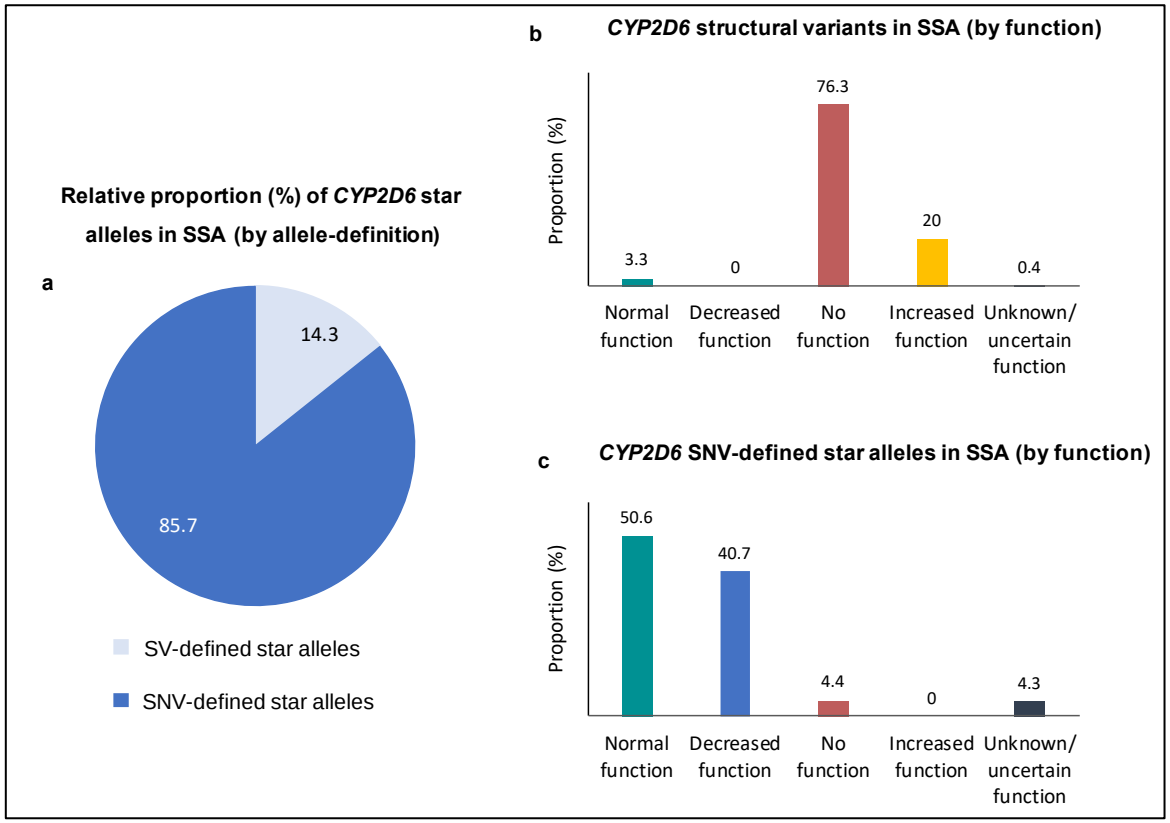
Characterisation of *CYP2D6* pharmacogenetic variation in sub-Saharan African populations

Supplementary Materials

Figure S3: Proportion of *CYP2D6* star alleles defined by structural variants (270 alleles) and core SNVs (1598 alleles) in sub-Saharan African populations



Panel (**a**) shows the relative proportion *CYP2D6* star alleles defined by structural variations (SVs) — e.g. the gene deletion (**5*), gene duplications, hybrids and tandems — compared to the relative proportion alleles defined by various combinations of key SNVs including rs28371706 (**17*), rs61736512 and rs59421388 (**29*), and rs1065852 (**10*). Panel (**b**) depicts the relative proportion of structural variants by function across SSA. *CYP2D6*5* accounts for the high proportion of no function alleles. Normal function SV-defined alleles arise from duplication of decreased function SNV-defined alleles e.g. *CYP2D6*17x2* and **29x2*, while increased function SV-defined alleles mainly include duplications of normal function alleles e.g. *CYP2D6*1xN* and **2xN*. Panel (**c**) shows the relative proportions of SNV-defined alleles grouped by CPIC function. *CYP2D6*17* and **29* account for the high proportion of decreased function alleles across SSA.

