

Warfarin Dosage Prediction

Assessing the Warfarin dosage requirements based on CYP2C9 and VKORC1 Genotypes



- Validated with 400+ Patients' DNA samples
- 100% Confirmation with DNA sequencing results¹
- strong patent positions in US, Europe, Japan, Mexico, New Zealand, Taiwan and Singapore²
- genomic DNA to results in ~2 hours

Warfarin, a commonly prescribed oral anticoagulant drug to prevent thromboembolism in patients with deep vein thrombosis, atrial fibrillation, or prosthetic heart valve replacement. It has been shown that the dose requirement for warfarin is highly variable among different ethnic populations. Excess bleeding is often associated with overdosing. Therefore, currently the dose has to be closely monitored by serial determinations of blood prothrombin time using standardized international normalized ratio (INR). However, such practice requires multiple visits to the clinic and may also increase medical complications in patients, especially in emergency situation.

Studies^{3, 4, 5} have shown that the single nucleotide variants of the gene CYP2C9 and the promoter of VKORC1 are associated with inter-individual and inter-ethnic difference in warfarin sensitivity.

CYP2C9 & VKORC1 genotype detection

- Comprehensive survey of relevant subtypes
 - CYP2C9*3 (c.1075): AA, AC, CC
 - CYP2C9*2 (c.430): CC, CT, TT
 - VKORC1 (-1639): GG, GA, AA
- 100% confirmation with DNA sequencing results
- Real-time PCR & TaqMan® based design^{7, 8}
- CE Marked & Research Use

In 2007 FDA has released an announcement⁶ that new genetic information of CYP2C9 and VKORC1 may help providers improve initial dose estimates of warfarin for individual patients .

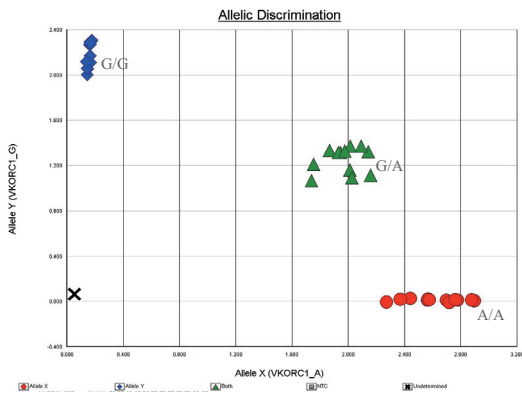
Genomic DNA	Samples	DNA sequencing vs. Pharmigene RT-PCR based detection 100% Agreement								
		VKORC1 -1639 (G>A)			CYP2C9*3 c.1075 (A>C)			CYP2C9*2 c.430 (C>T)		
Ethnicity of Healthy Volunteers		GG	GA	AA	AA	AC	CC	CC	CT	TT
Han Chinese	100	1	19	80	90	10	0	100	0	0
Asian	246	35	78	133	231	14	1	242	4	0
Caucasian	100	38	48	14	87	12	1	67	32	1
Total	446	74	145	227	408	36	2	409	36	1

1. Table 1.
2. US20060166239, EP1381402, JP4516990, MX270342, NZ556461, TWI334886 and SG133256 are properties of Academia Sinica, Taiwan, and are licensed exclusively to Pharmigene, Inc.
3. Yuan, H. et al., A novel functional VKORC1 promoter polymorphism is associated with inter-individual and inter-ethnic differences in Warfarin sensitivity. (2005) Human Molecular Genetics, vol:14, 13:1745-1751.
4. Wen M. et al., Prospective study of Warfarin dosage requirements based on CYP2C9 and VKORC1 genotypes. (2008) Pharmacology and Therapeutics, 2008, Jul, 84(1):83-89.
5. The International Warfarin Pharmacogenetics Consortium: estimation of the Warfarin does with clinical and pharmacogenetics data. (2009) New England Journal of Medicine. vol. 360, 8:753-764.
6. FDA News released in Aug 16, 2007 FDA Approves Updated Warfarin (Coumadin) Prescribing Information.
7. TaqMan is a registered trademark of Applied Biosystems, Life Technologies, Corp.
8. Additional license may be needed for various usage of RT-PCR in specific territory.

Purchase & Distribution

License & Tech Transfer

Contract Manufacturing

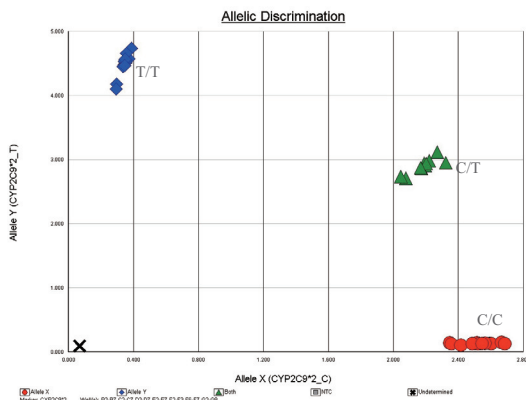


VKORC1 Scatter plot

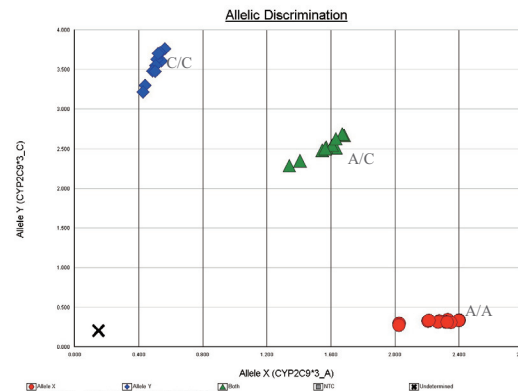
Warfarin Sensitivity Detection Kit

- PCR Master Mix (2x conc.)
- VKORC1, CYP2C9*2, CYP2C9*3 Detection Mix
- Positive Control Template

Recommended Sample Requirement:
0.2 ml of Blood or 0.2 µg of Genomic DNA



CYP2C9*2 Scatter plot



CYP2C9*3 Scatter plot

About Us...

At Pharmigene, Inc. we focus our efforts in developing, patenting, licensing, and commercializing technologies that address the prevention of adverse drug reactions. Our technologies includes HLA-B*1502 detection, HLA-B*5801 detection, Warfarin sensitivity detection (CYP2C9 detection & VKORC1 detection), etc. Pharmigene is an ISO 13485/9001 & GMP certified company since 2007.

Pharmigene, Inc.

USA : Tel:+1-650-847-1416 / Fax:+1-650-847-1415

Taiwan : Tel:+886-2-2695-9800 / Fax:+886-2-2695-7707

E-Mail : service@pharmigene.com

<http://www.pharmigene.com>