Supplementary tables

Supplementary table 1.ABCB4 gene variation in 118 patients with PFIC3

Case number	gender	Age of Onset	Exon/intron position	cDNA change	Amino acid change	variation type	Zygosity	PMID
1	Male	10	Exon 7	c.572A>G	p.Lys191Arg	Missense	Homozygous	37575491
			Exon 7	c.572A>G	p.Lys191Arg	Missense		
2	Female	25	Exon 22	c.2696C>G	p.Ala899Gly	Missense	Complex heterozygous	37488596
			Exon 27	WES [hg19]7q21.12 (87032513-87033422)	909bp deletion	Frameshift		
3	Male	16	Exon 7	c.646C > T	p.L216F	Missense	Complex heterozygous	37137858
			Exon 9	c.927T > A	p.Y309X	Nonsense		
4	Female	17	Intron 22	c.2784-1G > A	/	Splicing	Complex heterozygous	
			Exon 6	c.504C > T	p.N168N	Missense		
			Exon 7	c.646C > T	p.L216F	Missense		
5	Female	3	Exon 24	c.2906G>A	/	Missense	Homozygous	36644077
			Exon 24	c.2906G>A	/	Missense		
6	Male	23	Exon 18	c.2177 C > T	Pro726Leu	Missense	Complex heterozygous	36569137
			Exon 15	c.1756G > T	Val586Leu	Missense		
7	Female	4.2	Exon 22	c.2782A>G	p.Arg928Gly	Missense	Complex heterozygous	36550572
			Intron 3	c.136-2A>G	/	Splicing		
8	Fema	11	Exon 7	c.602C>T	p.Thr201Met	Missense	Complex heteroz	

	le		Exon 14	c.1645C>T	p.Arg549Cys	Missense	ygous	
9	Female	3	Exon 15	c.1801G>A	p.Ala601Thr	Missense	Complex heterozygous	
			Exon 13	c.1406G>A	p.Arg469Lys	Missense		
10	Female	0.083	Exon 26	c.3220G>A	p.Gly1074Arg	Missense	Complex heterozygous	
			Exon 10	c.955G>C	p.Gly319Arg	Missense		
11	Male	0.0082	Exon 15	c.1768C>T	p.Arg590*	Nonsense	Complex heterozygous	
			Intron 10	c.1006-2A>G	/	Splicing		
12	Female	0.5	Exon 25	c.3100_3101insA	p.Ile1034Asnfs*4	Nonsense	Complex heterozygous	
			Intron 2	c.80+1G>C	/	Splicing		
13	Male	1	Exon 8	c.716C>T	p.Ser239Leu	Missense	Complex heterozygous	
			Exon 23	c.2869C>T	p.Arg957*	Nonsense		
14	Female	3	Exon 26	c.3230C>I	p.Thr1077Met	Missense	Complex heterozygous	
			Exon 14	c.1621A>T	p.Ile541Phe	Missense		
15	Male	6.2	Exon 24	c.2914G>A	p.As972Asn	Missense	Complex heterozygous	
			Exon 10	c.965T>C	p.Leu322Pro	Missense		
16	Male	5	Exon 13	c.1436C>T	p.Pro479Leu	Missense	Homozygous	
			Exon 13	c.1436C>T	p.Pro479Leu	Missense		
17	Male	4.3	Exon 9	c.879dupA	p.Ala294SerfsTer62	Frameshift	Complex heterozygous	
			Exon 25	c.3152T>C	p.Val1051Ala	Missense		
18	Male	16	Exon 10	c.959C > T	p.Ser320Phe	Missense	Complex heterozygous	36330364
			Exon 13	c.1429C > A	p.Gln477Lys	Missense		
19	Fe	16	Exon	c.2950C>T	p.A984V	Miss	Complex	35317165