Table S3: Full table showing frequencies of all *CYP2D6* star alleles called in all populations in this study (sub-Saharan African and global populations)

		Allele frequencies (%)						
***CYP2D6* allele**	**CPIC function**	**SSA in this study (n=947)**	**Previous SSA studies[a] (n=2248)**	**African American/ Afro-Caribbean (n=157)**	**EUR (n=498)**	**AMR (n=345)**	**SAS (n=481)**	**EAS (n=502)**
**1*	Normal	24.7	7.8	31.5	35.8	45.1	39.5	26
**2*	Normal	13.4	19.8	9.6	15.9	18.3	20.8	7.8
**13+*1*	Normal	0		0	0.1	0	0	0
**13+*2*	Normal	0		0	0.2	0.4	0.1	0
**27*	Normal	0.3	0.5	0.3	0	0.3	0	0
**33*	Normal	0		0	0.6	0.3	0.2	0
**34*	Normal	0.1		0	0	0	0	0
**35*	Normal	0	0	1	4.8	2.6	0.6	0
**39*	Normal	0.1	0	0.3	0.1	0.1	0.4	0.3
**45*	Normal	3.7	4.2	2.2	0	0.3	0	0
**46*	Normal	0.5	0.2	1	0	0.1	0	0
**17x2*	Normal	0.2		0	0	0	0	0
**29x2*	Normal	0.3		0.3	0	0	0	0
**9x2*	Normal	0		0	0.1	0	0	0
**41x2*	Normal	0	0.2	0	0	0	0	0
**68+*2*	Normal	0		0	0.1	0	0.1	0
**83+*2*	Normal	0		0	0	0.1	0	0
**9*	Decreased	0	0	0.3	2.4	1.3	0	0
**10*	Decreased	3.9	5.6	3.8	1.2	1.6	3.5	15.2
**10x2*	Decreased	0	0	0	0	0	0	0.4
**14*	Decreased	0		0	0	0	0	1
**17*	Decreased	19.5	19.3	16.9	0.2	0.9	0	0
**29*	Decreased	10	12.1	5.7	0	0.3	0	0

		Allele frequencies (%)						
***CYP2D6* allele**	**CPIC function**	**SSA in this study (n=947)**	**Previous SSA studies[a] (n=2248)**	**African American/ Afro-Caribbean (n=157)**	**EUR (n=498)**	**AMR (n=345)**	**SAS (n=481)**	**EAS (n=502)**
**36+*10*	Decreased	0		0.3	0	0.1	1.2	34.5
**36+*10.003*	Decreased	0		0	0	0	0	0.1
**36x2+*10*	Decreased	0		0	0	0	0	1.7
**36+*10x2*	Decreased	0		0	0	0	0	0.5
**36+*10≥3*	Decreased	0		0	0	0	0	0.1
**36x2+*10x2*	Decreased	0		0	0	0	0	0.1
**36x2+*10≥3*	Decreased	0		0	0	0	0	0.1
**41*	Decreased	0.8	11.5	2.9	8.5	6.1	11.4	3.4
**49*	Decreased	0	0	0	0	0	0	0.5
**59*	Decreased	0		0	0.2	0.1	0	0
**84*	Decreased	0.1		0.3	0	0	0	0
**3*	No function	0	0.2	1	1.8	0.6	0.2	0
**4*	No function	1.7	3.4	4.1	11.8	9.6	8.2	0.2
**4x2*	No function	2.2		3.8	0.3	0.1	0	0
**4x3*	No function	0.1		0.1	0	0	0	0
**4+*4.013*	No function	0		0	0.7	0	0	0
**5*	No function	8.1	5.2	7	2.4	2.2	2.5	3.5
**6*	No function	0	0	0.3	2.1	0.3	0.1	0
**7*	No function	0	0	0	0	0	0.9	0
**11*	No function	0		0.3	0	0	0	0
**12*	No function	0.2	0.3	0	0	0	0	0
**13*	No function	0.1		0.3	0.2	0.1	0.1	0
**15*	No function	0.2	0.6	0	0	0	0	0
**20*	No function	0		0	0	0	0	0.1
**21*	No function	0	0	0	0	0	0	0.5

