

ABCmdb reloaded: updates on mutations in ATP Binding Cassette proteins

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Supporting Information

Table S1. Variations queried from ClinVar. Genetic alterations were filtered and categorized as missense, nonsense, and synonymous mutations. Genes were ordered by the number of variations. D: deleterious, N: neutral, ?: unspecified.

gene	all	coding	unique	synonymous total	missense				nonsense			
					D	N	?	total	D	N	?	total
CFTR	901	747	731	38	100	10	440	550	52	0	91	143
ABCA4	476	372	370	52	28	10	234	272	7	0	39	46
ABCC9	115	91	91	33	14	2	38	54	1	1	2	4
ABCC8	66	49	49	16	24	3	2	29	4	0	0	4
ABCD1	50	43	43	4	28	0	5	33	6	0	0	6
ABCA3	27	26	26	7	6	1	11	18	1	0	0	1
ABCC2	25	20	20	5	4	6	3	13	2	0	0	2
ABCC6	23	21	21	1	13	3	1	17	3	0	0	3
ABCB4	21	19	19	2	6	2	7	15	2	0	0	2
ABCC1	21	5	5	2	0	0	3	3	0	0	0	0
ABCA1	15	14	14	0	12	0	1	13	1	0	0	1
ABCB11	15	14	14	4	2	3	3	8	2	0	0	2
ABCG8	13	12	12	1	3	1	3	7	4	0	0	4
ABCB7	11	9	9	2	5	2	0	7	0	0	0	0
ABCG5	10	9	9	1	2	0	2	4	4	0	0	4
ABCB6	9	9	9	0	6	0	2	8	1	0	0	1
ABCA12	8	8	8	0	7	0	0	7	1	0	0	1
ABCB1	5	5	5	1	1	3	0	4	0	0	0	0
ABCG2	5	5	5	0	0	0	2	2	1	0	2	3
TAP1	3	3	3	0	1	2	0	3	0	0	0	0
TAP2	3	3	3	0	0	2	0	2	0	1	0	1
ABCC4	1	1	1	0	0	0	1	1	0	0	0	0
ABCC5	1	1	1	0	0	0	1	1	0	0	0	0
ABCD3	1	1	1	0	0	0	1	1	0	0	0	0
ABCD4	1	1	1	0	1	0	0	1	0	0	0	0
ABCG4	1	1	1	0	0	0	1	1	0	0	0	0
ABCA5	1	0	0	0	0	0	0	0	0	0	0	0
ABCA10	0	0	0	0	0	0	0	0	0	0	0	0
ABCA13	0	0	0	0	0	0	0	0	0	0	0	0
ABCA2	0	0	0	0	0	0	0	0	0	0	0	0
ABCA6	0	0	0	0	0	0	0	0	0	0	0	0
ABCA7	0	0	0	0	0	0	0	0	0	0	0	0
ABCA8	0	0	0	0	0	0	0	0	0	0	0	0
ABCA9	0	0	0	0	0	0	0	0	0	0	0	0
ABCB10	0	0	0	0	0	0	0	0	0	0	0	0
ABCB5	0	0	0	0	0	0	0	0	0	0	0	0
ABCB8	0	0	0	0	0	0	0	0	0	0	0	0
ABCB9	0	0	0	0	0	0	0	0	0	0	0	0
ABCC10	0	0	0	0	0	0	0	0	0	0	0	0
ABCC11	0	0	0	0	0	0	0	0	0	0	0	0
ABCC12	0	0	0	0	0	0	0	0	0	0	0	0
ABCC3	0	0	0	0	0	0	0	0	0	0	0	0
ABCD2	0	0	0	0	0	0	0	0	0	0	0	0
ABCG1	0	0	0	0	0	0	0	0	0	0	0	0

Table S2. Performance of SNAP2 and PROVEAN does not increase largely and consequently for the conserved nucleotide binding domains as compared to curated mutations from databases.

NBD:

gene	effect	curated	SNAP2	PROVEAN
ABCB11/BSEP	deleterious	75	52 (69%)*	54 (72%)
	neutral	18	7 (39%)	6 (33%)
	unspecified	5		
ABCC6/MRP6	deleterious	79	55 (70%)	56 (71%)
	neutral	0		
	unspecified	0		
ABCC7/CFTR	deleterious	121	63 (52%)	70 (58%)
	neutral	14	4 (29%)	6 (43%)
	unspecified	213		

TMD:

gene	effect	curated	SNAP2	PROVEAN
ABCB11/BSEP	deleterious	57	37 (65%)	36 (63%)
	neutral	26	17 (65%)	10 (38%)
	unspecified	8		
ABCC6/MRP6	deleterious	71	50 (70%)	49 (69%)
	neutral	1	0 (0%)	0 (0%)
	unspecified	0		
ABCC7/CFTR	deleterious	151	91 (60%)	68 (45%)
	neutral	7	1 (14%)	4 (57%)
	unspecified	279		

* The number of correctly predicted mutation effects (true positive hits)

Table S3. Significant portion of conservative and non-conservative amino acid replacements can lead to deleterious and neutral changes, respectively. Variants with premature stop and silent amino acid changes were not counted.

a.a. change:	conservative		non-conservative	
	deleterious	neutral	deleterious	neutral
ABCB11/BSEP	51% (25/49)	49% (24/49)	80% (105/131)	20% (26/131)
ABCC6/MRP6	100% (39/39)	0% (0/39)	98% (117/120)	3% (3/120)
ABCC7/CFTR	87% (48/55)	13% (7/55)	94% (206/218)	6% (12/218)

Figure S1. The major changes in the web interface associated with novel data, such as predicted effect of mutations by SNAP2 and PROVEAN, effect of mutations collected from databases (top panel), and mutations in non-coding regions (bottom panel).