	male		24			ense	heterozygous	
			Exon 8	c.667A>G	p.I223V	Missense		
20	Female	17	Exon 10	c.959C > T	p.S320F	Missense	Complex heterozygous	34376370
			Exon 14	c.1529A > G	p.Asn510Ser	Missense		
21	Male	27	Exon 10	c.959C > T	p.S320F	Missense	Complex heterozygous	
			Exon 14	c.1529A > G	p.Asn510Ser	Missense		
22	Female	14	Exon 26	c.3227G > A	p.S1076N	Missense	Complex heterozygous	33256620
			Exon 27	c.3431T > C	p.I1144T	Missense		
23	Male	0.916	Exon 20	c.2489insA	p.T830NfsX11	Frameshift	Complex heterozygous	33215027
			Exon 25	c.3139_3141delGCAinsCC	p.A1047PfsX8	Frameshift		
24	Female	1.58	Exon 10	c.955G>C	p.G319R	Missense	Complex heterozygous	
			Exon 26	c.3220G>A	p.G1074R	Missense		
25	Male	5	Exon 13	c.1436C>T	p.P479L	Missense	Homozygous	
			Exon 13	c.1436C>T	p.P479L	Missense		
26	Female	0.01	Exon 26	c.3143delA	p.N1048TfsX	Frameshift	Complex heterozygous	
			Exon 25	c.3139G>C	p.A1047P	Missense		
27	Female	7	Exon 11	c.1195G>C	p.V399L	Missense	Homozygous	32626542
			Exon 11	c.1195G>C	p.V399L	Missense		
28	Female	17	Exon 17	c.2137G > A	p.V713M	Missense	Complex heterozygous	32321542
			Exon 6	c.504C > T	p.N168N	Nonsense		
29	Male	8	Exon 28	c.3838T>A	p.Ter1280Arg	Missense	Homozygous	31000363

			Exon 28	c.3838T>A	p.Ter1280Arg	Missense		
30	Male	5	Intron 10	c.1006-2A>G	/	Splicing	Complex heterozygous	30298496
			Exon 27	c.3580C>T	p.R1194X	Nonsense		
31	Male	18	Exon 15	c.1798A>G	/	Missense	Complex heterozygous	29390323
			Exon 19	c.2362C>T	/	Missense		
32	Male	1	Exon 14	c.1621A>T	p.I541F	Missense	Homozygous	26474921
			Exon 14	c.1621A>T	p.I541F	Missense		
33	Female	0.41	Exon 14	c.1667T>G	p.L556R	Missense	Homozygous	
			Exon 14	c.1667T>G	p.L556R	Missense		
34	Male	0.25	Exon 10	c.1037G>T	p.S346I	Missense	Homozygous	
			Exon 10	c.1037G>T	p.S346I	Missense		
35	Female	1	Exon 12	c.1270A>G	p.T424A	Missense	Complex heterozygous	
			Exon 24	c.2925-10_2925-9insC	/	Frameshift		
			Exon 24	c.2925-10_2925-9insC	/	Frameshift		
36	Male	4	Exon 23	c.2860G>A	p.G954S	Missense	Complex heterozygous	
			Exon 16	c.1954A>G	p.R652G	Missense		
37	Female	0.5	Exon 23	c.2860G>A	p.G954S	Missense	Complex heterozygous	
			Exon 16	c.1954A>G	p.R652G	Missense		
38	Male	0.5	Exon 7	c.523A>G	p.T175A	Missense	Complex heterozygous	
			Exon 10	c.1069T>C	p.F357L	Missense		
			Exon 19	c.2324C>T	p.T775M	Missense		

39	Female	15	Exon 14	c.1529A>G	p.N510S	Missense	Complex heterozygous	
			Exon 18	c.2177C>T	p.P726L	Missense		
40	Male	1.5	Exon 21	c.2564A>T	p.Q855L	Missense	Homozygous	
			Exon 21	c.2564A>T	p.Q855L	Missense		
41	Female	1.5	Exon 27	c.3559C>T	p.R1187X	Nonsense	Complex heterozygous	
			Intron 28	c.3633+2 T>A	Splicing defect	Splicing		
42	Female	1	Exon 4	c.202G>A	p.G68R	Missense	Homozygous	
			Exon 4	c.202G>A	p.G68R	Missense		
43	Female	1.5	Exon 4	c.202G>A	p.G68R	Missense	Homozygous	24594635
			Exon 4	c.202G>A	p.G68R	Missense		
44	Female	2	Exon 13	c.1375G>C	p.D459H	Missense	Complex heterozygous	
			Exon 13	c.1436C>T	p.P479L	Missense		
45	Male	0.7	Exon 7	c.602C>T	p.T201M	Missense	Complex heterozygous	
			Exon 27	c.3352G>A	p.E1118K	Missense		
46	Female	24	Exon 12	c.1217 G > A	p.Arg406Gln	Missense	Complex heterozygous	22331132
			Exon 3	c.140 G > A	p.Arg47Gln	Missense		
47	Male	3	Exon 15	c.1783 C > T	p.R595X	Nonsense	Complex heterozygous	21514256
			Exon 9	c.937 942delGCACTG/ins55	p.A313MfsX72	Frameshift		
48	Female	4	Exon 15	c.1783 C > T	p.R595X	Nonsense	Homozygous	
			Exon 15	c.1783 C > T	p.R595X	Nonsense		
49	Fema	0.5	Exon 7	c.523A>G	p.T175A	Missense	Complex heteroz	21119540

