

More than 30 genes are involved in the metabolism of drugs. Mutations in these genes determine variation in the enzyme activity leading to poor, intermediate, fast or ultrafast breakdown and excretion of many drugs.

Poor metabolisers are at risk for adverse drug reactions, whereas the efficacy of the medication in ultrafast metabolisers is reduced.

The most prominent examples of such pharmacogenetic tests used are given in the table below.

Gene	Alleles*	Effect	Test Number
<b>CYP2D6</b>	*3, *4, *5, *6, *7, *8, *9, *14, *19	Poor metaboliser	19
	*XN	Ultrafast metaboliser	20
	*3, *4, *5, *6, *7, *8, *9, *14, *19, *XN	Poor and ultrafast metaboliser	21
<b>CYP2D6/CYP2C19</b>	AMPLICHIP CYP450 WITH 34 ALLELES OF CYP2D6/CYP2C19:  CYP2D6 alleles: *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *14A, *14B, *15, *17, *19, *20, *25, *26, *29, *30, *31, *35, *36, *40, *41, 1XN, 2XN, 4XN, 10XN, 17XN, 35XN, 41XN  CYP2C19 alleles: *2, *3	Poor and ultrafast metaboliser	22
<b>CYP2C19</b>	*2, *2B, *3, *4, *5, *6, *7, *8, *9, *10, *11	Poor metaboliser	23
<b>CYP2C9</b>	*2, *3, *4, *5, *6, *11	Poor metaboliser	24

A large amount of variations have been described in the genes encoding phase I and phase II enzymes.

A complete table of all variations offered is listed below.

Gene	Allele	Mutation	Effect on Protein	Effect on Enzyme Activity*	Test Number
<b>Cytochrome P450 (CYP)</b>					
<b>CYP1A2</b>	*1C	g.-3858G>A		decreased activity	25
	*1E	g.-740T>G			26
	*1F	g.-164C>A		higher inducibility	27
	*1J	g.-740T>G g.-164C>A			28
	*1K	g.-740T>G g.-730C>T g.-164C>A		decreased activity	29
	*1E, *1F, *1J, *1K				30
	*2	g.63C>G	F21L		31
	*3	g.2116G>A	D348N		32
	*4	g.2499A>G	I348N		33

	*5	g.3497G>A	C406Y		34
	*6	g.5090C>T	R431W		35
	*7	g.3534G>A	splicing defect	decreased activity	36
<b>CYP2A6</b>	*1H	g.-745A>G			37
	*2	c.479T>A	L160H	no activity	38
	*4	deletion	no protein	no activity	39
	*5	c.1436G>T	G479V	no activity	40
	*6	c.383G>A	R128Q	decreased activity	41
	*7	c.1412T>G	I471T	decreased activity	42
	*9	c.-48T>G	decreased protein	decreased activity	43
	*10	c.1412G>T c.1454G>T	I471T, R485L	decreased activity	44
	*11	c.670T>C	S224P	decreased activity	45
	*12	partial deletion	altered protein	decreased activity	46
	*17	c.1093G>A	V365M	decreased activity	47
	*1x2	gene duplication	increased protein	increased activity	48
<b>CYP2B6</b>	*2	c.64C>T	R22C		49
	*3	c.777C>A	S259R		50
	*4	c.785A>G	K262R		51
	*5	c.1459C>T	R487C		52
	*6	c.516G>T c.785A>G	Q172H, K262R		53
	*7	c.516G>T c.785A>G c.1459C>T	Q172H, K262R, R487C		54
	*8	c.415A>G	K139E	decreased activity	55
	*9	c.516G>T	Q172H		56
<b>CYP2C8</b>	*2	c.805A>T	I269F	increased activity	57
	*3	c.416G>A c.1196A>G	R139K, K399R	decreased activity	58
	*4	c.792C>G	I264M		59
	*5	c.475delA	T159fs177X	no activity	60
	*7	c.556C>T	R186X	no activity	61
	*8	c.556C>G	R186G	decreased activity	62
<b>CYP2C9</b>	*2	c.430C>T	R144C	decreased activity	63
	*3	c.1075A>C	I359L	decreased activity	64
	*4	c.1076T>C	I359T	decreased activity	65
	*5	c.1080C>G	D360E	decreased activity	66
	*6	c.818delA	frameshift	no activity	67
	*7	c.55C>A	L19I		68
	*8	c.449G>A	R150H	increased activity	69
	*9	c.752A>G	H251R		70
	*10	c.815A>G	E272G		71
	*11	c.1003C>T	R335W	decreased activity	72
	*12	c.1465C>T	P489S	decreased activity	73
	*16	c.485C>A	T299A	decreased activity	74
	*18	c.1075A>C	I359L	decreased activity	75
	*2, *3, *4, *5, *6, *11			poor metaboliser	24
<b>CYP2C19</b>	*2	c.681G>A	splicing defect	no activity	76
	*3	c.636G>A	W212X	no activity	77
	*4	c.1A>G	start codon mutation	no activity	78
	*5	c.1297G>A	R433W	no activity	79
	*6	c.395G>A	R132Q	no activity	80
	*7	1VS5+2T>A	splicing defect	no activity	81
	*8	c.358T>C	W120R	no activity	82
	*9	c.431G>A	R144H	decreased activity	83
	*10	680C>T	P227L	decreased activity	84
	*11	c.449G>A	R150H		85
	*2, *2B, *3, *4, *5, *6, *7, *8, *9, *10, *11			poor metaboliser	23
<b>CYP2D6</b>	*3	g.2549delA	frameshift	no activity	86
	*3B	g.1749A>G	N166D,	no activity	87

