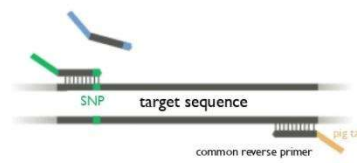


**- 1st round of PCR**

Amplification using allele specific primers

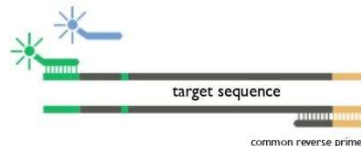
- MI3F (-20) tailed forward primer for wild type
- MI3F (-40) tailed forward primer for mutant



**- 2nd round of PCR**

Amplification using universal fluorescent primers

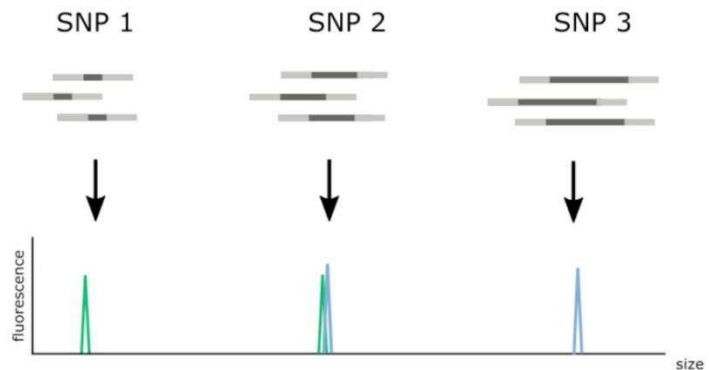
- HEX universal forward primer for wild type
- FAM universal forward primer for mutant



x cycles

**- Fragment analysis**

**SNP identification**  
SNP are identified by size



**Genotype identification**  
Genotypes are identified by dye color



**Figure S1: Principle of the assay**

The first round of amplification used allele specific primers designed to obtain different fragment sizes for each genetic location. The last nucleotide of the 3' flanking forward primers was specific to the genotype (wild-type or a variant allele). The reverse primer was the same for both allele (wild-type or a variant allele). A Pigtail GTTTCTT was added to 5' flanking reverse primers to improve the amplicon migration. A second round of amplification used universal primers combined with fluorescent probes.

A M13 sequence (-20) GTAAAACGACGGCCAGT in the 5' flanking forward wild-type primers allowed hybridization and amplification of the wild type allele and a M13 sequence (-40) GTTTTCCCAGTCACGAC in the 5' flanking forward variant primers allowed hybridization and amplification of the variant allele. After denaturation, PCR products were loaded on a sequencer. The color of the fluorescence of the fragment allowed allelic discrimination and the size of the fragment allowed genetic position discrimination.

**Table S1: Repeatability results. Eight internal control samples were analyzed in duplicate 4 different days.**

**QC1**

[illegible]

**QC2**

[illegible]

ABCB1-rs2032582-GT	DM	DM	DM	DM	DM	DM	DM	DM	100%
ABCB1-rs2229109	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP1A2-1F	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP2C9-2	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C9-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-2	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-17	DM	DM	DM	DM	DM	DM	DM	DM	100%
CYP2D6-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-4	DM	DM	DM	DM	DM	DM	DM	DM	100%
CYP2D6-6	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP2D6-9	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP3A4-22	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP3A5	DM	DM	DM	DM	DM	DM	DM	DM	100%
VKORC1-rs9923231	HM	HM	HM	HM	HM	HM	HM	HM	100%

### QC3

	Day1		Day2		Day3		Day4		
position	status R1	status R2	status R1	status R2	status R1	status R2	status R1	status R2	repetability
ABCB1-rs1045642	DM	DM	DM	DM	DM	DM	DM	DM	100%
ABCB1-rs1128503	DM	DM	DM	DM	DM	DM	DM	DM	100%
ABCB1-rs2032582-A	-	-	-	-	-	-	-	-	100%
ABCB1-rs2032582-GT	DM	DM	DM	DM	DM	DM	DM	DM	100%
ABCB1-rs2229109	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP1A2-1F	DM	DM	DM	DM	DM	DM	DM	DM	100%
CYP2C9-2	DM	DM	DM	DM	DM	DM	DM	DM	100%
CYP2C9-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-2	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-17	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-4	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-6	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-9	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP3A4-22	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP3A5	DM	DM	DM	DM	DM	DM	DM	DM	100%
VKORC1-rs9923231	HM	HM	HM	HM	HM	HM	HM	HM	100%

