Supplementary Table 1. *In silico* prediction of the functional impact of *ATP7B* variants based on their location and pathogenicity

No.	Type of variant	Exon/intron	Variant nomenclature	Protein	Classification	CADD phred scale	REVEL	Mutation Taster	Polyphen-2 HumDiv	Polyphen-2 HumVar	GERP++	SIFT	Frequency in the cohort
1	NT	Exon 2	c.1124A>G	p.H375R	VUS	19.64	0.311	PM	B	B	5.89	BS	1
2	NT	Exon 5	c.1771G>A	p. G591S	LP	24.7	0.924	DC	PD	PD	5.95	DS	1
3	NT	Exon 6	c.1924G>C	p. D642H	LP	24.9	0.793	DCA	PD	PD	5.46	U	2
4	NT	Exon 7	c.2072G>A	p. G691E	LP	24.6	0.964	N/A	PD	PD	5.38	DS	3
5	NT	Exon 8	c.2339T>C	p. L780P	LP	27.3	0.937	N/A	PD	PD	5.39	DS	1
6	NT	Exon 16	c.2128G>A	p.G710S	P	23.7	0.894	DCA	PD	PD	5.37	DS	1
7	NT	Exon 8	c.2145C>T	p. Y715=	VUS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	3
8	NT	Exon 8	c.2293G>A	p. D765N	P	28.2	0.846	DCA	PD	PD	4.54	U	1
9	NT	Exon 8	c.2300C>T	p.P767L	P	25.7	0.944	DCA	PD	PD	5.39	U	1
10	NT	Exon 8	c.2210C>G	p.T737R	LP	25.8	0.96	DC	PD	PD	5.54	DS	1
11	NT	Exon 9	c.2363C>T	p.T788I	P	27.5	0.923	DCA	PD	PD	5.05	DS	3
12	NT	Exon 10	c.2522T>G	p.V841G	LP	26.9	0.944	N/A	PD	PD	5.73	DS	3
13	NT	Exon 11	c.2668G>T	p.V890L	LP	23.8	0.735	N/A	PD	PD	5.73	U	1
14	NT	Exon 13	c.2906G>A	p.R969Q	P	25.2	0.754	DCA	PD	PD	5.15	BS	5
15	NT	Exon 13	c.2951C>T	p.P984L	LP	27.4	0.968	N/A	PD	PD	5.15	DS	1
16	NT	Exon 13	c.2993G>A	p.G998D	LP	25.2	0.944	DC	PD	PD	4.3	U	1
17	NT	Exon 13	c.3008C>T	p.A1003V	P	24.3	0.871	DCA	PD	PD	5.05	U	2
18	NT	Exon 13	c.3007G>A	p.A1003T	P	23.6	0.86	DCA	PD	PD	5.15	U	1
19	NT	Exon 13	c.2930C>T	p.T977M	P	27.2	0.89	DCA	PD	PD	5.15	DS	2
20	NT	Exon 13	c.2944G>C	p.A982P	LP	26.6	0.963	N/A	PD	PD	5.15	DS	1
21	NT	Exon 14	c.3182G>A	p.G1061E	P	25.3	0.928	DCA	PD	PD	5.43	U	10
22	NT	Exon 14	c.3089G>A	p.G1030D	LP	34	0.992	DC	PD	PD	5.28	DS	1
23	NT	Exon 14	c.3188C>G	p.A1063G	LP	27.2	0.841	N/A	PD	PD	5.43	DS	1
24	NT	Exon 16	c.3556G>C	p.G1186R	LP	29.2	0.867	DC	PD	PD	5	U	3
25	NT	Exon 16	c.3446G>C	p.G1149A	P	25.2	0.954	DC	PD	PD	5	DS	1
26	NT	Exon 16	c.3517G>A	p.E1173K	P	27.4	0.916	DCA	PD	PD	5	U	1
27	NT	Exon 17	c.3818C>T	p.P1273L	P	27.4	0.928	DCA	PD	PD	4.73	DS	1
28	NT	Exon 17	c.3626T>C	p.L1209P	LP	25.7	0.991	N/A	PD	PD	5.15	DS	1
29	NT	Exon 17	c.3646G>A	p.V1216M	P	24.6	0.948	DCA	PD	PD	5.15	DS	2
30	NT	Exon 17	c.3601G>A	p.E1201K	VUS	25.5	0.893	DC	PD	PD	5.15	DS	1
31	NT	Exon 18	c.3809A>G	p.N1270S	P	23.3	0.896	DCA	PD	PD	4.73	DS	18
32	NT	Exon 18	c.3859G>A	p.G1287S	P	24.4	0.898	DC	PD	PD	3.88	DS	1
33	NT	Exon 18	c.3895C>T	p.L1299F	P	23.8	0.915	DCA	PD	PD	4.73	DS	3
34	NT	Exon 18	c.3741C>G	p.H1247Q	P	21.7	0.692	DC	PD	PD	3.88	DS	2
35	NT	Exon 19	c.3962T>A	p.I1321K	LP	24.8	0.933	DC	PD	PD	5.34	DS	1
36	NT	Exon 20	c.4039G>A	p.G1347S	P	27.9	0.942	DCA	PD	PD	5.13	DS	1
