Supplementary Materials

Supplementary Table S1. Aggregate conclusive molecular findings identified in index cases and carrier relatives

Gene	Reference transcript	cDNA change	Protein change	Classification	Index cases, n	Carrier relatives, n	Total carriers, n
APOB	NM_000384	c.10580G>A	p.(Arg3527Gln)	Pathogenic	1	0	1
LDLR	NM_000527	c.1027G>A	p.(Gly343Ser)	Pathogenic	9	13	22
LDLR	NM_000527	c.(1060+1_1061-1)_(1586+1_1587-1)del	p.(?)	Pathogenic	1	9	10
LDLR	NM_000527	c.1072T>G	p.(Cys358Gly)	Likely pathogenic	1	5	6
LDLR	NM_000527	c.1187-10G>A	p.(?)	Pathogenic	1	3	4
LDLR	NM_000527	c.1291G>A	p.(Ala431Thr)	Pathogenic	2	0	2
LDLR	NM_000527	c.12G>A	p.(Trp4*)	Pathogenic	8	10	18
LDLR	NM_000527	c.1342C>T	p.(Gln448Ter)	Likely pathogenic	1	0	1
LDLR	NM_000527	c.1358+1G>A	p.(?)	Likely pathogenic	1	5	6
LDLR	NM_000527	c.1414G>T	p.(Asp472Tyr)	Likely pathogenic	1	3	4
LDLR	NM_000527	c.1502dupC	p.(Asp502GlyfsX34)	Likely pathogenic	1	0	1
LDLR	NM_000527	c.1567G>A	p.(Val523Met)	Pathogenic	1	4	5
LDLR	NM_000527	c.1639del	p.(Leu547Ter)	Pathogenic	4	3	7
LDLR	NM_000527	c.1690A>C; c.2393_2401del	p.(Asn564His), p.(Val800_Leu802del)	Pathogenic	1	3	4
LDLR	NM_000527	c.1690A>C; c.2397_2405del	p.(Asn564His), p.(Val800_Leu802del)	Pathogenic	4	3	7
LDLR	NM_000527	c.1706-187_1724del	p.(?)	Likely pathogenic	1	0	1
LDLR	NM_000527	c.1775G>A	p.(Gly592Glu)	Pathogenic	8	10	18
LDLR	NM_000527	c.1783C>T	p.(Arg595Trp)	Pathogenic	1	0	1
LDLR	NM_000527	c.1845+1G>C	p.(?)	Pathogenic	10	36	46
LDLR	NM_000527	c.1879G>C	p.(Ala627Pro)	Likely pathogenic	1	2	3
LDLR	NM_000527	c.1897C>T	p.(Arg633Cys)	Pathogenic	2	3	5
LDLR	NM_000527	c.191-2delinsCT	p.(?)	Likely pathogenic	1	1	2

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LDLR	NM_000527	c.1999T>C	p.(Cys667Arg)	Pathogenic	1	0	1
LDLR	NM_000527	c.2207dup	p.(Arg737fs)	Pathogenic	1	3	4
LDLR	NM_000527	c.2389G>A	p.(Val797Met)	Pathogenic	1	0	1
LDLR	NM_000527	c.2393_2405del	p.(Val800_Leu802del)	Likely pathogenic	1	3	4
LDLR	NM_000527	c.2399_2403delinsGGGT	p.(Val800Glyfs*129)	Pathogenic	1	5	6
LDLR	NM_000527	c.241C>T	p.(Arg81Cys)	Likely pathogenic	1	0	1
LDLR	NM_000527	c.324_325insAG	p.(Cys109SerfsTer98	Likely pathogenic	1	0	1
LDLR	NM_000527	c.346T>C	p.(Cys116Arg)	Pathogenic	2	1	3
LDLR	NM_000527	c.443G>A	p.(Cys148Tyr)	Likely pathogenic	1	0	1
LDLR	NM_000527	c.530C>T	p.(Ser177Leu),	Pathogenic	2	2	4
LDLR	NM_000527	c.682G>A	p.(Glu228Lys)	Pathogenic	2	0	2
LDLR	NM_000527	c.695?940+?del	p.(?)	Likely pathogenic	1	2	3
LDLR	NM_000527	c.800A>C	p.(Glu267Ala)	Likely pathogenic	1	3	4
LDLR	NM_000527	c.862G>A	p.(Glu288Lys)	Pathogenic	2	0	2
LDLR	NM_000527	c.890A>C	p.(Asn297Thr)	Likely pathogenic	1	1	2
LDLR	NM_000527	c.97C>T	p.(Gln33*)	Pathogenic	1	0	1
TOTAL					81	133	214

Supplementary Table S2. Variants reclassified from likely pathogenic to variant of uncertain significance at database lock

Gene	Reference transcript	cDNA change	Protein change	Initial classification	Final classification at database lock	Index cases, n	Carrier relatives, n	Included in S1
LDLR	NM_000527	c.2479G>A	p.(Val827Ile)	Likely pathogenic	Variant of uncertain significance	2	0	No
LDLR	NM_000527	c.80G>A	p.(Cys27Tyr)	Likely pathogenic	Variant of uncertain significance	1	0	No