### QC4



**QC6**

[illegible]

**QC7**

[illegible]

CYP3A4-22	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP3A5	HM	HM	HM	HM	HM	HM	HM	HM	100%
VKORC1- rs9923231	HM	HM	HM	HM	HM	HM	HM	HM	100%

#### QC8

	Day1		Day2		Day3		Day4		
position	status R1	status R2	status R1	status R2	status R1	status R2	status R1	status R2	repetability
ABCB1-rs1045642	WT	WT	WT	WT	WT	WT	WT	WT	100%
ABCB1-rs1128503	WT	WT	WT	WT	WT	WT	WT	WT	100%
ABCB1-rs2032582-A	-	-	-	-	-	-	-	-	100%
ABCB1-rs2032582-GT	WT	WT	WT	WT	WT	WT	WT	WT	100%
ABCB1-rs2229109	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP1A2-1F	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP2C9-2	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C9-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-2	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2C19-3	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP2C19-17	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP2D6-3	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-4	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-6	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP2D6-9	WT	WT	WT	WT	WT	WT	WT	WT	100%
CYP3A4-22	HM	HM	HM	HM	HM	HM	HM	HM	100%
CYP3A5	DM	DM	DM	DM	DM	DM	DM	DM	100%
VKORC1- rs9923231	DM	DM	DM	DM	DM	DM	DM	DM	100%

WT: wild-type allele; varHz: heterozygous for the variant allele; varHm: homozygous for the variant allele

QC: internal quality control DNA

R: replicate

**Table S2: Genotyping results of clinical cases and genes involved in the pharmacokinetics of treatments**

	ABCB1- rs1045642	ABCB1- rs1128503	ABCB1- rs2032582-A	ABCB1- rs2032582-GT	ABCB1- rs2229109	CYP1A2*1F	CYP2C9*2	CYP2C9*3	CYP2C19*2	CYP2C19*3	CYP2C19*17	CYP2D6*3	CYP2D6*4	CYP2D6*6	CYP2D6*9	CYP3A4*22	CYP3A5*3	VKORC1- rs9923231
P1	WT	WT	<b>varHm</b>	WT	WT	<b>varHm</b>	WT	WT	WT	WT	<b>varHz</b>	<b>varHz</b>	WT	WT	WT	WT	varHm	<b>varHz</b>
Haloperidol																		
Clozapine																		
P2	<b>varHz</b>	<b>varHz</b>	-	<b>varHz</b>	WT	varHm	WT	WT	varHz	WT	WT	WT	WT	WT	WT	<b>varHz</b>	varHm	WT
P3	<b>varHm</b>	<b>varHm</b>	-	<b>varHm</b>	WT	WT	varHz	WT	WT	WT	WT	-	-	-	-	WT	varHm	varHz
Vincristine																		

Results of the PCR-Multiplex analysis

	Polymorphism on a gene not significantly involved in the drug pharmacokinetics
	Polymorphism on a gene moderately involved in the drug pharmacokinetics
	Polymorphism on a gene strongly involved in the drug pharmacokinetics

P1, P2, P3: patient ID

WT: wild-type allele; varHz: heterozygous for the variant allele; varHm: homozygous for the variant allele