		Allele frequencies (%)						
***CYP2D6* allele**	**CPIC function**	**SSA in this study (n=947)**	**Previous SSA studies[a] (n=2248)**	**African American/ Afro-Caribbean (n=157)**	**EUR (n=498)**	**AMR (n=345)**	**SAS (n=481)**	**EAS (n=502)**
**31*	No function	0		0	0.2	0.6	0	0
**36*	No function	0.4		0.3	0	0	0	0.2
**36x2*	No function	0		0	0	0	0	0.3
**40*	No function	1.4	1.3	0.3	0	0	0	0
**42*	No function	0.1		0	0	0	0	0
**56*	No function	0.2		0	0	0	0	0
**69*	No function	0.1		0	0.1	0	0.2	0.3
**68*	No function	0		0	0	0.1	0.1	0
**68+*4*	No function	0.1		1	5.7	2.6	2.2	0
**68x2+*4*	No function	0		0	0	0.3	0	0
**99*	No function	0		0	0	0	0.2	0
**1x2*	Increased	0.4	1.1	0.3	0.5	1.2	0.6	0.3
**1x3*	Increased	0.2		0	0	0.1	0	0
**1x2+*83*	Increased	0		0	0	0	0.1	0
**2x2*	Increased	1.9	1.7	1.3	1.5	0.6	0.4	0.5
**2x3*	Increased	0.1		0	0.1	0	0	0.1
**2x4*	Increased	0.2		0	0	0	0	0
**35x2*	Increased	0	0	0	0	0.1	0	0
**45x2*	Increased	0.1		0	0	0	0	0
**45x3*	Increased	0.1		0	0	0	0	0
**1+*90*	Uncertain	0		0	0	0	0	0.1
**22*	Uncertain	0		0	0.3	0	0	0
**28*	Uncertain	0	0	0	0.5	0.1	0	0
**32*	Uncertain	0	0.3	0	0.3	0	0.2	0
**43*	Uncertain	0.8	1.7	1	0.1	0	1	0

		Allele frequencies (%)						
***CYP2D6* allele**	**CPIC function**	**SSA in this study (n=947)**	**Previous SSA studies[a] (n=2248)**	**African American/ Afro-Caribbean (n=157)**	**EUR (n=498)**	**AMR (n=345)**	**SAS (n=481)**	**EAS (n=502)**
**43x2*	Uncertain	0.1		0	0	0.1	0	0
**52*	Uncertain	0	0.8	0	0	0	0	0.1
**71*	Uncertain	0		0	0	0	0	0.6
**73*	Unknown	0.2	0.5	0	0	0	0	0
**74*	Unknown	0.1	0.5	0	0	0	0	0
**82*	Unknown	0		0	0	0.4	0	0
**86*	Unknown	0		0	0	0	2.3	0
**106*	Unknown	1.5		0	0	0.1	0	0
**108*	Unknown	0		0	0.3	0	0	0
**111*	Unknown	0		0	0.4	0	0.8	0
**112*	Unknown	0		0	0	0	0.2	0
**113*	Unknown	0		0	0	0	0.8	0
**117*	Unknown	0		0	0.4	0	0	0
**119*	Unknown	0		0	0	0	0	0.1
**121*	Unknown	0		0.3	0	0	0	0
**122*	Unknown	0.1		0.3	0	0	0	0
**125*	Unknown	0.3		0.3	0	0	0	0
**139*	Unknown	0.1		0	0	0	0.1	0
**144*	Unknown	0		0	0	0	0	0.1
**149*	Unknown	0.3		0	0	0	0	0.1