	le		Exon 10	c.1069T>C	p.F357L	Missense	ygous	
			Exon 19	c.2324C>T	p.T775M	Missense		
50	Male	0.5	Exon 11	c.1135_1136insAA	p.S379KfsX413	Frameshift	Complex heterozygous	
			Exon 17	c.2102T>C	p.L701P	Missense		
51	Male	1.25	Exon 22	c.2662G>T	p.E888X	Nonsense	Complex heterozygous	
			Exon 8	c.748G>C	p.A250P	Missense		
			Exon 16	c.1888A>G	p.M630V	Missense		
52	Female	16	Exon 10	c.959C>T	p.S320F	Missense	Complex heterozygous	
			Exon 9	c.857C>T	p.A286V	Missense		
53	Male	1.1	Exon 5	c.377G>A	p.G126E	Missense	Complex heterozygous	
			Exon 14	c.1531G>A	p.A511T	Missense		
54	Male	0.1	Exon 5	c.377G>A	p.G126E	Missense	Complex heterozygous	
			Exon 14	c.1531G>A	p.A511T	Missense		
55	Male	2	Exon 17	c.2176C>A	p.P726T	Missense	Complex heterozygous	
			Exon 15	c.1769G>A	p.R590Q	Missense		
			Exon 18	c.2284G>T	p.G762X	Nonsense		
56	Male	0.8	Exon 10	c.1091C>T	p.A364V	Missense	Complex heterozygous	
			Exon 18	c.2210C>T	p.A737V	Missense		
57	Female	1.8	Exon 21	c.2519C>A	p.A840D	Missense	Complex heterozygous	
			Exon 13	c.1424T>C	p.V475A	Missense		
58	Fema	0.16	Exon 14	c.1672G>A	p.E558K	Missense	Complex heteroz	

	le		Exon 17	c.2168G>A	p.G723E	Missense	ygous	
			Exon 27	c.3577G>A	p.A1193T	Missense		
59	Male	1.1	Exon 14	c.1672G>A	p.E558K	Missense	Complex heterozygous	
			Exon 17	c.2168G>A	p.G723E	Missense		
			Exon 27	c.3577G>A	p.A1193T	Missense		
60	Male	1	Exon 23	c.2860G>A	p.G954S	Missense	Homozygous	
			Exon 23	c.2860G>A	p.G954S	Missense		
61	Female	0.3	Exon 10	c.959C>T	p.S320F	Missense	Complex heterozygous	
			Exon 9	c.837T>A	p.Y279X	Nonsense		
62	Male	2.7	Exon 17	c.2169_2170insG	p.L724AfsX744	Frameshift	Homozygous	
			Exon 17	c.2169_2170insG	p.L724AfsX744	Frameshift		
63	Female	0.5	Exon 17	c.2169_2170insG	p.L724AfsX744	Frameshift	Homozygous	
			Exon 17	c.2169_2170insG	p.L724AfsX744	Frameshift		
64	Male	0.25	Exon 11	c.1207T>C	p.Y403H	Missense	Homozygous	
			Exon 11	c.1207T>C	p.Y403H	Missense		
65	Male	17	Exon 4	c.208G>C	p.G70R	Missense	Complex heterozygous	
			Exon 15	c.1769G>A	p.R590Q	Missense		
			Exon 10	c.959C>T	p.S320F	Missense		
66	Male	6.8	Exon 4	c.208G>C	p.G70R	Missense	Complex heterozygous	
			Exon 15	c.1769G>A	p.R590Q	Missense		