(-): no amplification because of full gene deletion

**Table S3. Design of primers used in the assay**

Gene and variant	Primer ID	Primer sequences (5'-3')	amplicon size (pb)	Primer final concentration in the mix (pmol/μL)
CYP1A2*1F rs762551	F-CYP1A2*1F - WT	<u>GTAAAACGACGGCCAGT</u> CAAAGGG TGAGCTCTGTGGTCC	160	0.02
	F-CYP1A2*1F - var	<u>GTTTCCCAGTCACGAC</u> CAAAGGG TGAGCTCTGTGGACA		0.02
	R-CYP1A2*1F	<u>GTTTCTT</u> TGGAGACATTCATTCATTC ATTCC		0.3
CYP2C9*2 rs1799853	F-CYP2C9*2-WT	<u>GTAAAACGACGGCCAGT</u> GGGAAGA GGAGCATTGAGCAC	127	0.02
	F-CYP2C9*2-var	<u>GTTTCCCAGTCACGAC</u> GGGAAGA GGAGCATTGAGCACT		0.01
	R-CYP2C9*2	<u>GTTTCTT</u> AGGTCAGTGATATGGAGT AGGGT		0.2
CYP2C9*3 rs1057910	F-CYP2C9*3-WT	<u>GTAAAACGACGGCCAGT</u> GTGCACG AGGTCCAGAGAAACA	328	0.03
	F-CYP2C9*3-var	<u>GTTTCCCAGTCACGAC</u> GTGCACGA GGTCCAGAGAAACC		0.01
	R-CYP2C9*3	<u>GTTTCTT</u> TAAATCTGGAGAACACAC ACTGCC		0.4
CYP2C19*2 rs4244285	F-CYP2C19*2-WT	<u>GTAAAACGACGGCCAGT</u> TTCCCACT ATCATTGATTATTTGCCG	164	0.01
	F-CYP2C19*2-var	<u>GTTTCCCAGTCACGAC</u> TTCCCACT ATCATTGATTATTTGCCA		0.01
	R-CYP2C19*2	<u>GTTTCTT</u> ATCAATAAAGTCCCGAGG GTTGT		0.4
CYP2C19*3 rs4986893	F-CYP2C19*3-WT	<u>GTAAAACGACGGCCAGT</u> GGATTGT AAGCACCCCGTG	183	0.01
	F-CYP2C19*3-var	<u>GTTTCCCAGTCACGAC</u> GGATTGTA AGCACCCCGTGA		0.005
	R-CYP2C19*3	<u>GTTTCTT</u> TACCCCATGGCTGTCTAG G		0.2
CYP2C19*17 rs12248560	F-CYP2C19*17-WT	<u>GTAAAACGACGGCCAGT</u> GGCGCAT TATCTTTACATCAGACATG	202	0.04
	F-CYP2C19*17-var	<u>GTTTCCCAGTCACGAC</u> GGCGCAT ATCTCTTACATCAGACATA		0.01
	R-CYP2C19*17	<u>GTTTCTT</u> GTGGTTCTATTTAATGTGA AGCCTGTTTATG		0.8
CYP2D6*3 rs35742686	F-CYP2D6*3-WT	<u>GTAAAACGACGGCCAGT</u> GATGAGC TGCTAACTGAGGACA	478	0.02
	F-CYP2D6*3-var	<u>GTTTCCCAGTCACGAC</u> GATGAGCT GCTAACTGAGGACG		0.005
	R-CYP2D6*3	<u>GTTTCTT</u> CGGCCCTGCACTGTTTC GTAAAACGACGGCCAGTCCGCATC		0.2
CYP2D6*4 rs3892097	F-CYP2D6*4-WT	<u>GTAAAACGACGGCCAGT</u> CCGCATC TCCACCCTCA	450	0.02
	F-CYP2D6*4-var	<u>GTTTCCCAGTCACGAC</u> CCGCATCT CCACCCTCAA		0.01
	R-CYP2D6*4	<u>GTTTCTT</u> TCTCTGACGTGGATAGGA GGTACA		1.6
CYP2D6*6 rs5030655	F-CYP2D6*6-WT	<u>GTAAAACGACGGCCAGT</u> CCTCCTCG GTCAGCCA	227	0.04
	F-CYP2D6*6-var	<u>GTTTCCCAGTCACGAC</u> CCCTCCTCG GTCAGCCC		0.01
	R-CYP2D6*6	<u>GTTTCTT</u> CCAGGGGGAGCATAGGGT T		2
CYP2D6*9 rs5030656	F-CYP2D6*9-WT	<u>GTAAAACGACGGCCAGT</u> CTTCCTGG CAGAGATGGACAAAG	410	0.02
	F-CYP2D6*9-var	<u>GTTTCCCAGTCACGAC</u> CTTCCTG GCAGAGATCGAG		0.01
	R-CYP2D6*9	<u>GTTTCTT</u> CGGCCCTGCACTGTTTC		1.6



