

**Table 1S.** Mutation data from the UniProt humsavar database used for the training dataset (TS270).

UniProt ID Gene	Mutation	dbSNP identifier	Disease
P05108 CYP11A1	L141W	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	A189V	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	L222P	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	E314K	rs6161	-
	R353W	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	A359V	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	V415E	-	Adrenal insufficiency congenital with 46,XY sex reversal (AICSR) [MIM:613743]
	P15538 CYP11B1	C10Y	rs6405
P42S		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
R43Q		rs4534	-
D63H		rs5282	-
P94L		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
N133H		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
M160I		rs5287	-
K173R		rs4539	-
T248I		rs34620645	-
F257L		rs5288	-
S281N		rs5291	-
L293V		rs5292	-
T318M		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
T318R		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
T319M		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
A348T		rs6407	-
R374Q		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
G379V		-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
A386V		rs4541	-
R404H		rs4998896	-
Y439H		rs5294	-
R448H		rs28934586	Adrenal hyperplasia type 4 (AH4) [MIM:202010]

	R454C	-	Adrenal hyperplasia type 4 (AH4) [MIM:202010]
	F494C	-	-
P19099 CYP11B2	A29T	rs6438	-
	R30Q	rs6441	-
	K173R	rs4539	-
	R181W	rs28931609	Corticosterone methyloxidase type 2 deficiency (CMO-2 deficiency) [MIM:610600]
	T185I	-	Corticosterone methyloxidase type 2 deficiency (CMO-2 deficiency) [MIM:610600]
	E198D	-	Corticosterone methyloxidase type 2 deficiency (CMO-2 deficiency) [MIM:610600]
	N222T	rs5308	-
	I248T	rs4547	-
	N281S	rs4537	-
	I339T	rs4544	-
	E383V	rs5312	-
	V386A	rs4541	Corticosterone methyloxidase type 2 deficiency (CMO-2 deficiency) [MIM:610600]
	V403E	rs5315	-
	G435S	rs4545	-
	L461P	-	Corticosterone methyloxidase type 1 deficiency (CMO-1 deficiency) [MIM:203400]
	F487V	rs5317	-
	T498A	-	Corticosterone methyloxidase type 2 deficiency (CMO-2 deficiency) [MIM:610600]
P05093 CYP17A1	C22W	rs762563	-
	P35L	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	Y64S	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	F93C	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R96W	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	S106P	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	F114V	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	D116V	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	N177D	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	Y329D	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	P342T	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R347H	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]

	R347C	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R358Q	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R362C	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	H373L	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	W406R	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	F417C	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	P428L	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R440H	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R496C	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
	R496H	-	Adrenal hyperplasia type 5 (AH5) [MIM:202110]
P11511 CYP19A1			
	W39R	rs2236722	-
	T201M	rs28757184	-
	R264C	rs700519	-
	R365Q	-	Aromatase deficiency (AROD) [MIM:613546]
	R375C	-	Aromatase deficiency (AROD) [MIM:613546]
	R375L	-	-
	R435C	-	Aromatase deficiency (AROD) [MIM:613546]
	C437Y	-	Aromatase deficiency (AROD) [MIM:613546]
Q16678 CYP1B1			
	S28W	-	Primary open angle glaucoma (POAG) [MIM:137760]
	R48G	rs10012	-
	P52L	-	-
	W57C	-	Primary open angle glaucoma (POAG) [MIM:137760]
	G61E	rs28936700	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
	Q68R	rs9282670	-
	L77P	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
	Y81N	rs9282671	Primary open angle glaucoma (POAG) [MIM:137760]
	A115P	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
	A119S	rs1056827	-
	M132R	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
	Q144H	-	-

Q144P	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
Q144R	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R145W	-	Primary open angle glaucoma (POAG) [MIM:137760]
G184S	-	-
D192V	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
P193L	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
V198I	rs59472972	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
N203S	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
S206N	rs9341248	-
S215I	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
E229K	rs57865060	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
G232R	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
S239R	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R266L	rs9341250	-
V320L	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
A330F	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
L345F	-	Primary open angle glaucoma (POAG) [MIM:137760]
V364M	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
G365W	rs55771538	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R368H	rs28936414	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
D374N	rs28936413	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
P379L	rs56305281	-
E387K	rs55989760	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
A388T	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R390H	rs56010818	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R390C	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R390S	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
I399S	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
V409F	-	Primary open angle glaucoma (POAG) [MIM:137760]
V422G	-	-