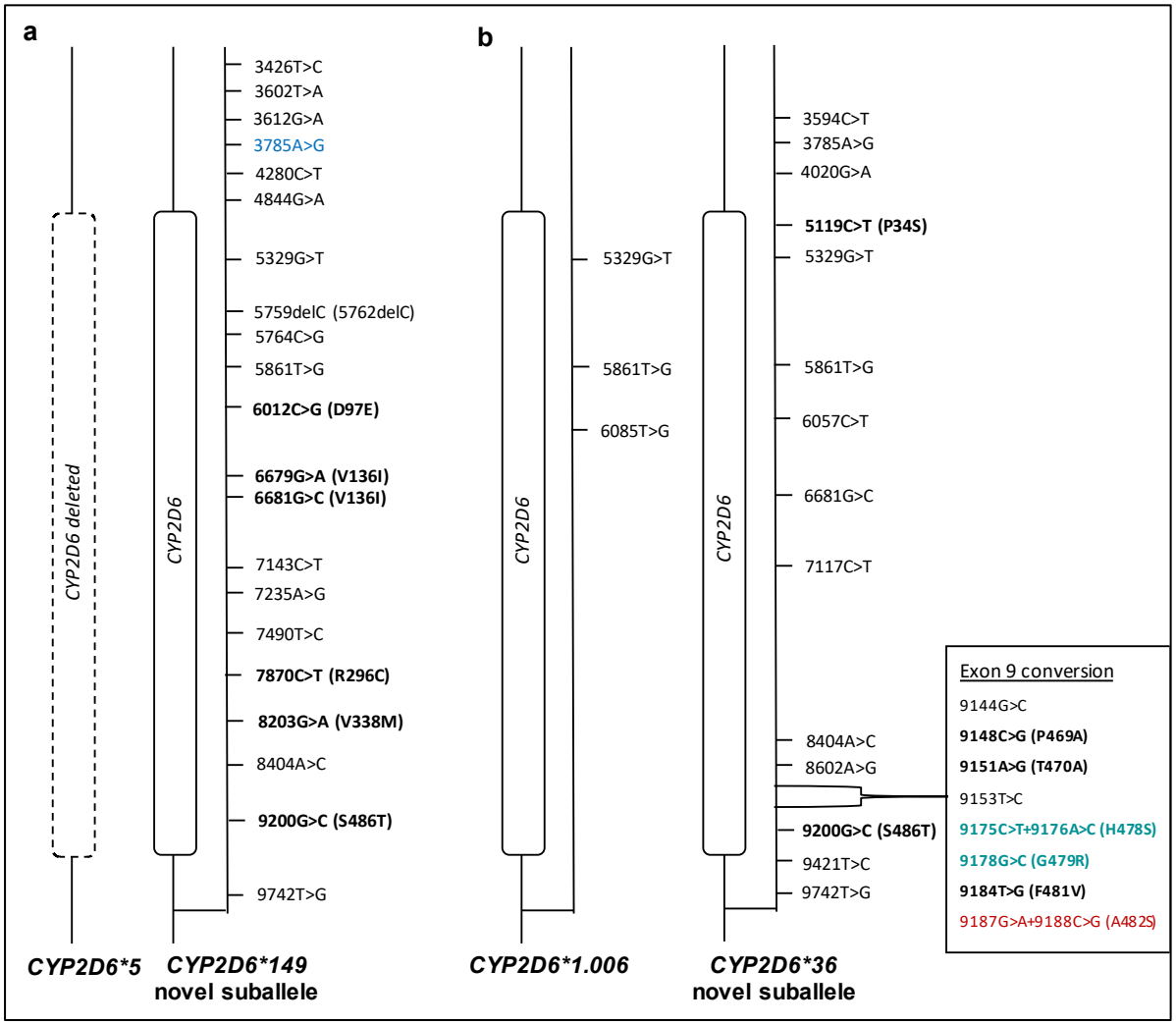
n, individuals; SSA; sub-Saharan African participants; EUR, European participants; SAS, South Asian participants; EAS, East Asian participants; CPIC, Clinical Pharmacogenetics Implementation Consortium; PharmGKB, Pharmacogenomics Knowledge Base; [a] See PharmGKB and CPIC *CYP2D6* reference materials (https://www.pharmgkb.org/page/cyp2d6RefMaterials)