CYP3A4*22 rs35599367	F-CYP3A4*22-WT	<u><b>GTAAAACGACGGCCAGT</b></u> AGTGTCT CCATCACACCGAGC	118	0.02
	F-CYP3A4*22-var	<u><b>GTTTTCCCAGTCACGAC</b></u> AGTGTCTC CATCACACCGAGT		0.01
	R-CYP3A4*22	<u><b>GTTTCTT</b></u> GATCTACTAGATCACCTTC TATCACACTCCA		0.4
CYP3A5*3 rs776746	F-CYP3A5-WT	<u><b>GTAAAACGACGGCCAGT</b></u> TGTGGTC CAAACAGGGAAGAGTTAT	305	0.02
	F-CYP3A5-var	<u><b>GTTTTCCCAGTCACGAC</b></u> TGTGGTCC AAACAGGGAAGAGTTAC		0.01
	R-CYP3A5	<u><b>GTTTCTT</b></u> AGATGACACAGCTCTAGA TGTCC		0.8
VKORC1- rs9923231	F-VKORC1- rs9923231-WT	<u><b>GTAAAACGACGGCCAGT</b></u> GACCTGA AAAACAACCATTTGGACG	397	0.01
	F-VKORC1- rs9923231-var	<u><b>GTTTTCCCAGTCACGAC</b></u> GACCTGAA AAACAACCATTTGGACA		0.04
	R-VKORC1- rs9923231	<u><b>GTTTCTT</b></u> CCTGACACCTAGTGGCTG GT		1.6
ABCB1- rs1045642	F-ABCB1- rs1045642-var	<u><b>GTAAAACGACGGCCAGT</b></u> CTCCTTTG CTGCCCTGACA	319	0.02
	F-ABCB1- rs1045642-WT	<u><b>GTTTTCCCAGTCACGAC</b></u> CTCCTTTG CTGCCCTGACG		0.005
	R-ABCB1- rs1045642	<u><b>GTTTCTT</b></u> TACACAAACTTTTCCTTA ATCTCA		0.8
ABCB1- rs1128503	F-ABCB1- rs1128503-var	<u><b>GTAAAACGACGGCCAGT</b></u> ACTCTGC ACCTTCAGGTTGAGA	338	0.02
	F-ABCB1- rs1128503-WT	<u><b>GTTTTCCCAGTCACGAC</b></u> ACTCTGCA CCTTCAGGTTGAGG		0.005
	R-ABCB1- rs1128503	<u><b>GTTTCTT</b></u> AGCCAAGTATTGACAGCT ATTCG		0.6
ABCB1- rs2032582	F-ABCB1- rs2032582-var-T	<u><b>GTAAAACGACGGCCAGT</b></u> ATTTAGTT TGACTCACCTTCCGAGA	424	0.02
	F-ABCB1- rs2032582-WT-G	GTTTTCCCAGTCACGACATTTAGTTT GACTCACCTTCCGAGC		0.005
	F-ABCB1- rs2032582-var-A	<u><b>GTTTTCCCAGTCACGAC</b></u> CATATTTA GTTTGACTCACCTTCCCTGT	427	0.005
	R-ABCB1- rs2032582	<u><b>GTTTCTT</b></u> CTGAAGTCATGGAAATTCT TACTGT	424/427	0.8
ABCB1- rs2229109	F-ABCB1- rs2229109-WT	<u><b>GTAAAACGACGGCCAGT</b></u> CCTTAACT TCTTTTCGAGATGGGAAAC	360	0.02
	F-ABCB1- rs2229109-var	<u><b>GTTTTCCCAGTCACGAC</b></u> CCTTAACT TCTTTTCGAGATGGGAAAT		0.01
	R-ABCB1- rs2229109	<u><b>GTTTCTT</b></u> GGACAGGCATCTCCAAGC AT		0.4

F: forward; R: reverse; WT: wild type; var: variant

**GTAAAACGACGGCCAGT**: M13 sequence (-20) added to 5' flanking forward primers

**GTTTTCCCAGTCACGAC**: M13 sequence (-40) added to the 5' flanking forward primers

**GTTTCTT**: "Pigtail" added to 5' flanking reverse primers

**X**: mismatch nucleotide in bold

**X**: position of the polymorphism

For the design of primers, the term "variant" was assigned to the lowest frequent allele compared to wild type in the total human population and according to the database dbSNP

<https://www.ncbi.nlm.nih.gov/snp/>