

Supplementary Table: Overview of genotypes, results of the 48-hour BH4 loading test and the BH4 extension phase

Allele 1	Allele 2	Phe load [†]	T=0	Max Phe ↓ (%)	Extension phase	
IVS2+5G>C‡§	c.168+5G>C	p.W187*‡	c.561G>A	No	741 4	No
IVS2+5G>C‡§	c.168+5G>C	p.W187*‡	c.561G>A	No	326 17	No
IVS2+5G>C‡	c.168+5G>C	p.R243*‡	c.727C>T	No	1049 25	No
IVS2+5G>C‡	c.168+5G>C	p.R261Q¶	c.782G>A	No	491 15	No
IVS5-21del177‡	c.510-21_665del	p.G272*‡	c.814G>T	No	855 5	No
IVS7+1G>A‡	c.842+1G>A	p.R243Q‡	c.728G>A	Yes	626 5	No
IVS7+5G>A‡	c.842+5G>A	p.R158Q¶	c.473G>A	Yes	896 -1	No
IVS7+5G>A‡	c.842+5G>A	p.Y414C	c.1241A>G	No	503 36	Yes positive
IVS7-5T>C‡	c.843-5T>C	p.P281L‡	c.842C>T	No	949 22	No
IVS10-11G>A‡	c.1066-11G>A	IVS10-11G>A‡	c.1066-11G>A	No	1224 22	No
IVS10-11G>A‡	c.1066-11G>A	IVS10-11G>A‡	c.1066-11G>A	Yes	550 14	No
IVS10-11G>A‡	c.1066-11G>A	IVS10-11G>A‡	c.1066-11G>A	No	705 3	No
IVS10-11G>A‡§	c.1066-11G>A	p.L48S	c.143T>C	Yes	478 56	No
IVS10-11G>A‡§	c.1066-11G>A	p.L48S	c.143T>C	No	845 27	No
IVS10-11G>A‡§	c.1066-11G>A	p.L48S	c.143T>C	Yes	459 48	No
IVS10-11G>A‡	c.1066-11G>A	p.D222G¶	c.665A>G	Yes	936 23	No
IVS12+1G>A‡	c.1315+1G>A	IVS12+1G>A‡	c.1315+1G>A	No	769 9	No
IVS12+1G>A‡	c.1315+1G>A	p.S16* ‡	c.47_48delICT	Yes	715 -4	No
IVS12+1G>A‡	c.1315+1G>A	p.S16* ‡	c.47_48delICT	No	451 12	No
IVS12+1G>A‡	c.1315+1G>A	p.S16* ‡	c.47_48delICT	No	599 0	No
IVS12+1G>A‡	c.1315+1G>A	p.L48S	c.143T>C	Yes	304 69	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.I65T	c.194T>C	Yes	587 60	No
IVS12+1G>A‡§	c.1315+1G>A	p.II74N¶	c.521T>A	Yes	692 35	Yes negative
IVS12+1G>A‡§	c.1315+1G>A	p.II74N¶	c.521T>A	Yes	663 17	No
IVS12+1G>A‡	c.1315+1G>A	p.W187*‡	c.561G>A	No	514 7	No
IVS12+1G>A‡§	c.1315+1G>A	p.P211T‡‡	c.631C>A	Yes	367 81	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.R241C	c.721C>T	Yes	464 45	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.R243*‡	c.727C>T	Yes	588 21	No
IVS12+1G>A‡	c.1315+1G>A	p.R261P¶	c.782G>C	Yes	591 -4	No
IVS12+1G>A‡	c.1315+1G>A	p.R261Q¶	c.782G>A	No	852 -1	No
IVS12+1G>A‡	c.1315+1G>A	p.R261Q¶	c.782G>A	No	408 16	No
IVS12+1G>A‡	c.1315+1G>A	p.R261Q¶	c.782G>A	Yes	709 22	No
IVS12+1G>A‡	c.1315+1G>A	p.R261Q¶	c.782G>A	No	577 21	No
IVS12+1G>A‡	c.1315+1G>A	p.Y277D¶	c.829T>G	No	557 -18	No
IVS12+1G>A‡§	c.1315+1G>A	p.P281L‡	c.842C>T	Yes	950 22	No
IVS12+1G>A‡§	c.1315+1G>A	p.P281L‡	c.842C>T	No	650 19	No
IVS12+1G>A‡	c.1315+1G>A	p.P281L‡	c.842C>T	Yes	469 7	No
IVS12+1G>A‡	c.1315+1G>A	p.A300S	c.898G>T	Yes	321 62	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.L348V	c.1042C>G	Yes	593 33	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.L367Pfs*27‡	c.1099_1100insC	Yes	397 -5	No