Table S4: Unresolved *CYP2D6* diplotypes with potential novel alleles in sub-Saharan African populations

#	Background alleles	Additional core variant(s)	Variant type	Number of participants	Country/dataset [a]
1	**1/*43*	rs61731586~8330G>A	Missense (R380H)	1	Nigeria (1000G)
2	**2/*4*	rs61736512 6679G>A; possible *CYP2D6* duplication	Missense (V136M)	1	Sierra Leone (1000G)
3	**2/*17*	rs778690377~6968C>T	Missense (L203F)	1	Kenya (1000G)
4	**2/*17*	rs373243894~5141C>T	Missense (P41L)	1	Kenya (1000G)
5	**2/*29*	rs556882139~6879G>A	Missense (R173H)	1	Gambia (1000G)
6	**2/*139*	rs566108360~8209G>C + rs1135829~7838A>G; possible *CYP2D6* duplication	Missense (G340R, N285S)	1	Congo (SGDP)
7	**17/*29*	rs532668079~9065G>A	Missense (R441H)	1	Nigeria (1000G)
8	**1/*2*	**4, *17*, and **29*-defining variants in the same sample		1	South Africa
9	**1/*2*	Possible **68*-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	Structural variant	1	South Africa
10	**1/*2*	Duplicated *CYP2D6* haplotype (**1* + rs565013903~7600G>A)	Structural variant	1	Namibia (SGDP)
11	**45/*46*	Possible **68*-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	Structural variant	1	Gambia (1000G)
12	**29/*45*	Possible **68*-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	Structural variant	1	Kenya (1000G)
13	**45/*45*	Possible **68*-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	Structural variant	1	Kenya (1000G)

SGDP, Simons Genome Diversity Project; 1000G, 1000 Genomes Project; [a] IDs for Coriell and SGDP samples are provided in Table S5 as these samples can potentially be used as reference materials.

Figure S4: Examples of novel and confirmatory *CYP2D6* suballeles in SSA characterised via XL-PCR and HiFi sequencing



Panel (**a**) shows a novel *CYP2D6*149* suballele from this study. *CYP2D6*149* is defined by rs76802407 (D97E) in phase with the **29*-defining variants, and it has recently been assigned a novel major star allele status (with definitive evidence) by PharmVar (https://www.pharmvar.org). The allele depicted here differs from *CYP2D6*149.001* as it has the NG_008376.4:g.3785A>G variant. Panel (**b**) shows a novel *CYP2B6*36* suballele called in a participant from Burkina Faso. HiFi data facilitated the detection of the exon 9 conversion SNVs. However, some of these SNVs were not called by the variant detection tool DeepVariant possibly due to lack of sufficient read support. The SNVs indicated in teal were observed during manual inspection in the Integrative Genomics Viewer (IGV) while there were virtually no reads supporting the SNVs indicated in red text. These haplotypes are currently under review by PharmVar and could instead be integrated as confirmatory suballeles if appropriate.

Table S5: Sample information for participants with publicly available high coverage WGS data containing potential novel *CYP2D6* star alleles. The Coriell DNA samples from these participants could potentially be added to GeT-RM reference materials for *CYP2D6* genotyping in pharmacogenomics testing laboratories.