		g.2549delA	frameshift		
	*4	g.1846G>A	splicing defect	no activity	88
	*5	gene deletion	no protein	no activity	89
	*6	g.1701delT	frameshift	no activity	90
	*7	g.2935A>C	H374P	no activity	91
	*8	g.1758G>T	Stop codon	no activity	92
	*9	g.2613-2615delAGA	K281del	decreased activity	93
	*14	g.1758G>A	G169R	no activity	94
	*17	g.1023C>T g.2850C>T	T107I, R296C	decreased activity	95
	*20	g.1973insG	frameshift	no activity	96
	*21	g.2573insC	frameshift	no activity	97
	*24	g.2853A>C	I297L		98
	*38	g.2587-2590delGACT	frameshift	no activity	99
	*44	g.2950G>C	splicing defect	no activity	100
	*XN	gene amplification	increased protein	increased activity	20
	*3, *4, *5, *6, *7, *8, *9, *14, *19			poor metaboliser	19
	*3, *4, *5, *6, *7, *8, *9, *14, *19, *XN			poor and ultrafast metaboliser	21
<b>CYP2D6 / CYP2C19</b>  AmpChip (Roche Diagnostics)	*2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *14A, *14B, *15, *17, *19, *20, *25, *26, *29, *30, *31, *35, *36, *40, *41, 1XN, 2XN, 4XN, 10XN, 17XN, 35XN, 41XN + CYP2C19 *2, *3				22
<b>CYP2E1</b>	*1C	6 minisat			101
	*1D	8 minisat		increased activity	102
	*2	g.1132G>A	R76H	decreased activity	103
	*5	g.-1293G>C g.-1053C>T			104
	*6	g.7632T>A			105
	*1C, *1D				106
<b>CYP2J2</b>	*2	c.427A>G	T143A	decreased activity	107
	*3	c.472C>T	R158C	decreased activity	108
	*4	c.575T>A	I192N	decreased activity	109
	*5	c.1024G>A	D342N	decreased activity	110
	*6	c.1210A>T	N404Y	decreased activity	111
	*7	g.-76G>T	decreased protein	decreased activity	112
<b>CYP3A4</b>	*1B	g.-392A>G			113
	*2	g.15713T>C	S222P	decreased activity	114
	*3	g.23172T>C	M445T		115
	*4	g.13871A>G	I118V		116
	*5	g.15702C>G	P218R		117
	*6	g.17662-17663insA	frameshift		118
	*7	g.6004G>A	G56D		119
	*8	g.13908G>A	R130Q		120
	*9	g.14292G>A	V170I		121
	*10	g.14304G>C	D174H		122
	*11	g.21867C>T	T363M		123
	*12	g.21896C>T	L373F		124
	*13	g.22026C>T	R416L		125
	*14	g.44T>C	L15P		126
	*15	g.14269G>A	R162Q		127
	*16	g.15603C>G	T185S		128
	*17	g.15615T>C	F189S	decreased activity	129
	*18	g.20070T>C	L293P	increased activity	130
	*19	g.23237C>T	P467S		131
<b>CYP3A5</b>	*2	g.27289C>A	T398N		132
	*3C	g.6986G>A	splicing defect	no activity	133
	*4	g.14665A>G	Q200R		134
	*5	g.12952T>C	splicing defect		135