IVS12+1G>A‡	c.1315+1G>A	p.L367Pfs*27‡	c.1099_1100insC	No	934 10	No
IVS12+1G>A‡	c.1315+1G>A	p.A403V	c.1208C>T	Yes	314 85	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.R408W‡	c.1222C>T	No	890 -1	No
IVS12+1G>A‡	c.1315+1G>A	p.Y414C	c.1241A>G	No	896 63	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.Y414C	c.1241A>G	Yes	681 72	Yes positive
IVS12+1G>A‡	c.1315+1G>A	p.Y414C	c.1241A>G	Yes	576 83	Yes positive
IVS12+1G>A‡§	c.1315+1G>A	p.Y414C	c.1241A>G	No	535 56	Yes positive
IVS12+1G>A‡§	c.1315+1G>A	p.Y414C	c.1241A>G	No	390 45	Yes positive

Allele 1	Allele 2	Phe load [†]	T=0	Max Phe ↓ (%)	Extension phase	
(Continued from previous page)						
IVS12+1G>A [‡]	c.1315+1G>A	p.Y414C	c.1241A>G	No	465 38	Yes positive
p.L48S	c.143T>C	p.R158Q	c.473G>A	Yes	316 52	No
p.L48S §	c.143T>C	p.R241C	c.721C>T	Yes	365 49	Yes positive
p.L48S §	c.143T>C	p.R241C	c.721C>T	Yes	532 59	Yes positive
p.L48S	c.143T>C	p.R261Q	c.782G>A	No	530 28	No
p.L48S	c.143T>C	p.P281L [‡]	c.842C>T	Yes	525 63	Yes positive
p.L48S	c.143T>C	p.R408W [‡]	c.1222C>T	No	815 36	Yes positive
p.F55Lfs*6 [‡]	c.165delT	p.P281L [‡]	c.842C>T	No	411 -7	No
p.I65T	c.194T>C	p.L311P [‡]	c.932T>C	Yes	530 33	Yes negative
p.I94del [‡]	c.283_285delATC	p.P314H ^{‡‡}	c.941C>A	Yes	436 65	Yes positive
p.I94del [‡]	c.283_285delATC	p.Y414C	c.1241A>G	No	521 72	Yes positive
p.A104D ^{††}	c.311C>A	p.A104D ^{††}	c.311C>A	Yes	660 57	Yes positive
p.A104D ^{††}	c.311C>A	p.R158Q	c.473G>A	No	646 31	Yes positive
p.A104D ^{††}	c.311C>A	p.R241C	c.721C>T	Yes	574 42	No
p.A104D ^{††}	c.311C>A	p.R408W [‡]	c.1222C>T	Yes	486 34	Yes positive
p.R111* [‡]	c.331C>T	p.R408W [‡]	c.1222C>T	No	766 14	No
p.R158Q	c.473G>A	p.R158Q	c.473G>A	No	633 34	Yes negative
p.R158Q	c.473G>A	p.R158Q	c.473G>A	No	535 5	No
p.R158Q	c.473G>A	p.V190A	c.569T>C	No	327 53	Yes positive
p.R158Q	c.473G>A	p.V190A	c.569T>C	Yes	511 52	Yes positive
p.R158Q	c.473G>A	p.R243* [‡]	c.727C>T	No	323 4	No
p.R158Q	c.473G>A	p.R261P	c.782G>C	No	1348 6	No
p.R158Q	c.473G>A	p.Y277D	c.829T>G	Yes	257 40	Yes negative
p.R158Q	c.473G>A	p.R408W [‡]	c.1222C>T	Yes	655 -1	No
p.R158Q	c.473G>A	p.Y414C	c.1241A>G	No	366 68	Yes positive
p.R158Q	c.473G>A	p.Y414C	c.1241A>G	Yes	362 74	Yes positive
p.I174N §	c.521T>A	p.P211T ^{††}	c.631C>A	Yes	360 67	Yes positive
p.I174T	c.521T>C	p.F299C [‡]	c.896T>G	No	1049 -24	No
p.E178G	c.533A>G	p.Y343C	c.1028A>G	Yes	353 64	Yes positive
p.W187* [‡]	c.561G>A	p.W187* [‡]	c.561G>A	No	505 17	No
p.W187* [‡]	c.561G>A	p.T193I ^{††}	c.578C>T	No	365 62	Yes positive
p.W187* [‡]	c.561G>A	p.L367Pfs*27 [‡]	c.1099_1100insC	Yes	689 -2	No
p.V190A	c.569T>C	p.S231F [‡]	c.692C>T	Yes	448 41	Yes positive