Coriell/SGDP IDs	Predicted Consensus Diplotype	Country/ population	Primary project
HG02570	*1/[*1+rs140900383~7471C>T (A226V)]	GWD	1000G
LP6005441-DNA_A11	[*2/*1 + rs565013903~7600G>A (R269P)]; (cn=3)	Namibia	SGDP
LP6005443-DNA_G08	[*1+rs565013903~7600G>A]/[*1+rs565013903~7600G>A]	Namibia	SGDP
HG03428	*5/[*1+rs567606867~7004G>A (E215K)]	MSL	1000G
NA19468	*1/[*2+rs368858603~7609_7610insA (fs)]	LWK	1000G
SS6004471	*2/[*2 + rs368858603~7609_7610insA (fs) + rs374616348~6628G>T (V119L)]	Congo	SGDP
NA19314	*5/[*2 + rs28371704~6002A>G (H94R) + rs28371703~5992C>A (L91M)]	LWK	1000G
HG03559	*2/[*2+rs376636053~6655T>C (W128R)]	MSL	1000G
HG03469	*2/[*2+rs769157652~8873G>A (E410K)]	MSL	1000G
LP6005592-DNA_C05	*5/[*17+rs1450231864~8231T>C (M347T)]	South Africa	SGDP
HG02666	*1/[*29 + rs76802407~6012C>G (D97E)]	GWD	1000G
HG02870	*1/[*29+rs76802407~6012C>G (D97E)]	GWD	1000G
HG03442	*2x2/[*29 + rs76802407~6012C>G (D97E)]	MSL	1000G
NA18933	*5/[*29+rs201006451~6767C>T (A165V)]	YRI	1000G
HG02840	*17/[*29+rs536109057~5173C>T (stop-gained)]	GWD	1000G
HG02860	*2/[*29+rs536109057~5173C>T (stop-gained)]	GWD	1000G
NA19130	*106/[*29+rs760940331~9096G>A (M451I)]	YRI	1000G
HG02807	*17/[*29+rs760940331~9096G>A (M451I)]	GWD	1000G
NA19316	*2/[*41 + rs141824015~8206A>C (I339L)]	LWK	1000G
HG02623	*2/[*45 + rs3915951~8177G>T (R329L)]	GWD	1000G
HG02642	*17/[*45 + rs3915951~8177G>T (R329L)]	GWD	1000G
NA19222	[*1/*43] + rs61731586~8330G>A (R380H)	YRI	1000G
HG03470	[*2/*4] + rs61736512~6679G>A (V136M); cn=3	MSL	1000G
NA19472	[*2/*17] + rs778690377~6968C>T (L203F)	LWK	1000G
NA19026	[*2/*17] + rs373243894~5141C>T (P41L)	LWK	1000G
HG02852	[*2/*29] + rs556882139~6879G>A (R173H)	GWD	1000G
LP6005441-DNA_A08	[*2/*139] + rs566108360~8209G>C (G340R) + rs1135829~7838A>G (N285S)	Congo	SGDP
HG03313	[*17/*29] + rs532668079~9065G>A (R441H)	ESN	1000G
HG02621	[*45/*46] + Possible *68-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	GWD	1000G
NA19017	[*29/*45] + Possible *68-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	LWK	1000G
NA19456	[*45/*45] + Possible *68-like *CYP2D6/2D7* hybrid (lacking 5119C>T)	LWK	1000G

cn, copy number; fs, frameshift; 1000G, 1000 Human Genomes Project; SGDP, Simons Genome Diversity Project; ESN, Esan in Nigeria; LWK, Luhya in Webuye Kenya; GWD, Gambian from Western Divisions (Mandinka); MSL, Mende in Sierra Leone; YRI, Yoruba in Ibadan, Nigeria; GeT-RM, Genetic Testing Reference Materials Coordination Program.

Table S6: VEP plugin predictions of the deleteriousness of core variants defining potential novel African ancestry *CYP2D6* star alleles identified in the study.

Core variants	Consequence	CADD	SIFT/ SIFT Indel	Polyphen-2	LRT	PROVEAN	VEST	LOFTEE	Consensus
rs140900383	Missense (A226V)								
rs141756339	Missense (R474Q)								
rs565013903	Missense (R269P)	X	X	X	X	X	X		X
rs567606867	Missense (E215K)						X		
rs368858603	Frameshift (T272TX)		X					X	X
rs374616348	Missense (V119L)								
rs28371704	Missense (H94R)					X			
rs28371703	Missense (L91M)	X	X	X	X				X
rs375715419	Missense (T458A)	X	X		X	X			X
rs376636053	Missense (W128R)	X	X	X		X	X		X
rs769157652	Missense (E410K)	X							
rs747089665	Missense (R414C)	X				X			
rs1450231864	Missense (M347T)	X		X	X	X	X		X
rs201006451	Missense (A165V)						X		
rs536109057	Stop-gained (Q52*)							X	
rs760940331	Missense (M451I)	X	X	X	X	X	X		X
rs141824015	Missense (I339L)			X	X		X		X
rs3915951	Missense (R329L)	X	X						
rs61731586	Missense (R380H)	X			X	X	X		X
rs61736512	Missense (V136I)								
rs778690377	Missense (L203F)			X					
rs373243894	Missense (P41L)	X	X	X	X	X	X		X
rs556882139	Missense (R173H)	X	X						
rs532668079	Missense (R441H)	X	X	X	X	X	X		X
rs566108360	Missense (G340R)	X	X	X	X	X	X		X
rs1135829	Missense (N285S)					X			

