

Allele	Target SNPs	Frequency in Major Ethnicity (%)				Enzyme Activity
		East Asia	Americas	Europe	Africa	
*1	None	19.5~93.8	38.8~81.2	31.9~68.9	16.8~56.1	Normal
*2	2850C>T	7.7~42.7	11.3~45.6	10.5~40.6	4.2~40.0	Normal
*3	2549delA	0.0~0.03	0.0~7.9	0.0~3.2	0.0~0.6	None
*4	1846G>A	0.0~4.4	0.2~24.0	8.1~33.4	0.9~8.0	None
*5	Deletion	0.0~9.6	0.0~5.3	0.0~6.9	1.0~17.2	None
*6	1707delT	0.0~0.5	0.0~4.2	0.0~2.5	0.0~0.6	None
*9	2613 delAAG	0.0~1.3	0.0~4.4	0.0~5.0	0.0~1.2	Decrease
*10	100C>T	8.6~64.1	0.0~14.9	0.4~14.5	2.5~8.6	Decrease
*14	1758G>A 2850C>T	0.0~3.0	0.0~1.8	0.0	0.0~0.5	Decrease
*17	1025C>T	0.0~0.2	0.0~16.5	0.0~2.2	9.0~34.0	Decrease
*18	4125_4133dup GTGCCCACT	0.0~0.5	0.0	0.0	0.0	None
*21	2573 _2574insC	0.0~1.7	¶ND	0.0	0.0	None
*29	3183G>A	0.0	0.0~8.7	0.0~0.3	4.6~19.8	Decrease
*41	2580C>T 2988G>A	0.0~6.6	0.0~13.5	2.7~12.4	1.4~25.3	Decrease
*49	100C>T 1611T>A	0.0~1.4	0.0	¶ND	0.0	Decrease
*52	3877G>A	0.0~1.0	0.0	¶ND	¶ND	Decrease
*60	1887insTA	0.0~0.2	0.0	¶ND	¶ND	None
Dupli -cation	Duplication	0.0~6.0	0.8~10.7	0.8~7.4	0.6~16.0	None Decrease Increase Normal

¶ND: Not determined

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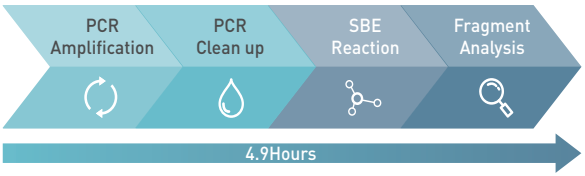
Features & Benefits

Analytical Merits

- Multiplex high-throughput analysis
- Meaningful 18 alleles in comprehensive coverage considered ethnicity
- Reliable and confident result derivation
  - Completely eliminated pseudogenes
  - High specificity and sensitivity with HotStart PCR system
  - Validated accuracy with 3000 samples compared with DNA sequencing
  - Not only the peak color but fragment size, double checking validation
- Easy-to-use master mix
- Simple and user-friendly protocols
- Reliable control DNA
- Haplotype information for analysis (Needed sample: 100~200ng DNA from whole blood or dried blood spot)

Figure 1.

The schematic workflow of "SPMED™ Genotyping Kit: CYP2D6"

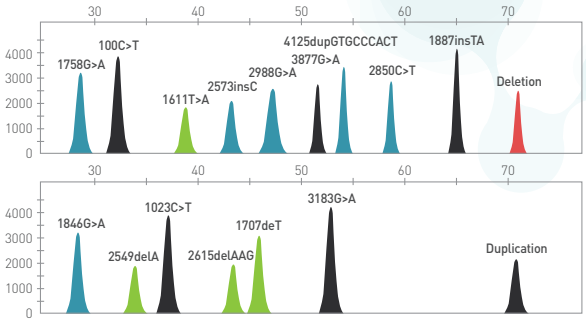


Contents

- 2X PCR Amplification Mix
- CYP2D6 Amplication Primer Mix 1
- CYP2D6 Amplication Primer Mix 2
- CYP2D6 Amplication Primer Mix 3
- SNaPshot Multiplex Reagent
- CYP2D6 SNaPshot Primer Mix 1
- CYP2D6 SNaPshot Primer Mix 2
- Wild Type DNA
- Nuclease Free Water

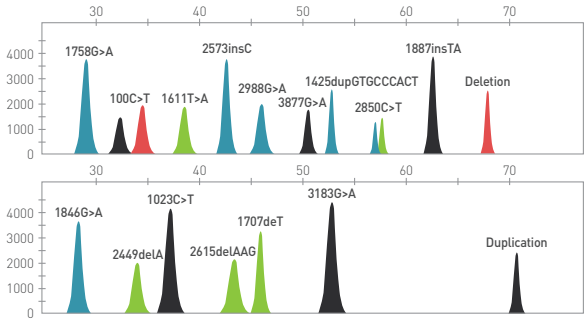
Performance

- **Wild Type DNA: CYP2D6*1/*1**



Example Results of CYP2D6 Genotyping

- **Sample DNA: CYP2D6*2/*10B**



Reference

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