37	T	Exon 2	c.813C>A	p.C271X	P	27.9	N/A	DCA	N/A	N/A	-1.8	N/A	54
38	T	Exon 2	c.174dup	p.T59Hfs*19	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
39	T	Exon 2	c.841C>T	p.Q281X	P	35	N/A	DCA	N/A	N/A	3.11	N/A	1
40	T	Exon 2	c.700_701delinsTGA	p.R234X	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
41	T	Exon 5	c.1869+5_1869+8delGTAA	Nil	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
42	T	Exon 8	c.2304dup	p.M769Hfs*26	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	3
43	T	Exon 8	c.2312_2313del	p.F771Cfs*23	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
44	T	Exon 10	c.2497dupG	p.V833Gfs*21	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
45	T	Exon 13	c.3026_3028del	p.I1009del	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
46	T	Exon 14	c.3147del	p.T1050Hfs*71	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
47	T	Exon 16	c.3467_3468del	p.R1156Gfs*7	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
48	T	Exon 18	c.3745del	p.V1249Wfs*81	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
49	T	Exon 18	c.3700dup	p.V1234Gfs*25	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
50	T	Exon 18	c.3895del	p.I1300Sfs*30	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
51	T	Exon 20	c.4112_4114del	p.L1371del	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
52	T	Exon 21	c.4174del	p.M1392X	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
53	T	Exon 21	c.4258_4264del	p.D1420Sfs*12	LP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
54	T	Intron 1	c.51+1G>C	Nil	LP	28.9	N/A	N/A	N/A	N/A	2.91	N/A	2
55	T	Intron 3	c.1544-3C>G	Nil	VUS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
56	T	Intron 3	c.1544-5T>C	Nil	VUS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
57	T	Intron 4	c.1708-1G>C	Nil	P	34	N/A	DCA	N/A	N/A	5.95	N/A	1
58	T	Intron 6	c.1946+1del	Nil	P	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2
59	T	Intron 7	c.2122-1G>C	Nil	P	33	N/A	DC	N/A	N/A	5.37	N/A	1
60	T	Intron 8	c.2355+3A>G	Nil	VUS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	3
61	T	Intron 16	c.3557-8C>A	Nil	VUS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1
62	T	Intron 20	c.4125-1G>A	Nil	LP	33	N/A	DC	N/A	N/A	5.69	N/A	1

VUS, variant of uncertain significance; P, pathogenic; LP, likely pathogenic; B, benign; DCA, disease causing automatic; DC, disease causing; PM, polymorphism; PD, probably damaging; DS, deleterious supporting; DM, deleterious moderate; BS, benign supporting; BM, benign moderate; NT, nontruncating mutations; T, truncating mutations; U, uncertain; CADD, combined annotation-dependent depletion; REVEL, rare exome variant ensemble learner; GERP++, genomic evolutionary rate profiling; SIFT, scale-invariant feature transform; N/A, not available.