X, indicates that the variant was predicted to be deleterious by the corresponding plugin; CADD, Combined Annotation Dependent Depletion; SIFT, Sorting Intolerant from Tolerant; Polyphen-2, Polymorphism Phenotyping (version 2); LRT, Likelihood Ratio Test; PROVEAN, Protein Variation Effect Analyzer; VEST, Variant Effect Scoring Tool (version 4); LOFTEE, Loss-Of-Function Transcript Effect Estimator. For each plugin a variant was considered deleterious if the scores met the following ADME-optimised thresholds suggested by Zhou et al. (2017): CADD PHRED (>19.19), SIFT (<0.0376), Polyphen-2 (>0.3841), LRT (<0.0025), PROVEAN (<-3.28), VEST4 (>0.4534). The consensus indicates a deleteriousness prediction where at least half the plugins used to assess the variant predicted it to be deleterious.

References:

Zhou, Y., Mkrtchian, S., Kumondai, M., Hiratsuka, M. and Lauschke, V. M. (2019). An optimized prediction framework to assess the functional impact of pharmacogenetic variants. *Pharmacogenomics J* 19, 115–126.

Table S7: Potential novel *CYP2D6* star alleles identified in participants from global biogeographical groups included for comparison in the study. The Coriell DNA samples from these participants could potentially be added to GeT-RM reference materials for *CYP2D6* genotyping in pharmacogenomics testing laboratories.

Coriell IDs	Predicted Consensus Diplotype	Population	Primary project
HG02318	*1/[*1+rs575708064~8332G>A (D381N)]	ACB	1000G
HG01491, HG01372, HG01149, HG01072 HG01086 HG01363	*1/[*1 + rs538707090~6935G>A (G192R)] *31/[*1 + rs538707090~6935G>A (G192R)] *2/[*1 + rs538707090~6935G>A (G192R)]	AMR	1000G
HG01139, HG01341 HG01551 HG01133	*4/[*2 + rs28371696~5096G>A (R26H)] *5/[*2 + rs28371696~5096G>A (R26H)] *2/[*2 + rs28371696~5096G>A (R26H)]	AMR	1000G
HG01565	*1/[*1 + rs563185985~6058G>A (G113R)]	AMR	1000G
HG01992	*1/[*1 + rs534682262~7609C>T (T272I)]	AMR	1000G
NA19750	*1/[*1 + rs1135828~7630T>A (M279K)]	AMR	1000G
HG01101	*41/[*2 + rs538036869~8916A>C (Q424P)]	AMR	1000G
HG01097	*31/[*13 + (*2 + rs78762568~8867G>A; V408I)]	AMR	1000G
HG01257	*2/[*2 + rs565444796~5909G>A (R63H)]	AMR	1000G
HG01403	[*1/*2] + rs544790460~7461G>T (V223L)	AMR	1000G
HG01083	[*1/*2] + rs376636053~6655T>C (W128R)	AMR	1000G
NA20320	*5/[*2 + rs146819268~7518C>T (R242C)]	ASW	1000G
NA20340	*29/[*29 + rs76802407~6012C>G (D97E)] now *CYP2D6*149*	ASW	1000G
HG02384, HG00693, NA18559	*1/[*1 + rs769258~5050G>A (V11M)]	EAS	1000G
NA19074	*5/[*10 + rs3915951~8177G>T (R329L)]	EAS	1000G
HG02379	*36+10/[*1 + rs567606867~7004G>A (E215K)]	EAS	1000G
HG01600, HG02121	*36x2+*10/[*10 + rs774778807~6907_6909delGAG (S183del)]	EAS	1000G
NA18641	*36+*10/[*1 + rs528725654~6776C>A (S168Y)]	EAS	1000G