ABCMdb: Database for Mutations in ABC proteins

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Mutations in ABCG2

reference sequence

Region	Mutation	Publications	Sentences	MutMiner_hits	SNAP2	PROVEAN	Effect_dbs
CL0	p.Ser 2 Ala details homologous mutations	1	1	1	N	N	?
CL0	p.Val 12 Met details homologous mutations	146	660	725	N	N	?
CL0	p.Val 12 Asn details homologous mutations	2	4	4	D	N	?
CL0	p.Ser 13 Leu details homologous mutations	1	6	7	D	N	?
CL0	p.Gly 15 Trp details homologous mutations	2	2	2	D	N	?
CL0	p.Thr 17 Asn details homologous mutations	1	1	1	N	N	?
CL0	p.Ala 24 Val details homologous mutations	5	5	5	N	N	?
CL0	p.Ser 25 Pro details homologous mutations	1	1	1	N	N	?
CL0	p.Ser 25 Arg details homologous mutations	1	1	1	N	N	?
CL0	p.Phe 31 Ser details homologous mutations	1	1	1	N	N	?
CL0	p.Phe 31 Trp details homologous mutations	2	2	2	N	N	?
CL0	p.Gly 34 Ala details homologous mutations	71	298	323	N	D	?

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Browse

ABCA [show]

ABCB [hide]

ABCB1	[mined mutations (mm)]	[map mm]	[m in coding regions]	[TF binding sites]
ABCB2	[mined mutations (mm)]	[map mm]	[m in coding regions]	
ABCB3	[mined mutations (mm)]	[map mm]	[m in coding regions]	
ABCB4	[mined mutations (mm)]	[map mm]	[m in coding regions]	[m in non-coding regions]
ABCB5	[mined mutations (mm)]	[map mm]		
ABCB6	[mined mutations (mm)]	[map mm]	[m in coding regions]	
ABCB7	[mined mutations (mm)]	[map mm]	[m in coding regions]	[m in non-coding regions]
ABCB8				
ABCB9	[mined mutations (mm)]	[map mm]		
ABCB10	[mined mutations (mm)]	[map mm]		
ABCB11	[mined mutations (mm)]	[map mm]	[m in coding regions]	[m in non-coding regions] [TF binding sites]

ABCC [show]

ABCD [show]

ABCG [hide]

ABCG1	[mined mutations (mm)]	[map mm]		
ABCG2	[mined mutations (mm)]	[map mm]	[m in coding regions]	[TF binding sites]
ABCG4			[m in coding regions]	
ABCG5	[mined mutations (mm)]	[map mm]	[m in coding regions]	[m in non-coding regions]
ABCG8	[mined mutations (mm)]	[map mm]	[m in coding regions]	[m in non-coding regions]

Figure S2. Mutations identified in an automatic way in full text papers are connected to entries in other data sources such as ClinVar and LSDBs and to *in silico* predictions by SNAP2 and PROVEAN to deliver as much information on phenotype as possible.


ABCmdb: Database
for Mutations in ABC proteins

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ABCC6 p.Arg518Gln

ClinVar: [c.1552C>T , p.Arg518Ter D](#) , Pathogenic

LOVD-ABCC6: [p.Arg518Gln D](#)
[p.Arg518* D](#)

Predicted by SNAP2: A: **D** (95%), C: **D** (95%), D: **D** (95%), E: **D** (95%), F: **D** (95%), G: **D** (95%), H: **D** (95%), I: **D** (95%), K: **D** (95%), L: **D** (95%), M: **D** (95%),
Predicted by PROVEAN: A: **D**, C: **D**, D: **D**, E: **D**, F: **D**, G: **D**, H: **D**, I: **D**, K: **D**, L: **D**, M: **D**, N: **D**, P: **D**, Q: **D**, S: **D**, T: **D**, V: **D**, W: **D**, Y: **D**,

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Publications

[\[hide\]](#) [Uitto J, Pulkkinen L, Ringpfeil F](#)
Molecular genetics of pseudoxanthoma elasticum: a metabolic disorder at the environment-genome interface?
Trends Mol Med. 2001 Jan;7(1):13-7., [\[PMID:11427982\]](#) [\[PubMed\]](#)

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[\[hide\]](#) [Le Saux O, Beck K, Sachsinger C, Silvestri C, Treiber C, Goring HH, Johnson EW, De Paepe A, Pope FM, Pasquali-Ronchetti I, Bercovitch L, Marais AS, Viljoen DL, Terry SF, Boyd CD](#)
A spectrum of ABCC6 mutations is responsible for pseudoxanthoma elasticum.
Am J Hum Genet. 2001 Oct;69(4):749-64. Epub 2001 Aug 31., [\[PMID:11536079\]](#) [\[PubMed\]](#)

Figure S3. Querying variations at the DNA level and batch queries are also novel additional changes in the web interface.

ABCMdb: Database for Mutations in ABC proteins

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Search

This function can be used to search for mutations that are in homologous positions to a certain amino acid in an ABC protein.

Select a protein:

Amino acid position: (valid range: 1 to 1280)

cDNA location: (valid range: 1 to 3840)

Chromosome location: (valid range: 87503863 to 87713323)

You can paste protein, cDNA, a genomic positions here, such as p.234, c.3456, g.16851502.
! If you do not select a protein, references to protein and cDNA positions will be ingored !
Here you can include also complex cDNA reference, such as c.3883-24G>A.

List of positions:

Examples for ABCC6:
g.16177623
g.16157810
g.16154767
g.16182799
p.Gly226Arg
p.Glu1400Lys
c.3634-3C>A
c.*38G>A
c.220-1G>C
16182799