			Exon 10	c.959C>T	p.S320F	Missense		
67	Female	8.4	Exon 4	c.208G>C	p.G70R	Missense	Complex heterozygous	
			Exon 15	c.1769G>A	p.R590Q	Missense		
			Exon 10	c.959C>T	p.S320F	Missense		
68	Male	8.3	Exon 10	c.959C>T	p.S320F	Missense	Homozygous	
			Exon 10	c.959C>T	p.S320F	Missense		
69	Female	23	Exon 3	c. 139C>T	p.R47X	Nonsense	Complex heterozygous	
			Exon 7	c. 523A>G	p.T175A	Missense		
70	Female	16	Exon 3	c. 139C>T	p.R47X	Nonsense	Complex heterozygous	18482588
			Exon 7	c. 523A>G	p.T175A	Missense		
71	Male	27	Exon 14	c. 1615G>A	p.A539T	Missense	Complex heterozygous	
			Exon 15	c. 1769G>A	p.R590Q	Missense		
72	Female	7	Exon 6	c.431G>A	p.Arg144Gln	Missense	Homozygous	/
			Exon 6	c.431G>A	p.Arg144Gln	Missense		
73	Male	7	Exon 10	c.1054C＞T	p. P3525	Missense	Complex heterozygous	DOI: 10.19538/j.Ek2022070610
			Exon 27	c. 3345—3353del9	p. R1116—Q1118del	Frameshift		
74	Male	16	Exon 7	c.646C>T	p.L216F	Missense	Complex heterozygous	DOI:10.3760/cmma.j.cn501113-20230217-00061
			Exon 9	c.927T>A	p.Y309X	Nonsense		
75	Male	1.25	Exon 25	c.3230C＞T	p. T1077M	Missense	Homozygous	DOI: 10.3969/j.issn.0253-9802.2022.07.008
			Exon 25	c.3230C＞T	p. T1077M	Missense		
76	Male	15	Exon 21	c. 2570C＞T	p.T857I	Missense	Complex heterozygous	doi: 10. 3969/j. issn. 1001—
			Exon	c. 2212A	p.I738F	Miss		

			18	＞ T		ense		5256. 2020. 07 . 032
			Exon 15	c. 1694C ＞ G	p.T565R	Missense		
77	Male	4	Exon 21	c. 2570C ＞ T	p.T857I	Missense	Complex heterozygous	
			Exon 18	c. 2212A ＞ T	p.I738F	Missense		
			Exon 15	c. 1694C ＞ G	p.T565R	Missense		
78	Female	5	Intron 3	c.136-2A>G	/	Splicing	Complex heterozygous	《Three cases of progressive familial intrahepatic cholestasis type 3 children and literature review》
			Exon 22	c.2782A >G	p.Arg928Gly	Missense		
79	Male	9	Exon 14	c. 1645C>T	p.Arg549Cys	Missense	Complex heterozygous	
			Exon 7	c.602C> T	p.Thr201Met	Missense		
80	Male	11	Exon 14	c. 1645C>T	p.Arg549Cys	Missense	Complex heterozygous	
			Exon 7	c.602C> T	p.Thr201Met	Missense		
81	Male	3	Exon 22	c.2766delA	p.K922Nfs*43	Frameshift	Complex heterozygous	《Clinical characteristics and gene mutation analysis of a child with type 3 progressive familial intrahepatic cholestasis》
			Exon 2	c.52G>T	p.E18X	Nonsense		
82	Female	17	Exon 24	2950C>T	p.A984V	Missense	Complex heterozygous	35317165
			Exon 7	667A>G	p.I223V	Missense		
83	Male	15	Exon 4	c.175 C>T	p.L59L	Synonymous	Complex heterozygous	25593501
			Exon 6	c.504 C>T	p.N168N	Synonymous		
			Exon 8	c.711 A>T	p.I237I	Synonymous		