HG00542	*36+*10/[*1 + rs770277909~6725A>G (Q151R)]	EAS	1000G
HG02026	*36+*10/[*10 + new_rsID~8823delCAAGGGA]	EAS	1000G
NA18630	*36+*10/[*2 + rs1135822~6631T>A (F120I) + rs1135823~6637G>T (A122S)]	EAS	1000G
HG00566	*36+*10/[*2 + rs377591409~6638C>T (A122V)]	EAS	1000G
NA18942	*2/[*2 + rs78762568~8867G>A (V408I)]	EAS	1000G
HG02187	*10/[*1 + rs140513104~7958C>T (P325L)]	EAS	1000G
NA19682	*10/[*1 + rs28371703~5992C>A (L91M) + rs28371704~6002A>G (H94R)]	EAS	1000G
HG00595	[*10/*36x2+*83+*10] (unresolved diplotype)	EAS	1000G
HG00458	[*1/*36xN+*10xN] – unresolved diplotype	EAS	1000G
HG00346	*1/[*1 + rs199722016~9212A>G (T490C)]	EUR	1000G
NA12872	*9/[*35 + rs1058172~8285G>A (R365H)]	EUR	1000G
NA12776	*1x2/[*1 + rs200234159~7946T>C (M321T)]	EUR	1000G
NA20815	[*41/*9] + rs3915951~8177G>T (R329L)	EUR	1000G
NA11919	[*10/*2] + rs371793722~7017T>C (F219S)	EUR	1000G
NA20798	[*1/*41] + rs141289473~7942C>T (L320F)	EUR	1000G
NA11830	[*1/*4] + rs138229048~9129G>C (Q462H)	EUR	1000G
HG01785	[*1/*2] + rs150216909~7969C>T (R329C)	EUR	1000G
HG03941	*1/[*1 + rs566833518~9227T>C (V495A)]	SAS	1000G
HG03709	*1/[*1 + rs3021084~8934C>T (P430L)]	SAS	1000G
HG02774	*86/[*2 + rs777691989~7480delTCC (L231del)]	SAS	1000G
HG03870	*41/[*41 + rs565013903~7600G>A (R269Q)]	SAS	1000G
HG04214	*2/[*1 + rs267608295~8218C>T (R343W)]	SAS	1000G
HG03803	*13/[*1 + rs542114265~8232G>A (M347I)]	SAS	1000G
HG04182	[*2/*41] + rs149686350~8298C>G (I369M)	SAS	1000G
HG03898	[*2/*41] + rs1135823~6637G>T (A122S)	SAS	1000G
HG03772	[*2/*4] + rs567340138~7840C>A (P286T)	SAS	1000G

HG04014	[*2/*4] + rs558523758~7563G>C (E257Q)	SAS	1000G
HG03593	[*1/*41] + rs1135830~7916C>T (stop-gained)	SAS	1000G
HG03800	[*1/*2] + rs544811063~8324C>T (T378I)	SAS	1000G
HG04194	[*1/*2] + rs531010318~7013G>C (G218R)	SAS	1000G
HG03802	[*1/*10] + rs556882139~6879G>A (R173H)	SAS	1000G
HG04002	*2/(*1x2+*83) – unresolved diplotype	SAS	1000G
HG02778, NA07347	*1/(*68-like + *2); has intron 1 breakpoint; lacks rs1065852	SAS, EUR	1000G

cn, copy number; fs, frameshift; 1000G, 1000 Human Genomes Project; GeT-RM, Genetic Testing Reference Materials Coordination Program; ACB, African Caribbean in Barbados; ASW, People with African Ancestry in Southwest USA; EUR, European participants; AMR, Admixed American participants; EAS, East Asian participants; SAS, South Asian participants.