	*6	g.14690G>A	splicing defect	no activity	136
	*7	g.27131-27132insT	frameshift		137
	*8	g.3699C>T	R28C	decreased activity	138
	*9	g.19386G>A	A337T	decreased activity	139
	*10	g.29753T>C	splicing defect	decreased activity	140
<b>CYP3A7</b>	*1C	c.-291G>T -284T>A -282T>C -281A>T -270T>G -262T>A -232A>C		increased activity	141
	*2	c.1226C>G	T409R	increased activity	142
<b>CYP4B1</b>	*2	c.881-882delAT	frameshift		143
<b>Epoxidhydroxylases (EPHX)</b>					
<b>EPHX1</b>	n.a.	c.128G>C	R43T		144
	*3	c.337T>C	Y113H		145
	*4	c.416A>G	H139R		146
<b>EPHX2</b>	n.a.	c.229A>G	K55R	increased activity	147
	n.a.	c.307C>T	R103C		148
	n.a.	c.461G>A	C154	increased activity	149
	n.a.	c.860G>A	R287Q	decreased activity	150
	n.a.	c.1208-1209insTCG	403-404insR	decreased activity	151
<b>Glutathione S-transferases (GST)</b>					
<b>GSTM1</b>	*0	gene deletion	no protein		152
<b>GSTT1</b>	*A	wild type			153
	*B	c.301A>C	T104P		154
	*0	gene deletion	no protein		155
<b>GSTP1</b>	*A	wild type			156
	*B	c.313A>G	I105V		157
	*C	c.313A>G c.341C>T	I105V, A114V		158
<b>Sulfonyl transferases (SULT)</b>					
<b>SULT1A1</b>	*2	638 G>A	R213H	decreased activity	159
	*3	667 G>A	M223V		160
	*2, *3				161
<b>SULT1A2</b>	*2	20 T>C	I7T		162
	*3	56 T>C	P19L		163
	*2, *3				164
<b>N-Acetyltransferase type 2 (NAT2)</b>					
<b>NAT2</b>	*4	wild type			165
	*5	c.341T>C	I114T	decreased activity	166
	*6	c.590G>T	R197Q	decreased activity	167
	*7	c.857G>A	G286E	decreased activity	168
	*10	c.499G>A	E167K		169
	*11B	c.481C>T;859del	frameshift		170
	*12	c.803A>G	K268R		171
	*13	c.282C>T	none		172
	*14	c.191G>A	R64Q	decreased activity	173
	*17	c.434A>C	Q145P	decreased activity	174
	*18	c.845A>C	K282T		175
	*19	c.190C>T	R64W		176
	*4, *5, *6, *7, *10, *11B, *12, *13, *14, *17, *18, *19				177
<b>Thiopurine methyltransferases (TPMT)</b>					
<b>TPMT</b>	*2	c.288G>C	A80P	decreased activity	178
	*3A	c.460G>A c.719A>G	A154T, Y240C	decreased activity	179
	*3B	c.719A>G	Y240C	decreased activity	180
	*3C	c.719A>G	A154T	decreased activity	181
<b>Uridine diphosphate-glucoronyltransferases (UGT)</b>					
<b>UGT1A1</b>	*1	promoter repeat [TA] 6	wild type		182

	*6	226A>G	G71R	decreased activity	183
	*28	promoter repeat [TA] 7		decreased activity	184
	*36	promoter repeat [TA] 5		increased activity	185
	*37	promoter repeat [TA] 8		decreased activity	186
	*28, **36, *37				187
<b>UGT1A6</b>	*1		wild type		188
	*2	637A>G 648A>C	T181A, R184S	decreased activity	189
<b>UGT1A7</b>	*1		wild type		190
	*2	387T>G 391C>A 392G>A	N129K, R131K	decreased activity	191
	*3	387T>G 391C>A 392G>A 622T>C	N129K, R131K,W208R	decreased activity	192
	*4	622T>C	W208R	decreased activity	193
	*1, *2, *3, *4				194
<b>UGT2B4</b>	*2	1411T>A	D458E	no activity	195
<b>UGT2B7</b>	*2	816C>T	H268Y	decreased activity	196
<b>UGT2B15</b>	*2	276T>G	D85Y	increased activity on androgens	197
<b>Multidrug resistance 1 ( MDR1, ABCB1)</b>					
	n.a.	1236C>T	decreased protein	decreased activity	198
	n.a.	2677G>T or 2677G>A	A893S or A893T	decreased activity	199
	n.a.	3435C>T	decreased protein	decreased activity	200
<b>5-@Hydroxytryptamine transporter (5-HTT, SLC6A4)</b>					
	L, S	44 bp insertion/deletion in the promotor region	increased protein for L (insertion) variant	increased activity for L variant	201