N423Y	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
L432V	rs1056836	-
P437L	rs56175199	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
D441H	rs4986887	-
A443G	rs4986888	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]; Primary open angle glaucoma (POAG) [MIM:137760]
R444Q	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
F445C	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
D449E	rs1056837	-
N453S	rs1800440	-
G466D	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
R469W	rs28936701	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
E499G	-	Primary congenital glaucoma type 3A (GLC3A) [MIM:231300]
S515L	-	Primary open angle glaucoma (POAG) [MIM:137760]
V518A	-	-
R523T	-	Primary open angle glaucoma (POAG) [MIM:137760]
D530G	-	Primary open angle glaucoma (POAG) [MIM:137760]

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A15T	rs63749090	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
P30L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
P30Q	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G56R	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
H62L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G64E	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
I77T	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G90V	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
K98R	-	-
K102R	-	-
P105L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
L107R	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
K121Q	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R124H	rs72552750	Adrenal hyperplasia type 3 (AH3) [MIM:201910]

L142P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
L167P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
C169Y	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
I172N	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G178A	rs72552751	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
D183E	rs1040310	-
V211L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
I230T	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R233K	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
I236N	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
V237E	rs12530380	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
M239K	rs6476	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
L261P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
S268T	rs6472	-
V281L	rs6471	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
V281G	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
M283L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G291S	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G291R	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G291C	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
G292D	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
L300F	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
S301Y	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
L317M	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
E320K	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R339H	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R341W	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R341P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R354C	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R354H	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R356P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R356Q	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
R356W	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]

	A362V	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	L363W	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	H365Y	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R369W	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	E380D	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R408C	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	G424S	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R426H	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R435C	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	P453S	rs6445	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R479L	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	P482S	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R483P	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R483Q	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	R483W	-	Adrenal hyperplasia type 3 (AH3) [MIM:201910]
	N493S	rs6473	-
Q07973 CYP24A1			
	R157Q	rs35051736	-
	R159Q	-	Hypercalcemia infantile (HCAI) [MIM:143880]
	E322K	-	Hypercalcemia infantile (HCAI) [MIM:143880]
	M374T	rs6022990	-
	R396W	-	Hypercalcemia infantile (HCAI) [MIM:143880]
	L409S	rs6068812	Hypercalcemia infantile (HCAI) [MIM:143880]
Q9NR63 CYP26B1			
	S146P	-	Radiohumeral fusions with other skeletal and craniofacial anomalies (RHFCA) [MIM:614416]
	V181M	-	-
	A185V	-	-
	R191H	-	-
	D227N	-	-
	L264S	rs2241057	-
	R363L	-	Radiohumeral fusions with other skeletal and craniofacial anomalies (RHFCA) [MIM:614416]

	E380K	rs2286965	-
	A420G	rs7568553	-
	R473C	-	-
	V479I	-	-
Q02318 CYP27A1	G145E	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	A169V	rs59443548	-
	T175M	rs2229381	-
	R395C	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	R395S	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	R405Q	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	R474Q	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	R474W	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
	R479C	-	Cerebrotendinous xanthomatosis (CTX) [MIM:213700]
O15528 CYP27B1	Q65H	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R107H	rs28934604	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	G125E	rs28934605	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	V166L	rs8176344	-
	E189G	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	E189K	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	T321R	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	S323Y	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R335P	rs28934606	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	L343F	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	P382S	rs28934607	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R389H	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R389G	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R389C	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	T409I	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R429P	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	R453C	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	V478G	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]



Q6VVX0 CYP2R1	P497R	-	Rickets vitamin D-dependent type 1A (VDDR1A) [MIM:264700]
	L99P	rs61495246	Rickets vitamin D-dependent type 1B (VDDR1B) [MIM:600081]
Q6NT55 CYP4F22	F59L	-	Ichthyosis lamellar type 3 (LI3) [MIM:604777]
	S178C	rs16980531	-
	R243H	-	Ichthyosis lamellar type 3 (LI3) [MIM:604777]
	R372W	-	Ichthyosis lamellar type 3 (LI3) [MIM:604777]
	H435Y	-	Ichthyosis lamellar type 3 (LI3) [MIM:604777]
	H436D	-	Ichthyosis lamellar type 3 (LI3) [MIM:604777]
	K505Q	rs7256787	-
	Q6ZWL3 CYP4V2	L22V	rs1055138
W44R		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
G61S		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
E79D		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
I111T		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
M123V		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
S213N		rs34331648	-
Q259K		rs13146272	-
E275K		rs34745240	-
H331P		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
S341P		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
V372I		-	-
R443Q		-	-
R508H		-	Bietti crystalline corneoretinal dystrophy (BCD) [MIM:210370]
O75881 CYP7B1		G57R	-
	F216S	-	Spastic paraplegia autosomal recessive type 5A (SPG5A) [MIM:270800]
	S363F	-	Spastic paraplegia autosomal recessive type 5A (SPG5A) [MIM:270800]
	R417H	-	Spastic paraplegia autosomal recessive type 5A (SPG5A) [MIM:270800]