			Exon 9	c.874 A>T	p.K292X	Nonsense		
			Exon 15	c.1804 G>T	p.G602W	Missense		
84	Female	7	Exon 25	c.3152T > C	p.V1051A	Missense	Complex heterozygous	DOI: 10.19538/j.ek2022040617
			Exon 25	c.3250C> T	p.R1084W	Missense		
85	Male	5	Exon 9	c.874A>T	p.Lys292*	Nonsense	Complex heterozygous	30755924
			Exon 27	c.3680T>C	p.Ile1227Thr	Missense		
86	Female	14	Exon 10	c.959C>T	Ser320Phe	Missense	Complex heterozygous	
			Exon 18	c.2301dupT	p.(Thr768TyrfsTer26)	Frameshift		
87	Female	23	Exon 10	c.959C>T	p.(Ser320Phe)	Missense	Complex heterozygous	35288833
			Exon 18	2301dupT	p.(Thr768TyrfsTer26)	Frameshift		
88	Female	25	Exon 10	c.959C>T	p.(Ser320Phe)	Missense	Complex heterozygous	
			Exon 18	c.2301dupT	p.(Thr768TyrfsTer26)	Frameshift		
89	Female	23	Exon 16	c.1954A > G	p.Arg652Gly	Missense	Complex heterozygous	31568708
			Exon 8	c.711A > T	p.Ile237=	Missense		
90	Male	7.2	Exon 7	c.602C>T	p.Thr201Met	Missense	Complex heterozygous	
			Exon 14	c.1645C>T	p.Arg549Cys	Missense		
91	Male	0.83	Exon 17	c.2123G>A	p.Trp708*	Nonsense	Complex heterozygous	36550572
			Exon 28	c.3789delA	p.Gly1264Alafs*38	Frameshift		
92	Male	11.5	Exon 6	c.431G > A	p.Arg144Gln	Missense	Homozygous	29973134
			Exon 6	c.431G > A	p.Arg144Gln	Missense		

93	Female	4.5	Exon 7	c.475C > T	p.Arg159*	Nonsense	Complex heterozygous	
			Exon 16	c.1954A > G	p.Arg652Gly	Missense		
94	Male	15	Exon 21	c.T2525C	p.L842P	Missense	Complex heterozygous	33842647
			Exon 25	c.T3152C	p.V1051A	Missense		
95	Male	0.5	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	33915153
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
96	Female	0.91	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
97	Female	5	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
98	Female	2.5	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
99	Male	6	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
100	Female	0.5	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
101	Male	4	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
102	Male	0.083	Exon 22	c.2692G>A	p.Glu898Lys	Missense	Homozygous	
			Exon 22	c.2692G>A	p.Glu898Lys	Missense		
103	Female	0.83	Exon 4	c.221T>G	p.Met74Arg	Missense	Homozygous	
			Exon 4	c.221T>G	p.Met74Arg	Missense		

104	Male	2	Exon 24	c.2906G>A	p.R969H	Missense	Homozygous	
			Exon 24	c.2906G>A	p.R969H	Missense		
105	Male	0.66	Exon 24	c.2906G>A	p.R969H	Missense	Homozygous	
			Exon 24	c.2906G>A	p.R969H	Missense		
106	Female	1.41	Exon 24	c.2906G>A	p.R969H	Missense	Homozygous	
			Exon 24	c.2906G>A	p.R969H	Missense		
107	Male	0.5	Exon 6	c.456G>A	p.K152K	Missense	Complex heterozygous	
			Exon 14	c.1584G>C	p.E528D	Missense		
108	Male	0.083	Exon 24	c.2908T>C	/	Missense	Homozygous	
			Exon 24	c.2908T>C	/	Missense		
109	Female	1	Exon 7	c.526C>T	p.R176W	Missense	Homozygous	
			Exon 7	c.526C>T	p.R176W	Missense		
110	Female	0.5	Exon 7	c.526C>T	p.R176W	Missense	Homozygous	
			Exon 7	c.526C>T	p.R176W	Missense		
111	Female	0.5	Exon 7	c.526C>T	p.R176W	Missense	Homozygous	
			Exon 7	c.526C>T	p.R176W	Missense		
112	Male	0.5	Exon 7	c.526C>T	p.R176W	Missense	Homozygous	
			Exon 7	c.526C>T	p.R176W	Missense		
113	Female	3	Exon 5	c.296C>T	p.Ser99Phe	Missense	Homozygous	
			Exon 5	c.296C>T	p.Ser99Phe	Missense		
114	Male	0.916	Exon 13	c.1378A>T	p.Ile460Phe	Missense	Homozygous	
			Exon 13	c.1378A>T	p.Ile460Phe	Missense		

115	Male	0.083	Intron 17	c.2064+G>C	r.spl?	splicing	Homozygous	
			Intron 17	c.2064+G>C	r.spl?	splicing		
116	Male	0.166	Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift	Homozygous	
			Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift		
117	Female	3	Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift	Homozygous	
			Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift		
118	Male	3	Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift	Homozygous	
			Exon 7	c.628_643del	p.Phe210Serfs*5	Frameshift		