p.V190A	c.569T>C	p.L311P [‡]	c.932T>C	Yes	592 76	No
p.L197Lfs [‡]	c.590_611del	p.D415N	c.1243G>A	Yes	302 73	Yes positive
p.C203Y	c.608G>A	p.L348V	c.1042C>G	Yes	486 25	No
p.P211Hfs [‡]	c.632delC	p.S231P [‡]	c.691T>C	Yes	474 -8	No
p.T238A ^{††}	c.712A>G	p.P281L [‡]	c.842C>T	Yes	549 59	Yes positive
p.R243* [‡]	c.727C>T	p.R261Q	c.782G>A	No	620 39	Yes negative
p.R243* [‡] §	c.727C>T	p.S349P [‡]	c.1045T>C	Yes	719 37	No
p.R243* [‡] §	c.727C>T	p.S349P [‡]	c.1045T>C	Yes	693 22	No
p.R243* [‡] §	c.727C>T	p.S349P [‡]	c.1045T>C	Yes	352 31	No
p.R243* [‡] §	c.727C>T	p.A403V	c.1208C>T	Yes	515 87	Yes positive
p.R243* [‡] §	c.727C>T	p.A403V	c.1208C>T	Yes	420 74	No
p.R243X [‡]	c.727C>T	p.Y414C	c.1241A>G	Yes	634 49	Yes positive
p.R243* [‡]	c.727C>T	p.E440 * [‡]	c.1318G>T	No	560 21	No
p.R252W [‡]	c.754C>T	p.P281L [‡]	c.842C>T	No	882 -2	No
p.R261P	c.782G>C	p.Y414C	c.1241A>G	No	572 30	Yes positive

Allele 1		Allele 2		Phe load [†]	T=0	Max Phe ↓ (%)	Extension phase
(Continued from previous page)							
p.R261Q¶§	c.782G>A	p.R261Q¶	c.782G>A	No	758	25	No
p.R261Q¶§	c.782G>A	p.R261Q¶	c.782G>A	Yes	510	7	No
p.R261Q¶	c.782G>A	p.E280K‡	c.838G>A	Yes	654	25	No
p.R261Q¶	c.782G>A	p.E280K‡	c.838G>A	No	1476	25	No
p.R261Q¶	c.782G>A	p.P281L‡	c.842C>T	No	1237	29	No
p.R261Q¶	c.782G>A	p.P281L‡	c.842C>T	Yes	488	79	Yes positive
p.G272*‡	c.814G>T	p.Y414C	c.1241A>G	Yes	462	84	Yes positive
p.Y277D¶§	c.829T>G	p.P314H††	c.941C>A	Yes	206	33	Yes positive
p.Y277D¶§	c.829T>G	p.P314H††	c.941C>A	Yes	213	68	No
p.E280K‡	c.838G>A	p.Y414C	c.1241A>G	Yes	481	73	Yes positive
p.P281L‡§	c.842C>T	p.P281L‡	c.842C>T	No	581	-6	No
p.P281L‡§	c.842C>T	p.P281L‡	c.842C>T	No	1317	4	No
p.P281L‡	c.842C>T	p.P281L‡	c.842C>T	No	1020	15	No
p.P281L‡	c.842C>T	p.A300S	c.898G>T	Yes	480	66	Yes positive
p.P281L‡	c.842C>T	p.Y356*‡	c.1068C>G	Yes	1181	38	Yes negative
p.P281L‡§	c.842C>T	p.R413P‡	c.1238G>C	No	921	9	No
p.P281L‡§	c.842C>T	p.R413P‡	c.1238G>C	No	640	-1	No
p.A300S	c.898G>T	p.R408W‡	c.1222C>T	Yes	260	42	Yes positive
p.G352Vfs*48 ‡	c.1055delG	p.G352Vfs*48 ‡	c.1055delG	No	570	60	Yes negative
p.K363Nfs*37 ‡§	c.1089delG	p.K363Nfs*37 ‡	c.1089delG	No	817	3	No
p.K363Nfs*37 ‡§	c.1089delG	p.K363Nfs*37 ‡	c.1089delG	Yes	576	19	No
p.L367Pfs*27 ‡	c.1099_1100insC	p.Y414C	c.1241A>G	No	458	78	Yes positive
p.R408Q††	c.1223G>A	p.R408Q††	c.1223G>A	Yes	315	36	Yes positive
p.Y414C	c.1241A>G	p.Y414C	c.1241A>G	Yes	339	49	Yes positive
† Phe supplementation, ‡ Putative null mutation, § siblings/family, ¶ unclassified mutation, mutation associated with long-term BH4 responsiveness, †† mutation in this study newly associated with long-term BH4 responsiveness, novel mutations are in bold.							